ABSTRACTS

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Basic Sciences 1
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0001
PRORESOLVING ANTIINFLAMMATORY MECHANISMS ARE NOVEL POTENTIAL TARGETS AGAINST EPILEPTOGENESIS
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Purpose: Resolution of inflammation is an active homeostatic process controlled by proresolving lipids and peptides. We characterized this process during epileptogenesis to test whether boosting resolution mechanisms prevents epileptogenesis or mediates disease modifications.

Method: Our analyses were done in the hippocampus of mice exposed to status epilepticus (SE) and their sham controls, and patients who died ≤5 or ≥7 days from SE and autopsy controls. Mice were studied 2 h, 24 h and 72 h after SE (epileptogenesis) evoked by intraamygdala injection of kainic acid. We measured by RTqPCR and/or immunohistochemistry: proinflammatory cytokines (IL-1β; TNF-α), proresolving lipid’s biosynthetic enzymes (LOX5; LOX15), key proresolving receptors (ALXR; ChemR23) and peptides (AnnexinA1; IL-1Ra). Proresolving lipids and related molecules were measured in mouse hippocampus by LC-MS/MS lipidomic analysis. The AnnexinA1 fragment Ac2-50, BML111 or PD1 n-3DPA-Me, stable analogues of LipoxinA 4 and neuroprotectin PD1 n-3DPA, or their respective vehicles, were injected individually icv in mice twice/day for 4 days starting 1 h post SE, then mice were killed for neuroinflammation analysis.

Results: IL-1β and TNF-α mRNA levels increased by 2 h and remained elevated for 72 h post SE. LOX5 and LOX15 mRNA levels were induced 72 h post SE. ALXR and ChemR23 expression was limited to pyramidal cells and hilar interneurons in sham mice and autopsy controls while it was induced in activated astrocytes 72 h post SE in mice and in patients; AnnexinA1 and PD1 n-3DPA were upregulated by 2- and 20-fold, respectively. PD1 n-3DPA-Me injection abolished IL-1β increase during epileptogenesis while BML111 and Ac2-50 were ineffective.

Conclusion: The activation of proresolving mechanisms occurs with a delay after the onset of neuroinflammation during epileptogenesis. The anticipation and potentiation of the resolution response with PD1 n-3DPA-Me inhibited neuroinflammation. PD1 n-3DPA-Me is an ideal candidate for testing potential neuroprotective and anti-epileptogenic actions by boosting resolution mechanisms of neuroinflammation.

0002
NOVEL DRUG-SCREENING IN “EPILEPTIC” ZEBRAFISH UNCOVERS HISTONE DEACETYLASE (HDAC) 1 AND 3 AS A NOVEL ANTICONVULSANT TARGET
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Rationale: Epilepsy is a common neurological condition that affects approximately 1–2% of the general population. 30–40% of patients are unresponsive to drugs and continue to suffer from unremitting recurrent seizures, suggesting a need for drugs with new mechanisms of action. We created a drug-screening platform that harnesses the power of zebrafish (ZF) genetics and the measurement of whole animal bioenergetics to unbiasedly uncover novel agents with unexpected mechanisms of action. Previously, we identified vorinostat (a broad HDAC-inhibitor) as a potent and efficacious anticonvulsant agent. In the present study, we further investigated class I, IIa, IIb, and IV HDAC inhibitors to identify the specific class of HDACs that might be responsible for the anticonvulsant properties observed with vorinostat.

Methods: We introduced mutations into the zebrafish ortholog (kcnal1) of Kv1.1 epilepsy-associated gene, and analyzed their bioenergetics profile using the XF24 Extracellular Flux analyzer. Systematic analysis of bioenergetics activities of 26 HDAC inhibitors in kcnal1-null zebrafish was conducted. All HDAC inhibitors that restored mitochondrially-mediated bioenergetics to baseline levels were further validated using video electroencephalogram (EEG) recording in Kv1.1 mutant rodent models.

Results: HDAC 1 and 3 inhibitors (class I HDAC) effectively restored elevated mitochondrially-mediated metabolism (p < 0.01), and reversed the abnormal metabolic bioenergetics profile observed in kcnal1-null zebrafish. Also, treatment of the spontaneously seizing Kv1.1 mutant mice with HDAC 1 and 3 inhibitor led to >50% (p < 0.01) in the frequency of seizures observed in these mice. This further suggests that inhibition of HDAC 1 and 3 activity can serve as a potential anticonvulsant target.

Conclusions: Our metabolic approach to drug screening represents a new direction that could be used to identify therapeutics with novel mechanisms of action, which might be effective for the treatment of monogenic intractable epilepsy.
Purpose: Current pharmacotherapy for TLE has no disease-modifying effect on epileptogenesis. T-type Ca\(^{2+}\) channels have been strongly implicated in the pathogenesis of TLE. Therefore, in this study we set out to evaluate the effects of Z944, a potent and selective T-type Ca\(^{2+}\) antagonist, on epileptogenesis in the post-status epilepticus (post-SE) model of TLE.

Method: Wistar rats underwent implantation of EEG recording electrodes and kainic acid induced SE for 4 hours. Sham animals received saline injections only. SE was terminated with diazepam and animals were assigned to one of five treatment groups: post-SE + saline; post-SE + Z944 (60 mg/kg/day, n = 8); post-SE + vehicle (n = 8); sham + vehicle (n = 6) or sham + Z944 (60 mg/kg/day, n = 6). Treatments were delivered by continuous subcutaneous infusion for four weeks. Four weeks after completion of treatment, the animals had two weeks of continuous video-EEG monitoring to evaluate the effects of the different treatments on epileptogenesis. Behavioural tests were performed to evaluate anxiety, depression, learning, and memory.

Results: Following drug washout, post-SE + vehicle animals had the highest average number of seizures per day (0.77 ± 0.09), followed by post-SE + levetiracetam (0.536 ± 0.076). Treatment with Z944 greatly reduced the number of seizures per day (0.017 ± 0.012) which was significantly different when compared to vehicle and levetiracetam treated groups. Only 2 post-SE + Z944 animals had seizures recorded (one seizure each during the two weeks of recordings), whereas all of the animals in the other post-SE groups had several seizures. Depressive-like behaviour was assessed using the sucrose preference test. Z944 treatment significantly improved depressive like behaviour (p < 0.05 in comparison to post-SE + vehicle) in both tests.

Conclusion: This indicates that pharmacologically targeting T-type Ca\(^{2+}\) channel with Z944 may be an effective disease-modifying treatment for TLE. Z944 has been found to have a favourable safety profile indicating strong EKP-antagonist activity in freely moving animals, might be particularly interesting for future anti-epileptic or anti-epileptogenic drug discovery strategies.

0005
THE NINDS/NIH EPILEPSY THERAPY SCREENING PROGRAM (ETSP)
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Building on the success of the longstanding NINDS/NIH Anticonvulsant Screening Program (ASP), the recently-renamed Epilepsy Therapy Screening Program (ETSP) has a refocused mission to facilitate the discovery and characterization of novel agents for addressing the significant remaining unmet medical needs in epilepsy, most notably treatment-resistance, and disease prevention and modification. With ongoing feedback provided by an External Consultant Board (ECB), the ETSP has implemented significant changes in its testing strategies. The ETSP has developed a refined two-stage flow chart to evaluate the potential of compounds for clinically-differentiated treatments for drug refractory epilepsy. An initial “Identification” phase utilizes two acute seizure models in neurologically-intact rodents, the maximal electroshock (MES) seizure test, and the mouse 6 Hz 44 mA model of pharmacoresistant seizures. To help identify mechanistically-novel agents that interact with aberrant processes in the epileptic brain and therefore may not be detected by acute seizure tests, the Identification phase has two additional assays with “disease-like” characteristics, corneal kindled seizures, and an intravital spontaneous electrical bursting slice model. A subsequent “Differentialization” phase utilizes three advanced disease models: the lamotrigine-resistant amygdala-kindled rat model; mouse mesial Temporal Lobe Epilepsy (mTLE) model, and chronic epileptic rat model with video/EEG recording. The ETSP has also incorporated models of special epilepsy populations: a mouse model of viral-induced encephalitis [Theiler’s murine encephalitis virus (TMEV) model], and a rat model of benzodiazepine pharmacoresistant status epilepticus. The mTLE mouse and chronic epileptic rat models are also adapted for evaluating potential anti-epigenetic activities, and we encourage further discussions with external investigators. Finally, the ETSP established the publicly-accessible PANACHE database that provides methodological information and a searchable repository for non-confidential data generated on compounds.

0004/p0137
INHIBITION OF GLUTAMATE DECARBOXYLASE (GAD) BY ETHYL KETOPENTENOATE (EKP) INDUCES TREATMENT-RESISTANT EPILEPTIC SEIZURES IN ZEBRAFISH
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Purpose: Epilepsy is a chronic brain disorder characterized by recurrent seizures due to abnormal, excessive and synchronous neuronal activities in the brain. It affects approximately 65 million people worldwide, one third of which are still estimated to suffer from refractory seizures. Glutamic acid decarboxylase (GAD) that converts glutamate into GABA is a key enzyme in the dynamic regulation of neural network excitability. Importantly, clinical evidence shows that lowered GAD activity is associated with several forms of epilepsy which are often treatment resistant. We have previously shown that (D,L)-allylglycerine (AG) reduced GABA content and as a consequence induced epileptiform activity in zebrafish larvae and mice. The oxidative metabolite of AG, 2-keto-4-pentenoic acid (KPA), was proven to be a far more potent GAD inhibitor.

Method: We explored the possibility to use ethyl ketopentenoate (EKP), a lipid-permeable form of KPA to induce refractory seizures in zebrafish larvae. We performed locomotor tracking, local field potential (LFP) recording and neourlulnescence monitoring to phenotypically and pharmacologically characterize this model.

Results: Our results demonstrate that EKP evoked robust convulsive locomotor activities, excessive epileptiform discharges and upregulated c-fos expression in zebrafish. Moreover, transgenic animals in which neuronal cells express apoaequorin, a Ca\(^{2+}\)-sensitive bioluminescent photoprotein, displayed large luminescence signals indicating strong EKP-induced neuronal activation. Molecular docking data indicated that this pronounced anticonvulsant activity resulted from the direct inhibition of both gad67 and gad65. Limited protective efficacy of trials anti-seizure drugs (ASDs) demonstrated a high level of treatment resistance of EKP-induced seizures.

Conclusion: We conclude that EKP is more effective than AG in inducing refractory seizures and can serve as a high-throughput model to discover novel ASDs. Furthermore, it is anticipated that the neourlulnescence technique as a tool to monitor whole brain neuronal activity in freely moving animals, might be particularly interesting for future anti-epileptic or anti-epileptogenic drug discovery strategies.
tested by the ETSP. Together, these efforts are aimed at identifying promising agents that will comprise the next-generation of pharmacological treatments for significantly reducing the burden of epilepsy.

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0006 SPINDLE OSCILLATIONS TRIGGER ROLANDIC DISCHARGES IN BENIGN CHILDHOOD EPILEPSY

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Purpose: Rolandic discharges (RDs) are the hallmarks of interictal epileptic discharges in benign childhood epilepsy with centro-temporal foci (BECT). The RD rate increases during non-REM sleep. Our preceding study on the cross-correlation between the RD rate and background EEG power showed that the development of RD rate precedes that of delta-band power, but synchronize with sigma-band power. While the results showed a close link between RDs and spindle oscillations, the one-to-one temporal relationship between RDs and spindle oscillations still remains to be solved.

Method: Seven children diagnosed with BECT, with predominant unilateral RDs, were enrolled in the study (4 boys and 3 girls, aged from 6 to 11 years), 8-channel EEGs were recorded throughout a night, and sampled (1.25-Hz sampling frequency). The RDs were detected semi-automatically, and the EEG data with growing periods of delta-band power during the first sleep cycle were subjected to the analysis. We applied wavelet analysis on the contralateral lead of RDs (Fp1-C3 or Fp2-C4, 8192 points / frame) with the fixed point of RDs (6144-point in a frame), then averaged (spike-triggered wavelet average, STWA). The results of STWA were accumulated within the spindle range (spindle power: 10.2 – 13.5 Hz), and divided into 32 blocks (8192 / 256 points; 0.205 s for a block). They were tested for the significance of time series by one-way repeated measure ANOVA.

Results: The results showed the significant time-series changes around the RDs (F = 2.74, p < 0.001). The spindle power increased around 0.6 s before the onset of RDs.

Conclusion: Spindle oscillations trigger RDs in BECT.

0007 LOCALIZING NON-EPILEPTIC ABNORMAL BRAIN FUNCTION IN CHILDREN USING HIGH DENSITY EEG (hEEG): LECTRIC SOURCE IMAGING OF FOCAL SLOWING

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Purpose: A proportion of pediatric patients who are candidate for epilepsy surgery show the absence of interictal epileptiform discharges or multifocal spikes on interictal EEG. The “Non-spiking” pathological brain activity such as abnormal low-frequency activity could provide important localisation information. This study aims to map the brain source of pathological focal slowing in children with drug resistant epilepsy in order to validate a new electrical imaging source (ESI) index able to identify the epileptic focus.

Method: We selected 17 children (7F/10M), who underwent high density EEG (hEEG), presurgical assessments and surgical treatment. Mean age at the evaluation was 12 ± 4 yrs, mean duration and onset of disease were, respectively 7 ± 5 yrs and 4 ± 5 yrs. For each patient, we exported about 15 epochs of pathological focal slowing lasting 2sec. We applied for each channel the S-transform to obtain the frequency content of the signal across time, taking in account only the dominant FS frequency: 1–4 Hz or 4–5 Hz. Then, for each frequency and time point, we applied the inverse solution obtaining the spectral power at each solution point, which was averaged in order to identify the frequency and time that correspond to the maximal spectral power providing the FS source localization. Finally, we computed the Euclidian distance between this solution point and the nearest solution point included in the resection. In patients with seizure free outcome (16/17), the median distance was 2.7 mm, and the distance between ESI focal slowing and resection was smaller than 5 mm in the 65% (41% into resection). One patient had Class III outcome and a distance superior to 10 mm from resection.

Conclusion: These findings suggest that the analysis of focal slowing activity could be useful for the estimation of the epileptogenic zone.

0008 ASSOCIATION OF DEFAULT MODE NETWORK (DMN) REGIONS AT ABSENCE SEIZURE ONSET UNCONSTRAINED BY THEIR FREQUENCY CONFINEMENT

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Purpose: We investigated the leading generators of electrographic absence seizures, at different frequency bandwidths (1–200 Hz), during MEG.

Methods: Nineteen patients (M: F = 10:9; age:10.25 ± 3.39 years), with childhood (n = 11) and juvenile (n = 8) absence seizures underwent MEG. Generalized spike-wave discharges (GSD) for >5 seconds (s), were regarded ‘electrographic absence seizures’. Data was analyzed at 3 frequency bandwidths: 1–30 Hz (C), 30–80 Hz (G) and 80–200 Hz (R). At each frequency band, for every subject, leading 300 ms of ictal GSD of seizures were concatenated and subjected to source localization over a cortical grid using adaptive spatial filtering. At each frequency band, group statistics was computed with t-test, corrected for multiple comparisons using cluster permutation approach (n = 500p < 0.05).

Cortical regions with significant cluster thresholds were segregated and termed as generators of absence seizures.

Results: There were 5135 (232.37 ± 49.82) independent ictal GSD in 19 patients, among which 119 were electrographic seizures (5.95 ± 1.2s). The frequently localized cortical regions, at 3 frequency bands (C, G and R) were superior, middle and inferior frontal gyri, frontal operculum, supplemental motor area, somatosensory cortex, angular gyrus, inferior parietal lobule, precuneus, middle temporal gyrus, cuneus, calcarine and middle occipital gyri, and anterior cingulate gyrus. Brain regions responsible for generating all seizures (n = 49) were expressed in proportions and grouped pertaining to the lobes: frontal (C = 49.28%; G = 47.39%; R = 43.44%); temporal (C = 9.44%;G = 11.33%; R = 9.37%); parietal (C = 20.9%;G = 30.9%;R = 24.17%); occipital (C = 14.33%; G = 7.06%; R = 19.18%) cortices and anterior cingulate (C = 6.94%;G = 10.38%; R = 3.85%) regions. There were no differences in the source localization regions acquired at 3 frequency bands (p > 0.05).

Conclusion: Multiple focal cortical regions were involved at 3 frequency bands in absence epilepsy. The excited regions for generating the absence seizure were positioned in the DMN, regardless of their excitation frequency (1–200 Hz), indicating under-modulation of intrinsic neuronal firing. These might suggest that unconsciousness in absence seizures could probably be related to the (multi)focal disruption of these specific networks.
0009 NEW HYBRID MICRO-MACROELECTRODES TO RECORD FAST-RIPPLES IN PATIENTS WITH DRUG-REFRACTORY EPILEPSY
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Purpose: Patients with drug-refractory epilepsy are explored using stereoelectroencephalography (SEEG) to identify the brain areas where epileptic seizures originate. When the seizure onset zone (SOZ) can be identified, surgical resection may be possible with usually good outcome. During SEEG, fast activities (gamma) but also high frequency oscillations like Ripples (> 80 Hz) and Fast Ripples (FR, > 200 Hz) can be recorded. FR are candidates to be new biomarkers of the SOZ. They are usually recorded with macroelectrodes (800–1300 μm) but microelectrodes (20–50 μm) - not currently used in clinical practice - appear to facilitate their recordings. The aim of our study is to assess whether newly designed hybrid micro-macro electrodes work correctly and if they present an interest.

Method: The EpiFaR study was accepted in 2014 and has been proposed to all epileptic patients undergoing a SEEG in the CHU of Toulouse since March 2015. When electrodes locations (based exclusively on clinical criteria) has been determined, the implantation of 4 micro-macroelectrodes instead of the classical macroelectrodes is scheduled. One is located in the presumed SOZ and the other anteriorly, posteriorly and contralaterally. The micro-macroelectrodes are provided by DIXI Medical. Each consists of several macrocontacts and 2 or 3 tetrodes (each with 4 microwires with a diameter of 20 μm). Each patient is recorded 24/24 using the clinical video-SEEG system from Micromed. In addition, 1 h of signal is recorded from the microwires everyday using a Blackrock amplifier sampling the signal at 30 kHz.

Results: Our results show that FR are preferentially recorded with microelectrodes as predicted. Other events are also recorded by microelectrodes like seizures, interictal spikes and single and multi-unit activities. The tetrode configuration allows a better identification of the neuronal activity. Cognitive task also generate specific potentials in the microspatial domain.

Conclusion: These data suggest that these new microelectrodes are highly promising.

0010 ELECTROENCEPHALOGRAPHIC ABNORMALITIES IN ANTI-NMDAR ENCEPHALITIS
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Purpose: Anti-NMDA (N-methyl D-aspartate) receptor encephalitis (anti-NMDARE) is an autoimmune encephalitis. Early treatment initiation improves its prognosis. The electroencephalogram (EEG) is an accessible tool, easy to achieve. The aim of our study was to describe the different EEG patterns in patients suffering from anti-NMDARE. We further looked for EEG abnormalities timeline in the course of the disease, their correlation with clinical data, and whether any EEG pattern could be a reliable predictor of outcome.

Method: We retrospectively analyzed 300 EEG recordings, including 60 days of EEG-monitoring, from 24 patients suffering of anti-NMDARE. Patients were hospitalized in the University Hospital of Clermont-Ferrand, Lyon and Saint-Etienne, between November 2007 and June 2016.

Results: Our study describes three typical EEG patterns in patients with anti-NMDARE: Excessive Beta Activity range 14–20 Hz (EBA) in 70.8% of our patients, Extreme Delta Brush (EDB) in 62.5% and Generalized Delta Activity (GDA) in 50%. A temporal organization and timeline in these EEG patterns could be evidenced in the course of disease: EBA appears first, followed by EDB and then GDA, as the median time of appearance for EBA, EDB and GDA was respectively 10, 15 and 22 days. GDA were correlated with the occurrence of abnormal movements; their presence at the time of EEG recordings increased the risk to observe abnormal movements at the same time by 4.7 (CI 95% 2.3–9.3, p < 0.001). The absence of GDA was significantly associated with a good outcome (modified Rankin Scale score < 4) at 6 months (p = 0.011), and 18 months of follow-up (p = 0.05).

Conclusion: These results provide new diagnostic and prognostic supports in the anti-NMDARE. The rhythmic aspect of GDA should not be misinterpreted as status epilepticus, to avoid antiepileptic treatments intensification and their adverse effects, we discussed potential electrophysiological generators of these EEG patterns, and their correlations with physiopathological hypothesis.

Epilepsy Surgery 1
Sunday 3rd September, 2017

0011 RELATIONSHIP BETWEEN CORTICAL RESECTION AND VISUAL FUNCTION AFTER OCCIPITAL LOBE EPILEPSY SURGERY
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Purpose: To describe the long-term clinical and visual outcomes of occipital lobe epilepsy (OLE) surgery and to analyze the relationship between visual cortical resection and visual function in OLE surgery.

Method: A total of 42 consecutive patients who were diagnosed with OLE and underwent occipital lobe resection from June 1995 to November 2013 were included. Clinical, radiological, and histopathological data were retrospectively reviewed. Seizure outcomes were classified according to the Engel classification. Visual function after surgery was assessed by the National Eye Institute Visual Functioning Questionnaire 25 (NEI-VFQ-25). The relationship between the resected area of the visual cortex and visual function was demonstrated by multivariate linear regression models.

Results: After a mean follow-up period of 102.2 months, 27 patients (64.3%) were seizure free, and six patients (14.3%) had Engel class II outcome. Nineteen of 33 patients (57.6%) were in the normal or quadrantantopia group after surgery. The normal or quadrantanopia group had better vision-related quality of life than the hemanopsia group. The resection of lateral occipital areas 1 and 2 (LO1, LO2) of the occipital lobe was significantly associated with difficulties in general vision, peripheral vision, and vision-specific roles. Additionally, the resection of intraparietal sulcus 3 or 4 (IPS3 or IPS4) was significantly associated with decreased social functioning.

Conclusion: We found a favorable seizure control rate of 78.6% (Engel class I or II), with 57.6% of the subjects having good visual function after OLE surgery (normal or quadrantanopia). Lateral occipital cortical resection had also a significant impact on visual function despite the preservation of the visual field.

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After anterior temporal lobectomy (ATL) for drug resistant mesial- temporal lobe epilepsy related to hippocampus sclerosis (MTLE-HS) in Brazilian patients.

Method: Multiple binary logistic regression analysis was performed to identify the clinical, demographic, radiological, and electrophysiological variables independently associated with MCIC in the QOLIE-31 overall score one year after anterior temporal lobectomy (ATL) in 77 consecutive patients with unilateral MTLE-HS.

Results: The overall QOLIE-31 score and all its subscale scores increased significantly (p < 0.0001) 1 year after ATL. The final logistic regression model, absence of pre-surgical diagnosis of depression (adjusted OR 4.4, CI 95% 1.1 - 16.1; p = 0.02) and complete postoperative seizure control (adjusted OR 4.1, CI 95% 1.2 - 14.5; p = 0.03) were independently associated with improvement equal to or greater than the MCIC in QOL after ATL. The overall model accuracy for MCIC improvement in the QOL was 85.6%, with a 95.2% of sensitivity and 46.7% of specificity.

Conclusion: These results in Brazilian patients reinforce the external validation of previous findings in Canadian patients showing that pre-surgical depression and complete seizure control after surgery are independent predictors for meaningful improvement in QOL after ATL, and have implications for the surgical management of MTLE patients.
**Abstracts**

0015

**STIMULATION INDUCED SEIZURES DURING EXTRAOPERATIVE DIRECT ELECTRICAL CORTICAL STIMULATION OR CORRECT MAPPING**

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**Purpose:** Direct electrical cortical stimulation (CS) is used routinely for mapping of eloquent cortex in patients undergoing intracranial EEG as part of their presurgical evaluation. CS can, as a by-product, elicit after-discharges, subclinical EEG seizures, stimulus induced seizures (SIS) and stimulus induced auras (SIA). SIS and SIA may have habitual or non habitual symptomatology compared to spontaneous seizures and auras. The purpose of this study is to: (1) determine the frequency of SIS with habitual or non habitual symptomatology and (2) estimate their potential diagnostic role in defining the seizure onset zone.

**Method:** We performed a retrospective review of 134 focal epilepsy patients who underwent intracranial electrode implantation and CS at the National Hospital for Neurology and Neurosurgery, Queen Square from 2008 until 2016.

**Results:** 46 (34%) of those had SIS, SIA or a subclinical EEG seizure during CS. Of those 46 pts, 29 experienced SIS (63%) in 14pts (30.4%) SIS were of habitual semiology, and 9 of those had concordance with the ictal onset zone of spontaneous seizures. In 15pts(32.6%)SIS were non habitual SIA were elicited in 16 pts (35%), 12 of those were of habitual semiology. Subclinical EEG seizures were elicited in 4 pts (8.7%)

**Conclusion:** In conclusion, our retrospective review of CS mapping revealed that about a third of all patients will experience unintended stimulation induced seizures. Those seizures are habitual or non habitual in equal proportion. In two thirds of cases the location of eliciting habitual SIS will be from the same location of the spontaneous seizure onset zone. This calls for caution to routinely use SIS to localize the seizure onset zone, although in some cases SIS mimicking the effect of spontaneous epileptic discharges on cortex during CS could be a potential additional diagnostic tool to localize the seizure onset zone.

Living with Seizures/Epilepsy 1
Sunday 3rd September, 2017

0016

**BEHAVIOURAL AND EMOTIONAL COMORBIDITY OF ACUTE SEIZURES IN YOUNG KENYAN CHILDREN: A POPULATION-BASED STUDY**

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**Purpose:** Acute seizures in young children in Africa may be associated with poor behavioural and emotional problems. It is unclear if behavioural and emotional comorbidities of acute seizures are related to the seizures, or shared genetic susceptibility and neurological damage.

**Method:** We conducted a population-based study on 3,273 young children aged 1–6 years on the Kenyan coast to examine the relationship between acute seizures and behavioural and emotional problems, and to determine the factors associated with the comorbidity. Prevalence of behavioural and emotional problems was derived from the inverse link of a logit model. Generalised linear models were used to measure the independent association between acute seizures and behavioural and emotional problems, and to determine associated risk factors. Sobel-Goodman mediation tests were used to perform mediation analysis.

**Results:** The crude prevalence of total behavioural and emotional problems was 30% (95% CI, 20%–43%) for children with acute symptomatic seizures and 25% (95% CI, 15%–38%) for those with febrile seizures; being greater than for those without seizures (11% (95% CI, 11%-12%); Chi-squared p ≤ 0.001). Behavioural and emotional scores were higher in acute seizures than in those without seizures (Cohens d = 0.44 (95% CI, 0.30–0.59)). Acute seizures were associated with total behavioural and emotional problems (risk ratio (RR) = 1.92 (95% CI, 1.34–2.77)) after accounting for sociodemographic and medical confounders. The proportion of total effects of acute seizures on behavioural and emotional problems mediated by epilepsy was small (15.3% (95% CI, 4.5–34.9%)). Among children with acute seizures, important risk factors for mental health comorbidity included family history of febrile seizures (RR = 3.36 (95% CI, 1.34–8.41)) for total problems, repetitive acute seizures (β=0.36 (95% CI, 0.15–0.57)) for externalizing problems and focal acute seizures (RR=1.80 (95% CI, 1.05–3.08)) for internalising problems.

**Conclusion:** Acute seizures are associated with substantial behavioural and emotional problems, which should be assessed and addressed in children with these seizures in this rural area of Kenya.

0017

**PARENTING STRESS AND PERCEIVED STIGMA IN MOTHERS OF CHILDREN WITH EARLY ONSET EPILEPSY: A POPULATION-BASED STUDY**

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**Purpose:** To provide population-based data on parenting stress and perceived stigma in mothers of young children with epilepsy, and to compare findings with those of mothers of developmental, age and gender matched children with non-epilepsy related neurodisability (i.e. neurological and/or neurodevelopmental difficulty).

**Method:** The mothers of young children (1–7 years) with epilepsy (n = 47) in a defined geographical area of the UK completed the Parenting Stress Index–4th Edition and a measure of perceived stigma (Austin et al. 2004). The responses of mothers of children with epilepsy are compared with parents of developmental, age and gender matched children with non-epilepsy related neurodisability (n = 48). Alpha level is p < 0.05.

**Results:** Significantly more mothers of children with epilepsy scored in the abnormal range (~85th percentile) on the Parent-Child Dysfunctional Interaction subscale (Epilepsy 45% vs. Controls 21%; p = 0.013), but not on the Parental Distress subscale (Epilepsy 32% vs. Controls 23%; p = 0.325), Difficult Child Subscale (Epilepsy 57% vs. Control 46%; p = 0.257) or Total Stress Score (epilepsy 38% vs. Controls 21%; p = 0.062). There was not a significant difference on the perceived stigma measure between mothers of children with epilepsy and mothers of children with non-epilepsy related neurodisability (p = 0.508).

**Conclusion:** Mothers of young children with epilepsy report high levels of parenting stress. They also showed higher levels of parenting stress on the Parent-Child Dysfunctional Interaction subscale compared with mothers of children with non-epilepsy related neurodisability. Levels of perceived stigma did not differ between the groups. Further analysis will attempt to identify factors associated with parenting stress and stigma in mothers of young children with epilepsy. Additionally we will also seek to identify why parent-child interaction may be more compromised in mothers of children with epilepsy.
0018
"SEIZURE MONITORING ON MY APP" A NURSING APPROACH IN THE IMPLEMENTATION OF A SEIZURE APP. PERSPECTIVES FROM CLINICAL PRACTICE
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Purpose: Various App’s have been introduced to the market which also includes Apps within the Health Sector. At the Danish Epilepsy Center, we therefore introduced a Seizure App for patients treated at our hospital in order to offer patients and their relatives a tool that could monitor their seizures in a safe and correct form. As the intention was also to ensure a fast track to the medical file, the App is designed in a way that enables the patient to register not only their seizures, but also acute medication and possible triggers and every 24-h have it sent directly to their own medical file at the Epilepsy Center. The overall purpose is to obtain a clinical precise overview over the seizure situation based on the particular seizures that the clinician has classified. As the seizures gets automatically registered in the patients’ medical file it ensures that there is always an updated clinical status in order for the MD to adjust and monitor treatment.

Method: In order to be able to distinguish amongst the vast numbers of different seizures, the patient/relatives are, before getting the password, introduced to only their specific seizure semiology. The process thereby includes and ensures a valuable introduction to an individual seizure semiology which is entirely based on the introduction and education from the nurses. It is also possible to send a seizure and after acceptance to the MD it can be sent directly to the hospital.

Results: So far we have 600 users, which is a gradually growing number.

Conclusion: The App has proven very useful in the clinical context. There is always a precise and updated seizure registration available and more important it is based on the patients clinically diagnosed seizures in an accurate manner.

0019
AN ECONOMIC EVALUATION OF A MULTI-COMPONENT SELF-MANAGEMENT INTERVENTION FOR ADULTS WITH EPILEPSY (ZMILE STUDY)
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Purpose: The objective of this (trial-based) economic evaluation was, from a societal perspective, to compare the cost-effectiveness of a multi component self-management intervention (MCI) with care as usual (CAU) in adult patients with epilepsy over a 12 month period. Method: In a randomized-controlled trial participants were randomized into intervention or CAU group. Adherence, self-efficacy (ESSES), quality adjusted life years (QALYs), health care costs, production losses, and patient & family costs were assessed at baseline and during the 12-month study period. Incremental cost-effectiveness ratios (ICERs) (i.e. cost per increased adherence, self-efficacy or QALY), and cost-effectiveness acceptability curves were calculated.

Results: In total, 102 patients were included in the study, of whom 52 were in the intervention group. Adherence rates over 6 months were 63.7% for the CAU group and 75.9% for the intervention group. Adherence, ESES and quality of life did not differ significantly between groups. An ICER of €54 per point increase in ESSES-scores at 6 months and €1105 per point increase at 12 months follow-up was found. The intervention resulted in an ICER of €88 per percentage of adherence increase at 6 months. ICERs of €8.272 and €15.144 per QALY gained were found at 6 and 12 months follow-up, respectively.

Conclusion: Although no statistically significant difference was found after baseline adjustments, cost-effectiveness estimates for MCI appear to be promising. As rules of inference are arbitrary, it has been argued that decisions should be based only on the net benefits, irrespective of whether differences are statistically significant. Hence, the MCI may be a cost-effective addition to the current standard care for adults with epilepsy.

0020
KNOWLEDGE AND ATTITUDES TOWARDS EPILEPSY OF PARENTS IN MALI
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Background: In Mali, epilepsy affects 15 persons per thousand yet its psychosocial impact remains to be explored.

Objectives: The objective of this study was to evaluate the knowledge and attitudes towards epilepsy of parents with children affected by epilepsy in Mali compared to unaffected parents.

Methods: We interviewed 720 adults in Bamaco (Capital of Mali), half of which were parents of children living with epilepsy. The groups were matched for age, sex, education and socio-economic status.

Results: In our population 78% of parents had seen at least one epileptic seizure. Of these, only 33% recognised the need to intervene while 22% believed their first action should be to pour fresh water on the head of the patient, 57% reported that their first action would be to take the patient to a traditional healer. Knowledge about the clinical characteristics of seizures was more accurate in the parents with affected children. But, the misconceptions about epilepsy were high in both groups and sometimes even more prevalent in the parents with affected children.

Conclusion: Our study demonstrates the widespread misconceptions towards epilepsy in parents whether affected or not. Our findings argue for the need of a focused effort on education towards the population of Mali, including traditional healers, to improve the quality of life of children living with epilepsy and their family by improving knowledge and reducing stigma.
Paediatric Epilepsies 1
Sunday 3rd September, 2017

0021
AETIOLOGY AND SUBCORTICAL STRUCTURE VOLUME ARE ASSOCIATED WITH SUBSEQUENT COGNITIVE DEFICITS IN CHILDREN FOLLOWING CONVULSIVE STATUS EPILEPTICUS (CSE)
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Purpose: Childhood CSE is associated with poorer neuropsychological outcomes with aetiology as a significant risk factor. We recently showed a wide spectrum of decreased subcortical structure volumes are associated with lower IQ in childhood epilepsy. We hypothesise that in childhood CSE, aetiology and decreased subcortical structural volumes are associated with cognitive measures.

Method: Structural MRI scans (Siemens Avanto, 1.5T) and cognitive measures (FSIQ, PIQ, VIQ (Wechsler Abbreviated Scale of Intelligence) and GMS (Children’s Memory Scale)) were collected from age and gender matched controls and patients at a mean 8.5 years post-CSE (Prolonged Febrile Seizures (PFS), n = 30; Symptomatic, n = 30; and Other, n = 12). Scans underwent quantitative volumetric analysis using FSL (Analysis Group, FMRIB, Oxford) to provide subcortical structure volume, grey/white matter volume, and intracranial volume (ICV).

Multivariable linear regression was performed for each subcortical structure of patients to identify significant predictors of cognition, whilst correcting for aetiology, age, gender and ICV; Bonferroni correction was applied. Due to significant collinearity between structures, an additional multivariable analysis was used with total subcortical volume instead of individual subcortical structures, whilst additionally correcting for white/grey matter volume.

Results: 72 controls (12 ± 2.9SD years; 43 male) and 72 patients (11.7 ± 3.4SD years; 36 male) underwent analysis. Aetiology is a significant predictor of long-term cognitive outcome post-CSE. Volumes of the left putamen and globus pallidus both significantly correlated with FSIQ (p < 0.05) and PIQ (p < 0.05). In the final model, total subcortical volume was independently associated with FSIQ (p < 0.05), PIQ (p < 0.05) and GMS (p < 0.05).

Conclusion: Our findings suggest that in addition to aetiology, decreased volumes of the left putamen and globus pallidus are associated with cognitive deficits following CSE. This, along with our findings with total subcortical volume, indicates that a subcortical network rather than individual structures may be associated with cognition.

0022
CANNABIDIOL (CBD) REDUCES CONVULSIVE SEIZURE FREQUENCY IN DRAVET SYNDROME: RESULTS OF A MULTI-CENTRE, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL (GWPCARE1)

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Purpose: Assess the effect of CBD added to antiepileptic drug (AED) therapy for the treatment of drug-resistant seizures in Dravet syndrome.

Method: This double-blind, placebo-controlled trial randomised 120 children aged 2–18 years with Dravet syndrome and drug-resistant seizures to receive CBD oral solution 20 mg/kg/day (n = 61) or placebo (n = 59) for 14 weeks (2 week titration; 12 week maintenance). The primary endpoint was the percentage change from baseline in convulsive seizures (tonic-clonic, tonic, clonic, and atonic) frequency over the 14-week treatment period.

Results: The groups were well-balanced at baseline for demographics. Mean age was 10 years, with 29% of patients <6 years. Patients had previously tried a median 4 AEDs, and were currently taking a median 3 AEDs. Convulsive seizure frequency per month decreased from a median of 12.4 to 5.9 (median reduction of 39%) with CBD vs. 14.9 to 14.1 (median reduction of 13%) with placebo (difference between groups of 23%; p = 0.012). The proportion of patients with ≥50% reduction in convulsive seizure frequency was 42.6% with CBD vs. 27.1% with placebo (OR=2.0; p = 0.078). Adverse events (AEs) occurred in 93.4% of CBD and 74.6% of placebo patients, and were mostly mild or moderate; the most common were somnolence, diarrhea, and decreased appetite. Serious AEs were reported in 16.4% of CBD and 5.1% of placebo patients, and were mostly mild or moderate; the most common were somnolence, diarrhea, and decreased appetite. Serious AEs were considered treatment-related in 8.2% of CBD patients, all of whom discontinued CBD. Some elevations in transaminases were noted and were considered treatment-related in 8.2% of CBD patients, all of whom discontinued CBD. Some elevations in transaminases were noted and were considered treatment-related in 8.2% of CBD patients, all of whom discontinued CBD. Some elevations in transaminases were noted and were considered treatment-related in 8.2% of CBD patients, all of whom discontinued CBD. Some elevations in transaminases were noted and were considered treatment-related in 8.2% of CBD patients, all of whom discontinued CBD. Some elevations in transaminases were noted and were considered treatment-related in 8.2% of CBD patients, all of whom discontinued CBD. Some elevations in transaminases were noted and were considered treatment-related in 8.2% of CBD patients, all of whom discontinued CBD. 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**Purpose:** SCN2A mutations are associated with a spectrum of epilepsies and neurodevelopmental disorders. In single functional investigations both gain- and loss-of-function effects on the sodium channel were found. Here, we report the phenotypic spectrum in a large cohort of novel patients, describe the effect of sodium channel blockers (SCB) on epileptic seizures, and correlate the findings with genetic and functional properties.

**Method:** 71 unpublished children with SCN2A mutations were collected across multiple centers in Europe and the US. Cases were analyzed regarding genotype, phenotype and response to SCB. Functional studies were performed in selected missense mutations using whole cell patch clamping.

**Results:** 28 had encephalopathy with early-infantile-onset epilepsy (< 3 months), including Ohtahara syndrome (8) and epilepsy of infancy with migrating focal seizures (5). 29 had encephalopathy with infantile/childhood-onset epilepsy (≥3 months), including West syndrome (9), Lennox-Gastaut syndrome (6), and focal epilepsies with an ESES-like EEG pattern (6). Five children had intellectual disability/autism without seizures. Nine children had benign neonatal/infantile seizures. The use of SCB was associated with significant seizure reduction/freedom in children with early infantile epilepsies, whereas SCB were rarely effective in epilepsies with later onset and sometimes induced seizure worsening. Truncating mutations were exclusively seen in patients with late onset epilepsies and lack of response to SCB. Missense mutations associated with early infantile epilepsy and a good response to SCB resulted in increased sodium channel activity with gain-of-function (GOF). In contrast, mutations in patients with late-onset forms and an insensitive response to SCB were associated with loss-of-function effects (LOF).

**Conclusion:** Our study reflects the large spectrum of SCN2A-related disorders. We establish two distinct main groups with seizure onset either before or after three months of age, which show phenotypic differences.

**Purpose:** Rotavirus infection has recently been reported to be associated with neonatal seizures and distinctive symmetric cerebral white matter lesions on magnetic resonance imaging (MRI). We investigated long-term outcomes and prognostic factors in newborns with rotavirus-associated leukoencephalopathy.

**Method:** We retrospectively reviewed the records and brain magnetic resonance (MR) images of 32 patients who fulfilled the following criteria: (1) neonatal seizures, (2) distinctive symmetric cerebral white matter lesions on diffusion-weighted MR images (DWI), (3) rotavirus infection, (4) absence of a specific etiology of seizures, except for the aforementioned DWI lesions, and (5) Korean Bayley Scales of Infant Development II (K-BSID-II) assessment after 12 months of age.

**Results:** The mean age at seizure onset was 4.7 ± 0.8 days. The age of the patients at the time of K-BSID-II assessment was 24.2 ± 8.0 months. Fourteen patients (43.8%) showed normal or accelerated performance in the mental and motor scales, while 18 patients (56.2%) had delayed performance in the mental and/or motor scales. Three patients (8.6%) were significantly delayed in both the mental and motor scales. The percentage of volume of diffusion-restricted lesions based on total brain volume was significantly delayed in both the mental and motor scales. The percentage of volume of diffusion-restricted lesions based on total brain volume was significantly delayed in both the mental and motor scales. The percentage of volume of diffusion-restricted lesions based on total brain volume was significantly delayed in both the mental and motor scales. The percentage of volume of diffusion-restricted lesions based on total brain volume was significantly delayed in both the mental and motor scales.

**Conclusion:** Rotavirus-associated leukoencephalopathy in newborns around 5 days of age can cause adverse neurodevelopmental outcomes with a wide range of severity. The extent of white matter lesion on initial DWI can predict neurocognitive outcome.

**Purpose:** Epileptic encephalopathy with electrical status epilepticus in sleep (ESES) is characterized by near-continuous epileptiform activity during sleep accompanied by acquired neurodevelopmental deficits. Perinatal thalamic injury has previously been reported to predispose to ESES. The aim of this study was to identify possible predictors for the occurrence of ESES after perinatal thalamic injury.

**Method:** We included patients with perinatal thalamic injury, diagnosed in our center in the neonatal period (incidence cohort), or referred later during childhood. Thalamic injury was classified as anterior, medial, ventral, lateral or pulvinar based on the conventional MRI sequences. Thalamic and caudate nucleus volumes were calculated after automatic segmentation of the DTI MRI-scans. Sleep EEGs distinguished patients into ESES (spike wave index [SWI] >85%), ESES-spectrum (SWI 50-85%) or no ESES (SWI<50%).

**Results:** 26 patients were included. Conventional MRI sequences were available in 22 neonates, at around three months in 18 and during childhood in 21 patients, with DTI images of sufficient quality in 4, 8 and 8 patients respectively. In the incidence cohort (n = 20), 8 had ESES, 7 ESES-spectrum and 5 had not developed ESES after a median sleep EEG follow-up of 7 years. In the total cohort (n = 26), 13 had ESES, and 8 ESES-spectrum. At three months of age, thalamic volume and volume ratio thalamus/caudate nucleus were lower in children who later developed ESES-spectrum (volume left thalamus 7650 vs. 4574 mm³ [p = 0.004]; ratio 4.1 vs. 3.2 [p < 0.001], volume right thalamus 6315 vs. 4930 mm³ [p = 0.004]; ratio 4.4 vs. 3.5 [p = 0.002]). Bilateral injury (p = 0.005) and involvement of the anterior thalamic nuclei (p = 0.006) were associated with lower IQ/DQ after ESES onset.

**Conclusion:** ESES-spectrum is seen in a majority of patients after thalamic injury. Smaller remaining thalamic volume is associated with development of ESES and bilateral injury and involvement of the anterior nuclei predict neurodevelopmental deficits.

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**0025 ELECTRICAL STATUS EPILEPTICUS IN SLEEP AFTER THALAMIC INJURY: CLINICAL AND NEOIMAGING PREDICTORS IN 26 CHILDREN**


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**Purpose:** Epileptic encephalopathy with electrical status epilepticus in sleep (ESES) after perinatal thalamic injury (THAL) is characterized by near-continuous epileptiform activity during sleep accompanied by acquired neurodevelopmental deficits. Perinatal thalamic injury has previously been reported to predispose to ESES. The aim of this study was to identify possible predictors for the occurrence of ESES after perinatal thalamic injury.

**Method:** We included patients with perinatal thalamic injury, diagnosed in our center in the neonatal period (incidence cohort), or referred later during childhood. Thalamic injury was classified as anterior, medial, ventral, lateral or pulvinar based on the conventional MRI sequences. Thalamic and caudate nucleus volumes were calculated after automatic segmentation of the DTI MRI-scans. Sleep EEGs distinguished patients into ESES (spike wave index [SWI] >85%), ESES-spectrum (SWI 50-85%) or no ESES (SWI<50%).

**Results:** 26 patients were included. Conventional MRI sequences were available in 22 neonates, at around three months in 18 and during childhood in 21 patients, with DTI images of sufficient quality in 4, 8 and 8 patients respectively. In the incidence cohort (n = 20), 8 had ESES, 7 ESES-spectrum and 5 had not developed ESES after a median sleep EEG follow-up of 7 years. In the total cohort (n = 26), 13 had ESES, and 8 ESES-spectrum. At three months of age, thalamic volume and volume ratio thalamus/caudate nucleus were lower in children who later developed ESES-spectrum (volume left thalamus 7650 vs. 4574 mm³ [p = 0.004]; ratio 4.1 vs. 3.2 [p < 0.001], volume right thalamus 6315 vs. 4930 mm³ [p = 0.004]; ratio 4.4 vs. 3.5 [p = 0.002]). Bilateral injury (p = 0.005) and involvement of the anterior thalamic nuclei (p = 0.006) were associated with lower IQ/DQ after ESES onset.

**Conclusion:** ESES-spectrum is seen in a majority of patients after thalamic injury. Smaller remaining thalamic volume is associated with development of ESES and bilateral injury and involvement of the anterior nuclei predict neurodevelopmental deficits.

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**0026 CANNABIDIOL (CBD) SIGNIFICANTLY REDUCES DROP AND TOTAL SEIZURE FREQUENCY IN LENNOX-GASTAUT SYNDROME (LGS): RESULTS OF A DOSE-RANGING, MULTI-CENTRE, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL (GWPCARE3)**


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Purpose: Evaluate efficacy of add-on CBD for the treatment of seizures associated with LGS.

Method: Eligible patients were 2–55 years old with a clinical diagnosis of LGS, ≥8 drop seizures during 4-week baseline, and documented failure of ≥1 antiepileptic drug (AED). Patients were randomised (1:1:1) to 20 mg/kg/day CBD, 10 mg/kg/day CBD, or placebo for 14 weeks (2-week titration; 12-week maintenance). The primary efficacy endpoint was percentage change from baseline in drop seizures/month over the 14-week treatment period for CBD vs. placebo; ≥50% responder rate and percentage change in total seizures were assessed.

Results: 225 patients were randomised (76 CBD 20 mg/kg, 73 CBD 10 mg/kg, 76 placebo); 9 CBD 20 mg/kg, 2 CBD 10 mg/kg, and 2 placebo patients withdrew. Groups were similar at baseline; mean age was 16 years (30% of patients ≥18 years) and median drop seizures/month was 85 (IQR: 44, 166). Patients had failed a median of 6 and were taking a median of 3 AEDs. Reduction in drop seizures was significantly greater for CBD 20 mg/kg (42%) and CBD 10 mg/kg (37%) than placebo (17%; p = 0.0047 and p = 0.0016), as were ≥50% responder rates (40% and 36% vs. 15%; p = 0.0006 and p = 0.0030) and reductions in total seizures (38% and 36% vs. 18%; p = 0.0091 and p = 0.0015). Adverse events (AEs) occurred in 94% of CBD 20 mg/kg, 84% of CBD 10 mg/kg, and 72% of placebo patients, and were mostly mild or moderate; the most common were somnolence and decreased appetite. Treatment-related serious AEs occurred in 5 CBD 20 mg/kg, 2 CBD 10 mg/kg, and 2 placebo patients. Some elevations in transaminases were seen. There were no deaths. Of 212 completers, 99% entered the open-label extension study.

Conclusion: Results suggest that add-on CBD for treatment of seizures associated with LGS may be efficacious, with more adverse events than placebo, but generally well-tolerated. (Funded by GW Research, Ltd; NCT02224560).

Purpose: Seizure-free persons with epilepsy may ask whether antiepileptic drug (AED) treatment is still necessary. Stopping AEDs carries the risk of seizure recurrence, and although many publications studied predictors of seizure outcome it is difficult to apply this knowledge to the individual patient. The aim was to create an individualised prediction model for seizure recurrence and long-term seizure outcome, through an Individual Participant Data meta-analysis.

Method: Systematic review of literature identified all candidate predictors and eligible publications, of which authors were contacted to provide individual participant data. Through regression analysis the strongest predictors were selected. Internal-external cross-validation was performed to ensure generalizability. Ultimately, nomograms were created to visually represent computed prediction models.

Results: Ten cohorts with 1769 patients were gathered, with both children and adults, of which 812 (46%) experienced seizure recurrence and 9% had seizures in the last year of follow-up (median 5.3 years, interquartile range 3–10 years). Prediction models for seizure recurrence (c-statistic: 0.65; 95%CI 0.65–0.66) and chance of long-term seizure freedom (c-statistic: 0.71; 95%CI 0.70–0.71) were created with good calibration and stable validation across all ten populations.

Conclusion: It is now possible to compute combined risks of seizure recurrence and the chance of long-term seizure freedom after AED withdrawal. The nomograms are based on a large cohort, validated in both children and adults, and will aid consultation of seizure free people with epilepsy. The nomograms may therefore guide the physician as well as the patient in person-tailored choices.

Purpose: CONSIDERING ANTI-EPILEPTIC DRUG WITHDRAWAL? A TOOL FOR INDIVIDUAL PREDICTION OF SEIZURE OUTCOMES

0027

CONSIDERING ANTI-EPILEPTIC DRUG WITHDRAWAL? A TOOL FOR INDIVIDUAL PREDICTION OF SEIZURE OUTCOMES


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Purpose: Seizure-free persons with epilepsy may ask whether antiepileptic drug (AED) treatment is still necessary. Stopping AEDs carries the risk of seizure recurrence, and although many publications studied predictors of seizure outcome it is difficult to apply this knowledge to the individual patient. The aim was to create an individualised prediction model for seizure recurrence and long-term seizure outcome, through an Individual Participant Data meta-analysis.

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0028

ADJUNCTIVE EVEROLIMUS IN PATIENTS WITH TREATMENT-REFRACTORY SEIZURES ASSOCIATED WITH TUBEROUS SCLEROSIS COMPLEX (TSC): ANALYSIS OF EXPOSURE-EFFICACY AND EXPOSURE-SAFETY RELATIONSHIPS IN THE RANDOMIZED, PHASE 3, EXIST-3 TRIAL


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Purpose: This exploratory analysis ofEXIST-3 (NCT01713946) evaluated the impact of time and serum concentration on the efficacy and safety of everolimus.

Method: Patients with TSC-associated treatment-refractory seizures were randomized (1:1:1) to receive placebo, low-exposure (LE, 3–7 ng/mL) or high-exposure everolimus (HE, 9–15 ng/mL) during the core phase (18-weeks). In the extension phase (24-weeks), target exposure for all patients was 3–15 ng/mL. Post-baseline average weekly seizure frequency

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Pharmacokinetic-efficacy analysis showed a 2-fold increase in TN-C min GABAbR patients (31%). In anti-LGI1 encephalitis carbamazepine used, TCS seemed to respond to levetiracetam in a minority of anti-Erasmus MC, Neurology, Rotterdam, Netherlands, concerns were observed with higher exposure. associated treatment-refractory seizures. No unexpected toxicities/safety gest a potential disease-modifying effect of everolimus for TSC- – HR:0.89; 95%CI:0.65–1.79. Conclusion: Reduction in SF with time. How- ever, HE achieved higher reduction in SF with time. These findings sug- gest a potential disease-modifying effect of everolimus for TSC- associated treatment-refractory seizures. No unexpected toxicities/safety concerns were observed with higher exposure.

0029 SYMPTOMATIC TREATMENT OF ANTI-GABAbR AND ANTI-LGI1 AUTOIMMUNE EPILEPSY

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Purpose: In this nationwide study we report anti-GABAbR and anti-LGI1 autoimmune epilepsy (AIE), with specific emphasis on response to anti-epileptic drug (AED) treatment.

Method: We collected patients with anti-GABAbR and anti-LGI1 encephalitis, confirmed with both cell-based assay and immunohistochemistry, from January 2007 till August 2016. Information on seizure type, seizure frequency, AED treatment, immunotherapy, response to treatment and adverse events was obtained in interviews and from medical records.

Results: Of 70 patients with autoimmune encephalitis (23 with anti-GABAbR and 47 with anti-LGI1 encephalitis), 87% suffered from seizures (21/23 and 41/47, respectively). Seizures were the presenting symptom in 51% of patients. Anti-LGI1 encephalitis patients initially presented with focal seizures (44%), faciobrachial dystonic seizures (FBDS; 29%) or tonic-clonic seizures (TCS; 27%), while most anti-GABA_B_R patients (75%) presented with TCS (86%). Status epilepticus occurred in 10/21 anti-GABA_B_R patients (48%) and in 6/41 anti-LGI1 encephalitis patients (15%; p = 0.012), twelve of them super-refractory. Patients were mainly treated with levetiracetam (n = 42), valproic acid (n = 33) and carbamazepine (n = 21), with a median use of 2 AED (0–6). Of AED used, TCS seemed to respond to levetiracetam in a minority of anti-GABA_B_R patients (31%). In anti-LGI1 encephalitis carbamazepine reduced focal seizures (32%) and valproic acid reduced TCS (32%). Overall, only 65/1 patients (12%) achieved seizure freedom with AED (2 anti-GABAbR and 4 anti-LGI1 patients). Contrarily, immunotherapy resulted in seizure freedom in 35/52 patients (67%; p < 0.0001), in 16 within 7 days (31%; 3 anti-GABA_B_R and 13 anti-LGI1 encephalitis). Seizure frequency was reduced in 41/52 patients (79%). Reported adverse events of AED were additional cognitive decline by valproic acid (12%); mood- and behavior disorders by levetiracetam (21%) and rash by carbamazepine (29%).

Conclusion: It is important to consider AIE in refractory epilepsy or in stereotypic focal seizures, as symptomatic treatment with AED is often insufficient and early, additional immunotherapy is essential.

0030 COMPARING THE EFFICACY OF SODIUM VALPROATE AND LEVETIRACETAM FOLLOWING INITIAL LORAZEPAM IN GENERALIZED CONVULSIVE STATUS EPILEPTICUS (GCSE) IN ELDERLY: A PROSPECTIVE RANDOMIZED CONTROLLED STUDY

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Purpose: This prospective randomized controlled study was conducted to compare the efficacy of sodium valproate (SVA) and levetiracetam (LVM) following initial lorazepam in elderly patients with GCSE and analyse the predictors for poor seizure control.

Method: One hundred and eighteen patients ≥60 years (mean: 67.5 ± 7.5 years, M:F = 1:6.1) with GCSE were recruited after obtaining consent and randomized into either SVA and LVM treatment arms. All patients received initial lorazepam (0.1 mg/kg) followed by par enteral SVA (20–25 mg/kg) or LVM (20–25 mg/kg). Those uncontrolled with 1st AED, crossed over to receive the 2nd AED. One hundred patients (SVA-50; LVM-50) completed the study. Analysis for seizure outcome and prognostic markers was performed in all 118 patients (SVA: 60, LVM: 58).

Results: SE could be controlled with lorazepam and one of AEDs (SVA/ LVM) in 71.18% (84/118). ITT analysis showed that the 2 groups didn’t differ significantly [SVA: 41/60 (68.3%); LVM: 43/58 (74.1%), p = 0.486]. Among the 100 patients who completed the study, SE control was achieved in SVA-38/50 (76%) and LVM-43/50 (86%) (p = 0.202). After crossing over to 2nd AED, SE could be controlled in: SVA (+LVM) group -6/12 (50%); LVM (+SVA) group -1/7 (14.3%). Overall, after the 2nd AED, it was achieved in 77.1% (91/118). Two patients were given anaesthetic medications for seizure control. Longer duration of SE (p = 0.038), lower systolic BP (p = 0.04), higher STESS (p = 0.038), lower GCS at admission (p = 0.016) and discharge (p = 0.007), higher mean mRS (p = 0.018) and lower mean GOS at discharge (p = 0.004) were significantly associated with poor therapeutic response. The 30-day mortality was 20.3% (23/113).

Conclusion: Efficacy of SVA and LVM following initial lorazepam in controlling SE in elderly population was statistically not different; hence the choice of AED could be individualised. Overall seizure control of 77.1% was achieved by adding 2nd AED, especially without the anaes thetic medication, which is encouraging in a resource limited setting.
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0031 FAMILIAL MESIAL TEMPORAL LOBE EPILEPSY AND THE BORDERLAND OF DÉJÀ VU


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Purpose: The cause of temporal lobe epilepsy is often unknown. We ascertained the frequency of familial mesial temporal lobe epilepsy (FMTLE) among patients presenting to a First Seizure Clinic with non-lesional mesial temporal lobe epilepsy (MTLE).

Method: We assessed all available first-degree relatives (cases) of patients presenting to the Austin Health First Seizure Clinic with MTLE with normal MRI (MTLE-NL) or hippocampal sclerosis (MTLE-HS) over a 10-year period. Cases and pairwise age- and sex-matched controls underwent a comprehensive epilepsy questionnaire. Interview transcripts were reviewed independently by two epileptologists blinded to participants’ group allocation, who classified each subject as follows: epilepsy, specifying if MTLE; manifestations suspicious of epilepsy; or unaffected. The presence of physiological déjà vu was noted.

Results: Forty-four patients with MTLE-NL or MTLE-HS were included. In only 2 of them, MTLE had been previously recognized to be familial. Among 242 participants interviewed, MTLE was diagnosed in 9/121 cases vs. 0/121 controls (p = 0.008). All affected cases had focal aware seizures with intense déjà vu and accompanying features; 6 had not been previously diagnosed. Déjà vu experiences which were suspicious, but not diagnostic of MTLE occurred in an additional 6 cases vs. none of the controls (p = 0.04). Physiological déjà vu was frequent, and did not differ between cases and controls. After completing the interviews, FMTLE was diagnosed in 8 of 44 patients (18.2%).

Conclusion: FMTLE accounts for almost one-fifth of new diagnoses of non-lesional MTLE, and is largely unrecognized. Relatives of patients with MTLE may experience déjà vu phenomena which lie in the ‘borderland’ between epileptic seizures and physiological déjà vu.

0032 SEIZURES AND HIGH-GRADE GLIOMAS: A UK SINGLE CENTRE RETROSPECTIVE ANALYSIS

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Purpose: High-grade gliomas (HGG) originate de novo (primary) or following transformation of a low-grade glioma (secondary), and can be considered as two different pathologies, influencing clinical behaviour. Despite this, both tumour types are currently managed similarly. Limited evidence exists investigating the two as separate entities in relation to seizure activity and biochemical markers, therefore forming the focus of our study.

Method: Retrospective analysis of 132 confirmed HGG cases in a single neurosciences centre. Variables recorded: patient demographics, tumour features (cytogenetics, location, primary or transformational, grade), seizure characteristics (type/onset), anti-epileptic drugs (AED) prescribed (prophylaxis/post-seizure) and operative intervention.

Results: 132 patients analysed: mean age at diagnosis 56 (range 21–82), 1.75:1 male:female, 48% males: 40% females experienced seizures. 105:27 primary: transformational HGG. Most common tumour location: frontal (38%) and temporal (23%). 30% HGG patients initially presented with seizures, 14% developed seizures post-diagnosis. 62/132 were prescribed AEDs; 84% post-seizure, 16% prophylactically. Compared to temporal lobe, frontal lobe HGG was a significant predictor of seizures (p < 0.05). Transformational HGG was significantly more likely to present with seizures (p < 0.05) compared to primary HGG (88%–58%). HGG with IDH1-IDH2 mutation was significantly more likely to present with seizures (p < 0.05), with a 2:1 prevalence of IDH1-IDH2 mutation in transformational:primary. Right-sided HGG was significantly more likely to cause seizures (p < 0.01). No significant difference was found between seizures and MGMT hypermethylation/1p-19q co-deletion.

Conclusion: The differing HGG pathologies appear to influence the likelihood of developing seizures. Transformational HGG and the presence of IDH1-IDH2 mutation are associated with increased likelihood of seizure at presentation. Right-sided and frontal lobe HGG are associated with both increased seizures at presentation and overall occurrence. With further analysis of AED impact, this could potentially lead to a change in management of patients with HGG. However, conclusions drawn remain complicated by the limitations of a retrospective analysis.

0033 IMPACT OF SEIZURES AFTER THROMBOLYSIS FOR ACUTE ISCHEMIC STROKE: THE ENCHANTED TRIAL


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Purpose: To determine the frequency, determinants and significance of seizures after thrombolysis for acute ischemic stroke.

Method: Data are from the Enhanced Control of Hypertension and Thrombolysis Stroke Study (ENCHANTED), an international, multicenter, randomized controlled trial where patients with acute ischemic stroke were randomized to low-dose (0.6 mg/kg) or standard-dose (0.9 mg/kg) intravenous alteplase. The protocol pre-specified prospective data collection on in-hospital seizures over 7-days post-randomization. Logistic regression models were used to determine variables associated with seizures and their significance on poor outcomes of death or disability (modified Rankin scale [mRS] scores 3–6), symptomatic intracerebral hemorrhage (sICH), and health-related quality of life (European Quality of life 5-Dimensions questionnaire [EQ-5D]) over 90 days.

Results: Data were available for 3139 acute ischemic stroke participants, of whom 42 (1.3%) had seizures at a median 22.7 hours after the onset of symptoms. Baseline variables associated with seizures were male (odds ratio [OR] 2.19, 95% confidence interval [CI] 1.07–4.50), severe neurological impairment (National Institutes of Health Stroke Scale [NIHSS] score ≥10, OR 2.16, 95% CI 1.06–4.40) and fever (OR 4.55, 95% CI 2.37–8.71). Seizures independently predicted poor recovery: death or major disability (OR 2.88, 95% CI 1.28–6.47), unfavorable ordinal shift of mRS scores (OR 1.94, 95% CI 1.10–3.39) and lower than median EQ-5D health utility index score (OR 3.50, 95% CI 1.37–8.91). There was no association of seizures with sICH in adjusted analyses.

Conclusion: In thrombolysis-treated patients with acute ischemic stroke, seizures are uncommon, occur early, relate to neurological severity, and predict poor recovery.
**0034**
CIRCUMSTANCES OF SUDEPS: A SWEDISH NATIONWIDE POPULATION-BASED STUDY OF 329 CASES

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**Purpose**: Given the importance of identifying high risk situations of sudden unexpected death in epilepsy (SUDEP) and for development of effective preventive measures, we analyzed SUDEP circumstances in a Swedish nationwide population-based case series including 329 SUDEPs.

**Method**: We identified all persons that at some point during 1998–2005 were registered in the National Patient Registry with an ICD code for epilepsy and were alive July 1st, 2006 (n = 78,524). All deaths in this study population from 1 July 2006 to 31 December 2011 with epilepsy mentioned on the death certificate, and all deaths during 2008, were identified by linkage to the National Cause-of-Death Registry. In all, 3166 deaths were included. Death certificates, medical charts, autopsy and police reports were reviewed to identify SUDEP cases and related circumstances.

**Results**: We found 329 cases of SUDEP (63% men) (167 definite, 89 probable and 73 possible) according to the Annegers’ classification. The average age at death was 50.8 (median 52) years. More than half, 58% (n = 191) died at night (between 00.00 and 08.00). A vast majority, 91% (n = 299) died at home. Among these, 65% (n = 195) were found dead in bed. Of all cases, 71% (n = 233) were living alone. Only 14% (n = 47) shared a bedroom. In 66% (n = 217) there was a witnessed (n = 46) or a suspected (n = 171) seizure. When documented, 70% (n = 100) were found prone.

**Conclusion**: This largest SUDEP study to date, illustrates that epilepsy patients who die of SUDEP, largely die at home, live alone, die at night in bed, in the prone position with indication of a previous seizure. This supports that lack of supervision may play a crucial role in SUDEP risk and illustrates challenges that need to be considered in the development of preventive strategies.

**0035**
INTER-ICTAL CARDIAC REPOLARIZATION ABNORMALITIES IN PEOPLE WITH EPILEPSY

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**Background and purpose**: It is well established that acute ventricular arrhythmia following repolarization disorders is a leading cause for sudden cardiac arrest. The occurrence of cardiac electrical disturbances in epilepsy patients was previously documented and may, in part, clarify the mechanism of sudden unexpected death in those patients. The aim of this study was to investigate the frequency of cardiac repolarization disorders among epilepsy patients and whether specific demographic or disease-related features are associated with their occurrence.

**Methods**: This cross sectional study was carried out on 1000 subjects with epilepsy who were compared to age and sex matched 2500 subjects without epilepsy. Clinical assessment, which included careful history taking and examination, was carried out for all subjects. A resting 12-lead electrocardiogram (ECG) was recorded in all participants. ECGs were reviewed by experienced cardiologists. ECG intervals were measured and morphological abnormalities were identified using standard guidelines.

**Results**: Repolarization abnormalities were found in 140 (14%) epilepsy patients. A statistically significant elevation in percentage of QTc prolongation among epilepsy patients compared to controls was documented (8.2% vs. 2%, p = 0.001). Affected patients were significantly older and the abnormality was significantly more prevalent among males and those with poor seizure control. On the other hand, early repolarization and Brugada-type ECG patterns were significantly more prevalent in subjects without epilepsy.

**Conclusion**: Our results demonstrated that epilepsy patients, especially if uncontrolled, are at higher risk for development of QTc interval prolongation. To prove the relationship between this type of arrhythmia and the occurrence of sudden unexpected death in epilepsy further studies are warranted.

**0036**
PRECISION THERAPY FOR EPILEPSY DUE TO KCNT1 MUTATIONS: AN ORDER-RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED CROSS-OVER TRIAL OF ORAL QUINIDINE

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**Purpose**: Gain-of-function mutations of the potassium channel encoded by KCNT1 cause severe epilepsy. Quinidine is a proposed precision therapy due to in vitro blockade of KCNT1 function; open label use has been successful in case reports or small series. We aimed to systematically evaluate quinidine for KCNT1 severe autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE).

**Method**: A single-center, inpatient, order-randomized, blinded, placebo-controlled, cross-over trial of oral quinidine included 6 patients with severe ADNFLE due to KCNT1 mutation. Order was block randomized and blinded. Four day treatment blocks were used with a two day wash-out between. Dose started at 900 mg over three divided doses then, in subsequent participants, reduced to 600 mg, then 300 mg. Primary outcome was seizure frequency measured on continuous video-EEG in those completing the trial.

**Results**: Prolonged QT-interval occurred in the first two patients at doses of 900 mg and 600 mg quinidine per day respectively, despite serum quinidine levels well below the therapeutic range (0.61 μg/ml and 0.51 μg/ml, reference range 1.3–5.0 μg/ml). Four patients completed treatment with 300 mg per day without adverse events. Patients completing the trial had very frequent seizures (mean 14 per day, SD 7, median 13, IQR 10–18). Seizures per day were non-significantly increased by quinidine (median 2, IQR -0.25 - 4.25, p = 0.15) and no patient had a 50% seizure reduction.

**Conclusion**: Quinidine did not show efficacy in adults and teenagers with ADNFLE. Dose-limiting cardiac side effects were observed even in the presence of low measured serum quinidine levels. Although small, this trial suggests use of quinidine in ADNFLE is likely to be ineffective coupled with considerable cardiac risks. It also demonstrates that small trials in severe epilepsy are practical and achievable without overwhelming expense and can provide definitive results that guide the implementation of precision medicine.

**Genetics 1**
Monday 4th September, 2017
0037
THE PHENOTYPIC SPECTRUM OF SCN8A MUTATIONS AND TREATMENT RESPONSE
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Purpose: Since 2012, SCN8A has been known to cause severe epileptic encephalopathy with seizures that are difficult to treat, and a high incidence of sudden unexpected death in epilepsy. Only recently it was discovered that SCN8A can cause more benign forms of epilepsy, where cognition is normal and seizures are treatable. The purpose of this study was to confirm and complete the phenotypic spectrum, and evaluate the treatment response in patients with SCN8A mutations.

Method: We collected a cohort of 131 published and unpublished patients with pathogenic mutations in SCN8A.

Results: The mutational landscape included one de novo 5'UTR mutation, one partial deletion of SCN8A, one in-frame deletion, four stop or frameshift mutations, whereas the remaining mutations were missense. The majority of the mutations occurred de novo, however we also observed nine familial cases. The phenotypic spectrum ranged from benign epilepsy with normal cognition, treatable epilepsy in patients with autism and/or slightly affected cognition, and patients with ID or autism without epilepsy to severe epileptic encephalopathies with severely affected cognition and ongoing seizures. Movement disorders such as paroxysmal dyskinesia, ataxia and choreoathetosis were seen in all patient groups. Treatment response was evaluated in each subgroup. All subgroups showed a good response in form of better seizure control to sodium channel blockers. In some of the milder forms respond well, and often got seizure free, with the aid of carbamazepine, whereas the more severely affected seemed to benefit more from high dosages of oxcarbazepine or phenytoin.

Conclusion: This study takes the first steps toward personalized treatment in SCN8A patients, however, further studies are needed to confirm the position of sodium channel blockers in the treatment protocol.

0039
KCNT1 PATHOGENIC VARIANTS CAUSE NOCTURNAL FRONTAL LOBE EPILEPSY AND MALFORMATION OF CORTICAL DEVELOPMENT
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Purpose: Pathogenic variants of KCNT1 sodium-dependent potassium channel gene have been recently demonstrated to cause nonlesional nocturnal frontal lobe epilepsy (NFLE). The aim of this study is to report the novel association of KCNT1-related NFLE with malformation of cortical development (MCD) in four subjects.

Method: Four patients (2 M, 2 F; two of them brother and sister) with drug-resistant focal epilepsies were submitted to wakefulness/sleep EEG, including long-term video-EEG monitoring for presurgical evaluation in three of them. MRI was performed in all, PET scanning in two. Next-generation sequencing of KCNT1 was performed in all subjects.

Results: Nocturnal seizures occurred in all patients; ictal semiology (bizarre movements, screaming, choking, tonic/dystonic stiffening, nocturnal wandering) was consistent with frontal lobe seizures, leading to the diagnosis of NFLE. Two patients (brother and sister) presented with mental retardation and psychotic features and one had behavioral disturbances and neuropsychological deficits (impulsivity, attention deficit, poor executive functions) consistent with a frontal lobe dysfunction. Neuroimaging investigations showed blurring plus PET hypometabolism of the left frontal operculum in one patient and transmantle heterotopia in another one. The two MRI-negative patients underwent surgical treatment after intracranial EEG recordings. Seizure outcome was Engel Class III in both (follow-up is 13 and 9 years respectively). Histopathology showed type I focal cortical dysplasia (FCD I) in both cases. Genetic testing revealed pathogenic missense variants of KCNT1 gene in all four patients.

Conclusions: We show for the first time that KCNT1 pathogenic variants causing drug-resistant NFLE can be associated with MCD. We can hypothesize that: a) KCNT1 and MCD may exert reciprocal influences in determining the mechanisms that underly seizure generation; b) ultimately, a role for ion channel disorders in the pathogenesis of migration brain abnormalities cannot be excluded.

0040
AETIOLOGIES AND COST-EFFECTIVENESS OF GENOMIC TESTING IN SEVERE EPILEPSIES OF INFANCY: A POPULATION-BASED STUDY
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Purpose: Many infants with severe epilepsies of infancy (SEI) have a genetic or presumed genetic aetiology, but access to genomic testing in clinical practice remains limited. The health economics of genomic testing has not been studied.

Method: Population-based study of the aetiologies and cost-effectiveness of genomic testing in infants with SEI born 2011–2013. SEI was defined as epilepsy onset before age 18 months, frequent seizures, pathways forming have not been studied.

Results: Population-based study of the aetiologies and cost-effectiveness of genomic testing in infants with SEI born 2011–2013. SEI was defined as epilepsy onset before age 18 months, frequent seizures, pathways forming have not been studied.
other ‘genetic’ disorders (16) and unknown (presumed genetic) (38). 86 infants had no aetiologic diagnosis at epilepsy onset. Simulation of diagnostic pathways showed higher yield with the revised pathway than the current pathway (47/86 (55%) vs. 39/86 (45%). Cost per diagnosis was lower with the revised pathway ($12,967AUD vs. $22,754AUD).

Conclusion: Implementation of WES into clinical practice early in the diagnostic pathway, and limiting metabolic testing, will increase diagnostic yield for less cost than current standard diagnostic testing in SEI.

Living With Seizures/Epilepsy 2
Monday 4th September, 2017

0041 THE IMPACT OF PHYSICAL ATTRACTIVENESS JUDGMENTS ON STIGMA OF EPILEPSY
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Purpose: We aimed to investigate whether the physical attractiveness judgment affects perception of epilepsy among healthy individuals and patients with multiple sclerosis (pMS). We tested hypothesis that subjects, in the absence of relevant clues, would catch upon the facial attractiveness when asked to speculate which person suffers epilepsy and select less attractive choices.

Method: Two photo-arrays (7 photos for each gender) selected from the Chicago Face Database (180 neutral faces of Caucasian volunteers with unknown medical status) were shown to subjects. Photos were evenly distributed along the continuum of attractiveness that was estimated by independent raters in pre-study stage. In each photo-array three photos had ratings 1–3 (unattractive), one photo had rating 4 (neutral), and three photos had rating 5–7 (attractive). High-quality printed photo-arrays were presented to subjects and they were asked to select a one person from each photo-array “who has been diagnosed as epilepsy”. Finally, all subjects were asked to complete questionnaire of self-esteem and 19-item Scale of stereotypes toward people with epilepsy.

Results: In total 71 students of psychology/anthropology/andragogy (mean age 21.6 ± 1.7; female 85.9%) and 70 pMS (mean age 37.9 ± 8; female 71.4%) were tested. Majority of students or pMS had no previous personal experience with individuals with epilepsy (63.4%; 47.1%, p = 0.052). Male photo was selected as epileptic in following proportions: students - 84.5% unattractive, 8.5% neutral, and 7% attractive; pMS - 62.9% unattractive, 8.6% neutral, and 28.6% attractive (p = 0.003). Female photo was selected as epileptic in following proportions: students - 38% unattractive, 52.1% neutral, and 9.9% attractive; pMS - 32.9% unattractive, 34.3% neutral, and 32.9% attractive (0.037). Both groups showed very low potential for stigmatization: significantly lower in pMS in 5 items, pMS showed significantly higher self-esteem than students (p = 0.007).

Conclusion: Both students and pMS seemed less willing to attribute epilepsy to attractive person of both gender.

0042 SELF-MANAGEMENT EDUCATION FOR ADULTS WITH POORLY CONTROLLED EPILEPSY (SMILE-UK)
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Introduction: Seizures are controlled with medication for 60–70% of people with epilepsy (PWE). For those with recurring seizures, self-management is important to prevent risks including injury, psychological co-morbidity and premature death. PWE want to know more about self-management but little training has been tested or provided, and none in the UK. In this context, we tested a two-day course delivered in groups for UK PWE with recurring seizures.

Objective: To evaluate by a randomized-control trial Self-Management education for adults with poorly controlled epilepsy (SMILE-UK).

Methods: Patients with ≥ 2 seizures in the previous year were randomised into the treatment or wait-listed control group and followed-up for 1 year. The primary outcome was quality of life measured by QOLIE-31-P. Secondary outcomes included: seizure frequency, anxiety and depression, stigma, self-mastery. Participants were purposefully selected for interview < 6 months after the course.

Results: 404 PWE participated, with a median 18 years since diagnosis, 54% were female, and 69% experienced ≥10 seizures in the prior year. Mean QOLIE-31-P score was 66 at enrolment. There was no difference between the two groups at baseline or 1 year later. In-depth interviews showed facilitated group learning helped participants overcome their sense of isolation, open up, discuss feelings, and improve confidence whilst comparing attitudes and practice.

Conclusion: People with drug-resistant epilepsy need to find ways to self-manage. Group education courses offer them the opportunity to learn from experts, and by talking together, to overcome their sense of isolation and build confidence. However, they are insufficient to change quality of life after 1 year. Trial registration: ISRCTN57937389. Funding: NIHR-HTA 09/165/01. The views and opinions expressed in this evaluation are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

0043 NEW EPILEPSY GUIDELINE IN NORWAY - AVAILABLE ON NET AND AS A FREE APP
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Purpose: For many years, the Norwegian Epilepsy Association has received feedback from their members about a very variable quality of the epilepsy care in Norway. Hence, in 2014 the Norwegian health authorities appointed a committee to prepare an evidence-based guideline on diagnostics, treatment, follow-up and education for people with epilepsy. The aim was to equalize the differences between the parts of the country and increase the quality of the care.

Method: A multidisciplinary committee was soon established, including child- and adult epileptologists, epilepsy nurses, a neuropsychologist, a physiotherapist, a social worker, an educationist, a dietician, representatives from the Epilepsy Association, and a librarian. A thorough search in different databases was undertaken, and in evaluating the quality of the documentation and the strength of our recommendations we employed the GRADE system - with some modifications.

Results: The guideline comprises a short introduction on epilepsy, followed by recommendations on diagnostic work-up in patients suspected
of epilepsy, different treatment options (drugs, surgery, neurostimulations, diets), handling of special patient groups (children, intellectual disabled, pregnant women, elderly, status epilepticus), practical handling of ongoing seizures, follow-up, and rehabilitation. After finalizing the guideline, we have made an e-learning aiming at informing the patients and their relatives about some of the highlights in the guideline, and how to make use of it.

**Discussion:** So far, the guideline has been warmly welcomed. The colleagues find it user friendly, it has a good search function, and it is easy to get access via mobile phone and as a free available app. The net address is: www.epilepsibehandling.no

**Conclusion:** We have made a new electronically available evidence based guideline on epilepsy in Norway. We believe it meet a need for updated information, not only for doctors treating patients with epilepsy, but also for other health personnel, patients themselves, and their relatives.

### 0044 ATTITUDES AND EXPERIENCES OF MEDICINAL CANNABIS USE IN EPILEPSY

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**Purpose:** To measure the Australian experience and attitudes of cannabis use in epilepsy of adults and parents/guardians of children living with epilepsy.

**Method:** Online distribution of a forty-one item survey measuring demographic and clinical factors plus attitudes and opinions of cannabis use in epilepsy. IP address capture was deactivated. Inclusion criteria required a response to question seventeen “Have you or the person with epilepsy tried any form of medicinal cannabis for seizures?”

**Results:** 1,277 responses received over a ten day period. 983 responses met analysis criteria with a distribution of 45% adults and 55% parents of children with epilepsy. 62% of children and 50% of adults identified as respondents have previously used, or currently use medicinal cannabis. 62% of children and 50% of adults identified as parents/guardians made comments themed as "willing to try anything". Respondents had previously used, or currently use medicinal cannabis for epilepsy. Of these people, 86% reported a positive response to cannabis use in managing seizures. 66% of survey respondents would be willing to participate in a medicinal cannabis research trial with 68% of the parents/guardians made comments themed as "willing to try anything".

**Conclusion:** This survey provides an insight into the attitudes, experiences and opinions of adults and parents of children living with epilepsy in Australia seeking cannabis as a viable treatment option for epilepsy. Findings support the need for information and education about the cannabis plant, the endocannabinoid system, medicinal uses of cannabinoids and current state of legislation and clinical trials.

### 0046 FUNCTIONAL CONNECTIVITY OF MPFC COMPENSATES EPISODIC MEMORY ENCODING NETWORK FOLLOWING MEDIAL TEMPORAL LOBE RESECTION

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**Purpose:** Although it is generally known that widespread functional reorganization occurs after brain damage, these functional recovery patterns in patients with medial temporal lobe resection (MTLR) in relation with memory are still poorly understood. In this study, we investigated whole brain memory encoding network in patients who showed normal range of memory function following unilateral MTLR.

**Method:** We studied 37 adult temporal lobe epilepsy patients who underwent unilateral MTLR (left–right, follow-up = 6.45 ± 2.75 years, seizure free=31/37) and 24 healthy controls.

**Results:** Both patient groups exhibited normal range of intelligence and memory function after surgery. Functional activations for both word and figure encoding were similar across the subject groups. However, group comparisons revealed that well-known task-negative areas including medial prefrontal cortex (mPFC) were less deactivated in MTLR patients. During successful encoding, both patient groups showed increased FC between mPFC and widespread memory-related brain areas including contralateral hippocampus when compared with healthy controls. Furthermore, FC of the right mPFC - left middle frontal gyrus was positively correlated with verbal recall scores in left MTLR patients. FC of the right mPFC - left hippocampus was positively correlated with visual recall scores in right MTLR patients.

**Conclusion:** Thanks to the relatively long follow-up period, we could investigate stable memory encoding network after functional reorganization process in postoperative patients with unilateral MTLR. Our data suggest that hyper-connectivity between the mPFC and contra-resected hippocampus together with remote neocortical areas may play a compensatory role in episodic memory function for the loss of functional connections in surgically removed MTLRs.
0047

SEIZURE CONTROL AND HIPPOCAMPAL SCLEROSIS ARE RELATED TO METABOLIC ALTERATIONS IN MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: We aimed to better characterize conflicting data on N-acetyl aspartate (NAA) and glutamate in mesial temporal lobe epilepsy (MTLE) with or without MRI signs of hippocampal sclerosis (HS) using proton magnetic resonance spectroscopy.

Methods: We included 94 unilateral MTLE patients and 50 healthy controls. Patients were divided per seizure control into poor (PSz, frequent seizures) and good (GSz, seizure-free or rare seizures), and per presence/ side of HS into left-HS, right-HS, right- and MRI-negative. Single-voxel spectra were acquired in a Philips 3T-scanner using PRESS sequence (PointResolved Spectroscopy, TR/TE=2000/35 msec) and quantified using LCModel. We used MANCOVA co-varying for age with Bonferroni corrections to compare total NAA (NAAt) and total glutamate (Glx) ratios to controls (p<0.001). We found an ipsilateral reduction of NAAt in PSz compared to GSz (p<0.0001) and controls (p<0.0001). NAAt was also reduced contralaterally in PSz group compared to controls (p=0.001). Glx was reduced only ipsilateral to HS in PSz compared to GSz (p=0.04) and controls (p=0.002). Regarding HS side, there was a significant difference between groups (F(12, 363)=2.44, p=0.004) only for NAA. It was decreased ipsi- and contralaterally in left-HS compared to controls (p<0.0001 and p=0.003). Right- HS showed only ipsilateral reduction compared to controls (p=0.003). Further analysis combining groups showed differences in NAAt and Glx (F(24, 472)=2.17, p=0.001), however only NAAt survived Bonferroni correction. NAAt was decreased ipsilaterally in PSz-left-HS compared to GSz-right-HS, GSz-MRI-negative and controls (p=0.039, p=0.04 and p<0.0001) and reduced contralaterally in PSz-left-HS compared to controls (p=0.009).

Conclusion: Our results suggest more pronounced NAA alterations in left-HS with poor seizure control than right-HS and MRI-negative TLE patients, whilst Glx alterations are more related with seizure control than left-HS with poor seizure control than right-HS and MRI-negative TLE.

0048

EEG SOURCE CONNECTIVITY TO LOCALIZE THE SEIZURE ONSET ZONE FROM CLINICAL ICTAL EEG IN REFRACTORY EPILEPSY PATIENTS

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Purpose: Accurate delineation of the seizure onset zone (SOZ) is important during the presurgical evaluation to assess whether the patient qualifies for epilepsy surgery. Currently, ictal EEG analysis happens visually, which is time-consuming, challenging and subjective. In this study, we validate a methodology to objectively localize the SOZ from ictal EEG.

Methods: We retrospectively analyzed 95 seizures recorded with 27 and 32 EEG electrodes in 26 patients from Ghent and Geneva University Hospital. All patients had Engel class I outcome with at least 1 year follow-up. For every seizure, an artifact-free epoch close to the electrographic seizure onset was selected. We applied EEG source localization (LORETA) followed by functional connectivity analysis using the spectrum-weighted Adaptive Directed Transfer Function to depict the brain region with most outgoing connections during the ictal epoch. For validation, the distance between the depicted SOZ and the border of the resected zone (RZ) segmented from the post-operative MRI was calculated. Moreover, we compared this error to the distance between the source with maximal power after ESI and the RZ, to assess the added value of functional connectivity analysis over ESI.

Results: ESI with subsequent connectivity analysis was able to localize the SOZ within 20 mm of the RZ in 88% of the seizures, within 10 mm in 59% and inside the RZ in 44%. When using only ESI these numbers dropped to 60%, 57% and 30%, respectively. ESI followed by connectivity analysis significantly outperformed SOZ localization based on maximal power after ESI. Furthermore, the intra-patient robustness was significantly higher.

Conclusion: ESI combined with subsequent functional connectivity analysis is able to localize the SOZ in a non-invasive and objective way. Therefore it could be a valuable tool in the presurgical evaluation of epilepsy.

0049

INTRANAT ELECTRODES: A FREE SOFTWARE TO VISUALIZE SEEG DATA IN PATIENT REFERENTIAL AND INITIATE GROUP STUDIES

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Purpose: Patients with drug-resistant focal epilepsy can be implanted with intracranial electrodes to find the seizure onset zone to be resected. In stereo-electroencephalography (SEEG), patient have around 120 electrode contacts, recording signal in a 3.5 mm sphere approximately. The spatial coverage is around 1% of the brain activity per patient and differs between patients. Group studies over different types of epilepsy thus need a large number of patients with a multicentric perspective in the long run. To facilitate them, we developed a software for visualizing electrode implantation and related epileptogenicity, functional and cognitive maps, on the basis of a patient database allowing various search criteria for highlighting various group features.

Methods: For each patient, imaging modalities (PET, anatomical MRI, fMRI, DTT, CT, Destrieux parcellation) are coregistered (using ANTs or SPM12) and MarsAtlas parcellation is performed (using Brainvisa). Using post implantation images the user can insert the 3D modelized electrodes. Each contact is labeled according to its position in MarsAtlas or Destrieux parcellation, Brodmann or AAL atlases, and resection mask (as assessed by subtracting the T1 brain segmentation after resection minus before implantation). Users can manually add more contact labels, such as clinical response after electrical stimulation cortico-cortical evoked potentials, gamma band activity during cognitive task or epileptogenicity during seizures.

Results: IntrAnat Electrodes provides a means to visualize SEEG implantations, resection over anatomical or functional imaging and to summarize epileptogenic and functional information provided by SEEG signals. The contact labeling allows to search for patient in the database according to criteria (contact position, resection localization, response to
stimulation, etc. ...). IntrAnat Electrodes will be available in the forthcoming release of BrainVisa (http://brainvisa.info/web/index.html).

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0050

IN-VIVO IMAGING OF ACTIVATED NMDA RECEPTOR ION CHANNELS WITH THE RADIOIGAND 18F-GE179

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Purpose: To validate the radioligand 18F-GE179 as a use dependent marker of NMDA receptor activity in the living brain by non-invasive detection of overactive NMDARs in the pre-surgical evaluation of patients with refractory focal epilepsy using Positron Emission Tomography (PET) and 18F-GE179, which selectively binds to open NMDAR ion channel (IC). This may lead to better detection and understanding of altered NMDARs.

Method: 18F-GE179 PET and MRI were performed during stimulation from electrodes unilaterally implanted into the amygdala/hippocampus of 21 rats and 6 pigs. EEG evident spiking and afterdischarge was electrically induced in rats and seizures were induced during DBS in pigs. Humans underwent anatomical MRI and functional 18F-GE179 PET with simultaneous interictal EEG.

Results: In rats, the implanted and stimulated animals (n = 5) showed significantly increased 18F-GE179 uptake adjacent to the electrode tip. Administration ketamine (NMDAR-IC antagonist) effectively blocked 18F-GE179 uptake during induced seizures (n = 3). No focal 18F-GE179 uptake was seen in the control rats (n = 13). In pigs, 18F-GE179 uptake was globally increased in a current dependent manner during DBS in all pigs. In humans, 18F-GE179 PET detected clusters of significantly increased interictal uptake in 8 of 10 patients, twice the detection rate of focal abnormalities by the simultaneously recorded EEG. Patients who had extensive clusters of raised 18F-GE179 uptake also showed the most clear-cut abnormalities on their simultaneously recorded EEG. No control showed focally increased 18F-GE179 uptake or EEG abnormalities.

Conclusion: 18F-GE179 PET may have capacity to map the distribution of abnormal NMDAR-IC activation and reveal subjects with increased susceptibility to seizures and identify subjects with a higher risk of epilepsy models. This has the potential to improve the efficiency and rigor of pre-clinical research and therapy development using these models.

Basic Sciences 2

Monday 4th September, 2017

0051

AN AUTOMATED TOOL FOR RELIABLE DETECTION OF SEIZURES IN RODENT MODELS OF EPILEPSY

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Purpose: Prolonged video-EEG monitoring in chronic epilepsy rodent models has become an important tool in pre-clinical drug development of new therapies, in particular for anti-epileptogenesis, disease modification and drug resistant epilepsy. We have developed an easy to use, reliable, computational tool for detection of electrographic seizures from prolonged EEG recordings in rodent models of epilepsy.

Method: We applied a novel method based on advanced time-frequency analysis which detects the episodes of EEG with excessive activity in certain frequency bands. The method uses an advanced technique of short term spectral analysis - the Similar Basis Function algorithm. The method was applied for off-line seizure detection from chronic EEG recordings from two spontaneously seizing, chronic epilepsy rat models, post-status epilepticus model of temporal lobe epilepsy and the fluid percussion injury model of post-traumatic epilepsy (n = 34 and 5 rats, n = 88 and 49 seizures respectively).

Results: High values of power spectrum in frequency band 20–23 Hz were found to specifically indicate seizures in both animal models. This peculiarity comes from the frequency composition of single discharges within the seizures in these animals. Focusing on this band, our computer program detected 100% of seizures in all 39 rats. Electrode artefacts, which are usually present in long-term EEG recordings, may also significantly contribute to this frequency band, so they were also selected by the program. This selection, however, generated a very low rate of false positives. For their elimination, a quick user inspection was needed. The overall processing time for 12 day-long recordings varied from few minutes (5–10) to an hour, depending on the number of artefacts.

Conclusion: Our seizure detection tool provides high sensitivity, with acceptable specificity, for chronic EEG recordings from chronic rat epilepsy models. This has the potential to improve the efficiency and rigor of pre-clinical research and therapy development using these models.

0052

MMP-9 ACTIVITY AFTER TRAUMATIC BRAIN INJURY AS A RISK FOR EPILEPSY DEVELOPMENT

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Purpose: Epilepsy in 20% of cases, develops as an effect of traumatic brain injury (TBI). Recent evidence indicate important role of extracellular matrix metalloproteinase-9 (MMP-9) in neuronal circuitry remodeling and synaptic plasticity. The aim of the present study was to evaluate the MMP-9 activity changes, dendritic spines density after brain injury and the influence of MMP-9 expression level on spontaneous seizures appearance after TBI.

Method: We used Controlled Cortical Impact (CCI) as a model of TBI in animals with altered MMP-9 levels (lacking: MMP-9 KO; overexpressing: MMP-9 OE) and their WT siblings. 12 weeks after CCI animals were subjected to continuous video EEG monitoring. To verify MMP-9 changes after TBI: gel zymography and in situ hybridization were used. For dendritic spine alterations staining using liophilic dye DiI were performed.

Results: TBI resulted in progressive cortex (Cx) degeneration during 30 days after TBI. This effect was MMP-9 dependent. In MMP-9 KO animals degeneration volume degree was significantly smaller compared to wildtype siblings and MMP-9 OE mice. Gel zymography analysis showed time-associated elevation of MMP-9 activity in ipsilateral Cx and Hp, also in the thalamus samples during 3 days after CCI. Moreover, in situ hybridization showed increase of MMP-9 mRNA expression which reached the peak 6 h post-CCI. Density of the dentritic spines measured 7 and 14 d after CCI was significantly decreased in ipsilateral Cx and CA1. EEG recordings with threshold test showed decreased seizure latency in MMP-9 OE mice while increased in MMP-9 KO. Interestingly total seizure number was the highest in MMP-9 OE animals.

Conclusion: We described the correlation between TBI and MMP-9 activity and action post trauma. We indicated that MMP-9 might be an important factor for major dentritic spine reshaping, observed after brain injury, which in consequence may lead to altered sensibility of neuronal circuits to trigger seizures.
Method: To investigate the underlying mechanisms of epileptogenesis, we generated Scn2a(A263V) knock-in mice by homologous recombination in embryonic stem cells and characterized the effect of the mutation on neuronal network activity and behavior.

Results: Homozygous and heterozygous A263V knock-in mice were born at the expected Mendelian ratio, but had a reduced body weight. Homozygous mice frequently showed spontaneous behavioral seizures in adulthood, while their mortality was increased from the third week of life onward. In vivo depth recordings in neonatal mutants revealed that epileptic network activity with the hippocampal CA1 region was present before the onset of motor seizures, i.e. as early as postnatal day 2. Spontaneous electrographic seizures were also recorded in about 20% of heterozygous mice, although less frequently. Behavioral characterization of adult mice revealed hyperactivity and cognitive impairment, being particularly pronounced in homozygous animals. Chronic treatment with the non-specific sodium channel blocker phenytoin during the first postnatal week was able to prevent the occurrence of electrographic hippocampal seizures when animals were recorded at the age of seven or fifteen days.

Conclusion: In summary, the Scn2a(A263V) knock-in mouse line represents a new channelopathy model giving us the opportunity to study epileptogenesis and behavioral comorbidities, and to develop and test new therapeutic strategies.

0054
THE MASHL+/- KNOCK-IN MOUSE AS A MODEL FOR HUMAN SUDEP SUITABLE TO SCREEN FOR POTENTIAL ANTI-SUDEP AGENTS

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Purpose: To demonstrate occurrence of sudden unexpected death in epilepsy (SUDEP) in Mashl+/- knock-in mice (carrying Atp1a3 D801N mutation); to determine at what age SUDEP is highest; and to investigate whether dextromethorphan (DXM), a medication that reduces spreading depolarization the mechanism, can ameliorate Mashl+/- predisposition to SUDEP as an illustration of the usefulness of this model to screen for anti-SUDEP agents.

Method: The natural time course of SUDEP in the Mashl+/- mice, known to manifest spontaneous recurrent seizures and vestibular stimulation induced seizures, was examined. Next, 4 groups were studied: 2 WT and 2 D801N Mashl+/- mice, one of each receiving vehicle and one of each receiving DXM (20 mg/kg). Animals underwent vestibular stimulation 20 min after receiving vehicle/DXM once/day for 10 days. Then animals were subjected to flurothyl-induced seizures.

Results: Mortality was significantly higher in the second quarter of life in Mashl+/- mice: n = 39, P < 0.05, x² test (7/39 in the 1st quarter; 16/39 in the 2nd; 11/39 in the 3rd; and 5/39 in the 4th). Spontaneous recurrent seizures were observed in 3/22 (14%) Mashl+/- mice as compared to 0/40 (0%) WT mice. After undergoing vestibular stimulation, all Mashl+/- mice had seizures irrespective of whether they received DXM or vehicle. Preliminary results show trends that DXM treatment decreases seizure latency in both WT and Mashl+/- mice (WT, n = 2, P = 0.058; Mashl+/-, n = 2, P = 0.052), and increases mortality in Mashl+/- mice (WT-Vehicle 0/2, WT-DXM 0/2, Mashl+/--Vehicle 1/4, Mashl+/--DXM 2/4).

Conclusion: SUDEP occurred most commonly during the second quarter of life. By virtue of the occurrence of stimulus-induced seizures, this model can be used to screen for potential anti-SUDEP medications. Preliminary data gathered regarding DXM in this model do not appear favorable for a positive effect.
0056
SEIZURE CONTROL AFTER SURGERY FOR INTRACRANIAL MENINGIOMA: A SINGLE CENTER COHORT STUDY
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Purpose: Meningiomas account for approximately 30% of primary CNS neoplasms in adults. Seizures occur frequently both pre- and postoperatively. The purpose of this study was to investigate the long-term seizure outcomes and antiepileptic drug (AED) prescription, and identify possible predictors of seizures before and after surgery in patients operated for cranial meningioma.

Method: Adult patients with newly diagnosed meningioma and operated at the Karolinska University Hospital between 2006 and 2008 were included and followed until end of 2015. Preoperative data and details on surgical procedures were obtained through chart review. Data on seizure outcome and AED prescriptions were obtained through chart review and telephone interview. Logistic regression and survival analysis was applied to identify risk factors for pre- and postoperative seizures.

Results: Of the 113 patients analyzed, seizures occurred in 21 (18.6%) patients before surgery of which 38.1% achieved completely seizure freedom after surgery. Thirteen (14%) patients had new-onset seizures after surgery. Tumor diameter ≥3.5 cm was a risk factor for preoperative seizures (OR: 3.83, 95% CI 1.14–12.87) while having no headache (OR: 0.19, 95% CI 0.05–0.76), and non-skull base location (0.14, 95% CI 0.04–0.44) were protective for preoperative seizures. Predictors for postoperative unprovoked seizures were tumor diameter ≥3.5 cm (OR: 2.65, 95% CI 1.06–6.62) and history of preoperative seizures (OR: 3.50, 95% CI 1.55–7.90).

Conclusion: Seizures are relatively common before and after intracranial meningioma surgery. Just over a third of patients with preoperative seizures become seizure free after operation while 14% acquire new seizures after operation. Size of the tumor and preoperative seizures are risk factors for postoperative seizures.

0057
HIGH EXPRESSION OF CYSTINE-GLUTAMATE ANTIPORTER xCT (SLC7A11) IS AN INDEPENDENT BIOMARKER FOR EPILEPTIC SEIZURES AT DIAGNOSIS IN GLIOMA
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Purpose: Epileptic seizures are an important cause of morbidity of glioma patients. Several lines of evidence support the concept of excitatory neurotransmitter glutamate being the crucial mediator of gliomas associated seizures. The main mechanism of glutamate secretion in glioma is secretion mainly via the cystine-glutamate exchanger xCT.

Method: In this retrospective cohort study, the journal records of 229 patients were analyzed with respect to the presence, time course and severity of anti-epileptic seizures. The expression of xCT was determined in three independent samples from the same biopsy using tissue microarrays. The maximal expression of the protein was determined and used for further analysis.

Results: 221 patients were included in the study (71.1% grade II, 67.4% grade III, 86.2% grade IV). In a multivariate analysis, high xCT expression but not tumor grade, vGlut1 expression, or IDH1 R132H mutations were significantly associated with epileptic seizures at diagnosis (Odds ratio 4.9, p = 0.02). In further exploratory analyses, low-grade gliomas with IDH1 R132H mutations were more likely to develop seizures irrespective of xCT expression (p = 0.07) and had significant lower xCT expression (p = 0.039). Both associations completely disappeared in glioblastoma (GBM). Although xCT expression was significantly increased in GBM, the extent of xCT expression was not associated with survival (log-rank p = 0.27) in our cohort.

Conclusion: xCT is an independent marker for glioma-associated seizures, more abundant in GBM and shows an inverse correlation with IDH1 R132H mutations in low-grade glioma. Our data clearly support the idea that glutamate release via xCT is crucial for glioma-associated seizures and a promising therapeutic target.
ICTAL VOCALIZATION IN FOCAL EPILEPSY

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Background: Systematic analysis of video recorded seizures established several localizing and lateralizing semiological signs. However, the significance of ictal vocalization is not yet well determined. This study investigates frequency and audio signal characteristics of ictal vocalization with regard to different focal epilepsy syndromes.

Methods: Up to four consecutive partial seizures were evaluated in 277 lesional focal epilepsy patients, excluding isolated auras and subclinical seizure patterns. Vocalization was considered to be present if observed in at least one of the analyzed seizures and not being of speech quality. Special audio-analysis software (Praat©, www.praat.org) was used to quantify the vocalization intensity of the first seizure in 14 patients with frontal (FE) and 17 with temporal (TE) epilepsy.

Results: Vocalization was observed in 37% of the patients (102/277). It was similarly frequent amongst different epilepsy syndromes (27/62 FE: 5/11 paracentral, 64/185 TE; 6/19 parieto-occipital epilepsy). Automotor seizures with ictal vocalization were significantly more common in TE than in extratemporal epilepsy (ETE, p < 0.0001) and identified TE patients with a sensitivity of 92% and specificity of 70%. Audio signal comparison of ictal vocalization in FE and TE did reveal a significant lower minimum (p = 0.0034) and a significant higher maximum intensity (p = 0.033), as well as a bigger intensity range (p = 0.0003) for FE than TE. Further, the intensity variation during the vocalization as well as the velocity of intensity increase at the beginning of the vocalization were significantly greater in FE than TE (p = 0.0001 and p = 0.0006). No significant difference was found for vocalization duration and mean intensity.

Conclusion: Ictal vocalization is similarly common in different focal epilepsies. It’s analysis permits differentiation of automotor seizures of temporal or extratemporal origin. Further, observer independent audio analysis is helpful to objectively distinguish between ictal vocalizations in FE and TE and adds another promising diagnostic entity to presurgical semiology analysis.

UTILITY OF HOME VIDEOS FOR DIAGNOSIS OF PNES

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Purpose/background: Psychogenic non-epileptic seizures (PNES) resemble epileptic seizures, and 10 to 50% of patients referred to epilepsy centers may be subsequently diagnosed with PNES. The objective was to assess the utility of home videos in the diagnosis of PNES.

Methods: Consecutive patients with suspected PNES were asked to make home video recordings of the events on their mobile phones, with instructions on how to record so as to get maximum information from the videos. Those subjects who, on a subsequent visit, had a video with at least one habitual episode were enrolled, and underwent short-term video-EEG monitoring. Both were assessed by different epileptologists blinded to each other’s findings. Diagnoses of PNES, epileptic seizures, both or other episodic events were arrived at using a checklist of clinical features in the case of home videos, and concordance with the video-EEG diagnoses noted, and statistics applied. Neuropsychiatric and quality of health (QOL) rating scales were also administered to these subjects.

Results: Sixty-nine of the seventy-three patients had habitual seizures during the video-EEG monitoring; six subjects’ home videos were inconclusive due to quality issues. Sixty-six home videos had been labelled correctly as PNES; with sensitivity of 98.51% and specificity of 83.33%. Of these patients, 34 were noted to have a major depressive episode, and 13 had anxiety.

Conclusion: Home videos made on care-givers’ mobile phones may be effectively used to diagnose PNES obviating the need for video-EEG monitoring, important in resource-poor settings.
variability in response to drug treatment are not fully understood. While the loss of feed-forward inhibition in the CTC circuitry has been implicated in several animal models of absence epilepsy, it is still unclear if this aberration is a direct consequence of loss of excitatory input to local inhibitory interneurons. The stargazer mouse model of absence epilepsy presents with a genetic deficit in stargazin, an AMPA receptor (AMPAR) trafficking protein, which is predominantly expressed in fast-spiking parvalbumin-positive (PV⁺) inhibitory interneurons. Hence, we investigated the impact of loss of stargazin on the synaptic expression of AMPAR GluA1-4 in cortical PV⁺ neurons, which could potentially alter their excitation and thus disrupt feed-forward inhibition to pyramidal cells.

**Method:** Samples were dissected from the cortex of adult epileptic stargazers and non-epileptic littermates (n ≥ 5 pairs). Cortical synaptic fractions were obtained using biochemical fractionation, and then processed by western blotting to analyze GluA1-4 expression. Double post-embedding immunogold-cytochemistry was also used to analyze the relative density of GluA1-4 at excitatory synapses on cortical PV⁺ interneurons.

**Results:** In synaptic fractions, AMPAR expression was significantly reduced in stargazers (23% GluA1, 39% GluA2, 48% GluA4; p < 0.005) compared to non-epileptic littersmates. Ultrastructural analyses revealed loss of AMPARs at excitatory synapses on PV⁺ neurons in stargazers (21% GluA1, 17% GluA2/3, 30% GluA4; p < 0.005, n = 200 synapses/subunit) compared to non-epileptic controls.

**Conclusion:** Our results show a significant loss of synaptic AMPARs, specifically at excitatory synapses on PV⁺ inhibitory interneurons, in the stargazer cortex. This could compromise AMPAR-mediated excitation onto cortical PV⁺ neurons and impair subsequent feed-forward inhibition within the cortical network, leading to pathological hypersynchronous SWDs.

# 0063
COMPARISON OF miRNA EXPRESSION PROFILES IN RAT MODEL OF EPILEPSY WITH HUMAN MTLE+HS PATIENTS

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**Purpose:** The primary aim of this study was to identify microRNAs (miRNA/miR) which were aberrantly expressed in both mesial temporal lobe epilepsy (mTLE) patients with hippocampal sclerosis (HS) and rats with pilocarpine-induced epileptogenesis.

**Method:** miRNA expression in samples from mTLE+HS patient was analysed using sequencing approach and validated by qPCR. We selected 28 miRNAs aberrantly expressed in patients for comparison with the animal model. Rats were exposed to LiCl/pilocarpine induced Status Epilepticus (SE) at P60. The miRNA was isolated from hippocampal tissues from 18 treated rats and 12 age matched controls. Expression of selected miRNAs was quantified using a technique specific for miRNA quantification, miQPCR.

**Results:** Our quantification analyses revealed that four of 28 selected miRNAs had significantly aberrant expression in treated rats (miR-19b-3p, miR-142-3p, miR-142-5p, and miR-374b-5p) in comparison with controls. miR-142-3p and miR-142-5p were upregulated in treated rats as well as in mTLE+HS patients. On the contrary, miR-374b-5p revealed opposite regulation in expression in comparison with patients. Other miRNAs were not differently expressed in rat model.

**Conclusion:** Our results revealed several miRNAs, which were aberrantly expressed in human patients as well as the animal model. This comparative analysis significantly increases the confidence that these miRNAs are directly involved in the biology of epilepsy and provide possible miR-therapeutic targets (miRNA mimics/inhibitors) that could be tested in rat model of epilepsy.

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# 0065
THE DYNAMICS OF THE EXCITATORY AND INHIBITORY NEURAL NETWORK DURING DEVELOPMENT AND INITIATION OF CHEMOCONVULSANT-INDUCED CORTICAL SEIZURES

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Under normal conditions, the cortical network is characterized by a balanced state between excitation and inhibition. The transition between the inter-ictal and ictal states during seizure initiation is probably caused by disruption of the excitation-inhibition (E-I) balance, favoring excitation over inhibition in the cortical network. In this study we used two photon calcium imaging of Ca2+MP6 expressing neurons in the S1 barrel cortex of adult mice to investigate the network dynamics during development and initiation of partial neocortical epileptic seizures in-vivo. We monitored the activity several sub types of excitatory and inhibitory neurons including layer 2–3 (WT mice) and layer 5 (SIM1 transgenic mice) pyramidal neurons; all inhibitory inter-neurons (GAD-Cre transgenic mice), and two sub-classes of inhibitory inter-neurons, somatostatin-expressing inter-neurons (SOM-Cre transgenic mice), and parvalbumin-expressing inter-neurons (PV-Cre transgenic mice). In our experiments we monitored calcium imaging from both the somata and dendrites of the different neurons. Seizures where induced by local application of the chemovulant 4-aminopyridine onto the neocortical surface, and seizure activity was monitored electrophysiologically, by a glass recording pipette. We found that dynamics markedly differed between different neuronal sub populations during development and initiation of seizures. While layer 2–3 neurons and PV-inter-neurons tended to fire in synchronously bursts with increasing intensity during development of seizures, layer-5 pyramidal neurons and SST inter-neurons were recruited gradually and asynchronously during the pre-ictal state. Moreover, seizure initiation was associated with a synchronized burst of layer 2–3, layer 5 and PV-inter-neurons followed by intense firing in these neurons. In contrast, SST-inter-neurons were only gradually recruited during the seizure. Our findings show that during the pre-ictal state different neuronal populations are recruited with different dynamics into the epileptic network. Our findings further suggest that the state transition associated with seizure initiation may be caused by delayed recruitment of SST-inter-neurons.

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# 0066
IMPACT OF COMORBIDITIES ON RISK FOR INJURIES AND ACCIDENTS IN EPILEPSY: A PROSPECTIVE, POPULATION-BASED COHORT STUDY

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**Purpose:** To study the impact of comorbidities on the future risk of injuries or accidents for people with newly diagnosed epilepsy (PWE).

**Method:** Between September 1st. 2001 and August 31st. 2008, all patients in northern Stockholm with incident unprovoked seizures (n = 2130) were included in the Stockholm Incidence Register on Epilepsy (SIRE). For every exposed (patient with incident seizure), eight unexposed controls were matched for sex, inclusion year and catchment area (n = 16992). To identify injuries/accidents patients and controls
were followed until December 31st, 2014 in the Swedish Outpatient Register, the Swedish Hospital Discharge Register and the Cause of Death Register. The two former registers were also used to identify the existence of comorbidities in cases and controls up to the end of follow-up.

**Results:** There were 1033 registrations for injuries/accidents among epilepsy and 6202 among controls, (Hazard Ratio, HR = 1.71, 95% CI: 1.60–1.83). Compared to controls without comorbidities HR was 1.17 (1.07–1.28) in epilepsy without comorbidities, 7.15 (6.49–7.87) in epilepsy with comorbidities, and 4.52 (4.18–4.88) in controls with comorbidities. Comparing risks with or without psychiatric comorbidities, the HR in epilepsy without such comorbidity was 1.55 (1.44–1.66), 6.35 (5.49–7.35) in epilepsy with, and 4.52 (4.08–5.02) among controls with psychiatric morbidity. The pattern was the same for subgroups of psychiatric disorders. A similar pattern with a modest but significant increase in HR of the existence of comorbidities.

**Conclusion:** As in the general population the HR for injuries/accidents associated with epilepsy without specific comorbidities, and much higher HR associated with epilepsy with comorbidities such as malignant and benign brain tumours, diabetes, and dementia.

**0067 INTERVENTION STRATEGY FOR THE MANAGEMENT OF EPILEPSY IN SOUTH-EAST ASIA**

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**Purpose:** The prevalence of epilepsy is 7.7‰ in Laos and 5.8‰ in Cambodia, the treatment gap exceeds 95% in both countries. Our research program aims to measure the effectiveness of two new community-based health care approaches using two different types of Domestic Health Visitors (DHV) trained to screen and follow patients with epilepsy (PWE): (1) in Laos DHV chosen from health center staff (2) a identical strategy in Cambodia where DHV duty was carried out by health volunteers residing in the villages.

**Method:** Between 2015 and 2017, these two quasi-experimental studies were conducted in rural districts over a 12-months period comparing an intervention area and a control area. Our intervention included an Information, Education and Communication campaign, training of the DHV staff, a number of surveys on general population about Knowledge, attitudes and practices (KAP) and regular monitoring.

**Results:** In Laos after a 12-month intervention period, the treatment gap was reduced by 5.5% (20 to 43 cases under treatment of the 418 expected) in the intervention vs. 0.5% (21 to 25 cases under treatment of the 788 expected) in the control area (p < 0.0001). In Cambodia, after a 6-month period in area with a treatment gap of 100%, he was reduced by 31.1% (55 cases out of the 177 expected) in the intervention compared to a 7.0% decrease (23 cases out of the 327 expected) in the control area (p < 0.0001).

**Conclusion:** The strategy is more successful when the DHV lives in the village where he/she is going to perform his/her duty. Observations on KAP in the general population and among health staff, in addition to the therapeutic pathway of PWE will enlighten our results. The results of the intervention in Laos have resulted in an Advocacy Policy Plan which has been favorably received by the Lao Ministry of Health.

**0068 THE INCIDENCE AND PREDICTORS OF RECURRENCE AFTER FIRST SEIZURE IN EMERGENCY DEPARTMENT AND OUTCOMES: A RETROSPECTIVE STUDY IN AN UNIVERSITY HOSPITAL**

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**Purpose:** The risk factors of seizure recurrence after first seizure have been generally studied. However, the risks and outcomes among adult and elderly attending emergency services have been scarcely reported. The authors aimed to demonstrate the risk factors of seizure recurrence after the first seizure presenting to emergency department (ED) among adult and elderly patients, as well as their final outcomes.

**Method:** The patients presented with first seizure at ED between January 2003 and December 2016 were recruited for this retrospective cohort study. Final seizure outcomes were evaluated by Glasgow outcome scale (1–3 unfavorable; 4–5 favorable). Risk factors associated with seizure recurrence and final outcomes were assessed using Cox’s proportional hazard analysis and multiple logistic regression.

**Results:** A total of 414 patients were recruited. They comprised of 267 adults (aged 16–64 years) and 147 elderly (aged ≥65 years) presented to ED with first seizure. The Incidence of recurrent seizure at 6 months, 1 year and 2 years were 0.63 (95% CI: 0.54–0.71), 0.76 (95% CI: 0.67–0.85) and 0.94 (95% CI: 0.88–0.97) respectively. Independent predictors of seizure recurrence were remote symptomatic etiology (adjusted HR = 2.21, 95% CI: 1.38–3.55) and nocturnal seizure onset (Adjusted HR = 1.53, 95% CI: 1.03–2.26). The factors predicted unfavorable final outcome were remote symptomatic etiology (adjusted OR = 2.34, 95% CI: 1.25–4.37), and age ≥65 years (adjusted OR = 4.35, 95% CI: 2.42–7.83). The anti-epileptic drug (AED) treatment was associated with unfavorable outcome.

**Conclusion:** Remote symptomatic etiology had significant association with seizure recurrence and poor outcome. However, advanced age associated merely with poor outcomes. The unfavorable outcomes of AED use might be related to presenting clinical severity.

**0069 ACCIDENTAL DEATHS IN PEOPLE WITH EPILEPSY: A NATIONWIDE COHORT STUDY**

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**Purpose:** Epilepsy is associated with increased premature mortality. We investigated the risk of premature mortality from accidents in people with epilepsy (PWE) compared to the general population.

**Methods:** We created cohort of 3,431,393 people born in Denmark between 1960 and 2011 who were alive in 1980 and residing in Denmark. The follow-up period was from 1980 to 2011, and people were followed until death, emigration or end of follow-up (31 December 2011). Poisson regression was used to calculate mortality rate ratios (MRRs).

**Results:** After 75,227,547 years of follow-up, 347 PWE had died from accidents. In PWE the mortality rate from accidents was more than three times higher compared to people without epilepsy (MRR: 3.12 (95% CI: 2.80–3.47)). Psychiatric comorbidity was associated with the risk of accidents. In people with both epilepsy and a psychiatric disease the MRR was 9.42 (95% CI: 8.28–10.73) compared to people with neither epilepsy nor psychiatric disease. After dividing cause of death from accidents into transport accidents and other accidents, the MRR was 1.35 (95% CI: 1.09–1.66) for transport accidents and 5.81 (95% CI: 5.12–6.60) for other accidents.
Conclusion: The mortality from accidents is significantly increased in PWE, especially in people with comorbid psychiatric diseases. Increasing the information and the attention to these high risk groups may help reduce the mortality associated with epilepsy.

0070
STATUS EPILEPTICUS IN AUCKLAND, NEW ZEALAND: A PROSPECTIVE, HOSPITAL-BASED INCIDENCE STUDY
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Purpose: To determine the incidence, causes and outcomes of Status Epilepticus (SE) in Auckland, New Zealand, using the EpiNet database.

Method: All patients aged more than 4 weeks who presented to the 5 public hospitals within Auckland city (population 1.6 million) with SE (seizure exceeding 10 min duration) between 6th April 2015 and 5th April 2016 were identified using multiple overlapping sources of information. Post anoxic SE was excluded. Baseline health economics, clinical details, treatments, and outcomes for each episode of SE were entered into the EpiNet Database. Patients will be followed for 2 years.

Results: Hospital records for >6000 presentations with possible seizures were reviewed. 638 episodes of possible SE were identified by study nurses. 623 of these presentations (97%) have been reviewed by a neurologist. 460 presentations in 360 patients were considered definite or probable SE; 56 patients had >1 episode of SE during the year; 3 patients had 5 or more episodes. The incidence of primary and recurrent SE in Auckland is 27 episodes (21 persons) per 100,000 per year. 60% of episodes occurred within 30 min of arrival at the ED, 50% of patients received benzodiazepines before presentation to hospital, 48% required intubation, 60% of episodes lasted >30 min. 56% of patients died within 6 months of the index event, 51% were discharged from hospital. 27 patients had SE lasting >15 min. 44% of episodes in children were associated with fever. 52% of patients had known epilepsy before the SE. 81% were back to normal by discharge, but 55% (10%) died during the study period.

Conclusion: This study has determined the incidence, aetiology, treatment and outcomes of SE in New Zealand. A form to collect comprehensive data on SE in the EpiNet database has been developed; it can be used for multicentre cohort studies and randomised controlled trials.

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0071
FAST RIPPLIES BEST DEFINE REGIONAL NETWORKS OF EPILEPTOGENESIS ON PEDIATRIC INTRAOPERATIVE ELECTROCORTICOGRAPHIES
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Purpose: High frequency oscillations are increasingly shown to be a spatial biomarker of the epileptogenic zone. We investigated the predictive value of unrectified interictal fast ripples (FR, 250–500 Hz) for postoperative seizure recurrence, and how well FR localized to the epileptogenic zone compared with other conventional electrocorticographic abnormalities.

Method: In 60 consecutive UCLA pediatric patients with medically refractory epilepsy who underwent surgical resection, interictal FR were visually identified on iECoG with standard anesthetic protocol. Initially these iECoGs were assessed retrospectively, subsequently prospectively and “live” in the operating room.

Resections were based on iECoG, iECoG-PET, TLE MEG, and conventional iECoG. Results: FR were identified in 80% (48/60) of iECoGs’ s, retrospectively (n = 30), prospectively (n = 19), or “live” (n = 11). Median post-operative follow-up was 4.1 years. Six of the 48 children (12.5%) had unrectified interictal FR, and all 6 had postoperative seizure recurrence. Time-to-first-postoperative-seizure was strongly associated with unrectified FR (hazard ratio = 25.4; p < 0.001). Furthermore, all seizures returned within 6 months postoperatively. Compared to other iECoG findings of focal slowing, focal attenuation, spikes, continuous epileptiform discharges, gamma, and ictal events, unrectified interictal FR was the best predictor of post-operative seizure recurrence, with 100% positive predictive value, 76% negative predictive value, 38% sensitivity, and 100% specificity.

Conclusion: Interictal FRs on pediatric iECoG suggest: 1) the epileptogenic network may be more extensive than that determined by ictal scalp EEG and neuroimaging; 2) interictal FR appears to be the best spatial indicator of the epileptogenic network amongst all conventional iECoG abnormalities, including ictal onset zone; 3) seizure recurs quickly within 6 months in all children with unrectified FR. 4) a small remnant of the epileptogenic network is sufficient for seizure recurrence. These findings together suggest interictal FR may be the best localizing biomarker of the epileptogenic network in children.
concordant with the PMG in only 8/49 (16%) cases of unilateral and perisylvian, and in none of multilobar PMG. The epileptogenic zone included remote cortical areas in 21 (43%) and localized predominantly in those in 5 (10%) cases, all related to the mesial temporal structures. Only patients with unilateral PMG had resective surgery; 21 unilateral resections, 13 multilobar resections, and 5 hemispherotomies. At last follow-up (mean 4.6 years, range 1–16), 28(72%) patients remained seizure free; 9 were off antiepileptic drugs. Shorter epilepsy duration to surgery was the only independent predictor of seizure freedom.

Conclusion: Our study demonstrates that SEEG is essential for guiding tailored resections in PMG-related refractory epilepsy, since the epileptogenic zone may only partly overlap with the PMG and often include remote cortical areas. In well-selected cases, epilepsy surgery is highly effective in terms of seizure control and antiepileptic drug cessation, even in patients with extensive unilateral but not in those with bilateral PMG. Our data also shows that in patients with PMG-related refractory epilepsy, early vs. delayed epilepsy surgery may be more beneficial.

0074
FOCAL CORTICAL DYSLASIA TYPE II IS MEG, MULTIMODAL NEURONAVIGATION AND INTRAOPERATIVE MR IMAGING HELPFUL FOR SURGERY?
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Purpose: Focal cortical dysplasia (FCD) is one important cause of drug-resistant epilepsy potenially curable by epilepsy surgery. As complete resection is one of the crucial factors for long term seizure control especially in FCDII, we integrated multimodal neuronavigation including magnetoencephalography (MEG) and intraoperative magnetic resonance tomography imaging (iopMRI) into surgery to maximize the resection and spare eloquent areas.

Methods: Between 2/2003 and 10/2016, altogether 62 FCD patients (29 female, 33 male, mean age 36 ± 12 yrs) suffering from drug-resistant epilepsy who had surgical resection were identified (39 FCDI/II, 23 FCDIII). Mean duration of epilepsy was 20.7 ± 12.9 years. Surgery was performed using multimodal neuronavigation (integration of functional MR/DTI imaging and MEG) and intraoperative 1.5T-iopMR imaging. Additionally, three-dimensional visualization of phase-2 electrodes had been integrated in 15 patients.

Results: Considering patients suffering from electro-clinical and radiological focal epilepsy, 24 patients were identified correlating with the postoperative histological report of FCD Ia (8 Patients) and FCD Ib (16 patients). Altogether, 71% (17/24) of that subgroup had an excellent Engel Grade I seizure outcome (13 Grade Ia), 1 patient after a second surgery. A positive significant correlation of the resection amount and the seizure outcome was found, patients with Engel Grade I outcome were quoted as complete resections intraoperatively, patients with worse outcome had suspected residual lesions in eloquent position during intraoperative scanning. Compared to 71% Engel Grade I outcome in FCDII patients, the total series including associated FCDs showed 64% Engel Grade I outcome. The surgical complication rate was 8% transient and 0% permanent severe deficits.

Conclusion: In FCD Grade II patients, functional neuronavigation including MEG data and intraoperative MR imaging contributed to enable a tailored resection of the epileptic zone, leading to an excellent seizure outcome and a remarkable low complication rate.

0075
CAN VOLUMES OF MESIAL TEMPORAL STRUCTURES PREDICT PRE AND POST-LASER ABLATION PSYCHIATRIC COMORBIDITIES IN PATIENTS WITH TEMPORAL LOBE EPILEPSY?
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Purpose: To determine whether volumes of mesial temporal structures are associated with pre and/or post-surgical psychiatric comorbidities in patients with mesial temporal lobe epilepsy (MTLE) who undergo an MRI-guided laser ablation (MRI-GLA) of mesial temporal structures.

Method: 30 consecutive patients who underwent a MRI-GLA had a psychiatric evaluation before surgery and were followed for post-surgical psychiatric symptomatology at 1, 4, 12, 24 and 52 weeks. Manual quantitative volumetric measurements of hippocampus and amygdala were performed in 3 Tesla high-resolution brain MRI studies. Patients had to have had a minimal follow-up period of six months to be included in this study. T-tests were used to identify significant differences in volumes between patients with and without psychiatric comorbidities before and after laser ablation.

Results: Among the 30 patients, 14 were women. Their mean age was 45 years old (range: 24 to 71) and the mean post-surgical follow-up period was 19.9 months (range 6 to 37 months). In 16 patients, the ablation was in the left side. Pre-surgical psychiatric comorbidities were identified in 18 patients (60%); 11 had a left ablation. Post-surgical exacerbation in the initial 4 weeks occurred in 14 patients (77% of symptomatic patients pre-surgically). No patient had de novo psychopathology. Persistent psychiatric symptomatology at last contact was present in 11 patients (36%), while 7 patients (39% of symptomatic patients pre-surgically) had a complete remission of psychiatric symptoms. Volumetric measurements revealed a significant association between pre-surgical mood/anxiety disorders and a larger amygdala volume in the left side (p = 0.04). No significant associations were identified between volumetric measurements and post-surgical psychiatric outcome.

Conclusions: A larger left amygdala is associated with pre-surgical mood and/or anxiety disorders. Ablation of mesial structures can yield an immediate exacerbation of pre-surgical psychiatric comorbidities and a complete psychiatric remission in 39% of patients in the long-term.

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Tuesday 5th September, 2017

0076
A COMPREHENSIVE ANALYSIS OF MISSENSE MUTATIONS IN SCN1A IN PATIENTS WITH DRAVET SYNDROME IMPROVES INTERPRETATION OF CLINICALLY RELEVANT VARIANTS
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Purpose: Interpreting the clinical significance of genetic variants found in molecular tests can be challenging, particularly for variants of unknown significance such as missense mutations. In order to access the rate of success in the classification of missense variants, we assessed algorithms to predict functional effects of SCN1A missense mutations in patients with Dravet syndrome (DS) reported in the literature and in our own molecular study.

Method: We assessed the use of ten different computer algorithms individually to predict putative deleterious effects of amino acid changes resulting from SCN1A missense mutations in patients with DS. In addition, we developed a classifier to obtain more reliable prediction

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0077 SOMATIC MUTATIONS ARE ABUNDANT IN FOCAL CORTICAL DYSPLASIA
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Malformations of cortical development (MCD), including focal cortical dysplasia (FCD), can cause epilepsy and are associated with reabsorptive seizures. FCD is characterized by alterations in the cortical cytoarchitecture also observed in other MCDs, such as in Tuberous Sclerosis (TS) and Hemimegalencephaly (HME). Recently, mosaic mutations were detected in TS, HME and in rare cases of FCD; however, it is still unclear if only a single mutation event may lead to FCD or whether somatic mosaicism is a more widespread genetic mechanism. Exome sequencing was performed on gDNA extracted from brain tissue resected by surgery (BTRS) and blood samples of 12 FCD patients. We performed capturing with Nextera® Expanded Kit (Illumina®). Samples were sequenced following a 200 bp paired-end protocol in a HiSeq2500 (Illumina®) to achieve at least 200x of average coverage. We aligned sequences and variant calling using BWA-MEM and GATK. We evaluated mosaicism using Mutec2. Effect of variants was evaluated using Variant Effect Predictor (VEP). In addition, we also focused in variants not described previously in the normal population (reference individuals) or variants whose minor allele frequency (MAF) is ≤ 0.01. We identified potentially deleterious mosaic mutations in BTRS in all 12 patients analyzed. Mosaic mutations were identified in 28 genes belonging to the mTOR pathway and in 40 genes belonging to the Tau pathway. More interestingly, all 12 patients have somatic mutations in BTRS in at least two genes. Somatic mutations were identified in genes with functional roles and expression in the central nervous system. Somatic mutations were abundant in FCD tissue, affecting several genes from the mTOR and Tau pathways, and were detected in all samples examined. Therefore, somatic mosaicism seems to be a much more abundant and widespread genetic phenomenon than previously described in FCD. Support: CEPID-FAPESP.

0078 ANALYSIS OF FACIAL ASYMMETRY AND DYSMORPHISM IN EPILEPSY
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Purpose: There is variable clinical expressivity in each specific form of epilepsy. Genotype-phenotype correlations are very helpful to understand the origin and the mechanisms underlying the spectrum of clinical variability in epilepsy. In the current study, we use novel phenotyping 3D stereophotogrammetry and dense surface models, to evaluate facial asymmetry and dysmorphism in people with focal epilepsies aiming to generate new tools to explore the genetic contribution to these epilepsies.

Method: We consecutively recruited 859 people with epilepsy attending the epilepsy clinics at the National Hospital for Neurology and Neurosurgery, London (UK). We used dense surface modeling of the full face and signature analyses of 3-dimensional facial photographs to discriminate between cases and 205 healthy controls and to determine agreement with epilepsy categorization.

Results: Cases with focal cryptogenic and idiopathic generalised epilepsy showed more asymmetry compared to controls (p = 0.018 and p = 0.014, two-sample t-test, respectively). There was no significant difference between focal symptomatic cases and controls. The opposite pattern was observed when considering the signature analysis: no difference emerged when comparing focal cryptogenic or idiopathic generalised epilepsy cases with controls, whilst cases with focal symptomatic epilepsy associated with unilateral lesions showed higher signature weights than controls (p < 0.001, two-sample t-test).

Conclusion: Facial structure development is driven by complex molecular interactions between surface ectoderm and underlying forebrain and neural crest cells. The increased level of facial asymmetry in cases with focal cryptogenic and idiopathic generalised epilepsy might be explained by a potential genetic cause, with underlying genetic pathways shared between face and brain development. 3D stereophotogrammetry and dense surface models could represent a powerful novel phenotyping process that will permit greater understanding of genetic data, improved discrimination between pathogenic and non-pathogenic variation, and further insight into genetics of facial and neural development.

0079 MOSAICISM OF DE SCN NOVO1A MUTATIONS IN EPILEPSY: AN EXPLANATION FOR VARIABLE PHENOTYPES?
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Purpose: Phenotypes associated with de novo SCN1A mutations are very variable, ranging from Dravet syndrome on the severe end of the spectrum, to GEFS+ on the other end. We investigate whether mosaicism is a major modifier of de novo SCN1A mutations.

Method: We tested 105 patients with de novo, pathogenic SCN1A mutations for mosaicism. Clinical data were collected from medical records and semi-structured telephone interviews. Next Generation Sequencing

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with high coverage was performed on DNA from blood, after capture of SCN1A by single molecule molecular inversion probes (smMIPs). Only unique reads from single molecules were counted, using the single-molecule tag to remove duplicate reads and provide unbiased estimates of gene copies. The percentages mutated reads of pathogenic mutations were used to determine whether mosaicism was likely, based on an expected binomial distribution and comparison with heterozygous neutral SNPs. Confirmation by droplet digital PCR and sequencing of buccal DNA is pending. Developmental outcome was classified, based on available data on IQ and school functioning/education, rated by a child neurol-
gist, neuropsychologist, and clinical geneticist.

Results: In 12 out of 105 patients, mosaicism is suspected (p-values ranging from 3.08x10-11 to 6.2x10-305). Three patients were classified as “very mild or unaffected”, four as “mild”, and five as “moderate or severe”, (10-34%, 33-41%, and 26-42% alternate allele respectively). Classification of the remaining part of the cohort and comparative statistical analyses are in progress.

Conclusion: Mosaicism is suspected in 11% of patients in our cohort, and could explain several mild cases. Confirmational tests and statistical analyses will be presented to make definite conclusions about the predictive value of mosaicism in blood.

0080 KCNB1 MUTATIONS ARE CAUSING A NEURODEVELOPMENTAL DISORDER INCLUDING EPILEPSY AND AUTISM

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Purpose: De novo mutations in KCNB1, encoding the Kv2.1 voltage-gated potassium channel, have recently been associated with epileptic encephalopathies (EEs). Our study aimed to describe the phenotypic spectrum associated with KCNB1.

Method: We used high-throughput sequencing of KCNB1 in 292 patients with a range of EEs and childhood epilepsies. In addition, we ascertained cases from other centers. A detailed clinical history including EEG data was obtained.

Results: In our screening cohort we identified 5 patients (1.7%) with KCNB1 mutations and ascertained 15 additional patients through collaborators, yielding a total of 20 novel patients. Fourteen patients carried missense mutations and 6 carried either nonsense or frameshift mutations. Detailed genotype-phenotype correlations were performed. All patients presented with developmental delay in the first year of life, preceding onset of epilepsy, and all had intellectual disability, which was mostly moderate to severe. The majority (80%) suffered from intractable epilepsy with seizure onset in early childhood (median onset: 12 months). Epileptic spasms were observed in 4 patients with a median onset at 11.5 months. Most patients developed multiple seizure types, including tonic, focal-clonic, myoclonic, GTCS and atypical absences. EEG was deeply abnormal in most patients, including hypersynchrony and general slowing of background activity together with multifocal or generalized spikes/polyspikes. Interestingly, several patients had an extreme accentuation of the epileptiform abnormalities during sleep, resembling an atypical ESES pattern. Psychiatric comorbidities including autistic features, stereotypies, hand-wringing and ADHD were common. The most severely affected patients consistently harboured missense variants within vital channel domains of KCNB1. The effect of the nonsense or frameshift mutations was less clear-cut, though a tendency existed towards less severe phenotypes.

Conclusion: De novo KCNB1 mutations are relatively frequent causes of intractable epilepsy and encephalopathy. Our data suggest a correlation between the type and position of the mutation with the severity of the disorder.

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**0081**  
**ABNORMAL ELECTROPHYSIOLOGICAL PROPERTIES OF A1783T MUTATION IN SCN1A MAY CAUSES SMEI**  
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**Purpose:** Mutations in the sodium channel gene, SCN1A (NaV1.1), have been linked to a spectrum of epilepsy syndromes, and many of these mutations obstruct the channel function. We identified a novel mutation, A1783T, in the SCN1A pore region of a child with SMEI (Severe Myoclonic Epilepsy in Infancy), try to investigate if mutation A1783T has impacts on channel function and expected to disclose the relationship between genotype and phenotype of sodium channelopathies.  

**Method:** A mutant plasmid was constructed with a SCN1A plasmid containing a gene mRNA sequence and a pair of primers with point mutations. RT-PCR and Western-blot were used to detect the expression of target genes and proteins and the differences were compared between mutant and wild-type. The plasmids were expressed in HEK293 and whole-cell patch-clamp recording was used to define electrophysiological properties between mutant and wild-type.

**Results:** Expression analysis in HEK293 cell from the gene and protein level had no significant difference between mutant and wild-type. Functional analysis demonstrated that SCN1A- A1783T had no measurable sodium current, indicating a complete loss of function, while wild-type of SCN1A had total channel activity.

**Conclusion:** This observation indicates that A1783T mutation in SCN1A cause loss of function. These abnormal electrophysiological properties may cause SMEI. This study may be helpful in understanding the function of sodium channel as well as the pathogenesis of epilepsy.

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**0082**  
**LONG-TERM SURGICAL OUTCOME IN PEDIATRIC PATIENTS WITH FOCAL CORTICAL DYSPLASIA**  
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**Purpose:** Focal cortical dysplasia (FCD) is the mayor cause of focal intractable epilepsy in childhood. Factors influencing the success of the surgical treatment remain controversial. We investigated seizure freedom following epilepsy surgery in one of the largest cohorts of children with histologically confirmed FCD.

**Method:** Retrospective study of patients younger than 18 years undergoing epilepsy surgery with histologically ascertained FCD. Data about age at epilepsy onset, seizure types, seizure frequency, disease duration, FCD visibility in the MRI and location, histological subtype, age at surgery, surgical strategy, postsurgical follow-up and pharmacological treatment were collected. Statistical analysis was made with IBM SPSS Statistics, MS Office Excel and R.

**Results:** 24 subjects were initially treated with cerliponase alfa in the phase 1/2 study (9 male, 15 female, mean (SD) age 4.3 years (1.24)); 23 subjects enrolled in the extension study (74–124 weeks total exposure). All had AEs; most were Grade 1–2. Common AEs included pyrexia, hypersensitivity and convulsion. Nineteen (79%) subjects had at least one serious AE, which were mostly consistent with neurodegenerative disease in a pediatric population. Significant attenuation of the rate of decline in ML score (mean (95% CI): 0.32 (0.13, 0.52) points/48 weeks, p < 0.0001) was observed compared with a rate of decline of 2.0 points/48 weeks in untreated patients. The responder (< 2 point loss) rate at 81 weeks (87%, p = 0.0002) was unchanged compared to that observed at 48 weeks, suggesting a persistent treatment effect.

**Conclusion:** These data suggest that enzyme replacement therapy with IVC-administered cerliponase alfa has an acceptable safety profile and a sustained effect over time.

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**0083**  
**LONG-TERM SAFETY AND EFFICACY OF INTRACEREBROVENTRICULAR ENZYME REPLACEMENT THERAPY WITH CERLIPONASE ALFA IN CHILDREN CLN WITH 2 DISEASE: INTERIM RESULTS FROM AN ONGOING MULTICENTER, MULTINATIONAL EXTENSION STUDY**  
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**Purpose:** CLN2 disease, a rare, inherited, pediatric, neurodegenerative lysosomal storage disorder caused by TPP1 deficiency, is characterized by seizures, ataxia, language and motor function loss, blindness and early death. A phase 1/2 study (NCT01907087) demonstrated that intracerebroventricular (ICV) infusion of 300 mg cerliponase alfa, a recombinant human TPP1 enzyme, every other week for 48 weeks was associated with attenuation of CLN2 disease progression. This extension study (NCT02485899) assesses long-term safety and efficacy of ICV-administered cerliponase alfa in children with CLN2 disease for up to 240 weeks.

**Method:** Subjects who completed the phase 1/2 study enrolled in this open-label extension study, and continued receiving 300 mg cerliponase alfa qow. Cumulative data from both studies were used to evaluate long-term safety (assessed by analysis of adverse events (AEs)) and efficacy (assessed by changes in motor and language (ML) functions using the CLN2 clinical rating scale).

**Results:** 24 subjects were initially treated with cerliponase alfa in the phase 1/2 study (9 male, 15 female, mean (SD) age 4.3 years (1.24)); 23 subjects enrolled in the extension study (74–124 weeks total exposure). All had AEs; most were Grade 1–2. Common AEs included pyrexia, hypersensitivity and convulsion. Nineteen (79%) subjects had at least one serious AE, which were mostly consistent with neurodegenerative disease in a pediatric population. Significant attenuation of the rate of decline in ML score (mean (95% CI): 0.32 (0.13, 0.52) points/48 weeks, p < 0.0001) was observed compared with a rate of decline of 2.0 points/48 weeks in untreated patients. The responder (< 2 point loss) rate at 81 weeks (87%, p = 0.0002) was unchanged compared to that observed at 48 weeks, suggesting a persistent treatment effect.

**Conclusion:** These data suggest that enzyme replacement therapy with IVC-administered cerliponase alfa has an acceptable safety profile and a sustained effect over time.
0084 HIGH AGREEMENT IN THE EVALUATION OF STRUCTURAL MRI CHARACTERISTICS IN TUBEROUS SCLEROSIS COMPLEX
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Purpose: The majority of patients with tuberous sclerosis complex (TSC) have severe and refractory epilepsy. Localization of the epileptogenic zone is often challenging. A reproducible evaluation of structural MRI lesions would aid in the identification of epileptogenic zone and subsequently candidates for epilepsy surgery, in patients in whom clinical and electrophysiological data are not clearly focal. In these preliminary data we assessed the interobserver variability in evaluating individual MRI characteristics of TSC.

Method: Presurgical MRIs of 31 patients (aged > 1 year) with TSC who underwent epilepsy surgery in Prague or Utrecht were retrospectively and independently evaluated by two neuroradiologists experienced in epilepsy. MRI characteristics typical of TSC (tubers, cysts, calcifications) and focal-cortical dysplasia (FCD) features (gray-white matter blurring, transmantle sign, increased cortical thickness), as well as the largest FCD-like affected area, were identified. Brain localisations were categorized as frontal (mesial, lateral, basal, polar, central), temporal (mesial or lateral), parietal (mesial or lateral) or occipital (mesial or lateral). Interobserver variability was calculated using kappa statistic for the general (total score kappa 0.98–0.96, p < 0.001), or almost perfect (0.81–0.99), fair (0.21–0.40), moderate (0.41–0.60), substantial (0.61–0.80), or almost perfect (0.81–0.99).

Results: We found the overall consistency to be almost perfect for all localisations, and for all individual imaging features (total score kappa 0.91; 0.91–0.92), p < 0.001), and also for the largest FCD-like affected area (0.98; 0.96–0.99, p < 0.001).

Conclusion: A scoring system of MRI characteristics in TSC patients evaluated for epilepsy surgery showed almost perfect reliability between two experienced neuroradiologists. We feel that this scoring system could be used for the standardized evaluation of brain pathology related to TSC. We aim to employ it for detailed characterization of epileptogenic brain regions, especially when evaluating patients for epilepsy surgery.


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Purpose: Cognitive impairments and emotional dysregulations are frequently encountered in children with all types of epilepsy. Retrospective studies highlight these difficulties but fail to determine their chronology of appearance which might be influenced by many factors (syndrome, seizure frequency, treatment...). Early detection of pre-existing or progressively developing deficits represent real challenges for global epilepsy-care programs.

Method: We developed a comprehensive approach for an early detection of behavioral and cognitive deficits in newly diagnosed epilepsies. During the first visit, children were received in a day hospital for a global evaluation including a sleep and awake EEG, somatic and neurological examination, an epilepsy nurse interview and a preliminary evaluation of behavior and social competences using the Child Behavior Checklist (CBCL, Achenbach, 1991). A first neuropsychological screening was conducted to assess attention abilities and executive functions using Epitrack Junior (Helmauder, 2013). Depending on the results, a full neuropsychological evaluation can be scheduled. At the follow-up outpatient clinics, an epilepsy nurse interviewed the patient and his family using questionnaires on AEDs side effects and on “living with epilepsy”. A re-test with Epitrack Junior is performed.

Results: Preliminary results of the CBCL evaluation for idiopathic epilepsies (IE) - 36 children without epilepsy (NE); 37 children with IE (11 under AED treatment) - showed that at maximum 6 months from epilepsy onset, even benign forms of epilepsy score lower than NE in the Competences scale, assessing scholar, extrascholar and social skills (t(71)=2.01, p < 0.05), especially when under AEDs (t(45)=2.53, p < 0.02). Externalization scale showed that IE have more aggressive and delinquent behaviors as compared to NE (t(71)=2.16, p < 0.03) especially when under treatment (t(45)=2.55, p < 0.01).

Conclusion: Our results underscore the need for an early multidisciplinary approach and detection of neuropsychological or behavioral deficits to engage appropriate reeducations.

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0086 MODULATION OF AUTONOMIC SYMPATHETIC ACTIVITY REDUCES EPILEPTIC SEIZURES: ROLE OF FRONTAL CORTEX - AMYGDALA FUNCTIONAL CONNECTIVITY
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Purpose: In 2004, Nagai and her colleagues introduced galvanic skin response (GSR) biofeedback therapy in patients with drug resistant epilepsy, demonstrating positive effects of a randomized controlled trial: 60% response rate. Accompanying neuroimaging investigations in healthy individuals showed that ventromedial prefrontal cortex/ orbitofrontal neural activity is inversely correlated to biofeedback-driven changes in the tonic level of GSR. The present study aimed to replicate and extend evidence for the efficacy of autonomic biofeedback therapy and investigate the underlying neural mechanisms.

Method: Forty patients with drug-resistant temporal lobe epilepsy (TLE) were allocated to either one of two groups; one group received therapy with GSR biofeedback (n = 20), and the other received treatment as usual for control (n = 20). Resting-state functional and structural MRI data were acquired before and after one month of therapy in the therapy group, and before and after a one-month interval in the control group. The percentage change of seizure frequency was the primary outcome measure. The second outcome was the change in default mode network (DMN) and limbic network functional connectivity tested for effects of therapy.

Results: There was a significant difference in reduction of seizure frequency between the therapy and control groups (p < 0.001). The seizure frequency in the therapy group was significantly reduced (p < 0.001) following GSR biofeedback, with a mean seizure reduction of 43% (SD = ±
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32.12, median = -37.26. 45% of patients in the therapy group showed greater than 50% seizure reduction. Neuroimaging analysis revealed that post-therapy seizure reduction was linearly correlated with enhanced functional connectivity between amygdala and the orbitofrontal cortex (OFC).

Conclusion: Autonomic biofeedback therapy is an effective and potent behavioral intervention for patients with drug-resistant epilepsy, mediated through fronto-limbic change.

0087 PROSPECTIVE IDENTIFICATION OF FAST Ripples (FRs) HELPS DEFINE THE SPATIAL EXTENT OF THE EPILEPTOGENIC NETWORK

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Purpose: Observations from humans and animal models of epilepsy suggest that pathological high frequency oscillations (HFOs) may serve as a biomarker of epileptogenic zone. Prior retrospective studies analyzing extra-operative ECoG (electrocorticography) recording in neocortical epilepsy in children demonstrated wide distribution of interictal and ictal HFOs (Nariai et al. Epilepsia 2011 and Akiyama et al. Epilepsia 2011), suggesting the high prevalence of extensive epileptic network in this population. The purpose of this study is to evaluate HFOs prospectively to investigate the spatial extent of the epileptic network before the resection.

Method: Here we prospectively analyzed interictal fast ripples (FRs: 250–500 Hz) in seven patients with intractable focal epilepsy (the etiology includes cortical dysplasia and tumour) who underwent extra-operative ECoG (electrocorticography) recording before determining the resection margin. Interictal FRs were sampled at 2000 Hz, and were visually identified in 10 min of slow wave sleep from the early phase of the recording.

Results: Interictal FRs were observed in at least one of the seizure onset electrode(s) in all seven patients. The spatial distribution of FRs was more extensive than that of the seizure onset electrode(s), but less extensive than that of the spikes. Five out of seven patients showed widely distributed FRs. 2 had similar diffuse or multi-lobe neuroimaging abnormalities (MRI and/or PET) preoperatively; 3 had focal or normal neuroimaging findings preoperatively, yet there were widely distributed FRs discernible in multiple electrodes. Those 5 patients also showed other neurophysiological abnormalities including widely distributed areas with spikes, slowing, and seizures, resulting in extended resection margins.

Conclusion: The topological extent of network abnormalities in neocortical epilepsy may exceed what is discernible by multimodal neuroimaging and traditional electrocorticographic methods, and may be defined more completely by an investigation of FRs.

0088 EVIDENCE OF FOCALITY IN INFANTILE SPASMS AS INDICATED BY INTERHEMISPHERIC ONSET LATENCY DIFFERENCES IN ICTAL GAMMA AND BETA ACTIVITY ON EEG

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Purpose: The typical EEG correlate to infantile spasms in West syndrome (WS) is the electrodecremental response, which usually has a generalized electrographic appearance. However, focal lesions can produce infantile spasms in both humans and animal models, and it has been suggested that spasms may have a focal onset. We investigated ictal gamma and beta activity on scalp EEG during infantile spasms in patients with WS to evaluate for evidence of focal onset.

Method: A total of 1033 spasms from 34 patients with WS of various etiologies were analyzed using time-frequency analysis. Ictal gamma (35–90 Hz) and beta (15–30 Hz) activities were correlated with visual semiology of spasms and ictal EEG, and with objective EMG (electromyography) analysis, and etiology of WS. Interhemispheric latency differences were measured for the onset of ictal gamma and beta activity.

Results: Interictal gamma and/or beta EEG activities were present, temporally associated with spasms, and preceded the ictal motor manifestations in all cases. Focal onset of ictal gamma activity was present in 24/34 (71%), including 8/10 patients with asymmetric semiology of spasms and 16/24 patients with symmetric semiology of spasms. Focal onset of ictal beta activity was present in 23/34 (68%), including 6/10 patients with asymmetric spasms and 17/24 patients with symmetric spasms. All patients with asymmetric spasms and 21/24 patients with symmetric spasms had interhemispheric onset latency differences ≥10 ms in either gamma or beta activity.

Conclusion: Interhemispheric latency differences in the onset of ictal gamma and beta activity were present in the majority of spasms, regardless of observed symmetric vs. asymmetric semiology. This supports the theory that infantile spasms may have a focal electrographic onset, even in cases with apparent generalized semiology. When present, asymmetry of ictal gamma or beta activity may provide additional evidence of focality, assisting in the identification and lateralization of possible underlying lesions.

0089 EEG (ICHTAL AND INTER-ICHTAL) CONNECTIVITY PATTERNS AND 3-D SPIKE SOURCE ANALYSIS IN FOCAL EPILEPSY AND ITS RELATION TO NUCLEAR MEDICINE IMAGING

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Purpose: In this study we suggest a methodology for the connectivity investigation of EEG networks of inter-ictal and ictal epileptiform discharge activities and its correlation to nuclear medicine studies.

Method: Focal epileptiform discharges (FEDs) have specific patterns that can be determined using EEG connectivity analysis. Metabolic changes in nuclear medicine imaging are seen in epileptogenic regions at different states (ictal or inter-ictal). In this study we present a time and frequency domain analysis of FEDs based on the number of connections (significance threshold p < 0.05) identified in the regions of interest that belong to potentially activated networks. Cross-correlation coefficients for Delta, Theta, Alpha and Beta bands were calculated for each electrode pair using a time lag of ±500 ms, where the maximum value was selected. Furthermore, time domain analysis was performed using phase synchronization among scalp electrodes, by adopting a nonlinear data-driven method. Inverse solution was also applied to FEDs to help localize the activation regions. These results are then correlated to metabolic changes in nuclear medicine imaging during ictal and inter-ictal states.

Results: There are significantly less connections (symmetry and density) in the surrounding non-epileptic regions than in the epileptic region in the inter-ictal phase that correlate to hypo-metabolism in imaging. Hence in FEDs, the focal pattern of abnormal activity is reflected in the connectivity maps by higher number of within region connections and lower number of between region connections. As expected, during ictal phase
activity, connections become more apparent and widespread, also correlating positively with hyper-metabolic activity shown on the PET/SPECT brain imaging. These changes were calculated using the SUVR (standardized uptake value ratio).

Conclusion: Propagation characteristics are likely related to connectivity network activation in focal ictal events. The strength of the connections and their spreading behavior are directly related to metabolic changes found on nuclear medicine imaging.

0090 USEFULNESS OF AUTOMATED EEG ANALYSIS TO DETECT INTERICTAL EPILEPTIC ACTIVITY IN DIAGNOSTIC EEG RECORDINGS: A STUDY IN 38 PATIENTS

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Purpose: In clinical practice, the detection of interictal epileptiform discharges in diagnostic overnight EEG is a labor-intensive and time consuming task. In this study, we investigate the usefulness of automatically generated EEG reports that show detected epileptic spikes to aid in the visual clinical interpretation of diagnostic EEG.

Method: Thirty-eight patients had a diagnostic EEG recording of approximately 17 h (3 pm–8am) at the University Hospital of Geneva, Switzerland. Visual “clinical” interpretation, performed by an expert electrophysiologist (MS), was compared to automatically generated EEG reports (Epilog, Belgium) that visualized the detected spikes in the EEG. The average waveform of the epileptic spike clusters, their topography, the detections over time and 10 examples of single spikes were depicted in the report. A blinded expert electrophysiologist (SV) reviewed the patients solely based on the reports by indicating whether the report showed genuine epileptic spikes in each patient or not. We assessed the correspondence between the labor-intensive visual analysis and the analysis based on the automatically generated reports.

Results: Visual interpretation revealed that 12 of the 38 admitted patients had epileptic spikes present in the overnight EEG. The diagnosis based on the report corresponded with the visual analysis in 33 of the 38 patients. The sensitivity of epileptic diagnosis was 75%, the specificity 92%, positive predictive value 82% and negative predictive value 89%, which corresponds to a diagnostic odds ratio of 36.

Conclusion: We showed that automatically generated, objective and standardized EEG reports can aid in the visual interpretation of overnight EEG. This can help the neurologists decrease their time spend for visual interpretation. The visual clinical interpretation of the EEG was informed by clinical details, whereas the reviewer of the automated reports was blinded. In future studies we will adjust this to allow a more clinically relevant comparison between both approaches.

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p0091 ASSOCIATION BETWEEN ENVIRONMENTAL OZONE LEVELS AND INCREASED EPILEPTIC SEIZURES IN PATIENTS WITH EPILEPSY IN A HOSPITAL IN MEXICO CITY

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Purpose: In 2016, an environmental contingency was registered in Mexico City due to alarming levels of pollution in the metropolitan area. This study attempts to determine if there was a relationship between levels of airborne pollutants, specifically ozone, and increased seizure frequency of patients with epilepsy treated at the National Medical Center “20 de Noviembre” in Mexico City.

Method: We studied 65 adult patients with different types of epilepsy treated at the neurology service of the National Medical Center “20 de Noviembre”. These patients recorded daily epileptic seizures during March, April, and May 2016. During this time, we recorded daily reports of environmental ozone concentrations, published by the state Environment Ministry. We recorded the levels according to the corresponding score of the air quality index. We compared the total epileptic seizures of all patients each day with ozone levels using the Spearman correlation coefficient for random variables.

Results: We found a significant correlation (p < 0.05) between ozone levels and the frequency of epileptic seizures, mainly on days with levels classified as dangerous according to the air quality index.

Conclusion: Our results suggest that environmental contamination, specifically ozone levels, may be a factor in increasing seizures in patients with epilepsy. Further studies are required to determine the exact nature and implications of this association.

p0094 PREDICTORS OF OUTCOME IN PATIENTS WITH ACUTE SYMPTOMATIC SEIZURE

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Purpose: Very few studies from developing nation have looked into the predictors of outcome in patients with acute symptomatic seizures (AS).

We analyzed the predictors of outcome in patients with AS.

Methods: Between December 2014–August 2016, we retrospectively analyzed the clinical records of patients with AS and abstracted their clinical, laboratory, EEG and radiological data. Patients were dichotomized to have good and poor outcome at discharge based upon modified rankin scale (poor outcome= mRS 4 and above, good outcome mRS 3 or less). Appropriate statistical methods were applied.

Results: Out of 200 patients, 137 (68.5%) were males. One hundred and forty-three (72.6%) patients had good outcome and 54 (27.4%) patients had poor outcome. The etiology of AS were vascular (infarct - 71, cortical venous sinus thrombosis- 20, parenchymal bleed-10, posterior reversible leukoencephalopathy-7, subarchnoid hemorrhage-5, arterio-venous malformation-4, dural arterio-venous fistula-2), infection (42), metabolic (17), traumatic brain injury (5), autoimmune encephalitis (4), alcohol related (3), tumor (3) focal cortical dysplasia (1) and sturge weber syndrome (1). One hundred and fifty patients presented with generalized seizures. Complex partial seizures and simple partial seizures were seen in 39 and 11 patients respectively. EEG data was available for 126 patients. Fifty-six patients (45%) had mild diffuse slowing of background activity (BGA) in theta range, 28 (23%) patients had moderate slowing of BGA and 4 (3%) patients had severe bitemporal dysfunction. Epileptiform abnormalities were seen in 36 (29%) patients. Factors predicting poor outcome were old age (p = 0.01), Glasgow coma scale (GCS) at entry (p = 0.001), vascular etiology (p = 0.003) and severe electrophysiological dysfunction in EEG (p = 0.005).

Conclusion: The most common etiology of AS was vascular due to ischemic stroke and cortical venous sinus thrombosis. Old age, low GCS at entry, vascular etiology and severe electrophysiological dysfunction in EEG predicted the poor outcome in patients with AS at discharge.
suggest the presence of amygdala enlargement in some patients with TLE. This study sought to investigate clinical characteristics and treatment outcomes in TLE patients with amygdala enlargement detected by magnetic resonance imaging (MRI).

**Method:** This study enrolled 7 TLE patients with amygdala enlargement (2 men, 5 women) and 20 TLE patients without abnormal MRI findings (11 men, 9 women). Clinical features, seizure semiology, EEG findings, and treatment outcomes were evaluated. Visual assessments of MRI findings were performed by an experienced neurologist and a radiologist, respectively.

**Results:** Average seizure onset age among TLE patients with amygdala enlargement and patients without abnormal MRI findings was 46.6 (SD 17.7) years and 38.9 (SD 23.3) years. All patients with amygdala enlargement had complex partial seizures and 3 patients had occasional generalized tonic-clonic seizures. Two patients had memory decline. Four patients suffered from depression or anxiety. Epileptiform discharges appeared predominantly in the anterior or inferior temporal area ipsilateral to amygdala enlargement. Six patients became seizure free or showed remarkable improvement on antiepileptic medication. Volume of the enlarged amygdala was reduced after treatment in 3 patients. Among TLE patients without abnormal MRI findings, 2 patients had depression and no patients had memory decline. Ten patients became seizure free or showed remarkable improvement on antiepileptic medication.

**Conclusion:** TLE patients with amygdala enlargement generally are older at epilepsy onset, have a tendency to non-convulsive seizure, and show a good response to antiepileptic drugs. These results suggest a difference in pathophysiology between TLE patients with amygdala enlargement and TLE patients without abnormal MRI.

**References**

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**Purpose:** Musicogenic epilepsy is a rare form of complex reflex epilepsy. The precipitation of seizures by music is a useful tool to investigate seizure initiation, propagation and human’s brain processing. Little is known about the pathophysiological origin of this exceptional phenomenon. We present a series of patients with music induced seizures with high titers of antibodies against glutamic acid decarboxylase 65 kD (GAD65).

**Patients and methods:** We determined neural antibodies using a broad panel of surface and intracellular antigens in serum only or in serum-cerebrospinal fluid (CSF) of patients who fulfilled the clinical criteria of potential (sub)acute limbic encephalitis or chronic autoimmune-mediated temporal lobe epilepsy. We identified the positive cases and characterized them clinically in order to uncover typical syndromatic profiles.

**Results:** Out of 167 patients, eight patients had GAD65-antibodies. Among those, four patients had musicogenic epilepsy (GAD65-antibody serum titers between 1:2500 and 1:40 000). Common characteristics of these four patients were female gender, late epilepsy onset, mood disturbances, slight memory decline, normal MRI and seizures induced by individually preferred music, recorded by video-EEG. Spontaneous seizures were rare and well controlled by antiepileptic drugs whereas occurrence of music induced seizures was not influenced by AED-treatment and could only be prevented by avoidance of the specific musical stimulus. Endocrinological comorbidities were seen in three of the four patients. Immunomodulatory treatment has not been initiated yet because of the missing proof of efficacy in intracellular antibodies.

**Conclusion:** To our best knowledge, this is the first report on musicogenic epilepsy in patients with high titer GAD65-antibodies. These intracellular antibodies have recently been considered as markers of an immunopathological process of limbic structures in some chronic temporal lobe epilepsies. Since music processing strongly implicates the limbic system, there might be a predisposition in patients with autoimmune-mediated temporal lobe epilepsy to develop music-induced seizures.
RELATION BETWEEN GENDER, PSYCHIATRIC AND COGNITIVE DISORDERS AND EXPERIENTIAL AURAS IN PATIENTS WITH TEMPORAL LOBE EPILEPSY

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Purpose: To determine whether the experiential auras in patients with temporal lobe epilepsy (TLE) are related to gender, educational level, psychiatric comorbidity, visual or verbal material-specific memory impairment, lateralization by video-EEG and epileptogenic lesions on brain MRI.


Results: We included 35 patients, 51.4% were male, mean age 35 years, mean epilepsy duration 20.3 years. Laterality of the epileptogenic zone was right (57.1%) and left (37.1%) temporal. An epileptogenic lesion was detected in most of cases and hippocampal sclerosis was the most common finding. Seventy-four percent of patients underwent epilepsy surgery (Engel I-II: 65.4%). Educational level was mainly primary and secondary. Most of patients presented visual or both memories deficits associated with executive dysfunction. Almost half patients had a psychiatric comorbidity. Déjà vu was the most frequent experiential aura (60%), followed by jamais vu (20%), strangeness (20%) and depersonalization (14.3%). Most patients had a single experiential aura (déjà vu 54.5%, jamais vu 18.2%, strangeness 13.6%, depersonalization 9.1%, prescience 4.5%) associated with non-experiential auras in the majority of cases.

Conclusion: Most of patients presented a single experiential aura, most frequently déjà vu, associated with non-experiential auras, mainly fear. A right temporal lobe seizure focus was the most frequent. In terms of gender, déjà vu was more common in male patients. A high prevalence of psychiatric comorbidity was observed and despite of the reduced number of cases, the 3 patients with psychosis presented déjà vu. Most of patients presented visual or both memories deficits associated with executive dysfunction. We did not find any relation between the experiential auras and educational level.
recurrence was more likely to recur in patients with a tumor, SE development, coma or ICU admission in the acute phase (P < 0.05). All patients with acute seizure who received follow-up for more than 2 years after the acute stage were seizure free.

**Conclusion:** Seizures are a common feature in the acute stage of anti-NMDAR encephalitis but not thereafter. The presence of tumor, SE, coma and/or ICU admission in the acute phase predict early seizure recurrence. Seizure freedom was typically achieved in our follow-up, and long-term use of AEDs may not be necessary.

**Results:** The mean CV of NAA value was 7.2% on the right side and 5.7% on the left side in the IGE group, and 7.2% and 6.1% in the PE group. In the IGE group, patients showed less than 10% CV were 78% on the right side and 96% on the left side. In the PE group, patients showed less than 10% CV were 78% on the right side and 89% on the left side. Seven out of 9 patients demonstrating more than 10% of CV showed a larger CV on the epileptic focus side than the unaffected side.

**Conclusion:** An increase or decrease in NAA values within 10% CV might include the normal variance of NAA measurements. The seizure focus side in the PE group demonstrated fluctuating patterns with more than 10% CV. The emotional or social environmental change, such as divorce, effected on the right hippocampus in the IGE group. Longitudinal NAA measurements are needed to estimate the seizure focus side and to exclude the normal variance for evaluation of ideal hippocampal function.

**Purpose:** The aims of the study were to assess the occurrence of post-stroke epilepsy (PSE) in patients with ischemic strokes, to identify predictors, and to investigate whether treatment in a stroke unit (SU) influenced the long-term outcomes of epilepsy.

**Method:** Patients with PSE, defined as those having two or more unprovoked epileptic seizures > or = 1 week after an ischemic stroke, were identified from a cohort of 484 patients with ischemic strokes. The patients were prospectively assessed 7–8 years after stroke or until death. Different variables were studied to look for possible predictors.

**Results:** From 448 patients with ischemic strokes, PSE developed in 11 (2.5%) and 14 (3.1%) patients during the first year and 7–8 years after stroke, respectively. Eight (53%) of these patients were treated in a stroke unit (SU), and seven (47%) were treated in a general medical ward (GMW). The mean age of those who developed PSE and those who did not was 74.3 years and 76.3 years, respectively. In a multivariate analysis, a Medical scale (MS) score < 30 on admission was a significant predictor for developing PSE [(odds ratio (OR), 4.9; p = 0.004).

**Conclusion:** The prevalence of PSE, 7 to 8 years after an ischemic stroke, was 3.1%. MS scores < 30 on admission were a significant predictor for PSE. Neither treatment in SU vs. GMW, cortical location, nor age at onset of stroke seemed to influence the risk of developing PSE.

**Purpose:** About 10–20% of patients with epilepsy suffer primarily sleep-related seizures. Differentiating between generalized and focal epilepsies may be challenging as nocturnal seizures are sometimes un witnessed, and routine electroencephalograms (EEGs) are often normal. We aimed to determine (i) proportion of generalized, focal, and unclassified epilepsies in this population, (ii) response to anti-epileptic drug (AED) therapy, and (iii) diagnostic yield of routine vs. sleep-deprived / prolonged video-EEG recording.

**Method:** We retrospectively identified 80 patients with sleep-related seizures from 1996–2016 using an EEG database at our institution. Patients aged ≥ 16 years were included if (i) >90% of seizures were sleep-related, (ii) EEG and CT/MRI brain were performed, and (iii) ≥ 6 months of clinical follow-up was available.
Results: Mean age at seizure-onset was 34.5 years (SD=20.1); 31 (38.8%) were male. Eleven (13.8%) had a family history of epilepsy. Fifty-nine (73.8%) were classified as having focal epilepsy (21 PLE, 13 TLE, 11 other focal and 14 non-localized), 5 (6.3%) as generalized epi-
lepsy, and 16 (20%) remained unclassified. Thirty-eight (47.5%) had < 2 seizures / year, 34 (42.5%) 2–12 seizures / year, and 8 (10%) > 12 seizures / year. Most patients responded favorably to AEDs, with 62 (77.5%) showing ≥50% reduction in seizure frequency with 1 AED; 63 (78.8%) were seizure-free in the 3 months preceding follow-up. Twelve (15%) had lesion-positive scans (3 malformations of cortical develop-
ment, 2 hippocampal sclerosis, 5 focal gliosis, and 2 benign neoplasms).

Epileptiform discharges were recorded in 28/98 (28.6%) and 3/11 (27.3%) of routine and sleep-deprived EEGs respectively. All 3 patients (78.8%) were seizure-free in the 3 months preceding follow-up. Twelve

Conclusion: A significant proportion (20%) of patients with sleep-related seizures in our series have unclassified epilepsy. Extending the duration of EEG recording may increase diagnostic yield in this popula-
tion.

p0112
FOCAL AND GENERALIZED EPILEPSY: WHICH SEIZURE-MODULATORY FACTORS ARE MOST FREQUENT?
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Purpose: Seizure-precipitating or inhibitory factors (modulatory factors - MF) are often neglected and underestimated as part of epilepsy treat-
ment. Therefore we aimed to identify self-perceived MFs in patients with focal vs. generalized epilepsy syndromes.

Method: This was a transcultural multicenter cross-sectional study. Epi-
lepsy syndromes were classified by board-certified epileptologists according to ILAE’s criteria. Patients were interviewed using a semistructured questionnaire on clinical and epidemiological data and were asked to identify all experienced MFs from a list.

Results: A total of 185 individuals were surveyed. 136 (73.5%) had a diagnosis of focal and 49 (26.5%) generalized epilepsy at the four univer-
sity reference centers for the treatment of neurological diseases involved in this study (Brazil, Guatemala, Lithuania and Turkey). Their mean age was 34.98 ± 11.70 vs. 24.88 ± 10.12 (p = 0.001), and 97 (52.4%) vs. 88 (47.6%) were female (p = 1.00). In total, more than 80% of patients reported experiencing provocative factors sometimes or fre-
quently, while more than 60% of patients never experienced an inhibitory factor, regardless of epilepsy syndrome. The main precipitating factors reported by focal epilepsy patients were (in order of appearance): negative feelings (66.2%; p = 0.040), emotional stress (61.8%; p = 0.029), lack of sleep (55.9%; p = 0.127), certain memories (37.5%; p < 0.001) and certain thoughts (36.8%; p < 0.001), while among generalized epi-
lepsy patients: lack of sleep (60.4%; p = 0.127), negative feelings (49.0%; p = 0.040), emotional stress (42.9%; p = 0.029), seizures at awakening (26.5%; p = 0.081) and working on computer, thinking/con-
centration and visual stimuli (all 18.4%; ns).

Conclusion: The top three seizure-modulatory factors were similar in focal and generalized epilepsy, only in different order of frequency, certain thoughts and memories appear specific to focal epilepsy.

p0114
INTERLEUKINS INTERICTAL DATA AND TAU-
PROTEIN IN PATIENTS WITH LONG-STANDING PHARMACO-RESISTANT EPILEPSY
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Purpose: We investigated tau-mediated neurodegeneration by determina-
tion of tau protein level in correlation with proinflammatory interleu-
kins (ILs) involved into microglial-neuronal interactions and latent neuroinflammation in patients with long-standing pharmaco-resistant epilepsy (PhRE).

Method: Tau was measured by immunofluorescent method using mono-
oclonal anti-mouse anti-tau-2 antibodies also specific for phosho-Tau in PhRE (n = 59; 34–62 years, mean disease duration 16.24 ± 8.51 years) and healthy controls (HC); 30–25–35; results were expressed as optical density (OD= log10(F0/F1) units of FITC-labelled binding sites; IL-6, IL-8 measured by standard immunoenzyme assays using Vector-Best reagents.

Results: In PhRE tau concentration was 0.37 ± 0.04 compare to HC 0.08 ± 0.002; PhRE showed average tau serum level: psychiatric complications found in 52.54%; patients; tau-mediated toxicity positively correlated with behavioral and neuropsychiatric changes. PhRE anamnesis: brain injury (8 patients), febrile seizures (6), post-aspithxia encephalopa-
thy (6), meningo/encephalitis virus (4), chicken-px infection (2). PhRE medicated with one AED (35.59%), 38 patients (64.41%) were on poly-
therapy. Seizure frequency: 1–2 per 6 months (18.64%), 1–2 per/month (72.88%), 1–2 per/week (8.48%). RhRE revealed high serum proinflammatory IL-6 level suggesting that increased IL-6 (Mean 26.34 ± 6.51 pg/ml, range: 19–38.69 vs. HC 5.23 ± 1.5) might be governed from activation of microglia-astrocyte network (p < 0.01; t = 2.8), high IL-6 data were associated in 76.27% patients with high sei-
zure frequency; influenced by long-course of antiepileptic treatment (69.49%). PhRE showed no differences in IL-8: 8.32 ± 3.88 vs. 5.6 ± 2.47 pg/ml. PhRE patients had focal neurological deficit (12), severe headaches (14), cognitive decline (25). Proinflammatory cytoki-
nies may lead to neuronal excitability or neuron destruction associated with cognitive impairment.

Conclusion: PhRE revealed elevated baseline proinflammatory IL-6 level associated with high seizure frequency and long antiepileptic ther-
apy. IL-6-dependent neuroinflammatory processes are important of PhRE understanding there maybe potential role for anti-inflammatory therapy targeting cytokines. PhRE found heightened hyperphosphory-
lated tau level where it might contribute to chronic progression and asso-
ciated with psychiatric complications or cognitive decline.

p0115
A PILOT STUDY ON RELATIONSHIP BETWEEN PLASMA HAPTOGLOBIN AND POSTTRAUMATIC EPILEPSY
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Purpose: Delay hemoglobin clearance following cerebral injury might exacerbate iron-dependent tissue damage and predispose to the develop-
ment of seizure disorders. Reduced plasma haptoglobin might interfere with the normal clearance of hemoglobin from the site of an injury. We evaluated the correlation between plasma haptoglobin level and posttrau-
matic epilepsy.

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doi: 10.1111/epi.13944
Method: Using an immunonephelometric technique, we measured plasma haptoglobin level in 30 patients with posttraumatic epilepsy, 35 non-epileptic patients with head trauma, and 35 normal controls.

Results: The plasma haptoglobin level in MTLE patients with head trauma was 77.57 ± 45.65 mg% in patients with posttraumatic epilepsy, 119.68 ± 59.33 mg% in non-epileptic patients with head trauma, and 117.20 ± 55.39 mg% in normal controls. The plasma haptoglobin level of patients with posttraumatic epilepsy was significantly lower than that of normal controls and non-epileptic patients with head trauma (p < 0.01).

Conclusion: Our study suggests that low level of plasma haptoglobin may be associated with development of posttraumatic epilepsy.

p0116 AUDIT OF EPILEPSY HEALTHCARE PROVISION IN A LARGE UK CATEGORY B PRISON

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Purpose: This audit was undertaken to review standards of care for UK prisoners diagnosed with epilepsy. Previous reports have highlighted poor compliance with national guidelines for epilepsy care in prison settings, although available data is sparse.

Methods: Standards were identified using the National Institute for Health and Care Excellence (NICE) guidance and UK Medicines information. Standards included access to annual specialist review, use of an optimized anticonvulsant regimen, information provision regarding rescue medications, restrictions on duties or cell arrangements. The audit was conducted in one of the largest category B prisons in the UK (A closed prison for individuals who although not requiring maximum security, are considered to be a risk to the public). Fifty five prisoners with a diagnosis of epilepsy were identified during the audit period. Anonymised audit data was collected using face to face interviews using a standardised data collection proforma.

Results: Our findings highlight some unique demographics of prisoners within the epilepsy patient population. There was an increased frequency of adult seizure onset. 81.8% had a history of recent illicit drug misuse; this has important implications for both seizure control and prescribing. As Benzodiazepines and Pregabalin have high rates of diversion in prison settings. Further optimization of anticonvulsant regimen was required in 67.3% of the sample and only 14.5% of participants had been seizure free for the last 12 months. This emphasized the need for regular specialist review; just 37% of participants had been reviewed in the last 12 months. Regular, timely delivery of anticonvulsant medication had been difficult in 43.6% of cases; reasons for this were multifactorial.

Rates of provision of safety information relevant to epilepsy ranged from 12.7% (cell arrangements) to 67.3% (Driving).

Conclusion: We are currently looking at ways to implement a comprehensive overhaul of epilepsy care in UK prison settings.

p0118 NEURONAL AUTOANTIBODIES ARE INFREQUENTLY ASSOCIATED WITH MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS

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Purpose: The occurrence of epileptic seizures is often the result of multifactorial mechanisms. In many epilepsy syndromes the etiology is little known. However, in recent years, autoantibodies against neuronal surface and synaptic proteins have been detected in patients with epilepsy without signs of previous encephalitis, including epilepsies previously said of unknown cause. Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) is characterized by its well-defined clinical profile, and its refractoriness. Limbic encephalitis (LE) is increasingly recognized as a precipitating factor of adult onset MTLE-HS. Some series have reported up to half the MTLE-HS patients with evidence consistent with an autoimmune process. The aim of this study is to analyze the prevalence of specific autoantibodies in a group of patients with definite diagnosis of MTLE-HS.

Method: A cross-sectional study was carried out with 66 consecutive patients and 16 healthy controls. All patients fulfilled Wieser’s criteria for MTLE-HS. Clinical and demographic data were obtained. Blood was collected from patients and controls and serum was stored at -80°C for subsequent analysis. Indirect immunofluorescence was performed for detection of the following autoantibodies: anti-NMDA receptor, anti-CASPR2, anti-LGI1, anti-GABA-B receptor, anti-AMPA-1 receptor and anti-AMPA-2 receptor.

Results: Patients’ mean age was 41.1 (±11.6) years and of controls, 40.2 (±13.6) years. As to gender, 57.6% of patients and 62.5% of controls were females. Mean duration of epilepsy was 28.1 (±13.4) years. Neuronal autoantibodies were not found in both groups.

Conclusion: This study indicates that MTLE-HS may be infrequently associated with the presence of the mentioned neuronal autoantibodies, despite the fact that one recent study had shown the opposite. This is an ongoing project and the presented results are preliminary.

p0120 COULD ADULT TEMPORAL LOBE EPILEPSY PREDICT COGNITIVE DECLINE?

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Purpose: Prevalence of dementia in the Spanish population is age dependent, being approximately 10% at ≥70 years. Little is known about how many dementia patients can suffer seizures at onset. In addition, the prevalence of dementia in epileptic patient is uncertain. Our purpose is to evaluate cognitive decline in adult onset temporal lobe epilepsy (A-TLE) and related risk factors.

Method: Retrospectively selected A-TLE patients visited in our outpatient department between May 2014–May 2015, older than 30 years, epilepsy onset ≥30 years, and follow up of ≥5 years. We excluded rapidly progressive dementia. We recorded clinical information, neuropsychological tests, paraclinical tests (autoimmunity tests, cerebral IRM, FDG-PET, and cerebral SPECT) and clinical and/or neuropsychological evidence of dementia and mild cognitive impairment (MCI). We defined dementia as a multidomain dysfunction including memory severe enough to interfere with daily life and MCI as a memory dysfunction (1SD below general population) not related to epilepsy focus. The aetiologies were grouped: (1) vascular/brain trauma, (2) low grade tumour/cortical malformation, (3) CNS infection, (4) autoimmune epilepsy, and (5) unknown.

Results: We included 87 A-TLE 47 were women (54%), median age was 68 years (SD 10) and median time of epilepsy duration was 20 years (SD 11). Developed dementia 15/87 (17%) patients and 16% had MCI. A-TLE patients with dementia were older than patients without dementia (75 vs. 66). The age at epilepsy onset and the disease duration were not different. Were seizure-free 9/15 (60%) A-TLE patients with dementia. The unknown group had the greater frequency of dementia 11/51 (21.6%) and the tumour group the lowest (0/7 patients) but without significant statistical differences.

Conclusion: 1. High proportion of patients with A-TLE will develop dementia. 2. Cryptogenic A-TLE should be screened or follow up carefully for cognitive decline.

*Abstracts*
p0130
EFFECT OF LACOSAMIDE ON EPILEPTIFORM ACTIVITY INDUCED IN HUMAN NEOCORTICAL AND HIPPOCAMPAL SLICES
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Purpose: To assess the anticonvulsant effects of the antiepileptic drug lacosamide on epileptiform activity induced in human neocortical and hippocampal slices.

Method: This study was performed on surgically resected hippocampal and neocortical tissue of 11 patients with drug-resistant temporal lobe epilepsy (TLE). Using in vitro electrophysiology technique, the extracellular field potentials were recorded in the granular cell layer of the dentate gyrus. A total of 78 slices were studied. The epileptiform activity was induced in the hippocampus with 10–12 mM [K+] + electrical stimuli, in neocortex with 8 mM [K+] + 50 μM of bicuculline methiodide. The activity was evaluated in 3 epochs, induction, drug application and washout, each one with a duration of 20–25 min. Control value was determined in other set of experiments as the mean of induction and washout epoch recording on slices which lacosamide was not applied.

Results: Lacosamide therapeutic concentration (40 μM) shown decrease effect on seizure-like events (SLE) induced with high potassium protocol. Prolongation application of lacosamide (40 min) and increase of dose concentration (80 μM) improved the antiepileptic effect, however, the epileptiform activity under lacosamide application only was reduced but never suppressed, the effect was observed affecting the amplitude, duration and number of epileptiform events. Lacosamide also was assessed in combination with other antiepileptic drugs such as carbamazepine and levetiracetam, nevertheless, the effect on SLE was not enhanced and a marked reduction on the epileptiform activity only was observed when lacosamide was applied.

Conclusion: The results indicate the potential of lacosamide in decrease epileptiform activity induced in human neocortical and hippocampal tissue. These results support the therapeutic possibility of use lacosamide in refractory temporal lobe epilepsy in cases where the surgery not be possible.

p0131
NAV1.2 IS EXPRESSED IN REELIN-POSITIVE INTERNEURONS
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Purpose: Mutations of SCN2A gene encoding voltage-gated sodium channel alpha-2 subunit Nav1.2 have been found in patients with a wide spectrum of epilepsies, intellectual disability and autism. To understand the basic physiological role of Nav1.2, here we investigated the detailed expression of Nav1.2 in mouse brain.

Method: Immunohistochemical investigation of Nav1.2 were performed in mouse brain tissues with multiple developmental stages.

Results: In addition to unmethylated fibers such as mossy fibers of hippocampal granule cells, axons of striatal medial spiny neurons, cerebellar parallel fibers, in early developmental stages major Nav1.2 immunosignals were observed in methylated axonic features of excitatory neurons including cortical and hippocampal pyramidal cells. Of interest, neocortical and hippocampal reelin-positive somatostatin-negative interneurons were also positive for Nav1.2 at those stages.

Conclusion: We for the first time showed that Nav1.2 is expressed in neocortical and hippocampal reelin-positive somatostatin-negative interneurons. This would contribute to understanding of the pathology of patients with SCN2A mutations.

p0133
ANALYSIS OF ION CHANNEL PROPERTIES AND RHYTHMIC OSCILLATORY ACTIVITY IN THE THALAMOCORTICAL SYSTEM FOLLOWING DEMYELINATION
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Purpose: To understand the interaction between demyelination, inflammation and the prevalence of seizure we used a mouse model of thalamocortical epilepsy in combination with demyelination and application of pro-inflammatory cytokines INF-α and IL-1β. We performed recordings in C57BL/6J wild type, C3H/HeJ (absence epilepsy model) and cuprizone treated C3H/HeJ mice having acute demyelination.

Method: Network Oscillatory activity: 400 μm thick horizontal brain slices were prepared and rhythmic burst activity was induced by stimulating the internal capsule using tungsten electrode and measuring the network activity in the ventrobasal complex (VB) of thalamus using glass electrode. Whole cell patch clamp: a. Voltage clamp recordings were performed to study I<sub>H</sub> current carried by hyperpolarization activated cyclic nucleotide gated (HCN) channels. 300 μm thick coronal brain slices were prepared. Thalamic relay neurons of VB were held at a holding potential of -40 mV and voltage steps were applied with an increment of -10 mV until -130 mV. b. To study firing pattern current clamp recordings were performed. It consisted of hyperpolarizing and depolarizing current steps with fixed increments which led membrane potential ranging from -100 mV to a potential saturated by action potentials.

Results: INF-α decreased I<sub>H</sub> current density, hyperpolarized half maximal activation (H.M.A) of HCN channels, decreased rhythmic burst activity in C57BL/6J, C3H control and Cuprizone treated C3H mice. INF-α hyperpolarized resting membrane potential (R.M.P) (-3.83 ± 1.03 mV) and decreased tonic firing in C57BL/6J. IL-1β decreased I<sub>H</sub> current density (3.2 ± 1.2 pA), hyperpolarized H.M.A (-2.5 ± 0.8 mV), depolarized R.M.P (-1.69 ± 0.61 mV) and increased low threshold calcium spikes (LTS) in C57BL/6J. IL-1β increased rhythmic burst activity in C57BL/6J and C3H control mice. Demyelination decreased rhythmic bursts and hyperpolarized R.M.P.

Conclusion: Our findings suggest that pro-inflammatory cytokines may cause improper functioning of HCN channels and can have modulatory effects on excitatory activities of thalamic relay neurons thus affecting thalamocortical activity.

p0134
IMPAIRED BAROREFLEX SENSITIVITY AFTER BILATERAL CONVULSIVE SEIZURES IN PATIENTS WITH FOCAL EPILEPSY
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Purpose: In the majority of cases, SUDEP is probably due to an autonomic failure in the early phase after bilateral convulsive seizures (BCS). The baroreflex sensitivity (BRS) is one of the most robust biomarker for autonomic function and sudden cardiac death. Here we investigate whether postictal BRS depends on seizure type.

Method: Systemic blood pressure and heart rate were continuously and non-invasively recorded with the ccNexfin® device in patients with focal epilepsy undergoing video-EEG telemetry. BRS was calculated using two methods (sequence and spectral method). A random mixed-effect linear regression model was applied to study the influence of seizure type on BRS during three different time periods of 15-min length each (interictal, preictal and postictal). In addition, possible influencing factors such as hypertension, hemispheric lateralization of ictal activity, body position...
Abstracts

p0138
NR4A1 KNOCKDOWN SUPPRESSES SEIZURE ACTIVITY BY REGULATING SURFACE EXPRESSION OF NR2B
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Nuclear receptor subfamily 4 group A member 1 (NR4A1), a downstream target of CREB that is a key regulator of epileptogenesis, has been implicated in a variety of biological processes and was previously identified as a seizure-associated molecule. However, the relationship between NR4A1 and epileptogenesis remains unclear. Here, we showed that NR4A1 protein was predominantly expressed in neurons and up-regulated in patients with epilepsy as well as pilocarpine-induced mouse epileptic models. NR4A1 knockdown by lentivirus transfection (lenti-shNR4A1) alleviated seizure severity and prolonged onset latency in mouse models. Moreover, reciprocal coimmunoprecipitation of NR4A1 and NR2B demonstrated their interaction. Furthermore, the expression of p-NR2B (Tyr1472) in epileptic mice and the expression of NR2B in the postsynaptic density (PSD) were significantly reduced in the lentishNR4A1 group, indicating that NR4A1 knockdown partly decreased surface NR2B by promoting NR2B internalization. These results are the first to indicate that the expression of NR4A1 in epileptic brain tissues may provide new insights into the molecular mechanisms underlying epilepsy.

p0139
PHYSICAL EXERCISE DURING PREGNANCY ATTENUATES THE NEGATIVE EFFECTS OF PTZ-INDUCED SEIZURES IN OFFSPRING FROM MOTHERS SUBMITTED TO PRENATAL STRESS
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Purpose: Prenatal stress is one important factor that can interfere on brain development and affects the susceptibility of the developing brain to epilepsy. Studies have shown that exercise during pregnancy has a positive influence on brain function in the offspring. Thus, physical exercise contributes to reduce seizure susceptibility before brain insult and seizure frequency in the chronic epilepsy condition. Although there are studies which highlight the deleterious influence of stress during pregnancy on offspring behavioral and seizure susceptibility, very little is known about how to minimize these negative effects. This work aimed to verify whether physical exercise during pregnancy in mothers submitted to prenatal stress minimizes offspring seizure susceptibility in the beginning of postnatal development.

Method: Pregnant rats were divided into the following groups: control (n = 6); exercise (treadmill) (n = 5); stress ( restraint) (n = 5); exercise/
p0148  ABLATION OF NEWBORN GRANULE CELLS AFTER EPILEPSY ONSET HALTS DISEASE PROGRESSION  
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Purpose: Aberrant integration of newborn hippocampal granule cells is hypothesized to contribute to the development of temporal lobe epilepsy. To test this hypothesis, we used a transgenic mouse model system to selectively ablate these cells from the epileptic mouse brain. If these cells promote epileptogenesis, then ablation should be therapeutic.

Method: Epileptogenesis was initiated using the pilocarpine status epilepticus model. Diphtheria toxin receptor production was driven in Nestin-expressing granule cell progenitors using a tamoxifen-inducible mouse model system. Granule cells born shortly before and after the insult were targeted; the population known to underlie dentate dysmophogenesis. Continuous EEG monitoring was begun 2–3 months after pilocarpine treatment. Four weeks into the EEG recording period, at a time when spontaneous seizures were frequent, mice were treated with diphtheria toxin to ablate newborn cells. Monitoring continued for another month following ablation.

Results: Ablation halted epilepsy progression relative to untreated epileptic mice; the latter showing a significant and dramatic 300% increase in seizure frequency in the post-treatment period. This increase was prevented in treated mice. Ablation did not, however, cause an immediate reduction in seizures, suggesting that newborn cells mediate epileptogenesis, but that seizures per se are initiated elsewhere in the circuit.

Conclusion: These findings demonstrate that targeted ablation of newborn granule cells can produce a striking improvement in disease course, and that the treatment can be effective when applied months after disease onset. This latter observation suggests that the treatment window for disease modifying therapy may extend for months beyond the initial insult.

p0149  ROLE OF INTER-ICTAL DISCHARGES: INITIATING OR DELAYING SEIZURES?  
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Purpose: Experimental observations provide contradictory evidence concerning the role of inter-ictal discharges with respect to the seizure dynamics. Two competing mechanisms have been proposed: either a pro-convulsive role by initiation of seizures, or anti-convulsive role manifested as longer inter-ictal intervals when inter-ictal discharges are present.

Method: To explore possible mechanisms behind the observed phenomena, we build a phenomenological mathematical model of the switching between bistable high-firing (seizure) and low-firing neural population state, that is driven by changes in global excitability. The excitability dynamics entail a steady slow increase during the low-firing state and a decreasing tendency during the seizure state.

Results: The dynamics give rise to periodic switching between the model inter-ictal and ictal state. External perturbation to the mean potential variable can lead to both initiation and delay of seizures, based on the timing and parameters of the perturbation. We further extend the study by exploring whether similar dual mechanism of perturbation can be demonstrated in more realistic computation models of epilepsy.

Conclusion: Using computational models of seizure generation, we have demonstrated the possible dual role of inter-ictal discharges in seizure initiation: both pro-convulsive and anti-convulsive, depending on the timing and parameters of the perturbations.

p0150  EFFECTS OF RO 53-1908 AND RO 04-5595 INTRAHIPPOCAMPAL MICROPERFUSION ON THE PICROTOXIN SEIZURE THRESHOLD IN FREELY MOVING RATS  
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Purpose: The role of NR2B-containing NMDA receptors in the development of epileptic seizures is not yet well established. On kindling and pilocarpine animal models, activation of NR2A-, but not NR2B-, containing NMDARs seems to be required for epileptogenesis. However, treatment with highly selective antagonists of NMDA receptors containing the NR2B subunit has been shown to reduce on the incidence of seizures on several animal models. We have investigated the anticonvulsant effect of the intrahippocampal microperfusion of Ro 53-1908 and Ro 04-5595, two NR2B-containing NMDA receptor antagonists on seizure threshold in picrotoxin-induced seizures in awake, freely moving rats.

Method: We used a CMA/120 system for freely moving animals. Rat hippocampus was perfused with ringer fluid or 200 μg/ml Ro 53-1908 or Ro 04-5595 dissolved in ringer fluid through CMA/12 microdialysis probes during 3 h, with continuous EEG and videotape recording. After 2 h, a picrotoxin solution (100–300 μM) was perfused during 5 min. We evaluated the lower picrotoxin concentration needed to induce a seizure and the total seizure duration by Student’s T test.

Results: Perfusion of Ro 53-1908 or Ro 04-5595 alone at the concentrations studied did not induce changes in the basal EEG. However, both Ro 53-1908 and Ro 04-5595 increased picrotoxin seizure thresholds in the 100% of the animals studied. Ro 53-1908 prevented seizures at picrotoxin threshold level in in the 100% of the rats studied, while Ro 53-1908 prevented seizures at picrotoxin threshold level in in the 80% of the animals.

Conclusion: Our results show that treatment with highly selective antagonists of NMDA receptors containing the NR2B subunit prevent picrotoxin-induced seizures when perfused into the rat hippocampus with no observable toxic effects. The NMDA receptor NR2B subunit remains an attractive target for potential antiepileptic drugs.
based SMAD inhibition. The single cell electrophysiology was used to assess the maturity of the differentiated neurons.

**Results:** NGN The2 based protocol provided homogenous populations of firing neurons in less than three weeks of differentiation. In contrast, embryoid body procedure required about three months to produce reliably firing populations of neurons, often including cells at the different stages of maturity. A more precise look into passive membrane characteristics including capacitance and input resistance, active membrane characteristics such as sodium and potassium currents, or single-cell firing and spontaneous network activity revealed significant differences between the two protocols. NGN The2-derived neurons presented with activity resembling early phases of neuronal development and were lacking synaptic activity, while more mature neuronal and synchronized network activity, resembling the activity of cortical neurons of human foetus/newborn were found for the embryoid body-derived neurons.

**Conclusion:** We suggest that the observed differences in neuronal and network maturity should be taken into consideration when designing epileptic encephalopathy human in vitro models in order to match timing of disease manifestation to the relevant neuronal maturity.

**p0153**

WHOLE GENOME SEQUENCING THE GENETIC ABSENCE EPILEPSY RAT FROM STRASBOURG, ITS RELATED NON-EPILEPTIC STRAIN AND THEIR PROGENY

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**Purpose:** The Genetic Absence Epilepsy Rats from Strasbourg (GAERS) are an inbred Wistar rat strain widely used as a model of genetic generalised epilepsy with absence seizures. As in humans, the genetic architecture that results in genetic generalised epilepsy in GAERS is poorly understood. Here we present the strain-specific variants found among the epileptic GAERS and their related Non-Epileptic Control (NEC) strain. The GAERS and NEC represent a powerful opportunity to identify neurobiological factors that are associated with the genetic generalised epilepsy phenotype.

**Method:** We performed whole genome sequencing on GAERS and NEC rats, a strain derived from the same original Wistar. We also generated whole genome sequencing on four GAERS and NEC F2 selected for high-seizing (n = 2) and non-seizing (n = 2) phenotypes.

**Results:** Specific to the GAERS genome, we identified 1.12 million single nucleotide variants, 296.5K short insertion-deletions, and 1,457 putative copy number variants that result in complete or partial loss/duplication of 65 genes. Based on overlaps with Mouse Genome Informatics only two NEC strain-specific non-intronic CNVs were identified: Kenj6 (GIRK2) and Scn8a (NaV1.6). Subsequent screening against the two F2 progeny sequences for having the highest and two F2 progeny for having the lowest seizure burden identified only the selected Cacna1h GAERS-private protein-coding variant as exclusively co-segregating with the two high-seizing F2 rats. In the NEC, filtering of the specific variants were found in genes that have been associated with epilepsy and segregate with the two non-seizing F2 rats; Abat (4-aminobutyrate aminotransferase), Cyp11b3 (11-beta-hydroxylase) and Cyp11b (aldosterone synthase).

**Conclusion:** This study highlights an approach for using whole genome sequencing to narrow down to a manageable candidate list of genetic variants in a complex genetic epilepsy animal model, and suggests utility of this sequencing design to investigate other spontaneously occurring animal models of human disease.

**p0155**

ANTIOXIDANT INTERVENTION DURING EPILEPTOGENESIS DELAYS DISEASE ONSET AND BLOCKS ITS PROGRESSION IN A RAT MODEL OF ACQUIRED EPILEPSY


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**Purpose:** We studied the role of oxidative stress generated during epileptogenesis in the onset and progression of epilepsy and whether anti-oxidant drugs in medical use display therapeutic effects in a rat model of acquired epilepsy.

**Method:** We studied oxidative stress during epileptogenesis in rats exposed to electrically provoked status epilepticus (SE), a model associated with progressive seizures, cell loss and cognitive deficits. We measured GSSG/GSH levels in the hippocampus by HPLC and analyzed oxidative stress markers (Nrf2, iNOS, Xcl) by immunohistochemistry. We also measured brain and plasma levels of disulfide HMGB1 by LC-MS/MS since this neuroinflammatory molecule is sensitive to the redox state and its oxidized (disulfide) isoform is implicated in seizures. We tested the effects of N-acetyl-cysteine (NAC) and sulfurophane (SPN), two anti-oxidant drugs in medical use –administered intraperitoneally 1 h post-SE for 2 weeks- on ROS production, HMGB1 oxidation, and seizure onset and their progression by EEG analysis. Cognitive deficits were assessed in the T maze and hippocampal neuronal death was quantified by immunohistochemistry.

**Results:** The combined drugs decreased oxidative stress more efficiently than each drug alone, and decreased the brain and blood generation of disulfide HMGB1. As compared to vehicle-injected rats, the treatment delayed the onset of spontaneous seizure (8.6 ± 0.7 vs. 11.7 ± 1.1 days, n = 9, p < 0.01), blocked the 5-fold progression in the number of seizures and reduced chronic spontaneous seizures by 70% (p < 0.05). Drugs prevented the cognitive deficit and the loss of calretinin-positive hilar interneurons and reduced CA1 pyramidal cells degeneration.

**Conclusion:** Reduction of oxidative stress during epileptogenesis with medically used drugs delays disease onset and blocks its progression, and is neuroprotective. This intervention should be considered for patients exposed to potential epileptogenic insults.

**p0160**

FURTHER EVIDENCE FOR A DIFFERENTIAL SITE OF ACTION OF THE ANTICONVULSANTS BRIVARACETAM AND LEVETIRACETAM ON THE SV2A PROTEIN

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Purpose: Brivaracetam (BRV) and levetiracetam (LEV) are antiepileptic drugs which interact with the synaptic vesicle 2A (SV2A) protein. BRV differs from LEV in exhibiting more potent and complete seizure suppression in animal models of epilepsy. We showed that an SV2A modulator had a differential effect on the binding of \(^{[3]H}\)BRV compared to \(^{[3]H}\)LEV. Thus, the modulator potentiated \(^{[3]H}\)BRV binding mainly by increasing affinity (K_d), but potentiated \(^{[3]H}\)LEV binding by increasing binding capacity (B_max). This suggested that BRV and LEV act at different sites or in a different way with the SV2A protein. We therefore hypothesised that mutation of specific amino acid residues in the SV2A protein may have a differential effect on this modulation.

Method: Based on modelling studies, several mutants were selected. Saturation studies were performed using \(^{[3]H}\)LEV and -BRV in the presence and absence of the modulator in membranes from HEK293 cells expressing human SV2A protein.

Results: A number of mutations reduced both \(^{[3]H}\)BRV and \(^{[3]H}\)LEV binding (e.g. W300F; F277A; V661A; W666A; D670A). However, mutation of two residues (S294A and I273A) had no effect on potentiation of \(^{[3]H}\)BRV binding by the modulator, but blocked potentiation of \(^{[3]H}\)LEV binding.

Conclusion: We have identified two residues which have a differential effect on the modulation of \(^{[3]H}\)BRV binding compared to that of \(^{[3]H}\)LEV, providing further evidence that BRV and LEV interact at different sites on the SV2A protein. These two residues have previously been shown to differentiate different chemical classes of SV2A ligand. This suggests that BRV and LEV interact at closely overlapping yet distinct sites on the SV2A protein, which may correlate with their different pharmacological profiles.

p0171

A SYSTEMATIC REVIEW ON DIAGNOSTIC ACCURACY AND CLINICAL VALUE OF NON-INVASIVE LONG TERM VIDEO-EEG MONITORING IN PRESURGICAL EVALUATION OF PATIENTS WITH EPILEPSY

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Purpose: The European Union-funded E-PILEPSY network aims to harmonize and optimize the presurgical diagnostic procedures by creating and implementing evidence-based guidelines and recommendations across Europe. We evaluated the current evidence on diagnostic accuracy and clinical value of Long-term video-EEG monitoring (LTM) in identifying the epileptogenic zone in patients with epilepsy.

Method: Studies were identified by searching the MEDLINE, EMBASE, CENTRAL and ClinicalTrials.gov databases. In order to evaluate the diagnostic accuracy of LTM, sensitivity and specificity were assessed in subgroups of lesional and nonlesional temporal and extratemporal lobe epilepsy (TLE and ETLE) patients. We analyzed data descriptively by logistic regression based on single patient analysis and calculated sensitivity and specificity with respect to predicting seizure freedom after surgery.

Results: 42 studies were included, comprising 424 patients who underwent resective epilepsy surgery. Statistical analyses yielded a sensitivity estimate of 0.83 (CI: 0.78–0.87) and a specificity estimate of 0.21 (CI: 0.14–0.30) in the lesional TLE group. In the lesional ETLE group, sensitivity and specificity were 0.50 (CI: 0.33–0.67) and 0.39 (CI: 0.24–0.57), respectively. In the nonlesional subgroups, sample sizes were too small to calculate accuracy measures. An evaluation of the impact of certain etiologies on diagnostic accuracy of VEEG using logistic regression analyses was possible only in the lesional TLE group. In the lesional ETLE group, sensitivity and specificity were higher than in the lesional TLE group, but association with higher diagnostic accuracy of LTM, as indicated by a sensitivity of 0.88 (SE 0.029) and a specificity of 0.17 (SE 0.051).

Conclusion: The study shows that the sensitivity of VEEG is remarkably higher in lesional TLE compared to lesional ETLE. Furthermore, sensitivity estimates within the lesional TLE group differ considerably from those in the nonlesional TLE group.
p0174
BURST SUPPRESSION IN FULL TERM NEONATES
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Burst Suppression (BS) pattern of EEG consists of high amplitude paroxysmal bursts alternating with suppression of EEG activity. It is a poor prognostic sign in most but not in all. Aetiology of BS in neonates includes; hypoxia, birth asphyxia, early infantile encephalopathy, metabolic errors and medications. Early diagnosis is essential for effective management and we present an illustrative case of non-ketotic hyperglycaemia (NKH) picked up because of BS on EEG. A full term male neonate, presented on day 1 of birth with grunting and feeding difficulties. He had normal birth. Day 2, he developed hiccups, hypotonia and poor respiratory drive, needing intubation and ventilation on day 4. He made some improvement; extubated, started breast feeding, but remained hypotonic. There were no clinical seizures, but EEG on day 9 showed BS and frequent bilateral sharp waves. In the absence of hypoxic injury, he was investigated further and diagnosis of NKH was made by detection of elevated glycine in cerebrospinal fluid (CSF) and raised CSF/plasma glycine ratio. MRI showed areas of high signal on T2 in keeping with NKH. He was commenced on Sodium Benzoate and Dextromethorphan. EEG at 3 weeks continuous background, sharp waves over the left hemisphere. L-Dopa was introduced to manage dystonia. At 9 weeks, developed frequent jerks, EEG showed focal seizures arising independently from both hemispheres. He was commenced on phenobarbitone, Levetiracetam and ketogenic diet. EEG at 3 months showed clusters of epileptic spasms, hypsarrhythmia and subclinical focal seizures. NKH is a rare autosomal recessive inborn error of glycine metabolism, characterised by a rapidly progressive course, often death within the first year. It is associated with BS pattern during neonatal period, later changing to hypsarrhythmia. There is no cure but early diagnosis and treatment may possibly improve the prognosis. In that respect EEG demonstrating BS had been helpful.

p0180
PATTERN OF ICTAL INTRACEREBRAL EEG AT THE START OF ALTERATION OF CONSCIOUSNESS
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Purpose: The alteration of consciousness (AOC) during seizures is one of the most striking features in patients with focal epilepsy and the subjacent mechanisms are incompletely known. Better defining of intracerebral EEG morphological signal at seizure-onset and its propagation could improve the understanding of such mechanisms.

Method: It was included 9 patients (45 seizures) with drug resistant epilepsy. All of them had RM and steroelectroencephalography (SEEG). The SEEG were analysed independently by two reviewers blinded to clinical information, and consensus was reached after discussion. We analysed the patterns and localization of seizure onset and propagation, time of propagation, beginning of clinical seizure, beginning of AOC, degree of AOC and duration of seizure.

Results: In mesial temporal epilepsy, the seizures with AOC were longer, the most commonly pattern of seizure-onset activity was sharp at ≤ 13 Hz and the AOC occurred with or following the propagation of activity to contralateral hippocampus. In frontal epilepsy, the most commonly pattern of seizure-onset activity was low-voltage fast activity >13 Hz and the AOC occurred following the propagation of the activity to adjacent areas of the seizure-onset (overage 16 s after) without hippocampal commitment. In insular epilepsy, the seizures with AOC were longer and affected both anterior and posterior insular electrodes, without commitment of hippocampus. The electrical beginning were sharp activity at ≤ 13 Hz without consideration of degree of AOC.

Conclusion: In our work, the AOC were mostly with of the propagation of the seizure-onset activity. In mesial temporal seizures, the most of the AOC seizures were with contralateral hippocampus compromised. Meanwhile in frontal and insular seizures the AOC occurred when the area of discharged is enlarged without hippocampus compromised. Future works that apply different techniques for signal analysis are necessary to characterize functional connectivity between spatially distributed regions and pathophysiological mechanisms during AOC.

p0183
POST TRAUMATIC EPILEPSY DUE TO TRAUMATIC BRAIN INJURY BY TRAFFIC ACCIDENTS IN NEUROPHYSIOLOGICAL EXPLORATIONS LABORATORY OF MARRAKESH UNIVERSITY HOSPITAL
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Purpose: Post traumatic epilepsy (PTE) is defined by two or more unprovoked seizures after brain traumatic injury (BTI). PTE after TBI can be secondary to traffic accidents. Its prevalence of 4 % increases after penetrating brain injury. Cortical lesions play a role of PTE genesis. Morocco face a real “Road War” and Marrakech city and its region is especially known by traffic accidents of motorcyclists.

Method: retrospective Study on PTE Cases registered over one year in university hospital neurophysiology laboratory of Marrakesh. All cases had a (EEG) with selection of cases with epileptic seizure caused by TBI.

Results: Among 385 patients with epilepsy who had EEG, 11 cases were associated with a TBI caused by a traffic accident (Among a total of 20 cases with TBI). TBI was severe in 9 cases, average age was 27.5 years (ranged from 17 to 72 years) with a male predominance (10 cases). PTE diagnostic delay was 4 years after accident. Epilepsy seizures were mainly partial (9 cases). The neurological examination was normal in 5 cases. Elsewhere we found confusion (2 cases), a limb motor paralysis (2 cases), pyramidal signs (1 case) and multifocal lesions (1 case). The EEG confirmed partial paroxysmal abnormalities in 8 cases and was normal in 3 cases. All patients have cerebral CT scan showing hemorrhagic contusions (3 cases), depressed skull (2 cases), frontal hematoma (2 cases). Five patients were treated by valproate at the time of EEG realization EEG.

Conclusion: PTE due to traffic accidents was seen in 55 % of all TBI cases seen in our neurophysiologic laboratory. The majority of victims of this “road war” are young active males with severe consequences in Marrakesh region. In spite of the deployed efforts to decrease road deaths, more prevention is needed with an early diagnostic and treatment of the PTE victims.

p0184
SLEEP RELATED EPILEPSY IN FOCAL CORTICAL DYSPLASIA TYPE II (FCD2): INSIGHTS FROM SLEEP RECORDINGS
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Purpose: Sleep related epilepsy (SRE) defined by >70% of seizures occurring during sleep, has been recently reported in FCD2, a common neuropathological entity found in epilepsy surgery. We aimed to determine in a cohort of patients with histologically confirmed FDC2 and SRE the relationship between ictal onset, sleep stage, preceding arousal, and its value for localisation of the dysplasia.
METHODS: From a single centre surgical series of 109 FCD2 patients, 64 (59%) with SRE were identified. We reviewed scalp video-EEG data of and selected patients in whom sleep recordings were available. FCD location was based on MRI, histology, and surgical outcome.

RESULTS: Sleep video-EEG with at least one recorded seizure were available for 53 patients (30 males, mean age 20.7 (SD ± 10.4) years, age at seizure onset: 5.7 (SD ± 4.5) years). MRI was negative in 18 (34%) cases or showed subtle abnormalities in 11 (21%), histological subtype was FCD2a: 11 [21%], FCD2b: 42 [79%]. FCDs were located in frontal lobe in 39 (74%) and in extra-frontal areas in 14 (26%); 2 temporal, 11 posterior, 1 insular. Seizure onset relation to sleep stage could be determined for 50/53 (94%) patients. Seizure onset occurred from NREM sleep in 35/50 (70%) patients (mostly from stage 2), after arousal in 13/50 (26%) and in both conditions in 2/50 (4%). NREM sleep seizures were significantly more frequent with frontal (29/34 [85.3%]) compared to extra-frontal location (6/14 [43%]), whilst arousal preceded ictal onset more often in extra-frontal (6/14 [43%]) compared to frontal location (5/34 [14.7%]). *Fisher’s Exact Test p = 0.005.

CONCLUSION: FCD2 occurs very frequently in drug-resistant SRE. The seizure onset pattern arising from NREM sleep or preceded by arousal can provide additional localising information and suggests topography dependent impact on sleep related functional networks.

p0185 USING MEG-VIRTUAL ELECTRODES AT DEPTH ELECTRODE LOCATIONS TO CHARACTERIZE THE SEIZURE ONSET ZONE IN REFRACTORY EPILEPSY PATIENTS

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PURPOSE: Epilepsy surgery can increase the chance of seizure freedom in focal refractory epilepsy, provided that the seizure onset zone (SOZ) is located and the epileptogenic zone removed safely. Depth electrode recording (dEEG) is considered the gold standard in locating the SOZ when non-invasive techniques fail, yet entails risk of complications. The purpose of this study was to determine if potential SOZ biomarkers (i.e. spectral analysis, functional connectivity and network centrality measures) derived from magnetoencephalography-based virtual electrodes (MEG-VEs) could provide an accurate characterization and location of the SOZ comparable to that of dEEG.

METHOD: DEEG and MEG recordings from nine refractory epilepsy patients (who underwent surgical treatment) were analyzed. Beamforming was used to place MEG-VEs at the exact dEEG electrode locations. For both modalities, we computed spectral (relative power and peak frequency) and connectivity measures (phase lag index and phase transfer entropy). A minimum spanning tree graph was constructed and centrality measures calculated. To characterize the SOZ, we compared the measures from the channels located in the resected area (SOZ channels) to the non-resected channels (rest). Correlation coefficient, intraclass correlation and Bland-Altman plots were determined between modalities for each measure.

RESULTS: The SOZ channels had significantly lower peak frequencies and increased relative delta power, while relative alpha and beta power decreased compared to the rest of the channels in both modalities. SOZ channels showed high connectivity (increased PLI) and information flow towards the rest of the channels (dPTI > 0.5). Peak frequency, relative power (delta, alpha2 and beta), PLI and PTE were correlated, reliable and agreed between modalities.

CONCLUSION: Spectral and functional connectivity measures characterized the SOZ in both modalities and can potentially be used as biomarkers. Non-invasive MEG-VEs measures gave comparable results to dEEG. We suggest that MEG-VEs provides a promising tool to accurately evaluate the SOZ.

p0186 ANALYSIS OF HEART RATE VARIATION AFTER ELECTRICAL STIMULATION OF THE INSULA DURING SEEG

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PURPOSE: The insular cortex has been suggested to have a prominent role in neurological control of the autonomic nervous system, but its specific function and the precise location of these autonomic regulatory areas are not completely known. We aimed to study the heart rate (HR) changes induced by intracranial electrical stimulation of the insular cortex, in epileptic patients submitted to invasive stereo-electroencephalography (SEEG) recordings.

METHOD: We selected 6 patients with non-insular epilepsy studied through SEEG, in whom the insular cortex was explored. Insular electrodes were precisely localized merging postoperative CT scans and pre-operative MRIs. HR was analyzed during periods of 10 s previous to stimulation (HRb), during insular stimulation (HReq) and during stimulation of non-insular electrodes selected randomly on the same side (HRe). Heart rate variability (HRV) was measured according to instantaneous variations of beat-to-beat interval (DNN) that corresponds to its first derivative.

RESULTS: Six right-handed patients, three with left insular implantation and three with right insular implantation, were enrolled. Thirty-six electrodes were analyzed: 8 were implanted in the right anterior insula, 10 in right posterior insula, 12 in left anterior insula and 6 in left posterior insula. Stimulation of the right insula, and specifically of the anterior region induced a significant decrease of DNN and an increase of 4 beats-per-minute (bpm) on average as compared to HRb and HReq (p < 0.01). Serendipitously, we also elicited an atypical insular seizure that provoked a steep increase of HR (88 to 111 bpm). Stimulation of other areas of the insular cortex did not produce significant HRV changes in comparison to HRb or HReq.

CONCLUSION: In our study the electrical stimulation of the right anterior insula induced a significant increase of the heart rate. Our data support an important role of the human right insular cortex in the control of heart rate dynamics.
(467.6 recording hours) were used to test the performance of the algorithm. We aimed to modify an existing QRS-detection algorithm to a more precise R-peak detection algorithm to avoid the possible jitter Q- and S-peaks can create in the tachogram, which causes error in short-term HRV-analysis.

**Results:** The proposed R-peak detection algorithm showed a high sensitivity (Se = 99.979%) and positive predictive value (P+ = 99.976%), which was comparable with a previously published QRS-detection algorithm for the ePatch® ECG device, when testing the same dataset.

**Conclusion:** The novel R-peak detection algorithm designed to avoid jitter has very high sensitivity and specificity and thus is a suitable tool for a robust, fast, real-time HRV-analysis in patients with epilepsy. The R-peak detection algorithm is the first important step in creating a portable fully automatic real-time seizure detection for these patients.

**p0189**

**THE IMPACT OF THE EEG FINDINGS ON THE STRATEGY OF TREATMENT IN CHILDREN WITH ADHD**

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**Purpose:** According to the literature approximately 15% children with ADHD have certain epileptic activity in long-term sleep EEG. In available literature we couldn’t find publications about the impact of EEG findings on ADHD therapy strategy. To determine paroxysmal EEG abnormalities in children with pure ADHD and treatment strategy depending on EEG paroxysmal disturbances.

**Method:** We’ve examined 28 children aged 6–10 years with ADHD (DSM-5 classification), without epilepsy and speech development delay. All children were conducted neurological and psychiatric examination, speech therapist examination and long-term sleep EEG recording. All children underwent neuroimaging (CT, MRI) without any disturbances. According to the EEG findings all children were divided into 2 groups: group I (18 children) with epileptic activity, hypnagogic hypersynchrony and it’s abnormal variants (with sharp waves on it); group II (10 children) with normal EEG.

**Results:** Traditional drug methods of ADHD treatment showed significant clinical improvement only in the group II.

**Conclusion:** Paroxysmal activity in EEG could be the reason for insufficient effect of traditional ADHD treatment.

**p0190**

**TRACKING HEART RATE CHANGES DURING SEIZURES: A NATIONAL STUDY USING RESEARCHKIT AND APPLE WATCH TO COLLECT BIOSensor AND RESPONSE DATA DURING SEIZURES**


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**Purpose:** Seizure apps using biosensors and mobile devices may be used to develop non-EEG seizure detection and help support patients with epilepsy. We implemented a national study called EpiWatch, which uses Apple Watch to track heart rate, movements, and responsiveness during seizures, with the goal of using this data to develop seizure detection. We report an initial analysis of heart rate changes associated with seizures.

**Method:** Participants were e-consented using ResearchKit with encrypted data transmission. Seizure tracking was initiated during auras or by caregivers with heart rate (HR), accelerometer, and responsiveness data collected for 10 min. This was followed by a post-seizure survey. We performed preliminary analysis of participant HR changes during various seizures.

**Results:** 704 participants (mean age: 31, range: 16–73), from nearly all states, enrolled in the EpiWatch study. 47% of participants tracked seizures (mean: 9.6 per participant), with 3026 seizures recorded. Seizure types were typical of those expected for a national epilepsy population: 28% focal seizures and 9% tonic-clonic seizures. During tonic-clonic seizures, HRs increased >30% in 38% and >50% in 23% of seizures. HR changes were more variable with focal seizures: >15% increases in HR in 42% and decreases in 14% of seizures. We observed several temporal patterns associated with HR changes: most seizures evolved with tachycardia over a 30 second period, preceding visible and brisk accelerometer fluctuations associated with bilateral seizure evolution; some seizure activations had immediate elevated HR increases compared with pre-seizure baselines, presumably due to late tracking activation.

**Conclusion:** Our study demonstrates that it is possible to rapidly implement a national study which collects biosensor and response data types using wearable technology to accelerate epilepsy research. Watch biosensors captured early heart rate accelerations, particularly during tonic-clonic seizures. These data, along with accelerometer and responsiveness data, are being used to test seizure detection algorithms.

**p0193**

**EFFECT OF EMBELIN IN CHRONIC EPILEPSY INDUCED COGNITIVE DYSFUNCTION IN THREE-AXIS MAZE MODEL OF ADULT ZEBRAFISH**

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**Purpose:** Chronic epilepsy is characterized by repeated unpredictable seizures. Abnormal neurons firing electrical impulses, which can cause the brain and body to behave strangely. Neurocognitive impairment is frequently observed in epileptic patients. Most cognitive complaints in adult patients are mental slowness, memory difficulties and attention deficits. Embelin is derived from plant Embelia ribes and used traditionally in the treatment of various brain disorders and also as a brain tonic. Zebrafish are capable of learning and executing spatial tasks from an egocentric frame of reference. The three-axis maze is a conventional method to test the learning ability and egocentric memory in zebrafish. In three-axis maze, fish requires to navigate a route based on x (forward/backward), y (horizontal) and z (vertical) axes. Egocentric navigation is an evidence based process, where fish navigates to the feeding ring independent of environmental cues and deals directly with the spatial relation between subject and reward goal. The study, therefore, aims to assess whether embelin can ameliorate chronic epilepsy (kindling) induced spatial memory impairment.

**Method:** Repeated administration of pentylentetrazole (PTZ) for 10 days successfully induces kindling effect in zebrafish and also worsen the memory function detrimental to egocentric navigation. Animal treated with embelin are observed for its cognitive performance, three-axis maze behavior, performance errors and biochemical changes.

**Results:** Results demonstrate that doses of embelin (0.156 mg/kg, 0.312 mg/kg and 0.625 mg/kg) significantly improve maze navigation times and reduced performance errors in three-axis maze.

**Conclusion:** Embelin improves both epileptic and egocentric spatial memory condition. Three-axis maze analysis, locomotor behavior and biochemical changes shows that embelin can reverse chronic epilepsy associated learning and memory in zebrafish model.
p0196

BONE METABOLISM SERUM MARKERS IN ADULT PATIENTS WITH EPILEPSY: EFFECT OF VITAMIN D SUPPLEMENTATION ON SEIZURES CONTROL

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Purpose: The aim of our study was to evaluate serum markers of bone metabolism in adult patients with epilepsy treated with different antiepileptic drugs (AEDs). Also, the effect of Vitamin D (VitD) supplementation on seizure frequency was addressed.

Method: In 160 patients with epilepsy (PWE) on chronic therapy with AEDs and 42 healthy control subjects serum levels of calcium, phosphate, intact parathyroid hormone (PTH) and 25-hydroxy Vitamin D (25OHD) were evaluated. The levels of these markers were analysed taking into account the different features of epilepsy and treatment. Finally, in a group of 48 patients the effect of oral administration of VitD for 3 months on seizures control was assessed at 6 months after the beginning of supplementation.

Results: PWE showed significantly lower serum levels of 25OHD compared to controls subjects, negatively correlated with the duration of treatment. In 33.1% of patients a severe deficiency of VitD was detected, VitD insufficiency in 41.9% and only 25% of PWE had normal values of 25OHD. Polytherapy and enzyme inducing AEDs showed more detrimental effects. Only in patients under the age of 65, a weak inverse correlation between seizure frequency and levels of 25OHD was found, but the administration of VitD for three months failed to significantly affect seizures control.

Conclusion: We confirmed in adult patients with epilepsy a significant decrease of serum levels of 25OHD, largely dependent on the features and duration of treatment. The administration of oral VitD in a group of patients did not show a clear anticonvulsant effect.

p0197

ASSOCIATION BETWEEN BONE MINERAL DENSITY AND USE OF ANTI-EPILEPTIC DRUGS

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Purpose: Many patients on antiepileptic drugs (AEDs) develop metabolic bone disease such as osteopenia and osteoporosis. This increases the risk of pathological bone fractures, increases the risk of morbidity and mortality and decreases life quality. Little is known regarding bone disease in patients with epilepsy and its relation to treatment with AEDs. The study aim was to investigate the occurrence of bone disease in an unselected cohort of patients with epilepsy and the associations between bone mineral density (BMD) and treatment with AEDs.

Methods: The study is a retrospective cohort study of 474 patients (male:female ratio 1:1.2; age 48 ± 16 years (mean±SD); duration of epilepsy 24 ± 16 years) followed at a tertiary epilepsy outpatient-clinic in Denmark. Data on BMD from Dual-energy X-ray absorptiometry (DXA) scans were collected including T- and Z-scores from lumbar region and femoral region. Information regarding the patient’s medical history and epilepsy treatment was obtained through the patient’s medical report.

Results: Of the 474 patients 59% received monotherapy and 40% received polytherapy. The most frequently used AEDs were lamotrigine (42%), levetiracetam (29%) and valproic acid (21%). In the cohort 12% of the patients had osteoporosis and 22% had osteopenia. The only monotherapy that was significantly associated with decreases in BMD was carbamazepine (p = 0.04) whereas polytherapy, including lamotrigine, levetiracetam, valproic acid, and carbamazepine were significantly associated with decreases in BMD (p ≤ 0.02). When looking at specific combinations of therapy levetiracetam and topiramate, levetiracetam and carbamazepine, and levetiracetam and valproic acid were all significantly associated with decrease in BMD (p ≤ 0.04).

Conclusion: In the unselected cohort of patients with epilepsy 12% had osteoporosis and 22% had osteopenia. Significant decreases in BMD were primarily associated with polytherapy. This suggests an additive negative effect of polytherapy on bone health. Our results further support the need for focusing on bone health in patients treated with AEDs.

p0199

HIGH PREVALENCE OF INTELLECTUAL DISABILITY, AUTISM, ADHD AND DIMINISHED ADAPTIVE FUNCTIONING IN DOOSE SYNDROME (MAE)

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Myoclonic atatic epilepsy (MAE) is a rare childhood epilepsy with unclear neurodevelopmental outcome. We aimed to deeply phenotype MAE patients utilising a series of standardised neuropsychological tests.

Patients with MAE were recruited from UK paediatric neurology centres from 2012 to 2016. Cases were assessed using the WPPSI III or Bayleys III for cognition; Developmental, Dimensional and Diagnostic Interview (3di) and/or Social Communication Questionnaire (SCQ) for autism spectrum disorder (ASD); the Conner’s Comprehensive Behavioural Rating Scale (CBRS) for attention deficit hyperactivity disorder (ADHD) (defined as T score > 70); the Strength and Difficulties questionnaire (SDQ) for behavioural screening; and Adaptive Behaviour Assessment system (ABAS) for adaptive functional skills.

67 (49 Male, 18 Females) MAE cases were recruited. The mean age of seizure onset was 33.9 (SD 14.8) months, and mean age at recruitment was 97.3 (SD 48.4) months. Seizure types were remarkably similar to previous published cohorts. Cognitive testing showed moderate to severe intellectual disability (IQ < 55) in 102/25 (40%), and 4/25 (16%) with mild intellectual disability (IQ 55–70). ASD symptoms were elicited in 206/4 (31.2%) cases through the 3di (9/22) and SCQ (16/61). Parents reported ADHD on the CBRS in 21/52 (41.1%) cases, with 7/52 (13.4%) reaching...
threshold for both parent and teacher CBRS (P < 0.0001). In the SDQ, high or very high scores were recorded in: conduct problems (19/60, P < 0.0001), hyperactivity (22/60, P < 0.0001), peer problems (26/60, P < 0.0001), prosocial problems (29/60, P < 0.0001) and psychosocial impact scores (35/60, P < 0.0001) compared to a normative population. In the ABAS, 36/59 (61.0%) reported extremely low adaptive scores (< 2nd centile) for conceptual, 25/59 (42.3%) for social and 42/59 (71.1%) for practical domains.

These findings reveal a surprisingly high severity and impact of neurodevelopmental comorbidity in MAE and highlight the need for comprehensive evaluation and continued monitoring to guide intervention.

p0200
FACIAL EMOTION PERCEPTION IN PEOPLE WITH EPILEPSY: A SYSTEMATIC REVIEW WITH META-ANALYSIS
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Purpose: The ability to perceive emotion is a fundamental social competence that develops from childhood into adulthood, and relies on a specialised, yet distributed, network of brain regions. Our aim was to determine whether facial emotion perception is impaired in patients with epilepsy, and related to epilepsy, treatment and demographic variables.

Method: Electronic databases were searched according to PRISMA guidelines. Thirty studies (27 adult studies and 3 child studies) met inclusion criteria, and comprised of patients with temporal lobe epilepsy (TLE; 24 studies), frontocentral epilepsy (FCE; 2 studies), genetic generalised epilepsy (GGE; 3 studies), and a mixed epilepsy sample (1 study).

Results: Meta-analysis revealed that compared to healthy controls (n = 739), patients with epilepsy (n = 821) displayed an overall deficit in facial emotion perception, as well as deficits of each individual emotion (happiness, sadness, surprise, fear, disgust, anger) examined. While the magnitude of the deficit was large in all epilepsy groups (Hedges g = 0.908 - 1.076), distinctive patterns of emotion-specific impairments were also found. Specifically, patients with TLE were significantly impaired on all emotions except surprise, while patients with GGE were significantly impaired on anger, disgust, and fear, but not happiness, sadness, or surprise. Meta-regression of emotion perception in patients with TLE revealed that younger age at testing was associated with lower accuracy. Other epilepsy, treatment and demographic variables (including side of seizure focus and surgical status) were not related.

Conclusion: Robust deficits in facial emotion perception are found in epilepsy, with broader emotion-specific deficits in TLE than GGE.

p0201
THE ACTUAL MECHANISM BY WHICH PHENYTOIN DISPLAYS MICHAELIS-MENTEN KINETICS
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Purpose: Phenytoin (PHT) may saturate the hepatic enzymes and therefore display a nonlinear concentration-dose relationship. This has been appropriately described by the Michaelis-Menten equation. However, an alternative hypothesis based on its ability of inducing efflux transporters was reported [Clin Pharmacokinet 50:75-80(2011)]. This inductive effect in rats was demonstrated to be time- and concentration-dependent [Pharmacol Rep 66:946-51(2014); Epilepsy Res 107:51-5(2013)].

Method: In order to evaluate this inductive-based mechanism in humans two different dosage regimes, both having the same input rate of 8.33 mg/h of PHT, were implemented in 6 healthy volunteers throughout a ten-day period, under a crossover design with a 5-day washout interval: A) 100 mg every 12 h, and B) 600 mg every 72 h. After the last dose, saliva and plasma PHT concentrations throughout time were measured.

Results: Treatment B yielded a higher (p < 0.01) mean plasma PHT concentration (3.85 ± 2.77 vs. 2.81 ± 1.99 mg/L). Secondary peaks were noticed after B. Being the liver the most relevant site where PHT is metabolized in humans, the induction of efflux transporter located at the apical side of the hepatobiliary membrane would deviate the drug from the inner space of the hepatocyte to the bile, and then recovered by the systemic space via intestinal reabsorption. Conversely, saliva-to-plasma drug concentration ratio was higher (p < 0.05) after treatment A (0.111 ± 0.019 vs. 0.089 ± 0.012). Since efflux transporters are also placed in the apical membrane of salivary ducts, a higher induction of their expression was attributed to the more sustained PHT level achieved under treatment A.

Conclusion: The final effect of increasing PHT concentration at the hepatocytes is a progressive loss of their metabolic capacity as it could be expected if the hepatic enzymes would become saturated. A higher brain-to-plasma transportation of PHT would be envisaged after frequent dosing.

p0203
ADVERSE EVENTS ARE THE MAIN REASON FOR NON-ADHERENCE TO PHARMACOLOGICAL TREATMENT OF EPILEPSY IN BRAZIL
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Purpose: Non-adherence rates among people with epilepsy (PWE) are widely variable, ranging from 26% to 95.4%. We aimed to identify non-adherence in Brazil, its predictive factors and its impact on patient’s management.

Method: A multicenter observational case-control study was conducted between March 2015 and October 2016, when 153 subjects were included. Subjects’ clinical-epidemiological data were surveyed along with the Morisky-Green Test (MGT), Liverpool Adverse Effect Profile (LAEP) and the Brief Medication Questionnaire (BMQ).

Results: 103 PWE and 50 controls with other chronic conditions were interviewed, both groups were matched according to age and socio-educational level. PWE were aged 36.5 ± 13.86 (range 18–67), 55% were women, mean age of epilepsy onset was 18.2 ± 12.5 years, 51% had uncontrolled seizures and 58% were in monotherapy. 74.8% of PWE were non-adherent to treatment according to MGT, while 74.0% among controls (p = 0.58); according to BMQ domains, “Recall barrier” was associated with non-adherence in 78% of PWE and 76% of controls (p = 0.84). Multiple binary regression analysis revealed only LAEP and self perception of frequency of forgetfulness on the last three months as the predictive factors for non-adherence [LAEP = OR 3.1 (95%CI = 1.2–8.3; p = 0.02] and forgetfulness [OR 17.2 (95%CI = 2.2–136.0; p = 0.007)]. Non-adherent subjects did not seek emergency treatment more than adherent ones.

Conclusion: Adherence assessment should be routine throughout epilepsy treatment as well as interventions aimed at improving it. Since adverse events are important predictors of adherence, they should be considered when choosing the initial antiepileptic drug.
p0206
USE PATTERN AND ADVERSE DRUG REACTION PROFILE OF NEWER AND CONVENTIONAL ANTIETEPILEPTIC DRUGS IN A TERTIARY CARE HOSPITAL
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Purpose: Newer anti-epileptic drugs (AEDs) are being preferred over conventional AEDs because of better safety profile and efficacy. The present study was conducted as part of Pharmacovigilence Programme of India and evaluated the use pattern and adverse drug reactions (ADRs) profile of AEDs prescribed in a tertiary hospital.

Method: This prospective, cross-sectional and observational study was conducted in persons with epilepsy (PWE) attending Neurology Outpatient Department, AIIMS, New Delhi from June 2014 to May 2016, who were presented with any ADR. Causality assessment of suspected ADRs was performed according to WHO-UMC scale.

Results: Of the 1452 PWE on AEDs, 905 were male; the ratio of adult- pediatric subject was 880/572; and 374 were on newer AEDs either as mono or polytherapy. Among PWE on monotherapy (34%), AEDs used were levetiracetam > valproic acid > carbamazepine > phenytoin > other AEDs. Commonly encountered ADRs in PWE on any AEDs vs. newer AEDs include anger and aggression (49.4% vs. 13.1%), somnolence (38.0% vs. 9.4%), memory loss (33.3% vs. 7.7%), tremor (16.8% vs. 4.1%), agitation (14.8% vs. 3.1%), appetite loss (14.3% vs. 3.8%), and hair loss (13.8% vs. 4.7%). Causality of ADRs revealed 81.7% were having possible, 16.6% probable, 1.0% unlikely and 0.7% certain in relation with AEDs. The major AEDs implicated for ADRs having certain and probable relationships are levetiracetam (39.4%), valproic acid (21.2%), phenytoin (18.3%) and carbamazepine (17.4%). Among these, the related AED was stopped (3.3 %), reduced in dose (96.3%) or continued as other (6.9%). All AEDs used were levetiracetam > valproic acid > carbamazepine > phenytoin > other AEDs. Commonly encountered ADRs in PWE on any AEDs vs. newer AEDs include anger and aggression (49.4% vs. 13.1%), somnolence (38.0% vs. 9.4%), memory loss (33.3% vs. 7.7%), tremor (16.8% vs. 4.1%), agitation (14.8% vs. 3.1%), appetite loss (14.3% vs. 3.8%), and hair loss (13.8% vs. 4.7%). Causality of ADRs revealed 81.7% were having possible, 16.6% probable, 1.0% unlikely and 0.7% certain in relation with AEDs. The major AEDs implicated for ADRs having certain and probable relationships are levetiracetam (39.4%), valproic acid (21.2%), phenytoin (18.3%) and carbamazepine (17.4%). Among these, the related AED was stopped (3.3 %), reduced in dose (96.3%) or continued as other (6.9%). All AEDs used were levetiracetam > valproic acid > carbamazepine > phenytoin > other AEDs.

Conclusion: ADR profile does not support the belief of lesser ADR with newer AEDs. In this study, levetiracetam is commonly prescribed newer AED and is typically associated with neurological ADRs. Thus the experience of better efficacy should still be the guiding consideration for AEDs use.

p0208
EPILEPTIC SPASMS AND TONIC SEIZURES IN CHILDREN WITH TUBEROUS SCLEROSIS COMPLEX: A NEW INDICATION FOR VIGABATRIN?
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Purpose: Vigabatrin (VGB) is recommended as first-line treatment for infantile spasms (IS) in Tuberous Sclerosis Complex (TSC). Outside of TSC, it is also approved as adjunct treatment for refractory complex partial seizures in adults, but other indications in pediatric patients with TSC are less known. Clinical experience in our TSC clinic suggested efficacy for epileptic spasms and tonic seizures, prompting the examination of VGB used for all indications other than infantile spasms.

Method: We reviewed 201 children with TSC seen in our Multidisciplinary Tuberous Sclerosis Program from 1995–2016 and identified 27 patients started on VGB after age 1 and collected data on demographics, history of IS, genetic testing, seizure types, age of onset, EEG prior to VGB and frequency of seizures targeted with VGB. Treatment variables included age of onset at VGB treatment, anti-epileptic drugs (AEDs) prior and during VGB use, the maximum dose of VGB, response to VGB, length of time from start of VGB to best perceived therapeutic response, timing of weaning of VGB, recurrence of seizures and medication regimen after the wean, and duration of follow up. Side-effects and ophthalmological surveillance during VGB treatment was reviewed.

Results: Six patients had insufficient data. In 21 patients, the indication for VGB was epileptic spasms (n = 13), tonic seizures (n = 5), both (n = 2), and status epilepticus (n = 1). The mean age of treatment onset was 4.0 years (range 1.1–18.3). All but one patient (95%) had a reduction in seizures. Ten patients (48%) became seizure free and four (19%) had an improvement of >90%. In nine patients, VGB was tapered successfully after 8–33 months. Side effects reported included rash (n = 1), behavioral decline (n = 1), and no retinal toxicity was detected.

Conclusion: In conclusion, VGB may be an effective and safe treatment for epileptic spasms and tonic seizures beyond the infantile age in patients with TSC.

p0211
EFFECT OF LEVATIRECETAM MONOTHERAPY ON COMPLETE BLOOD COUNT, IMMUNOGLOBULIN LEVELS AND LYMPHOCYTE SUBSETS IN CHILDREN AND ADOLESCENTS WITH EPILEPSY
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Purpose: The aim of this study is to investigate the effects of levatirecetam monotherapy on complete blood count parameters, immunoglobulin levels and lymphocyte subsets in children and adolescents with epilepsy.

Method: A total of 31 children and adolescents with epilepsy (23 generalized, 8 focal seizures; age range, 4–16 years; mean, 8.82 ± 3.92) and 43 aged- and sex- matched controls were included in the study. All the patients were investigated for frequency and types of infections in the past month and past year. Complete blood count parameters (haemoglobin, lymphocyte, leukocyte, neutrophil, platelet), immunoglobulin levels (IgA, IgM, IgG, IgE) and lymphocyte subsets (CD3, CD4, CD8, CD4/CD8 ratio, CD19, CD56, NKT cells and Treg cells) were measured in patients with epilepsy and those in controls.

Results: Both groups were similar in terms of frequency and types of infections in the past month and past year. There were no significant differences in complete blood count parameters, lymphocyte subsets, and immunoglobulin levels between patients with epilepsy and those in controls. In the epilepsy group, while complete blood count parameters and immunoglobulin levels were similar in patients with focal and generalized seizure, CD4/CD8 ratio was significantly lower in patients with focal seizure (p = 0.006).

Conclusion: This is the first study which evaluate the effect of levatirecetam monotherapy both on complete blood count, humoral and cellular immunity during interictal period in children and adolescents with epilepsy. It was shown that levatirecetam monotherapy did not increase the incidence of infection and there were no significant effects on humoral or cellular immune system in epileptic children and adolescents.
p0212
MODELLING COVARIATES WHICH INFLUENCE LAMOTRIGINE PHARMACOKINETICS IN PAEDIATRIC PATIENTS
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Purpose: Paediatric populations with epilepsy offer a specific challenge in dose individualisation since they undergo significant developmental changes from childhood to adulthood. Population pharmacokinetic modelling is able to analyze sparse data sets such as that frequently available in paediatric populations. This study investigated the population pharmacokinetics of lamotrigine, in a paediatric population.

Method: In this study, pharmacokinetic models were developed using nonlinear mixed effects modelling, NONMEM®, and used in the individualisation of new-generation anti-epileptic drug therapy in paediatric epilepsy. These models included the influence of covariates such as drug plasma concentration, age, body mass index and co-administered antiepileptic drugs.

Results: Seventeen patients were identified and plasma samples taken to determine various parameters including drug plasma levels needed in this study. Pharmacokinetic models developed using NONMEM® investigated the possible correlation of metabolising enzymes such as CYPs and UGTs, to population pharmacokinetics. The preliminary results obtained indicate that even though patients were of similar age and taking the same dose of LTG, plasma concentrations differed due to possible effect of these metabolising enzymes.

Conclusion: This research investigated how population pharmacokinetics can improve therapeutic outcomes for paediatric populations with epilepsy, by contributing to the individualization of drug therapy and development of personalised medicine.

p0214
SYSTEMATIC REVIEW OF ADJUNCTIVE PHARMACOTHERAPIES FOR PRIMARY GENERALIZED TONIC-CLONIC SEIZURES
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Purpose: This review compares the clinical efficacy and safety of adjunctive treatments for primary generalized tonic-clonic seizures (PGTCS) to assist decision-makers with making informed decisions on treatment and reimbursement.

Method: A systematic literature review was conducted by 2 reviewers searching Embase, Medline, and the Cochrane database. Inclusion criteria: randomized, controlled trials (RCT) of antiepileptic drugs (AEDs) approved for the adjunctive treatment of PGTCS; original research; phase III or phase II/III; primarily adult population; English language; and published in the years 1989–2014. Exclusion criteria: nonhuman; intravenous drugs or surgery; case reports; studies with less than 10 patients per arm; double-blind follow-up is less than 3 months; age groups cannot be clearly identified; and abstracts without full papers. Indirect treatment comparisons (ITC) were performed using a network meta-analysis approach based on Bayesian theory.

Results: Six trials were included, one each for: topiramate (TPM) [n = 80], lamotrigine (LTG) [n = 117], levetiracetam (LEV) [n = 164], lamotrigine-XR (LTG-XR) [n = 153], perampanel (PER) [n = 164], gabapentin (GBP) [n = 129]. LEV and PER were the only AEDs to report significant improvements over placebo on GTC seizure freedom. PER was the only AED with a significant improvement on total seizure freedom. A qualitative review of the individual adverse events (AEs) reveals a unique spectrum for TPM (gastrointestinal) and some similarities between LEV and PER (behavior). ITC results revealed no statistically significant differences between AEDs on 50% or 100% responder or seizure freedom variables for PGTCS or total seizures. No significant differences were observed between AEDs on withdrawal due to AEs.

Conclusion: ITC results did not show differences between AEDs on efficacy or withdrawal due to AEs. It is important to note that RCTs are not powered to show differences in ITCs. Qualitative reviews of between trial differences may be informative in making decisions to prefer some AEDs over others.

p0217
ANTIEPILEPTIC DRUG WITHDRAWAL FOR TERMINAL REMISSION IN PATIENTS WITH EPILEPSY IN THE GENERAL POPULATION
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Purpose: Rate, reasons and predictors of antiepileptic drug (AED) discontinuation for terminal remission in representative samples of patients with epilepsy are poorly understood.

Method: The history of AED usage in children and adults with epilepsy registered with 123 family physicians in an area of Northern Italy was recorded. Cumulative probabilities of AED withdrawal with specific reasons were estimated using cumulative incidence functions. The probability of withdrawing AEDs for terminal remission was evaluated. The roles of sex, age at diagnosis, seizure types, duration at diagnosis and syndrome were assessed with hazard ratios (HR) and 95% confidence intervals (95% CI).

Results: 731/747 individuals were treated with at least one AED. The three commonest drugs were valproate, carbamazepine and phenobarbital. Terminal remission was the most frequent reason for AED discontinuation followed by ineffectiveness and adverse events. The probability of withdrawing the first AED for terminal remission was 1.0% at one year and increased to 20.0% at twenty years. At 20 years, the variables associated with first AED withdrawal due to seizure freedom were age at diagnosis, sex and epilepsy syndrome. Corresponding rates for the second drug was 13.3% and for third drug 4.3%. The 20-year probability of withdrawal for terminal remission was 12.9% for carbamazepine, 14.8% for phenobarbital and 27.4% for valproate. Variables associated with drug withdrawal due to seizure freedom were sex for carbamazepine and age, sex and syndrome for valproate. No predictors were found for phenobarbital.

Conclusion: Terminal remission was the commonest reason for AED discontinuation, it could be predicted by age at diagnosis, sex and clinical characteristics and varies among drugs.
p0222
USE OF CANNABIDIOL (RSHO) IN THE TREATMENT OF REFRACTORY EPILEPSY (LENNOX-GASTAUT SYNDROME), EXPERIENCE OF 38 CASES
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Introduction: The LGS remains as one of the most severe childhood encephalopathies with high seizure frequency (sudden falls, myoclonic and tonic), progressive cognitive impairment and antiepileptic drugs (AED) resistance.
Method: Between January 2016 and February 2017 we included in the study 45 patients with Lennox-Gastaut Syndrome (According to the criteria of the ILAE) with persistence of various seizures per day despite taking at least three anti-epileptic drugs. Seven patients were excluded from the study (one having started with a THC-containing compound and six who decided not to start the treatment).
Result: The remaining 38 cases took cannabidiol 100 pure (RSHO 5000) in progressive doses of up to 5–7 mg/kg for at least 6 months of follow-up. All patients had imaging studies (CT or MRI) and at least two EEG studies. 50% presented hypoxic-ischemic encephalopathy or cortical malformations. All patients continued to take basal AED (3.7 per patient). The age was of 10.9 ± 6 years (23/38 patients are male). All patients had various types of seizures (3.5/patient), dominating the atonic (73%) and focal (86%). 4 patients were callotomized for refractory epilepsy. The age was of 10.9/C6. The remaining 38 cases took cannabidiol 100 pure (RSHO 5000) in progressive doses of up to 5–7 mg/kg for at least 6 months of follow-up. All patients had imaging studies (CT or MRI) and at least two EEG studies. 50% presented hypoxic-ischemic encephalopathy or cortical malformations. All patients continued to take basal AED (3.7 per patient). The age was of 10.9 ± 6 years (23/38 patients are male). All patients had various types of seizures (3.5/patient), dominating the atonic (73%) and focal (86%). 4 patients were callotomized for refractory epilepsy. The age was of 10.9/C6.

Conclusion: Addition treatment with 100% Cannabidiol is a good alternative for patients with LGS and reduces the use and potential effects of tetrahydrocannabinol (THC).

p0227
TOLERABILITY OF ANTIETEPILEPTIC DRUGS
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Purpose: To evaluate the rate of adverse effects in a cohort of adult patients with newly diagnosed epilepsy. We also aimed to assess the association between poor tolerability and associated factors, including individual antiepileptic drugs (AEDs), dosage, age, gender, epilepsy classification, psychiatric comorbidities and number of concomitant agents.
Method: We retrospectively reviewed the medical records of all newly diagnosed patients aged ≥18 followed up in the Epilepsy Unit for at least two years after starting AED therapy during a 30-year period from July 1982 until November 2012.
Results: The study cohort included 1526 patients aged 18 to 93 years (median 37 years). Overall, 849 (56%) were men and 1290 (84%) had focal epilepsy. The incidence of adverse effects was 28% (n = 815/2911). Tiredness was the most frequent problem associated with AED usage. The incidence was 5.2% (n = 152/2911), which represented 19% (n = 152/815) of all patients reporting adverse effects. Among seventeen different AEDs, lamotrigine appeared to be best tolerated (15%, n = 143/962), while retigabine had the highest level of reported adverse effects (42%, n = 8/19). The rash rate was higher with carbamazepine (6.6%, n = 33/496) than with lamotrigine (4.2%, n = 40/962). Levetiracetam was poorly tolerated in 9% (n = 46/514) of patients due to psychiatric side effects, which accounted for 41% (n = 46/112) of levetiracetam’s overall poor tolerability. Female gender, focal seizures and psychiatric comorbidities were associated with higher rates of adverse effects. Likewise, an increasing number of co-prescribed AEDs correlated with poor tolerability. However, older AEDs usage was not significantly associated with poorer outcomes.

Conclusion: The incidence of adverse effects with AEDs was 28%, of which tiredness was the most frequent problem. Lamotrigine was the best tolerated AED, while retigabine was associated with the highest rate of adverse effects. Poor tolerability was higher in females and in patients with focal epilepsy, psychiatric comorbidities and those established on AED polytherapy.
LACOSAMIDE IN PATIENTS WITH BRAIN TUMOR RELATED EPILEPSY: EFFECT ON SEIZURE CONTROL AND QUALITY OF LIFE
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Purpose: We propose a prospective study with a historical control group to evaluate the effect of Lacosamide (LCM) as add-on on seizure control and quality of life in patients with brain tumor-related epilepsy (BTRE). This study has been designed to test the superiority of Lacosamide over Levetiracetam as an add-on.

Method: We recruited 25 patients (M 18, F 7; mean age 41.9). Patients were evaluated at baseline, after 6 months and at final follow-up at 12 months. Patients underwent QoL tests and test for adverse events.

Results: Twelve patients had high-grade gliomas, thirteen low-grade gliomas. Thirteen patients underwent chemotherapy, three radiotherapy and five had disease progression. Four patients dropped out due to poor compliance and 1 for inefficacy. Mean number of seizures significantly decreased from baseline (9.4) to 3 months (0.8) (P = 0.005) and to 6 months (1.2) (P = 0.005). At final follow-up in the subgroup of 22 evaluable patients (i.e. LCM dose greater than 100 mg/day) 7 patients were seizure free, 12 patients have significant reduction of seizures ≥50%, 2 patients were stable and 1 patient number of seizures increased. The Responder Rate was 86.4%. No clinical side effects were observed. No significant differences were observed at 3 and 6 months for all QoL tests. We found a significant reduction in the mean score of Karnofsky Performance Status and Barthel Index between baseline and final follow-up (KPS p = 0.003; BI p = 0.007). Comparing the LCM with the historical group treated with LEV in add-on (n = 19), we observed that both drugs have comparable clinical efficacy.

Conclusion: Our preliminary data seem to indicate that LCM showed good efficacy in patients with BTRE and seems not to induce significant side effects. We did not observe any significant changes in QoL tests, indicating stability in all QoL domains explored, despite the objective worsening in their functional status.

AN OBSERVATIONAL, POST-MARKETING STUDY OF ADJUNCTIVE BRIVARACETAM IN PATIENTS WITH FOCAL SEIZURES IN EUROPE: INTERIM ANALYSIS OF 6-MONTH DATA
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Purpose: Brivaracetam (BRV), a selective, high-affinity ligand for synaptic vesicle protein 2A (SV2A), is a new antiepileptic drug (AED) for adjunctive treatment of focal (partial-onset) seizures in adults. This post-hoc analysis evaluated long-term efficacy and tolerability of adjunctive BRV in patients with baseline secondarily generalized tonic-clonic seizures (SGTCS; Type IC).

Method: Adults with focal seizures with SGTCS among their baseline seizures were identified from core Phase III studies (NCT00490035, NCT00464269, NCT01261325), as were those who entered the subsequent open-label, long-term follow-up (LTFU) studies (NCT00175916, NCT00150800, NCT01339559). Patients received BRV ≤200 mg/day during LTFU. Efficacy data for protocol-specified time points ≤60 months and tolerability data over 1–60 months of follow-up are reported for patients who had received placebo or BRV 50–200 mg/day in core studies.

Results: At core study baseline, patients had mean duration of epilepsy of 22.2 years; 28.4%, 38.9% and 32.8% had received 0–1, 2–4 and ≥5 previous AEDs. Baseline median seizure frequency/28 days was 8.1 (focal) and 3.0 (SGTCS only). Of 409 patients with baseline SGTCS, 325 entered LTFU studies. In the 12-, 24-, 36-, 48- and 60-month cohorts, respectively, 150, 89, 73, 68 and 57 patients had BRV exposure and seizure diary data, and ≥50% responder rates for SGTCS were 75.3%, 78.7%, 80.8%, 79.4% and 78.9%. Median percent reduction from baseline in SGTCS frequency/28 days was 81.1%, 84.0%, 89.2%, 91.0% and 90.6%, respectively. In 296 patients with SGTCS at baseline (safety population), incidence of treatment-emergent adverse events (TEAEs) over 1–60 months’ LTFU was 222/296 (75.0%); discontinuations due to TEAEs: 25/296 (8.4%); drug-related TEAEs: 11/296 (37.5%); serious TEAEs: 52/296 (17.6%); drug-related serious TEAEs: 14/296 (4.7%); deaths: 4/296 (1.4%).

Conclusion: Long-term adjunctive BRV treatment reduced SGTCS frequency and was generally well tolerated up to 60 months in patients with SGTCS at baseline. Study supported by UCB Pharma.
**p0236**

**BANISHING VALPROIC ACID DURING PREGNANCY: ALWAYS REWARDING? SEIZURE FREQUENCY AND ANTI-EPILEPTIC DRUG TREATMENT DURING PREGNANCY AND DELIVERY IN WOMEN WITH EPILEPSY – A RETROSPECTIVE SINGLE CENTER STUDY**

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**Purpose:** Antiepileptic drugs (AED) are common teratogenic drugs prescribed to women of childbearing age. AED can induce both anatomical and behavioral teratogenicity; the risk is markedly increased by the use of Valproic Acid (VPA). On the other hand, the benefit of preventing seizures by AED treatment during pregnancy is still controversial. Our primary goal was to observe and AED treatment policy regarding a relatively long period.

**Method:** We investigated all cases of female epileptic patients admitted for labor at the Rabin Medical Center, Petah Tikva, Israel, from 2005 to 2015.

**Results:** 297 deliveries were recorded in 235 women with known epilepsy. 135 labors occurred in 2005–2010 (27.7y) and 162 in 2011–2015 (32.4y; increase of 20%). The percentage of women experiencing seizures during pregnancy was 23.3% and unchanged during the observed period (2005–2010: 22.9% vs. 2011–2015: 23.0%; p = 0.92). A trend for decreased seizures at delivery was observed (13.3% vs. 10.5%) but not statistically by 50% regarding the two time episodes observed (18% vs. 9.3%; p = 0.05). The use of VPA for pregnant women with epilepsy was less (35% and 36% respectively; total: 60.9%). Their use did not change over the examined period (LTG: 35% vs. 36.4%; CBZ: 24% vs. 26%; used (35% and 36% respectively; total: 60.9%). We detected a general increase of pregnancies in epileptic patients during 2005–2015. There is a tendency for a reduction in seizure frequency on delivery without difference of seizures quantity during pregnancy. We can confirm a marked 50% decline in the use of VPA but with 20% elevation of AED combination use.

**Conclusion:** Perampanel shows large variation of its dose to serum concentration relationship depending on the concomitant AEDs, because its metabolism is highly susceptible to interactions with enzyme inducing drugs. Our findings show that therapeutic drug monitoring for perampanel is clinically useful to estimate CYP3A4-mediated metabolic reactions.

**p0238**

**TREATMENT WITH CANNABIDIOL (CBD) SIGNIFICANTLY REDUCES DROP SEIZURE FREQUENCY IN LENNOX-GASTAUT SYNDROME (LGS): RESULTS OF A MULTI-CENTRE, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL (GWPCARE4)**

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**Purpose:** Evaluate efficacy of CBD added to antiepileptic drug (AED) therapy for the treatment of seizures associated with LGS.

**Method:** Eligible patients were 2–55 years old and had a clinical diagnosis of LGS, ≥ 8 drop seizures during 4 week baseline (≥2/week), and documented failures on ≥ 1 AED. Patients were randomised (1:1) to receive 20 mg/kg/day CBD (oral solution) or matched placebo for 14 weeks (2-week titration; 12-week maintenance). The primary efficacy endpoint was change from baseline in drop seizure frequency over the entire 14-week treatment period for patients on CBD vs. placebo.

**Results:** 171 patients were randomised (86 CBD; 85 placebo); 14 CBD and 1 placebo patient withdrew. Groups were similar at baseline; mean age was 15 years (34% of patients ≥ 18 years) and median drop seizures/month was 74. Patients had previously taken a median of 6 AEDs, and were taking a median of 3 concomitant AEDs. CBD resulted in a significantly greater median percent reduction in monthly drop seizures than placebo (44% vs. 22%; p = 0.0135) and a significantly greater ≥ 50% responder rate (44% vs. 24%; p = 0.0043). The treatment difference was established in first 4 weeks of the maintenance period. Adverse events (AEs) were reported in 86% of CBD and 69% of placebo patients, and were mostly mild to moderate; those > 10% were diarrhoea, somnolence, pyrexia, decreased appetite, and vomiting. Treatment-related serious AEs were reported in 9 CBD patients and 1 placebo patient. Some elevations in transaminases were noted without elevations of bilirubin; most were on concomitant valproate and all resolved. There was 1 death (CBD group), considered unrelated to treatment.

**Conclusion:** Results from this trial suggest that CBD add-on therapy for the treatment of drop seizures associated with LGS may be efficacious, with more AEs than placebo, but generally well tolerated. (Funded by GW Research, Ltd; NCT02224690)
**Abstracts**

**p0240**

CANNABIODIL (CBD) IN DRAVET SYNDROME: A RANDOMISED, DOSE-RANGING PHARMACOKINETICS AND SAFETY TRIAL (GWP CARE1)

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**Purpose:** Evaluate the dose-ranging safety, tolerability, and pharmacokinetics (PK) of CBD in children with Dravet syndrome (DS)

**Method:** Patients aged 4–10 years completed a 4-week baseline period and were randomised 4:1 to 1 of 3 CBD doses (5, 10, 20 mg/kg/day) or placebo as add-on therapy for 3 weeks. CBD (25 or 100 mg/mL oral solution) was administered BID starting at 2.5 mg/kg/day and increasing by 2.5 mg/kg QOD to randomised dose. On Days 1 and 22, PK exposures were expressed as AUC(0-t). Dose proportionality was assessed on Day 22 by regression analysis. Adverse events (AEs) were recorded daily.

**Results:** 34 patients were randomised to CBD 5 mg/kg/day (n = 10), 10 mg/kg/day (n = 8), 20 mg/kg/day (n = 9), or placebo (n = 7). Patients took a median 3 antiepileptic drugs (AEDs). On Day 22, exposures to CBD and major metabolites increased dose-proportionally; there was minimal change in clobazam levels, but concentrations of clobazam’s metabolite, N-clobazam, increased independent of CBD dose, except in patients on stiripentol. There was no demonstrable effect on other AEDs (valproic acid, topiramate, stiripentol, levetiracetam). Most common AEs (CBD vs. placebo) were pyrexia (22% vs. 0%), somnolence (19% vs. 14%), decreased appetite (19% vs. 0%), and sedation (15% vs. 0%). Treatment-related serious AEs occurred in 2 patients on CBD and discontinuations due to AEs occurred in 2 patients on CBD. Increases in ALT or AST (levels > 3 × ULN) occurred in 6 patients on CBD, all on valproic acid; none had elevated bilirubin and all recovered.

**Conclusion:** CBD was well tolerated and 20 mg/kg/day was chosen for further development. Exposure to CBD and its metabolites increased dose-proportionally. A PK interaction of CBD on N-clobazam was observed, likely mediated through CYP2C19 inhibition, except with stiripentol, presumably from prior saturated inhibition of CYP2C19 by stiripentol. (Funded by GW Research, Ltd; NCT02091206)

**p0243**

EPIDEMIOLOGY IN PRECLINICAL EMERGENCY CARE IN EPILEPSY - VALIDATION OF PREHOSPITAL EPILEPSY EMERGENCY SCORE (PEES)

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**Purpose:** In preclinical emergency cases of sudden loss of consciousness it is difficult to distinguish between syncope and epileptic seizure. Therefore the risk of false diagnosis or mistreatment increases and this however leads to an increase in mortality and morbidity of status epilepticus. We aim to develop an easy to handle score for the preclinical setting which is able to discriminate between syncope and epileptic seizure based on easy clinical signs.

**Method:** Open label longitudinal epidemiological study with statistical analysis of all emergency care reports in patients with seizure or loss of consciousness in the emergency room in the time between 2016/01/01 and 2016/09/30. In the emergency room PEES will be raised by rescue service members of our medical team. After hospital stay and diagnostic investigation initial PEES will be compared to the final diagnosis in order to distinguish between syncope and seizure by a cut-off value ≥ 5 points in PEES. Additionally we will validate sensitivity and specificity.

**Results:** N = 141 are statistically analysed. Preclinical emergency medication given by rescue team n = 28 (20%), intravenous midazolam 62%, diazepam 35%, given by layman or family members n = 4 (5%), only lorazepam oral. Seizure associated injuries n = 27 (19%) from that 17% were serious cases with medical treatment consequences. Seizure relapse occurred in 3% during transportation to ER. The total-sum-score demonstrates results with respect to sensitivity 0.62 and specificity 0.71.

**Conclusion:** The PEES records basic clinical signs for both, syncope and epileptic seizures. By a cut-off value for seizures defined as 5 or more points the score system showed moderate sensitivity and better specificity. Due to the recent results under real conditions in the emergency room, the score should be tested in a field project in prehospital emergency situations. We expect even higher sensitivity and specificity.

**p0244**

SEROTONIN REUPTAKE INHIBITOR USE AND MORTALITY IN EPILEPSY: FINDINGS FROM A CONTEMPORARY LINKED ELECTRONIC HEALTH RECORDS COHORT STUDY

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**Purpose:** To examine whether serotonin reuptake inhibitors (SRIs) are associated with improved all-cause and possible seizure-specific mortality in patients with epilepsy.

**Methods:** We extracted a cohort of patients with epilepsy from The ClinicAI Research using Linked Bespoke studies and Electronic Health Records (CALIBER) resource. Active epilepsy patients were defined by failure to achieve 12-month seizure-freedom over the duration of follow-up. The outcomes were all-cause and possible seizure-specific mortality (a composite outcome) treating SRI use as a time varying covariate (exposure occurred after the second SRI prescription). Cox regression and competing risk models with Firth correction were used in these analyses.

**Results:** We identified 2,718,952 eligible patients in CALIBER of whom 16,379 (0.60%) had epilepsy and 11,938 had active epilepsy. Median age and follow-up were 44 (interquartile range [IQR] 30–62) and 5.9 years (IQR 2.7–10.2 years) respectively. A total of 1526 patients (1.3%) had at least two SRI prescriptions. The hazard of all-cause mortality was significantly elevated following a second prescription for an SRI (hazard ratio [HR] 1.61, 95% confidence interval [95% CI] 1.37–1.89; p < 0.001). A higher risk was found in 180,199 age, sex, and GP practice matched controls without epilepsy (HR 2.05, 95%CI 1.91–2.18; p < 0.001). There was no significant difference in the hazard of possible seizure-related death whether analysed by time- varying exposure to a second SRI (HR 1.01, 95% CI 0.46–2.20; p = 0.972) or during discrete 6- and 12-month epochs.

**Conclusion:** Patients with active epilepsy exposed to an SRI appear to have increased risk of all-cause mortality, though the risk is lower than that for a matched population without epilepsy. Randomized controlled trials are impractical based on these data, therefore indicating that large
studies with systematically collected clinical data are needed to shed further light on these findings.

p0248

ANTIEPILEPTIC DRUGS-INDUCED HYPONATREMIA: REVIEW AND ANALYSIS OF 560 PATIENTS

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Purpose: It has been supposed that eslicarbazepine acetate (ESL) might be an appropriate alternative to carbamazepine (CBZ) and oxcarbazepine (OXC) due to better efficiency. One crucial aspect of safety is the drug-induced hyponatremia. We investigated the impact on serum sodium levels in 560 adult patients under antiepileptic drug therapy including CBZ, ESL and OXC.

Method: We reviewed medical records of patients with epilepsy in our in-patient clinic for adults at our center in 2015. We analysed the serum sodium levels and attempted to identify the association between hyponatremia and various factors in epilepsy patients.

Results: Hyponatremia was present in 76 (14%) of our 560 patients. The hyponatremia was mostly mild (10%). After adjusting for age and gender, OXC and ESL remained a significant risk factor for hyponatremia. No statistically significant differences in frequency of hyponatremia between OXC (47%) and ESL (33%) groups were observed. We also found that the serum sodium level was correlated with the dose of OXC ($r = .19, p = .03$) and the blood serum level of OXC ($r = -.23, p = .01$) but not with the dose or the serum level of ESL. The multiple regression analysis identified the significant interaction between age and ESL on sodium serum level ($p < .03$), suggesting that the effect of age on the sodium serum level depended on whether or not the patients received ESL. In other words, elderly patients who received ESL were more susceptible to hyponatremia.

Conclusion: The frequencies of hyponatremia induced by ESL and by OXC are not different. Unlike the OXC-induced hyponatremia, the ESL-induced hyponatremia is not dose related and occurs more distinct in elderly epilepsy patients. In elderly patients ESL should be considered with caution.

p0251

BREAKTHROUGH SEIZURES - FURTHER ANALYSIS OF THE STANDARD VS. NEW ANTIEPILEPTIC DRUGS (SANAD) STUDY

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Purpose: A breakthrough seizure is an epileptic seizure that occurs following a period of seizure freedom on antiepileptic drugs. Despite the severity and consequences of breakthrough seizures very few publications exist that examine factors associated with a breakthrough seizure and outcomes following such a seizure. We therefore developed prognostic models for risk of a breakthrough seizure, risk of seizure recurrence after a breakthrough seizure, and likelihood of achieving 12-month remission following a breakthrough seizure.

Methods: We analysed data from the SANAD study. This long-term randomised trial compared treatments for patients with newly diagnosed epilepsy. Multivariable regression modelling was used to investigate how clinical factors affect the probability of each outcome.

Results: 34% of recruited patients had a breakthrough seizure. Of these, 44% achieved a subsequent period of 12-month remission. Significant factors for risk of a breakthrough seizure following 12-month remission were neurological insult, number of tonic-clonic seizures by achievement of 12-month remission, and time taken to achieve 12-month remission. Significant factors for risk of seizure recurrence following a breakthrough seizure were total number of drugs attempted to achieve 12-month remission, time to achieve 12-month remission prior to breakthrough seizure, and breakthrough seizure treatment decision. Significant factors for likelihood of achieving 12-month remission after a breakthrough seizure were gender, age at breakthrough seizure, time to achieve 12-month remission prior to breakthrough, and breakthrough seizure treatment decision.

Conclusions: The described models can be used to identify patients most likely to have a breakthrough seizure, most likely to have a seizure recurrence following a breakthrough seizure, and most likely to achieve 12-month remission following a breakthrough seizure. This will help to stratify patients for likely outcome following a breakthrough seizure, as for some the breakthrough heralds the development of treatment refractoriness, whilst for the majority seizure control will be regained.

p0252

A NATIONAL PROFILE OF NEURODEVELOPMENTAL DISABILITIES IN CANADIAN CHILDREN: DATA FROM THE NATIONAL LONGITUDINAL STUDY OF CHILDREN AND YOUTH

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Purpose: National data on the prevalence of various developmental disabilities in Canada are not presently available. There are larger implications for health care costs and development of targeted health care interventions.

Methods: We analyzed data from 3 cycles of Canada’s National Longitudinal Survey of Children and Youth. The presence of neurodevelopmental disabilities (NDD) was self-reported and included; Epilepsy, Cerebral palsy, Intellectual disability, Learning disability, Emotional and nervous difficulties. Information on parental income status (income adequacy groups; Low, Middle, High) and residence (Rural vs. Urban location) was also surveyed in cycle 3.

Results: Cross sectional prevalence rates for the four NDD in children from birth-15 years across cycle 1–3 of the NLSCY show an increasing trend over the years 1994 to 1999. Population based estimates were also calculated from Census data. There was a clear male preponderance observed across all the four neurological conditions surveyed. There was a statistically significant relationship between income adequacy and epilepsy (Low Exp(B)=1.105 (95% CI 1.053, 1.159), and emotional nervous disorders (Low, Exp(B)=1.50 (95% CI 1.03, 2.18; p = 0.035) High Exp (B)=0.55 (95% CI 0.41, 0.75; p = 0.001). Children in rural locations had a lower odds of learning disability (Exp(B)=0.73 (95%CI 0.58; 0.91), and emotional nervous difficulties (Exp(B)=0.68; 95% CI 0.48, 0.96; p = 0.030).

Conclusion: Prevalence rates show an incremental trend. Male children are more likely to experience NDD than females across the spectrum. Income adequacy (low income groups) carries higher odds of epilepsy and emotional nervous problems while children in rural locations carry lower odds for learning disabilities, emotional behavioural problems.
p0254
INCIDENCE OF ACUTE SYMPTOMATIC AND UNPROVOKED SEIZURES, EPILEPSIES AND EPILEPSY SYNDROMES IN A COHORT OF CHILDREN ACCESSING GOVERNMENT PRIMARY SCHOOLS AND ORGANIZATION OF SEIZURES AND EPILEPSIES USING ILAE 2010 SYSTEM: A STUDY IN SOUTH INDIA

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Purpose: There are no incidence studies of acute symptomatic seizures and unprovoked seizures and epilepsies in children from developing nations.

Method: Study cohort included 7408 children accessing education in 18 government primary schools in Hyderabad district, India. The children registered on rolls as on January 1, 2006 were followed through first to fifth standard for new-onset seizure between January 1, 2006 to December 31, 2012. The data collected included demographic data, seizure semiology, date of seizure, neurologic findings, CT and EEG findings, antiepileptic drugs, and follow-up data. The recent definition of epilepsy and the system for organization of seizures and epilepsies by ILAE (2010) were used to organize the seizure and epilepsies.

Results: During the study period, 58 children had new onset seizures: acute symptomatic seizures in 21 [annual incidence 40.5 (95%CI 25.1–61.9) per 100,000] and unprovoked seizures in 37 [annual incidence 71.35 (95%CI 50.2–98.35) per 100,000] children. Of the 21 children with acute symptomatic, in 19 it was due to NCC-solitary cysticercus granuloma [annual incidence 36.64 (95%CI 22.1–57.2) per 100,000]. Of the 37 children with unprovoked seizure, 30 (80%) met the criteria of the new definition of epilepsy. The annual incidence of epilepsy was 57.85 (95% CI 39.0–82.6) per 100,000 respectively. Using new organization system epilepsies were organized into (1) electro-clinical syndromes (genetic): 11 (36.6%), (2) non-syndromic epilepsy due to structural/metabolic lesions: 14 (46.6), and (3) non-syndromic epilepsies due to unknown cause: 5 (16.6%). The annual incidence rates per 100,000 were: genetic epilepsies, both focal and generalized, 21.21 (95% CI 10.6–38.0); epilepsies due to structural/metabolic: 27.0 (95% CI 14.8–45.3), and epilepsies due to unknown cause: 9.64 (95% CI 3.1–22.5).

Conclusion: This study suggests that the new definition of epilepsy and ILAE proposed organization of seizures and epilepsies can be practiced in the community-based studies with minimal data: seizure semiology, EEG and CT.

p0256
INCIDENCE OF SUDDEN UNEXPECTED DEATH IN EPILEPSY IN COMMUNITY-BASED COHORT IN CHINA

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Purpose: Sudden unexpected death in epilepsy (SUDEP) is associated to the high premature mortality observed amongst people with epilepsy. It is, however, considered a rare event in China, probably due to lack of awareness and limitation of studies in the country. We aimed to provide some initial estimation of the burden of SUDEP in China.

Method: We established a large Chinese community-based cohort of people with epilepsy between January 2010 and December 2011. For any participant who died during follow up, detailed information on cause of death was obtained using a specifically designed verbal autopsy questionnaire. All cases were reviewed by a multidisciplinary expert panel and re-investigated if necessary. SUDEP incidence rates were estimated and case details provided.

Results: The cohort consisted of 1,562 people with epilepsy and during a median 5 years follow-up, 72 deaths were reported. The all-causes death incidence was 11.23(95%CI 8.86–14.07) per 1,000 person-years. Fifteen of the deceased died suddenly and unexpectedly in a reasonable state of health in the week preceding death. We recorded detailed information of these 15 deaths. Thirteen were considered to be probable SUDEP and two possible SUDEP. The incidence of probable SUDEP was 2.03(95% CI 1.13–3.38) per 1,000 person-years and the incidence of all suspected (probable and possible) SUDEP was 2.34(95% CI 1.36–3.77) per 1,000 person-years.

Conclusion: The incidence of SUDEP was relatively high among Chinese people with epilepsy when compared with previous community-based studies from high-income countries. The burden of SUDEP in China requires assessments.

p0257
PREVALENCE, TREATMENT GAP AND MISCONCEPTIONS ABOUT EPILEPSY AMONG GENERAL POPULATION IN ECUADOR

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Purpose: To report epidemiological data from a cross-sectional door-to-door survey concerning prevalence, treatment gap and misconceptions about epilepsy in urban and rural areas in Ecuador.

Method: A study to determine the barriers to access to antiepileptic drugs was conducted in Ecuador from January 2015 until May 2016. A door-to-door survey was performed in Tunubamba (urban district in Quito city, Andean region) and Archidona (rural district in Napo province, Amazonian region). All study participants were 15 years of age or older and lived more than 6 months in the study areas. A probabilistic systematic sampling was used to determine the selected households. Participants were interviewed using a validated and standardized questionnaire for epilepsy in tropical countries. A neurologist evaluated all the suspected cases to confirm epilepsy diagnosis. Treatment gap was estimated to a direct method. A specific questionnaire was administered concerning knowledge, attitudes and practice toward epilepsy in general population.

Results: Two hundred eighteen suspect cases were identified from 1,531 screened subjects, and 17 cases were confirmed with epilepsy in the urban area. Two hundred fortythree suspect cases were identified from 1,551 screened, and 21 cases were confirmed in the rural area. The crude prevalence was 11.1/1,000 [confidence interval (IC) 95%, 5.8 - 16.3] in the urban area and 13.5/1,000 [IC 95%, 7.8 - 19.2] in the rural area. The treatment gap was 47.1% and 66.7% in the urban and rural area, respectively. Epilepsy was related to supernatural or insanity. Significant differences were found concerning misconceptions about epilepsy in the study areas and ethnic groups.

Conclusion: The crude prevalence is similar compared to reports from Latin America. Treatment gap continues to be a disturbing issue mainly in rural areas. Misconceptions about epilepsy compromise the access to
treatment. Thus, socio-cultural education strategies are needed to increase knowledge and understanding of epilepsy.

**p0268**

**POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME IN ACUTE CHILDHOOD LEUKEMIA**


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**Purpose:** Clinical and radiographic abnormalities of Posterior reversible encephalopathy syndrome (PRES) usually involve a transient course with favorable outcomes. However, clinical course of PRES varies, depending on the underlying diseases, especially, in hematologic-oncology patients. This study was designed to investigate clinical manifestations, radiographic features, predisposing factors and long-term neurologic and radiologic outcomes of PRES as a complication during treatment of acute childhood leukemia.

**Method:** 648 patients aged less than 18 years were treated for acute leukemia at the Department of Pediatrics, Seoul St. Mary’s hospital between January 2003 and May 2011. Among them, PRES was evident in 19 (12 males, 7 females) patients who were monitored for an average of 40.3 months after developing the complication of PRES. A retrospective chart review was conducted on these patients to evaluate demographic data, primary diagnoses, treatment protocols, clinical manifestations, types of acute therapy, brain MRI and EEG findings, and neurologic and seizure outcomes.

**Results:** The mean ages at time of diagnosis of PRES and primary leukemia were 6.7 years and 5.4 years, respectively. Seizures comprised the most common clinical sign (18 cases), followed by headache, confusion, or visual disturbance. Hypertension was observed before the onset of PRES in 6 patients. Among 18 patients who manifested seizures, 9 required long-term anticonvulatant therapy because of continued epileptiform discharges in EEG or repeated seizure episodes. 3 patients manifested recurrent seizures although they were receiving more than three kinds of antiepileptic drugs. High signal intensities were observed at the posterior parietal lobe (16 cases) or occipital lobe (19 cases) in brain MRI.

**Conclusion:** The main predisposing factors for PRES during induction chemotherapy seemed to include all chemotherapy regimens. When PRES develops as a complication of acute childhood leukemia, long-term anticonvulatant therapy is frequently required, and intractable seizures may develop.

**p0269**

**CLINICAL FEATURES OF SEIZURES IN HIV PATIENTS WITH TOXOPLASMA ENCEPHALITIS**


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**Purpose:** Toxoplasma encephalitis in human immunodeficiency virus (HIV) patients have a higher burden of seizures, but few studies in Africa have examined seizures due to toxoplasmosis in HIV infected patients.

**Methods:** A prospective study was conducted in Yaounde central hospital during 2 years. the aim of the study was to determine the epidemiology, clinical and CT-scan characteristics of seizures due to toxoplasma encephalitis in HIV infected patients.

**Results:** Among a total of 60 HIV infected patients with toxoplasma encephalitids; 24 (40%) had new-onset seizures, none of these individuals had epilepsy before HIV infection. Most patients exhibited low (below 100, n = 16) CD4 counts. The most common seizure presentation was partial (n = 14), followed by secondarily generalized (n = 6) and generalized seizure (n = 4). Imaging studies revealed brain lesions in all patients, all were heterogeneous with contrast enhancement in 80% of cases. Lesions were multiple, supratentorial in 70% of cases. Most seizures were controlled without antiepileptic drugs (n = 18) or with a single antiepileptic drugs (benzodiazepine n = 3, valproic acid n = 3 for a few weeks). All patients received treatment for toxoplasmosis and antiretrovirals.

**Conclusion:** Often occur in severe immunosuppressive conditions, new-onset seizures due to toxoplasma encephalitis in HIV infected patient are common, with a benign clinical course and few complications, these seizures do not require antiepileptic drugs.

**p0270**

**REDUCING THE EPILEPSY TREATMENT GAP IN RURAL NEPAL USING EPILEPSY FIELD WORKERS AND TELEPHONE TELEMEDICINE**

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**Purpose:** The epilepsy treatment gap is over 50% in poorer countries, often because of bad access to doctors. The WHO has suggested that non-physician health workers take a bigger role in management.

**Method:** We have trained two people with no previous training in health as epilepsy field workers (EFWs) and used them to identify people with epilepsy in their surrounding villages. They used an app to determine if epileptic seizures were likely. They then contacted a neurosurgeon by telephone. The neurosurgeon suggested treatment which the EFW started. The patient was reviewed by the neurosurgeon face-to-face to decide whether the management was appropriate.

**Results:** The EFWs identified 62 people with possible epilepsy during nine months (from May 2016 to January 2017). Out of 62 patients 16 were already diagnosed and treated as epilepsy while 46 were newly identified; two-thirds were male, most were 20–40 years old (53%, mean age 25 yr) and more than half (54%) were married. Of the 46, 33 had app scores suggesting epileptic seizures (≥80), 3 patients had scores which suggested non-epileptic episodes (<30) and in 10 the app score was uncertain (30–80). Telephone consultation suggested that five patients had epileptic events not requiring treatment (febrile convulsions, alcohol withdrawal seizures) while 14 had non-epileptic conditions like faints or non-epileptic attack disorder. Twenty-seven had epilepsy which was untreated. After in-person examination diagnosis and management was appropriate in 78%.

**Conclusion:** The epilepsy treatment gap can be significantly reduced in a rural setting by EFWs using mobile apps with telephone telemedicine to a specialized clinician. Regular training of EFWs and frequent communication with a physician might increase the reliability of management. This is a promising means to identify and treat epilepsy in rural settings in a country like Nepal where access to health care is very limited.
Abstracts

p0271 QUALITY OF CARBAMAZEPINE IN RESOURCE-LIMITED SETTINGS: ANCILLARY RESULTS FROM THE QUALADF (QUALITY OF ANTI-EPILEPTIC DRUGS IN SUB-SAHARAN AFRICA) STUDY

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Purpose: Epilepsy is a common disorder affecting 70 million people worldwide, with 90% in resource-limited countries. In these countries, few standard antiepileptic drugs (AEDs) are used and concerned with quality issues. Often, the attention is focused on assay of active ingredient (AI). However, other pharmaceutical parameters are important, such as the dissolution profile that could be influenced by environmental factors. The main objective was to assess the stability of AEDs under stressed conditions.  

Methods: This study has been performed on 8 solid formulations of carbamazepine. Eight were gathered on the field in Madagascar (4 manufactured in China, 1 in India) and three manufactured in Europe were purchased directly from the manufacturer. The samples were exposed during three months to: (i) 45°C + 75.0% of relative humidity (RH) and (ii) 45°C + 99.9% RH. Assay of AI (by liquid chromatography and UV detection), dissolution and chemical stability measured by attenuated total reflection-Fourier transform infrared spectroscopy and differential scanning calorimetry were performed at T0 (baseline), one (T1) and three months (T3).  

Results: The assay of AI was successful for all the samples within the three months. No chemical degradation of the AI has been observed between T0 and T3. The dissolution profile was unsatisfactory for all samples from India and China, with a final proportion of dissolution ranging under 73.3% to 3.2% (Norms: 75–100%). At T0, all samples showed the presence of the anhydrous polymorphic form III of carbamazepine. At T1 and T3, a dihydrate polymorphic form has been observed in sample from China and India.  

Conclusion: The modification of dissolution behaviors was due to the polymorphism of the carbamazepine. These results have shown that an inhomogeneity of manufacturing process could lead to inefficient product unable to release the AI, but further analyses will have to be performed to strengthen our conclusion.

p0274 HISTORY OF SURGERY FOR TEMPORAL LOBE EPILEPSY

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Purpose: The current work reviews the historical advancement from trepanation for the treatment of epilepsy in ancient times to stereotactic laser thermo-ablation for the treatment of drug-resistant TLE in the modern world.  

Method: This is a literature review.  

Results: Evidence of trepanation (making a Burr hole in the skull) was found in the excavated prehistoric human remains from Neolithic times, and cave paintings suggest that ancient people believed this procedure would cure epilepsy, migraines, and mental disorders; though, no firm evidence has been discovered to support any medical explanation for trepanation. Evidence for temporal lobe epilepsy (TLE) goes back thousands of years to the pharaohs of ancient Egypt’s eighteenth dynasty. The collaborative work of a team led by Penfield and Jasper in 1930s helped to define the significant role of neurophysiological studies in epilepsy surgery. As a result, the importance of removing the mesial temporal structures in patients with TLE became established. The first series of temporal lobectomies for the treatment of epilepsy were reported by Penfield and Flanigin (1950). They selected their patients for surgery based on the seizure pattern, EEG and pneumographic and roentgenologic evidence. Their practice was curative for 53% of their patients, and an additional 25% of their patients experienced a worthwhile (≥50%) improvement in seizure frequency. Subsequently, Bailey and Gibbs (1951) promoted identifying TLE (formerly called “psychomotor epilepsy”) by EEG and treating it by temporal lobe resective surgery.  

Conclusion: As neuroscience related technologies have progressed, our understanding of the underlying causes and pathophysiology of epilepsies has advanced tremendously. In addition, with the help of these ancillary technologies we may now offer surgery as a therapeutic option to more patients who are suffering from drug-resistant epilepsy. However, the progress in technologies has not been matched by the degree of improvement in surgery outcome in these patients.
FOCAL CORTICAL DYSPLASIA: SEIZURE FREEDOM AND IMPACT ON QUALITY OF LIFE AFTER SURGERY

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**Objective:** Focal Cortical Dysplasias (FCDs) represent a common cortical disorder underlying drug-resistant focal epilepsy. Data are still scarce concerning comparison between patients harbouring Type II FCD operated at young and adult age, investigating whether age at surgery is an important factor influencing surgical outcome. Aim of our study is comparing presurgical clinical features and surgical outcomes of patients with FCD type II that underwent surgery at an earlier or late age.

**Method:** We retrospectively analyzed 1660 consecutive patients operated at “Claudio Munari” Epilepsy Surgery Centre. Among 289 patients (17.4%) with neuro-pathological diagnosis of FCD, we included two different groups, the first one including patients operated on at less than 6 years, the second sharing the same onset age but with delayed surgery after the age of 20. Seizure characteristics, neuropsychological and post-operative seizure outcome were evaluated by study groups.

**Results:** Forty patients underwent surgery before age of 6 and 66 patients after age of 20. Surgical outcome was favorable in the population (72.6% were classified in Engel’s Class IIa-Ic), independently from age at surgery. In children group, 32 patients were classified in Class I, including 30 (75%) children in classes Ia and Ic. In adult group, 53 belonged to Class I of whom 47 (71%) patients to classes Ia and Ic. No statistically significant differences were found between groups concerning presence of permanent complications, surgical outcomes and AEDs withdrawal with age at surgery.

**Conclusion:** Our results indicate that there is no difference between the groups, permitting to hypothesize outcome depends mainly on the histological findings and not on timing of surgery.

SURGICAL OUTCOMES IN TWO DIFFERENT AGE GROUPS SHARING FOCAL CORTICAL DYSPLASIA TYPE II: ANY REAL DIFFERENCE?

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**Objective:** To compare seizure outcomes and neurological complications in dominant vs. non-dominant temporal lobectomy for temporal lobe epilepsy.

**Method:** Retrospective case note analysis of patients undergoing temporal lobectomy for TLE between 2008 and 2016. Engel Classification at one year follow up was recorded. Surgical and neurological complications were documented with a special focus on speech outcomes.
Dominant side surgery was restricted to 4.5 cm from the pole; non-dominant side surgery was extended to 5.5–6 cm.

**Results:** A total of 78 patients (41 adults and 37 children) underwent temporal lobectomy for epilepsy (40 female, 38 male). Age range 9 months - 60 years. Dominant side surgery in 32 cases (18 adults; 14 children). Histology included hippocampal sclerosis, focal cortical dysplasia, cavernomas and tumours. Good seizure control (Engel I and II) was achieved in 80% patients overall [35/37 (95%) paediatric cases and 27/41 (66%) adults]. 78% dominant side surgery had good seizure outcome compared to 83% non-dominant cases. 8 patients experienced expressive dysphasia (6 adults, 2 paediatric). 1 adult and 1 paediatric cases had persisting expressive dysphasia. Both were dominant side cases. 9 patients experienced visual field deficits (3 adult, 6 paediatric). This persisted in 2 adult and 5 paediatric patients. 5 patients had frontalis weakness, all resolved. 2 patients developed hemiparesis (1 adult, 1 paediatric). These were due to capsular infarcts. The paediatric case fully recovered. The adult case experienced ongoing hemiparesis. 2 paediatric patients developed pseudoneurog STORAGE economies; 1 required a subgaleal shunt. 1 adult and 1 paediatric patient suffered 4th nerve palsies. The adult case still persists 2 years post-operatively although has significantly improved. 2 patients had extra-axial collections requiring surgical evacuation.

**Conclusion:** Temporal lobe epilepsy surgery offers good seizure control with an acceptable complication profile. No statistical difference in seizure control was noted between dominant and non-dominant temporal lobectomy.

**p0285**

**DIAGNOSTIC AND OUTCOME AFTER SURGICAL TREATMENT OF TEMPORAL EPILEPSY IN CHILDREN**

**Purpose:** Demonstrate the results of complex diagnostic and surgical treatment in children with medically intractable temporal epilepsy.

**Method:** A retrospective study was analyzed a surgical treatment in 80 (41 male) children with medically intractable temporal epilepsy at the child’s department of the Russian Neurosurgical Institute in honor of professor Polenov A.L. during the period from 2011 to 2016. The age of the patients was 3 to 17 years. The follow-up was 1 to 6 years (on average 3.3 years).

**Results:** The duration of disease was from 3 months till 16 years (on average 71.75 months). According to magnetic resonance imaging (MRI) of 60 (75.9%) patients structural changes of the brain were revealed. Local epileptic foci in temporal lobe were found in 60% and 30% by EEG monitoring and ECoG respectively. Bitemporal foci were found in 10% cases by electrophysiological investigation. Epileptic foci were localized by PET in 28 of 29 cases. Right-side resection was performed in 34 (42.5%) cases, left-side resection was done in 46 (57.5%) cases. Favorable long-term outcome of surgical treatment epilepsy (class Engel I) are reached at 72.5%. Pathomorphologic investigation revealed: focal cortical dysplasia- 48.75% of cases (FCD Ia-2, FCD IIa-9, FCD IIIb-6, FCD IIa-1, FCD IIIb-5, FCD IIIc-1, FCD III-15), epileptic encéphalopathy- 11 (13.75%) cases, benign tumors- 9 (11.25%) cases, cystic-atrophic changes- 6 (7.5%) cases, malignant tumors of the brain- 4 (5%) cases, vascular malformations-2 (2.5%) cases, tuberous sclerosis- 2 (2.5%) cases, others- 7 (8.75%).

**Conclusion:** The most important predictive factors of achievement favorable results after surgical treatment of epilepsy are: identification of epileptogenic morphological changes of the brain, completeness of resection of the epileptic and epileptogenic zone, and lack of seizures after surgery as well.

**p0288**

**INDIRECT REVASCULARIZATION SURGERY IN CHILDREN WITH SYMPTOMATIC EPILEPSY**

**Purpose:** To study indirect revascularization surgery outcomes in patients with symptomatic epilepsy which started as a result of moyamoya disease or syndrome, ischemic strokes, birth traumas and hemorrhages.

**Method:** We analyzed study outcomes and surgical results in 11 patients who had been receiving treatment at the RNI Department of Pediatric Neurosurgery from 2002 to 2016 with effects of perinatal traumatization (7 patients) and effects of ischemic stroke (4 patients). We used neurologic and neuropsychological examinations, neurosonography, EEG, CT and MRI data, triple ultrasonography of the neck and head vessels, CT and MR angiography. MRI brain perfusion. Revascularization surgery as a method of choice was applied in 3 patients with moyamoya disease, in 8 patients - as a supplement to cysts excision, in 2 patients - as a supplement to ventriculoperitoneal shunting, in 2 patients - as a supplement to electrocorticography and seizure focus excision, in 2 patients - as a supplement to chronic hemotoma drainage.

**Results:** According to Engel epilepsy surgery outcome scale, Class I outcome was achieved in 7 children, 2 of which had moyamoya disease. Class II and Class III were achieved in 1 patient each. Two patients with effects of ischemic stroke showed negative dynamics in the form of increase in seizure frequency and transformation of the seizures structure.

**Conclusion:** Indirect revascularization have a positive impact on clinical and electroencephalographic manifestations of the disease, which indirectly indicates the value dissemina processes in the pathogenesis of epilepsy. The occurrence of epileptic seizures in some patients after revascularization operations due to changes in perfusion of the brain and the local irritative effect of the anastomosis. Indirect brain revascularization, removal of cysts, scars, calcifications (epileptic foci) are the method of choice in the treatment of occlusally processes in combination with epileptic seizures.

**p0291**

**LONG-TERM INVASIVE MONITORING VS. INTRAOPERATIVE CORTICOGRAPHY: DIAGNOSTIC EFFICACY IN SYMPTOMATIC EPILEPSY**

**Purpose:** In tumor related epilepsy (TRE) electrocorticography (ECoG) is routinely used for localizing the epileptogenic zone during surgery. At present the efficacy of this technique is debated. It is considered by some authors that epilepsy surgery approach for TRE may be beneficial for the patients. In this study we investigated the efficacy of intraoperative ECoG (iECoG) vs. prolonged extraoperative ECoG (peECoG).

**Method:** The study included 63 patients (37 females, age 26–76) with TRE assigned for presurgical evaluation and tumor resection at Prof. Polenov’s Neurosurgical Institute. All patients had epileptiform patterns on presurgical EEG-recordings, except one patients with left temporal lobe tumor and 10-year history of seizures.

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Results: In these patients during iEEG epileptiform activity was detected in 18 patients next to the tumor margin and these areas were resected with regard to eloquent cortex. Postoperatively, in 13 patients epileptiform activity was recorded on EEG. The patient without any epileptiform activity on EEG and video-EEG-monitoring was assigned for a staged surgery. As a first stage after the inconclusive iEECoG a subdural-grid-electrode (4x5 contacts) was implanted covering the presumable location of the tumor and adjoining areas. Prolonged electrocorticography was recorded for the next few days after the implantation of grid-electrodes until the area generating interictal epileptiform discharges was defined by neurophysiologists. This area was located beyond the standard margins of tumor resection and did not overlay any eloquent zone. During the second stage the tumor and the defined area were resected. No signs of epileptiform activity were registered in any accessible area of the cortex after resection. Postoperative EEG did not show any epileptiform patterns.

Conclusion: This observation suggests that in the context of prolonged TRE long-term invasive monitoring may be superior to traditional intraoperative EC0G, although a long-term follow-up is necessary to evaluate the seizure outcome.

p0295
EFFECTIVENESS OF TRANSCRANIAL MOTOR EVOKED POTENTIAL MONITORING DURING THE SURGICAL TREATMENT OF MESIAL TEMPORAL LOBE EPILEPSY

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Purpose: Anterolesional temporal lobectomy (AMTL) is the most commonly performed standard surgical procedure in patients with temporal lobe epilepsy. However, this has been associated with the occurrence of some rare but potentially serious motor deficits. We have assessed the effectiveness of transcranial motor evoked potential (TcMEP) monitoring and its influences on surgical complications after temporal lobe resection for the treatment of mesial temporal lobe epilepsy.

Method: We have evaluated motor deficits occurred before and after the adaptation of TcMEP monitoring to AMTL in patients with temporal lobe epilepsy during the period between January 1, 1995, and February 28, 2017. A total intravenous anesthesia was induced and maintained with continuous infusion of propofol and vecuronium and supplementation with intravenous opioid. Transcranial motor stimulation was carried out using subdural electrodes placed at C3 and C4 positions by constant voltage stimulation and MEP responses was recorded in the bilateral upper extremity muscles and lower extremity muscles. A more than 50% loss of MEP amplitudes compared with baseline data was used as warning criteria and promptly reported to the epilepsy surgeon. Neurological examination focused on the motor status was evaluated preoperatively, immediately after surgery, one day after surgery, and at discharge.

Results: Before the introduction of Tc MEP, a newly identified motor deficit was observed in 7 of 593 patients. On the other hand, no new motor deficit was occurred in 290 patients operated under Tc MEP monitoring. More than 50% decrement of MEP was recorded in 8 patients, and recovered in all after prompt corrective procedures by the epilepsy surgeon.

Conclusion: Transcranial MEP monitoring is a reliable and reproducible modality for the evaluation and prediction of the possible motor deficits during epilepsy surgery. The motor deficits will be significantly diminished through prompt corrective measures under the control of TcMEP monitoring during the epilepsy surgery.

p0296
OUTCOME AND PROGNOSTIC FACTORS OF EPILEPSY SURGERY IN CHILDREN WITH FOCAL CORTICAL DYSPLASIA

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Purpose: Focal cortical dysplasia (FCD) is the most common cause of intractable focal epilepsy in children. Epilepsy surgery is one of the valuable treatment options to achieve seizure freedom in these intractable focal epilepsy patients. We aimed to analyze surgical outcome and prognostic factors of epilepsy surgery in children with FCD.

Methods: Eighty four children who had resective epilepsy surgery from January 2004 to December 2013, histologically proven FCD, and a follow-up period of at least 2 years were included. Medical records regarding demographics, epilepsy details, types of FCD, presurgical evaluations, longitudinal analysis of seizure control, and postoperative complications were retrospectively analyzed.

Results: The mean age at epilepsy onset was 5.2 years and the mean age at epilepsy surgery was 10.7 years. The mean postoperative follow-up duration was 5.2 years. Patients with FCD II had significantly early onset of epilepsy, higher seizure frequency, and underwent surgery at a significantly younger age compared to the other types. Of 84 patients, Engel class I was achieved in 66% of patients at postoperative 1 year, 60% at
Conclusion: Postoperative seizure outcome was favorable in children with FCD. Comprehensive presurgical evaluations and multidisciplinary team approach would enhance the chance for detecting epileptogenic region associated with cortical dysplasia. Constant and systematic presurgical, or surgical variables to predict postoperative outcome would help selecting the ideal candidate for epilepsy surgery.

p0298
PRESURGICAL FEATURES AND OUTCOMES IN CHILDREN WITH FOCAL CORTICAL DYSPLASIA
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Purpose: The aim of the study was to characterize a cohort of FCD pediatric patients according to clinical, EEG, neuro-imaging, neuropsychological features, and surgical outcome.

Method: We retrospectively analysed consecutive children who undergone to surgical treatment from 2009 to 2015 with untreated focal epilepsy and a histopathologic diagnosis of FCD with at least 12 months follow-up.

Results: Forty-one children were identified. FCD type I was identified in 8, FCD type II in 19 patients and FCD III in 14. The mean age at seizure onset was 4.45 years (range, 0.5 -15): FCD III patients were significantly older than FCD I and II at epilepsy onset (p = 0.035). A developmental delay and an IQ less than 70 was more frequent in FCD I patients (p = 0.0008 and p = 0.002). Seizure frequency was higher in FCD I and II (p = 0.0003). Slow EEG abnormality were significantly more common in patients with FCD type I (p = 0.013) while a normal EEG was more frequent in FCD III patients. FCD I brain MRI were characterized by regional reduction of the white matter volume while FCD type II was characterized by increased cortical thickness, transmantle sign, grey matter signal change in FLAIR. FCD III had the same MRI characteristic of FCD. A binomial logistic regression was performed in order to find prognostic factor: incomplete resection of epileptogenic area and long disease duration before surgery were poor independent outcome predictors on multivariate analysis.

Conclusion: We confirmed the presence of important differences in children with distinct FCD subtypes.

p0300
MEANINGFUL COGNITIVE DECLINE AFTER MESIAL TEMPORAL LOBE EPILEPSY SURGERY IN BRAZILIAN PATIENTS
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Purpose: To investigate if subjective perception of cognitive decline correlates with objective cognitive decline in neuropsychological tests (NPT) following surgery and to determine the predictors of meaningful NPT impairment in Brazilian patients submitted to mesial temporal lobe epilepsy (MTLE) surgery.

Method: Forty-eight adult patients with MTLE (27 right HS, and 23 male) were classified as reporting (Decline group, n = 40) or not (No-Decline group, n = 40) a cognitive function decline based on the changes in their scores of the cognitive function domain of QOLIE-31 applied before and one year after surgery. Objective cognitive changes determined by the difference between the baseline pre-surgical raw scores of NPT were compared between the Decline and No-Decline groups. Sensitivity, specificity, and predictive values at the best cutoff points of the ROC curve (95% CI) were determined for the NPT significantly associated with cognitive decline reported by patients.

Results: Among the 25 cognitive tests analyzed, only baseline-retest difference in the Boston Naming Test (BNT) showed a concordance with the cognitive decline reported by patients. A reduction of more than 7 points in the raw score of BNT after surgery showed 88% of sensitivity and 50% specificity for meaningful cognitive function decline to the patient. Left-sided surgery and age > 40 years were more associated with a meaningful BNT decline reported by patients (overall accuracy of 91.7%).

Conclusion: Similarly to American patients, the BNT decline is the only meaningful NPT impairment in Brazilian patients after surgery. Surgical side and age are good predictors for no-decline in the BNT (95%), but showed a lower accuracy to predict its decline (75%). Our findings reinforce the external validation for the BNT as a patient centered measure of cognitive outcome with implications for the surgical management of MTLE patients.
**Abstracts**

p0306 EARLY-ONSET EPILEPSY AND SEVERE COGNITIVE IMPAIRMENT IN SIX PATIENTS WITH THE DE NOVO P.GLU590LYS VARIANT OF CUX2

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**Purpose:** Cut homeodomain transcription factor CUX2 plays an important role in dendrite branching, spine development, and synapse formation in layer II-III neurons of the cerebral cortex. Abnormal dendrites and synapses in Cux2(-/-) mice correlate with reduced synaptic function and defects in working memory. A de novo CUX2 p.Glu590Lys variant was reported in two patients involved in large-scale whole-exome sequencing (WES) studies on intellectual disability and epileptic encephalopathies. We report on clinical data of six patients carrying the de novo p.Glu590Lys variant.

**Methods:** We reviewed clinical, MRI and EEG data from 6 patients, including 2 previously reported and 4 additional cases. The p.Glu590Lys variant was identified by WES in 3 and through a targeted gene panel in including 2 previously reported and 4 additional cases. The p.Glu590Lys variant was significantly lower than that from SME, while the level of normal transcripts from p.Glu590Lys was significantly lower than that of Wild-type (WT). Mutation c.4853-25T>A resulted in 28.8% reduction of the normal transcripts than that from WT, and incomplete penetrance was observed in the family.

**Conclusion:** SCN1A intronic mutations found in pGlu590Lys extended the spectrum of SCN1A-associated epilepsy. It provides direct evidence and new insights into the mechanism that decreased expression of SCN1A, besides null expression that leads to haploinsufficiency, is associated with phenotype variation of epilepsy.

p0307 LESS DESTRUCTIVE AND INTRONIC SCN1A MUTATIONS ARE ASSOCIATED WITH PARTIAL EPILEPSY WITH ANTECEDENT FEBRILE SEIZURES

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**Purpose:** Partial epilepsy with antecedent febrile seizures (PEFS+) is common clinically. SCN1A mutations located in the intronic regions are mostly associated with severe myoclonic epilepsy in infancy (SME). It is suspected that SCN1A intronic mutations are also associated with milder PEFS+ and lead to epileptogenesis by affecting splicing but differ from SME.

**Method:** SCN1A intronic mutations were scanned in patients with PEFS+. The consequence of SCN1A intronic mutations and their impact on splicing were investigated qualitatively and quantitatively by using an in vitro minigene strategy. Mutations at variant splice-site junctions (ISJ), which were identified in SME and located within the minigene systems, were selected for comparison.

**Results:** Among the 27 heterozygous SCN1A mutations identified in 238 unrelated patients with PEFS+, three were outside exons. c.473 + 5G>A and c.473 + 5G>C were 3 bp away from ISJs; c.4853-25T>A was located deep in intronic sequences. Two minigene systems containing c.473 and c.4853 were established according to these mutations and two SME associated hot-spot mutations c.602 + 1G>A and c.4853-1G>C. All these mutations resulted in aberrant splicing, as shown by abnormal bands of RT-PCR products, indicating frameshift and truncation of Nav1.1 proteins. Mutations from PEFS+ produced normal transcripts also, while mutations from SME produced only aberrant transcripts visible. Real-time PCR determined that the level of aberrant transcripts from PEFS+ was significantly lower than that from SME, while the level of normal transcripts from PEFS+ was significantly lower than that of Wild-type (WT). Mutation c.4853-25T>A resulted in 28.8% reduction of the normal transcripts than that from WT, and incomplete penetrance was observed in the family.

**Conclusion:** SCN1A intronic mutations found in PEFS+ extended the spectrum of SCN1A-associated epilepsy. It provides direct evidence and new insights into the mechanism that decreased expression of SCN1A, besides null expression that leads to haploinsufficiency, is associated with phenotype variation of epilepsy.

p0308 DETERMINING THE BURDEN OF COPY NUMBER VARIATION IN PATIENTS WITH EPILEPSY

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Mesial temporal lobe epilepsy (MTLE) and genetic generalized epilepsy (GGE) are common epilepsies syndromes. Genomic copy number variations (CNVs) have been identified as a risk factor for some types of
epilepsy syndromes. We aim to investigate CNV distribution in patients with MTLE and GGE, as well as in control subjects; to evaluate CNVs recurrence in patients and to identify genes involved in predisposition to MTLE and GGE. We have studied 750 individuals (340 MTLE patients, 70 GGE patients, 340 control subjects). CNVs were assessed by SNP 6.0 array (Affymetrix). The analysis of MTLE patients identified 2,246 CNVs of the total, 20.3% CNVs were found only in patients and affect 652 genes. Analysis using Metacore software revealed genes associated with neurogenesis development, synaptogenesis, learning, memory, cognition, ion transport, protein complex involved in synapse maturation. In GGE patients, we identified 340 CNVs; 17.4% were found only in patients and affecting 59 genes. Analysis using Metacore revealed genes associated with lithium effect on synaptic transmission and autophagy, glutamic acid regulation, mitochondrial dysfunction in neurodegenerative diseases, dopamine-D2 receptor transactivation, GABA-B receptor-mediated regulation of glutamate signaling. Finally, analysis of the control group identified 2,100 CNVs. Chromosomal regions more affected in controls are 1q21.1, 1q21.2, 1p36.13, 2q11.2, 3q26.1, 4q13.2, 8p11.22, 8p23.1, 10q11.2, 14q11.2, 15q11.2, 15q11.1, 16p11.2, 17q21.31. Our results clearly show that there is an increased burden of CNVs in specific chromosomal regions of the genome in patients with epilepsy. These regions are distinct in patients with MTLE as compared to GGE, indicating that the genetic burden, in these different epilepsy syndromes, is distinct. Interestingly, CNVs previously associated with epilepsy syndromes in the literature were identified in our control group. Support: FAPESP, CNPq.

p0311
PROTEOMIC ANALYSIS OF SERUM FROM PATIENTS WITH TEMPORAL LOBE EPILEPSY
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Purpose: Epilepsy affects more than 0.5% of the world’s population. It has a large genetic component and is caused by electrical hyperexcitability in the central nervous system. Despite its prevalence, the disease lacks definitive diagnostic and prognostic biomarkers. To identify potential biomarkers for epilepsy by a convenient method, we analyzed the expression of serum proteins, reflecting alterations in the patient’s proteins. Method: We compared two-dimensional electrophoretic band patterns of human sera from eight patients with temporal lobe epilepsy (TLE) with those of eight control subjects. The differentially expressed bands were identified using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and electrospray ionization quadrupole time-of-flight mass spectrometry. Results: Twelve proteins were differentially expressed in the TLE group, of which 6 were identified. Expression of haptoglobin Hp2, PRO2675, immunoglobulin heavy chain constant region gamma 2, an unnamed protein, and three unidentified proteins were upregulated in serum from the patients with TLE, whereas those of major histocompatibility complex (MHC) class I antigen, plasma retinol-binding protein precursor, and three unidentified proteins were downregulated in these patients. After resection of the epileptogenic zone, the expressions of MHC class I antigen, immunoglobulin heavy chain constant region gamma 2, two of the downregulated unidentified proteins, and one of the upregulated unidentified proteins returned to the normal range. Conclusion: The 12 serum proteins in this study are potentially useful biomarkers for the diagnosis and monitoring of temporal lobe epilepsy.

p0312
DIFFUSION WEIGHTED MAGNETIC RESONANCE IMAGING IN CHILD CEREBRAL PALSY WITH SYMPTOMATIC EPILEPSY
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Purpose: The purpose of the study was to determine the characteristics of diffusion weighted Magnetic Resonance imaging indicators in children with symptomatic epilepsy with cerebral palsy.

Method: The study was based on the results of the study 54 children with symptomatic epilepsy with cerebral palsy aged 1 - 11 years. All patients underwent standard clinical and neurological examination, with the inclusion of routine MRI. All of 54 studied children underwent routine Magnetic Resonance imaging with diffusion weighted sequence. Main group consisted of 26 epilepsy patients with cerebral palsy. The control group consisted of 20 children without clinical manifestations of epilepsy symptoms, seizures, of all children on EEG FA (fractional anisotropy), values and MD (mean diffusion) were calculated on the same sections for all the resulting images.

Results: In the study these children with symptomatic epilepsy on the background of cerebral palsy we found a significant decrease in the FA values in fronto-temporal areas (P < 0.01). In other areas studied FA values were within the normative range. To evaluate the results of MRI diffusion was used as indicator of the mean diffusion (MD), an increase of values is associated with a defect in neurogenesis or loss of cells, followed by an increase in the extracellular space. In children with symptomatic epilepsy cerebral palsy was observed the significant increase the MD values in all studied areas (P < 0.01).

Conclusion: The obtained results prove that diffusion weighted MRI in children with symptomatic epilepsy and cerebral palsy reveals the structural changes of white matter of brain. A significant increase of diffusion capacity of the brain due to lower fractional anisotropy in the fronto-temporal lobe indicates the permeability and damage of the myelin sheath in white matter.

p0318
A MULTIMODAL NEUROIMAGING STUDY OF PSYCHOSIS OF EPILEPSY (POE)

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Purpose: Approximately 7% of epilepsy patients develop psychosis of epilepsy (POE), a devastating condition that carries a high risk of suicide. Unfortunately, we do not understand why some people with epilepsy develop psychosis while others do not. Moreover, there is no current model that accounts for the differing presentations and severity of POE. A leading model of psychosis in schizophrenia holds that the aberrant assigning of “salience” (i.e. significance) to stimuli underpins psychotic symptoms. Research suggests that aberrant salience reflects dysfunction in the ‘salience network’ (SN) - a brain network anchored on the insula and anterior cingulate cortex. The purpose of this study was to assess the salience model of POE through multimodal imaging analysis of white matter tracts and resting state functional connectivity of the SN. We hypothesised changes in fibre density and altered functional connectivity in the SN in POE relative to epilepsy patients without psychosis (EPY-NP) and healthy controls (HC). Method: POE patients were recruited from three major epilepsy services in Victoria, Australia. High resolution MRI scans of 12 POE patients were matched with 12 EPY-NP patients, and 12 HC, and analysed to assess changes in white matter and resting state functional connectivity in the SN. Results: Reduced fibre bundle cross-section in the longitudinal fasciculus was identified in POE as compared to EPY-NP (p < 0.05), and in the cingulum bilaterally in POE compared to HC (p < 0.05). Correlations in functional connectivity between nodes of the SN were similar between POE and HC, and were less extensive in EPY-NP group.
**Conclusion**: The results suggest that POE is characterised by structural macroscopic changes in white matter fibre bundles that do not appear to result in differences in resting state co-activation of the SN. This research highlights that altered structure of specific white matter tracts may constitute a neurobiological marker of POE.

**p0319**

**DATA MINING MR IMAGE FEATURES OF SELECT STRUCTURES FOR LATERALIZATION OF MESIAL TEMPORAL LOBE EPILEPSY**


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**Purpose**: This study systematically investigates the predictive power of volumetric imaging feature sets extracted from select neuroanatomical sites in lateralizing the epileptogenic focus in mesial temporal lobe epilepsy (mTLE) patients.

**Method**: A cohort of 68 unilateral mTLE patients who had achieved an Engel class I outcome postsurgically were studied retrospectively. The volumes of multiple brain structures were extracted from preoperative magnetic resonance (MR) images in each. The MR image data set consisted of 54 patients with qualitatively identified (positive) hippocampal sclerosis (HS-P) and 14 patients without (HS-N). Data mining techniques (i.e., feature extraction, feature selection, machine learning classifiers) were applied to provide measures of the relative contributions of structures and their correlations with one another. After removing redundant correlated structures, a minimum set of structures was determined as a marker for mTLE lateralization.

**Results**: Using a logistic regression classifier, the volumes of both hippocampus and amygdala showed correct lateralization rates of 94.1%. This reflected about 11.7% improvement in accuracy relative to using hippocampal volume alone. The addition of thalamic volume increased the lateralization rate to 98.5%. This ternary-structural marker provided a lateralization rate to 98.5%. This ternary-structural marker provided a lateralization rate to 98.5%.

**Conclusion**: The proposed ternary-structural MR imaging biomarker provides greater lateralization accuracy relative to single- and double-structural biomarkers and thus, may play a more effective role in the surgical decision-making process. Also, lateralization of the patients with insignificant atrophy of hippocampus by the proposed method supports the notion of associated structural changes involving the amygdala and thalamus.

**p0320**

**PHOTOSENSITIVE EPILEPSY IS ASSOCIATED WITH ABNORMAL EXCITABILITY OF ALPHA RHYTHM GENERATING NETWORKS**

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**Purpose**: To investigate the brain circuits generating spontaneous alpha rhythm fluctuations in photosensitive patients and in people without photosensitivity.

**Method**: 44 epileptic patients and 16 healthy controls underwent an electroencephalography-correlated functional magnetic resonance imaging study. In the patients group, 16 subjects were affected by Genetic Generalized Epilepsy (GGE) with documented photosensitivity (GGE PS+), 13 by GGE without photosensitivity (GGE PS-) and 15 by Focal Epilepsy (FE). The alpha power variations were convolved with the standard hemodynamic response function and used as a regressor in a single general linear model. Within and between groups second level analyses were performed as appropriate. Whole brain functional connectivity was evaluated for two thalamic regions of interest based on the BOLD findings that included the posterior thalamus (pulvinar) and the medio-dorsal thalamic nuclei.

**Results**: GGE PS+ demonstrated a significant greater mean alpha-power with respect to controls and other epilepsy groups. In photosensitive epilepsy, alpha-related BOLD signal changes demonstrated lower BOLD deactivation relative to all other groups at the occipital, sensory-motor, anterior cingulate and supplementary motor cortex. The same brain regions demonstrated an abnormal connectivity with the visual thalamus only in GGE PS+.

**Conclusion**: The cortical-subcortical network generating the alpha oscillation at rest is different in people with epilepsy and visual sensitivity with respect to other epilepsy syndromes and healthy controls. Such difference consists of a decreased alpha-related inhibition of the visual cortex and sensory-motor networks. Our findings provide evidences of a functional link between the circuits triggering the visual sensitivity phenomenon and the posterior alpha rhythm generation.

**p0321**

**THE ADDED VALUE OF HIGH-FIELD MRI AT 7T FOR PRE-SURGICAL EVALUATION OF DRUG-RESISTANT EPILEPSY**

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**Purpose**: High-field MRI offers higher resolution and signal to noise ratio for structural imaging, and is often utilized for detection of surgical targets in drug-resistant epilepsy when no definite lesion is seen on conventional clinical MRI. Here we evaluate whether 7T MRI improves the diagnostic accuracy for potential surgical candidates at a tertiary epilepsy surgery center.

**Method**: We obtained high-field 7T MRI on 13 patients who were undergoing standard pre-surgical workup. Four of these had no detected lesion (“non-lesional”) on conventional 3T MRI. 9 had at least one suspected abnormality on clinical 3T MRI. Ten patients had temporal
(including mesial and neocortical focus) and 3 had extra-temporal epilepsy, determined by their clinical picture and ictal EEG. Patients with large malformations or prior brain surgery were excluded. High-field MR images were obtained using a 7T scanner (Siemens, Germany) with a 32-channel coil prior to any invasive recording or procedure, and were interpreted by a neuroradiologist with expertise in high-field imaging. Institutional review board approval was obtained for this study and patients signed an informed research consent form.

**Results:** Of the patients with at least one suspected abnormality on their 3T MRI, 5/9 suspected abnormalities were confirmed and better characterized by 7T. Three were not confirmed using the higher resolution and contrast of 7T, hence were re-categorized as non-lesional. Of the 4 patients with no abnormalities on 3T, 1 was found to have a previously undetected focal cortical dysplasia.

**Conclusion:** The use of 7T MRI can improve diagnostic accuracy in the evaluation for epilepsy surgery, not only by finding relevant abnormalities in previously non-lesional cases, but also by further characterizing suspected abnormalities such as mild mesial temporal sclerosis, cortical dysplasias, and vascular lesions or anomalies. The additional information provided by 7T MRI can significantly affect planning for invasive recordings and surgical treatments.

**Abstracts**

**p0322**

**IS MTLE-HS A FOCAL EPILEPSY SYNDROME? A DIFFUSION TENSOR STUDY**


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**Purpose:** To study the extent of white matter abnormalities through diffusion tensor imaging and tractography in a large cohort of patients with TLE with unilateral mesial temporal lobe (hippocampal) sclerosis (MTLE-HS).

**Methods:** DTI measurements were obtained from tractography for arcuate fasciculus (ARF), cingulum, corticospinal tract, inferior longitudinal fasciculus (ILF); inferior fronto-occipital fasciculus (IFOF), optic radiation (OR), superior longitudinal fasciculus and uncinate fasciculus (UNF) in 50 patients with MTLE-HS and were compared to 50 age and sex-matched controls. Paired t-test was performed to compare the tracts in the affected left and right hemisphere of patients with corresponding left and right hemisphere in controls.

**Results:** Compared to controls, significant differences in fractional anisotropy (FA) values of ARF, IFOF, and OR and apparent diffusion co-efficient (ADC) of OR in right hemisphere of right MTS patients was noted. In left MTS patients, significant differences were found in both FA and ADC values of cingulum and IFOF and FA value alone in OR of left hemisphere. Results showed significant decrease in FA values of three tracts (ARF, p = 0.009; IFOF, p = 0.002 and OR, p = 0.0003) in the affected hemisphere in the case of right MTS patients compared to the normal controls. In left MTS patients, two tracts (cingulum, p = 0.004; OR, p = 0.001) showed significant decrease in FA values. ADC values of two tracts in left MTS patients (cingulum, p = 0.042; and IFOF, p = 0.002) also showed significant decrease as compared to controls. On comparison of left and right hemispheres, ADC values of UNF (p = 0.050) in right MTS patients and ARF (p = 0.022) in left MTS patients showed significant low values.

**Conclusions:** Widespread changes in other parts of limbic system occurs in MTLE-HS. This could account for a less than optimal outcome in patients even when a focal abnormality like HS is resected for drug-resistant TLE. An early surgery for MTLE-HS with drug-resistant TLE therefore should be advocated.
is an urgent need for more subtle biomarkers to individually predict SR and better understand epileptogenesis. Systematic longitudinal first seizure cohorts with research-driven MRI protocols are scant. The Halifax First Seizure Clinic cohort provided the opportunity to determine whether hippocampal malformation (HIMAL) and loss of hippocampal internal architecture (HIA) are biomarkers for SR.

**Method:** 51 adult patients (15-74 years) with FS or new-onset epilepsy (NOE ≥ 2 seizures in <12 months) were recruited excluding primary generalized epilepsy. Within 6 weeks, patients received 1.5 Tesla MRI imaging using an epilepsy protocol (3 mm coronal T2 FSE images, angled to the hippocampi, sagittal cube T2 and FLAIR, axial 3D-FSPGR, axial DTI whole brain, and single-voxel proton spectroscopy of mesial temporal lobes). Two independent readers examined HIMAL and HIA following a published scoring system.

**Results:** 28 FS and 23 NOE patients were identified. 10 FS patients converted to NOE (1-year follow-up). MRI pathologies encompassed hippocampal sclerosis (n = 1), dysembryoplastic neuroepithelial tumor (n = 1), occipital band heterotopia (n = 1), and a cystic temporal stem lesion (n = 1). Based on consensus scores, subtle hippocampal changes were found in 26 patients, 11 presenting with HIMAL and 15 with loss of HIA. No significant association was found between HIMAL and NOE, nor between HIMAL and conversion from FS to NOE. Loss of HIA and NOE at presentation was also not significantly correlated. However, loss of HIA was significantly associated with conversion from FS to NOE (p = 0.0427, one-tailed Fisher’s exact test).

**Conclusion:** Our data support that HIMAL represents a normal variation of the hippocampal structure. The loss of HIA is possibly a biomarker for epileptogenesis.

**p0328 ALTERED STRUCTURAL CORRELATION NETWORKS (SCN’S) IN CRYPTIC GENETIC LOCALIZATION-RELATED EPILEPSY (CLRE) ARE ASSOCIATED WITH SEIZURE FREQUENCY**

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**Purpose:** In previous studies, altered structural correlation networks (SCN’s) based on cortical thickness have been observed in patients with epilepsy. However, as SCN’s can only be determined on a group level, associating altered networks with clinical (e.g. epilepsy related) characteristics is not straightforward. In a previous study, a method to obtain individual variations in SCN’s was introduced (Sagger et al. Neuroimage 2015). We applied this method in cryptogenic localization-related epilepsy (CRLE) and investigated whether altered SCN’s are associated with full-scale IQ (FSIQ), seizure frequency, and onset age.

**Method:** Fifty-nine participants are included in this study, 38 patients with CRLE (18 females, age 40 ± 12y) and 21 controls (6 females, age 40 ± 14y). T1-weighted images (voxel size, 1x1x1 mm) obtained by a 3.0-T MRI scanner (Philips Achieva) were used to extract the mean cortical thickness for 68 regions. These thicknesses were first corrected for age, gender, and total intracranial volume. Adjacency matrices were obtained by calculating the Pearson’s correlation coefficient between the corrected cortical thicknesses for each region pair. Individual contribution of a patient is measured by adding the respective patient to the native control group before calculating the network. Two well-known network metrics, characteristic path length and cluster coefficient, were computed and both are normalized with respect to 100 random networks to correct for variations in network topology.

**Results:** A significant positive correlation was found for the cluster coefficient and seizure frequency (r=0.361, p = 0.026). A trend towards negative correlation was also found for local clustering and onset age (r=0.291, p = 0.076). Moreover, a significant negative correlation was found between clustering and FSIQ (r = -0.399, p = 0.013).

**Conclusion:** In the current study it is shown that an increase in clustering is related to worse seizure control and decreased cognitive performance. These results might hint that seizure propagation is accommodated by highly clustered cortical networks.

**p0329 FUNCTIONAL MRI OF LANGUAGE AND MEMORY LATERALISATION TO AID PRESURGICAL EVALUATION OF PAEDIATRIC EPILEPSY**

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**Purpose:** Temporal lobe surgery is an effective treatment for medication-resistant paediatric temporal lobe epilepsy (TLE); however, this procedure can result in language and memory deficits that compromise
eductional performance. It is therefore crucial to assess language and memory lateralisation prior to surgery. We have developed an IMRI paradigm to assess memory and language in children during a single scanning session.

Method: Functional scans were acquired on a 3T Siemens system in 18 healthy volunteers (aged 8-18 years). Language lateralization was assessed through a verb generation task. Memory laterality was assessed through cued recall, where cues were presented to guide recall of previously encoded words (in the verb generation task). The baseline task involved making an odd/even decision to numbers and served as a delay period between encoding and recall. Lateralisation in individual participants was determined using the LI toolbox.

Results: Across the group, block-wise comparisons for the language task demonstrated activations in posterior inferior frontal gyrus (Broca’s area) and in superior temporal gyrus bilaterally (p < 0.05, FWE corrected). Memory function was explored using event-related analyses for correctly retrieved words, and hippocampal activations were observed bilaterally (p < 0.01). At the individual level, laterality indices suggest that all participants were left lateralised for language, with LIs ranging from +0.61 to +0.98. Most participants were also left lateralised for memory (n = 11; LI: +0.25 to +1) whilst three had LI in the bilateral range (-0.16 to +0.12) and three were lateralised to the right (-0.37 to -0.67).

Conclusion: Our findings show robust activations in language and verbal memory networks and confirm the feasibility of assessing lateralisation of language and memory in children. This protocol has the advantage of lateralisng language and memory functions within one single scanning session and could prove useful for the pre-operative assessment of paediatric candidates for epilepsy surgery.

p0330 EXECUTIVE FUNCTIONS IMPAIRMENTS IN CHILDREN WITH ROLANDIC EPILEPSY

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Purpose: The primary aim of this study was to compare the core executive functions (EF) in children with rolandic epilepsy (RE) and healthy controls. As a secondary aim, we compared typical and atypical RE children’s EF.

Method: 24 children (11 females) with RE (typical, n = 18, or atypical, n = 6) and 33 healthy controls (19 females), aged 6 to 13 years, were assessed for intelligence (WASI), working memory (subtest DigitSpan-WISC IV and Corsi Block-Tapping task - CBT), inhibitory control (TAVIS 4) and cognitive flexibility (Five Points Test - FPT). Their parents answered sociodemographic questionnaires and a ADHD/ODD symptoms scale (MTA-SNAP-IV). The groups were homogeneous (p > 0.05) regarding age, intelligence, income and ADHD/ODD symptoms.

Results: Compared to controls, the clinical group had worse performance in the CBT-forward’s trials: (U = 264.5; r = -0.27; p < 0.05) and in the FPT total perseverative errors (U = 197.5; r = -0.36; p < 0.05), and better performance in FPT total drawings (U = 264.5; r = -0.27; p < 0.05). Children with typical and atypical RE didn’t differ in EF measurements. Compared to control group, children with atypical RE had lower weighted scores in Digits backward (U = 39.5; r = -0.37; p < 0.05). Children with typical and atypical RE didn’t differ in EF measurements. Compared to control group, children with atypical RE had lower weighted scores in Digits backward (U = 39.5; r = -0.37; p < 0.05). Children with typical RE showed worse performance than controls in the CBT-forward’s trials (U = 185.5; r = -0.3; p < 0.05), FPT total perseverative errors (U = 118.5; r = -0.46; p < 0.01) and perseverative errors percentage (U = 159.5; r = -0.32; p < 0.05), and a better performance in the FPT total number (U = 156; r = -0.38; p < 0.01) and correct (U = 195; r = -0.28; p < 0.05) drawings.

Conclusion: Impairments in working memory and cognitive flexibility in RE patients were observed. The results also point to failures in visuo-spatial attention and behavioral monitoring. Differences between RE forms may have been underestimated due to the size of the atypical RE group.

p0337 THE CONTRIBUTIONS OF COGNITIVE ABILITIES TO ACADEMIC PROFILE IN NEW-ONSET CHILDHOOD ABSENCE EPILEPSY

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Purpose: Neuropsychological studies indicate that new-onset childhood absence epilepsy (CAE) is associated with deficits in attention and executive functioning. However, the contribution of these deficits to impaired academic performance remains unclear. We aimed to examine whether attention and executive function deficits account for the academic difficulties prevalent in patients with new-onset CAE.

Method: Neuropsychological tests were used to assess the cognitive performance in several domains, including language, mathematics, psychomotor speed, spatial ability, memory, intelligence, attention, and executive functioning, in 35 children with new-onset CAE and 33 control participants. One-way analysis of variance (ANOVA) compared performance on all tests between the new-onset CAE group and the control group. Analysis of covariance (i.e., ANCOVA) was conducted to examine the relationships among general cognitive processing, language processing, and mathematical abilities.

Results: Patients with new-onset CAE exhibited deficits in mathematics, intelligence, attention, and executive functioning. They showed preserved performance in language, psychomotor speed, spatial ability and memory. Furthermore, attention deficits, as measured by a visual tracing task, accounted for impaired arithmetic performance in the CAE group.

Conclusion: Children with new-onset CAE exhibit deficits in attention and executive functioning, and is associated with impaired academic performance in mathematics. Attention deficits, rather than impaired intelligence or executive functioning, is the fundamental cognitive mechanism underlying mathematical performance impairments in patients with new-onset CAE.
commission errors (U = 3; r = −0.7; p < 0.01). LH was better than RH in TAVIS-T1’s commission errors (U = 0; r = −0.8; p < 0.01).

Conclusion: The earlier the onset and the longer the RE, the worse the children performance on working memory and inhibitory control. Bilateral epileptiform discharges also resulted worse performance in these functions. The relation between the number of AED and the inhibitory control may be due to their adverse effects or the disease severity.

p0340
WATCH THE LANGUAGE! LANGUAGE AND LINGUISTIC-COGNITIVE ABILITIES IN CHILDREN WITH NOCTURNAL EPILEPTIFORM ACTIVITY
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Purpose: The purpose of the study was two-folded: First, we wanted to explore in what ways the language abilities of children with nocturnal epileptiform activity (NEA) differ from those of typically developing children. Second, we wanted to explore how NEA-related factors affect the language abilities of children with NEA.

Method: We included a group of children with nocturnal epileptiform activity (NEA; N = 33) hospitalized at a tertiary epilepsy hospital (inclusion criteria: more than four times increase of epileptiform activity from daytime to sleep state, no seizures the last six weeks and not any known diagnosis such as mental retardation, cerebral palsy and autism). The children were compared with two groups of typically developing children: one group matched on age and gender (N = 33) and one group matched on language ability (vocabulary) and gender (N = 66).

Results: In general, the children with NEA showed delayed language abilities. The data suggested a trend for the children to perform especially poorly on phonology and naming speed. However, a subgroup of NEA-children who could read performed especially poorly only on phonology.

Overall, we did not find firm evidence that NEA-related factors (the amount of NEA, the use of antiepileptic drugs (AEDs), and the lateralization and localization of NEA) affected language abilities. Nevertheless, children with right-lateralized epileptiform activity seemed to have specific difficulties with naming speed and children with NEA located in the centrotemporal areas seemed to have specific difficulties with phonology and orthographic skills.

Conclusion: First, the children with NEA showed delayed language abilities and a trend for difficulties with phonology and naming speed in particular compared to typically developing children. Second, the NEA-related factors did not affect language abilities. However, we found some support for the idea that laterality and localization of NEA might affect the difficulties.

Results: Eight studies included a comparison group with typically developing children. The results showed that the odds of having IEA were six times greater for children with speech and language impairments than for typically developing children. In total, we found 55 unique estimates of the prevalence of IEA in children with speech and language impairments. Overall, the pooled prevalence of IEA was 27.3%. However, a wide variation was found between the unique estimates. This variation could be explained in different ways. First, type of speech and language impairment could to a certain degree explain the wide variation. IEA were found in 8.1% of children with speech impairments (e.g. dysfluent speech and speech sound disorder), 25.8% of children with language impairments (e.g., specific language impairments (SLI) and developmental dysphasia (DD)), and 51.5% of children with language regression. Second, sleep EEGs detected a significantly higher prevalence of IEA than awake EEGs. Last, significantly higher prevalence rates of IEA were found when epilepsy was present versus if epilepsy was not present. However, in additional analysis 33.5% of language-impaired children without epilepsy were found to have IEA in sleep EEGs.

Conclusion: IEA is a frequent finding in children with language impairment. We argue that while EEG is of questionable value when assessing children with solely speech impairments, sleep EEG would be valuable when assessing children with language impairments and children who experience language regression.

p0343
MRI-NEGATIVE TLE IS NOT COGNITIVELY BENIGN: LOOKING BEYOND LESIONS FOR CAUSES OF NEUROPSYCHOLOGICAL IMPAIRMENT
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Purpose: Cases of MRI-negative and lesional TLE are similar in their semiology and electroclinical profile. It remains unclear, however, whether they are also similar in their memory and mood profiles, as previous studies have generally been low powered and report mixed findings. This study aims to clarify whether a structural lesion leads to an additional decrement of neuropsychological function, over and above that caused by the brain network disruption that is characteristic of all epilepsies.

Method: In total, 152 adults participated: 79 TLE patients and 73 sociodemographically-matched healthy controls. On the basis of 3T-MRI, 19 (24%) of patients had a lesion consistent with hippocampal sclerosis (HS-TLE), 30 (38%) had a lesion other than HS (MRI-pos TLE), and 30 (38%) were deemed lesion negative (MRI-neg TLE). Memory and mood were assessed using measures well-established for use in epilepsy.

Results: Relative to controls, people with MRI-neg TLE showed significantly impaired verbal, visual, and autobiographic memory (p < 0.05–0.001); they also reported significantly higher depression and anxiety (p < 0.05–0.01). Mood and memory decrements in MRI-neg TLE were equivalent to those seen in patients with lesions (p > 0.05), but were predicted by distinct factors. In MRI-neg, memory deficits were underpinned by younger onset of seizures, reduced intellectual capability, and previous depressive disorder. Memory deficits of HS-TLE patients were linked to the refractoriness of seizures as well as depressive symptoms, and in MRI-pos TLE, more years of education. Conclusion: MRI-negative TLE is associated with memory and mood dysfunction equivalent to that seen in patients with HS and other structural pathologies. This suggests that neuropsychological impairments in TLE are not contingent upon a macroscopic structural lesion, and might be better conceptualised as an intrinsic property of the underlying network disease. Additional vulnerability to behavioural dysfunction is conferred by clinical, cognitive, and psychological mechanisms specific to TLE subtype.
p0344 NEUROPSYCHOLOGICAL PROFILE OF PATIENTS WITH SLEEP-RELATED HYPERMOTOR EPILEPSY (SHE)


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Purpose: To assess the cognitive functions of a representative cohort of SHE patients by a systematic neuropsychological study.

Methods: Cross-sectional study carried out over 2013–2016, including patients with video/video-EEG-documented SHE according to the novel diagnostic criteria. All patients underwent an assessment of intelligence (WAIS) and cognitive status (MMSE); individuals with normal scores (IQ > 80; MMSE ≥ 23.8) underwent a standardized neuropsychological battery. Fisher’s exact test and Wilcoxon Rank-Sum highlighted possible correlations with clinical determinants.

Results: We enrolled 60 individuals (M/F: 28/32, mean age 38.2 ± 12.43 years; mean age at onset 12.62 ± 8.15 years): 38 (63.3%) had unknown etiology, 11 (18.3%) showed brain lesions and 11 (18.3%) were genetic.

IQ scores (range: 45–148) were significant worse in verbal compared to performance abilities (mean: 93.38 ± 19.50 vs 101.35 ± 21.10; p < 0.0001). Thirteen patients (11 with cognitive deficits, 2 drop-out) did not complete the extensive battery. Of the remaining 49 individuals, 23 (46.9%) showed deficits in at least one test: phonemic fluency, 12 (24.5%); verbal/visuospatial memory, 12 (24.5%); Stroop, 11 (22.4%); working memory, 5 (10.2%). At univariate analysis, pathological neurological examination (NE) correlated with worse scores at WAIS (66.67% vs 7.69%, p: 0.029) and MMSE (24.52 ± 5.7 vs 28.03 ± 1.45, p: 0.010); “Any underlying brain disorder” (pathological NE and/or brain MRI) was associated with deficits in verbal memory (30% vs 2.63%, p: 0.025) and attention/inhibitory control (50% vs 15.38%, p: 0.033), with significant worse performances in shifting abilities (99.9 ± 30.9 vs 73.38, p: 0.027). This result regards also patients with status epilepticus (65.4 ± 18.51 vs 46.18 ± 23.15, p: 0.035) and poor prognosis (50.12 ± 23.47 vs 30.83 ± 8.9, p: 0.02). Bilateral convulsive seizures correlated with worse working memory (3.56 ± 1.04 vs 4.27 ± 1.06, p: 0.049).

Conclusions: Neuropsychological deficits are frequent in SHE. The profile of neuropsychological impairment is characterized by significant worse scores in verbal IQ and deficits in phonemic language, memory and selective executive functions. Pathological brain MRI and NE, together with variables of clinical severity (but not genetics) significantly correlated with worse performances in cognitive tests, long-term verbal memory and attention/inhibitory control.

p0352 RESPONSIVE NEUROSTIMULATION THERAPY FOR SUPER-REFRACTORY FOCAL STATUS EPILEPTICUS: A CASE REPORT

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Purpose: To describe one institution’s experience with responsive neurostimulation after urgent placement of the RNS System in a patient with super-refractory focal status epilepticus (FSE) due to focal cortical dysplasia (FCD) in primary motor cortex. Since FDA approval in 2013, this is the second known case in which the RNS System was urgently implanted for super-refractory FSE.

Method: Case report.

Results: A 35-year-old man with medically-refractory focal epilepsy (onset age 2) due to a 2.5 cm FCD in the right sensorimotor strip presented with his third episode of super-refractory FSE. Despite treatment with six AEDs, anesthetic agents and ketogenic diet, the patient’s right frontal-parietal seizures persisted for 3 weeks. The patient had previously been evaluated with Phase II monitoring confirming seizure localization to the FCD and had repeatedly refused lesionectomy given high risk of left hemiparesis; however, he was actively considering RNS System placement. Since he was in a therapeutic coma during the admission and sedation wean attempts were complicated by persistent FSE with failure to regain consciousness, his family consented for the procedure. RNS System placement with two cortical strip leads over the FCD was urgent due to persistent FSE with risk of left hemiparesis; however, he was actively considering RNS System placement. Since he was in a therapeutic coma during the admission and sedation wean attempts were complicated by persistent FSE with failure to regain consciousness, his family consented for the procedure. RNS System placement with two cortical strip leads over the FCD was urgently performed.

Conclusion: There may be a role for urgent RNS System placement in cases of refractory FSE with localized seizure onset, but further studies are needed to determine optimal seizure detection and stimulation parameters post-implant. FSE is a more dynamic process than chronic focal epilepsy given daily clinical and medication changes, so close monitoring and more frequent programming adjustments are required.

p0346 EXAMINING RELATIONSHIPS BETWEEN MEMORY SCORES AND DEPRESSION IN EPILEPSY PATIENTS WHO UNDGO MEMORY TRAINING

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Purpose: To investigate the relationships between subjective memory rating, performance on an objective measure of association memory and symptoms of depression in outpatients with epilepsy undergoing memory rehabilitation.

Method: One hundred and seven adult patients with epilepsy and memory complaints completed a group-based, 6-week memory rehabilitation training program (Radford et al., 2010) as well as pre- and post-training assessments. Scores included

1. a Likert-scale subjective Self-rating of overall memory function;
2. number correct on an Identity Association Memory Test (with two alternative versions and randomised administration; not practiced in the memory course.)
3. Depression symptom score from the Depression, Anxiety and Stress Scale. Non-parametric statistics were used to examine the relationships between subjective memory ratings, objective memory scores and presence of depression.

Results: Prior to memory training, Self-rating of memory and Depression were negatively correlated, but neither Depression nor Self-rating-of-memory score correlated with objective memory performance. Similarly, we found a negative correlation between change (pre- to post-training) in Depression and change in Self-rating of memory, but correlations between the other change scores were not significant. When subjects were divided into depressed and non-depressed groups, they both showed significant (and similar) pre- to post-training gains in Identity Association Memory.

Conclusion: Level of pre-training depression helps to predict memory self-ratings, but it does not predict objective memory test performance. Furthermore, changes in objective memory post-training were not reflected in patients’ self-rated memory. The presence of depression does not influence who will benefit from this memory training program.
RESULTS: The results from six subjects showed that the average detection rate of continuous or clustered epileptiform discharge was greater than 85% at acute stage but was slightly lower at chronic stage. The seizure suppression was successful in both the acute stage of status epilepticus (success rate: 72%) and the chronic stage of episodic attacks (success rate: 80%). The suppression was quicker in the chronic stage than in the acute stage. We think the reason is that the intensity of epileptiform discharge was lower in the chronic stage. Sometimes, the intensity of photic stimulation reached the upper limit during seizure suppression in the acute stage.

Conclusion: A novel optogenetic closed-loop control system was developed and the experiment results indicated that it could effectively suppress epileptiform discharges in both acute and chronic stages.

p0357
VAGUS NERVE STIMULATION (VNS): EXPLORATORY ANALYSIS WITH REAL LIFE DATA FROM A BELGIAN HEALTH INSURER, 2011–2015
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Purpose: To assess change in healthcare resources, consumption and costs from 12 months pre- to 12 months post-initiation of VNS among refractory epilepsy patients.

Method: 36 patients (1–36 years, 20 male) treated with anti-epileptic drugs (AEDs) and implanted with VNS were identified using a Belgian administrative database of health insurer MLOZ (2 million affiliates). Patients were studied in a mirror-image design to assess change in health care utilization variables (2011–2015). Costs were estimated from the health service payer’s perspective. Paired t-test compared epilepsy-associated annual direct healthcare costs and use of medical services: hospitalisations, consultations, ambulatory treatments, pharmaceuticals.

Results: There were no changes in hospitalizations in pre- and post-implant (p > 0.05), but hospitalization rates via emergency services declined by 50%, while the mean hospitalization duration remained around 3 days (3.2 vs. 3.5; p > 0.05). There was a significant decline in the median and Q3 length of stay (respectively from 2 to 1 day and from 4 to 2.6 days). Total health care costs declined from €9,059 to €7,786 (p > 0.05) and total AED costs increased by 10% (from €1,614 to €1,814; p > 0.05). The relative part of AEDs in the total pharmaceutical costs remained stable at 90%. Epileptic patients mainly consulted GPs and neurologists. After VNS initiation, only neurologist’s visits increased significantly from 2.7 to 5.7 visits a year and the number of AED molecules remained at 3 after one year.

Conclusion: VNS is relatively rare in Belgium but is rather expensive (€11,000). VNS was not associated with a decline in hospitalization variables except via emergency services. Volumes (hospitalizations, visits, DDDs...) remained stable. Total healthcare costs including pharmaceutical costs did not decline the year after initiation. Treatment with VNS may not be as cost-effective as expected from payer’s perspective, although patients may have clinical benefits (seizure reduction, quality of life, etc.).

p0355
REAL-TIME SUPPRESSION OF TEMPORAL LOBE EPILEPTIFORM DISCHARGES BY CLOSED-LOOP OPTGENETIC STIMULATION
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Purpose: The main goal of this study was to develop a control system to suppress temporal lobe epileptiform discharges in real time by optogenetic stimulation.

Method: Thy-1-ChR2-YFP transgenic mice were adopted as the subjects. Two electrodes, each to one side of hippocampus, for deep EEG recording and an optical fiber to the right hippocampus for photic stimulation were inserted by the stereotactic technique. Seizure was induced by lithium and pilocarpine. The EEG signal from the left hippocampus was digitalized to calculate approximate entropy (AE) as an indicator of the severity of epileptiform discharge. Proportional control was implemented and the magnitude of AE was used to regulate the intensity of photic stimulation using a piece-wise linear control law.
p0358

AUTOMATIC BAD CHANNELS DETECTION FROM INTRACRANIAL EEG DATASETS USING MACHINE LEARNING

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Purpose: Stereoelectroencephalogram (SEEG) recordings is an invasive method used to localise the epileptogenic zone for some patients with drug resistant focal epilepsy. However, SEEG recordings come with non-neuronal signals resulted from disconnected electrodes, sensors malfunctioning or other parasitic electrical activity picked up by amplifier and current drift. Those signals, known as bad channels, are excluded (so far manually) from datasets for further analysis. Our purpose is to design a method that detects automatically SEEG bad channels.

Method: We acquired datasets from 206 epileptic patients (93 from Rothschild Foundation, 67 from CHU Grenoble-Alpes, 32 from CHU Nancy, 11 from CHU Lyon, and 3 from Bucharest Hospital) who underwent SEEG recordings and direct electrical stimulation at 1 Hz as part of the presurgical evaluation. From stimulation runs, channel features (correlation, variance, deviation, amplitude, gradient, Hurst exponent and kurtosis) have been extracted. We then trained an ensemble bagging classifier on stimulation runs whose bad channels were visually identified by experts. The trained model was applied on new dataset for bad channels prediction.

Results: This method effectively detected different types of bad channels and showed a detection ability that matches a manual one by experts at an agreement of 99.77%. The classification performance is thus not impacted by the multicentric nature of data.

Conclusion: The proposed method demonstrated promising results and can be envisaged to be used on larger datasets for automatic quality control of SEEG data. The property of the method is the use of different features and ensemble bagging classifier not only to identify the bad channels but also to cope with datasets with imbalanced class distributions.

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p0361

FACTORS INFLUENCING THE CONFIDENCE OF TEACHERS IN THE MANAGEMENT OF EPILEPSY IN MAINSTREAM EDUCATION WITHIN THE BELFAST EDUCATIONAL AUTHORITY AREA

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Purpose: There is a relative paucity in the literature regarding the confidence of teachers in the management of epilepsy. The aim of this study was to establish what factors influenced this.

Method: School principals in Belfast Area were contacted via email to introduce the survey. A link to an electronic survey was subsequently forwarded to the schools for completion by the Special Educational Needs Co-ordinator (SENCO).

Results: Out of the 149 schools contacted 88 (59.1%) mainstream schools responded. Educational Stage: nursery 12, primary 47, post primary 24 and 1 primary with attached nursery unit (4 non-responders). Chi² = 0.2101. Health professional on site: Yes 13 (14.8%), No 71 (80.7%) (4 (4.5%) non-responders). Mean difference (1–5) 1.19. (95% CI 0.53–1.85, p = 0.0006). Awareness of epilepsy training: Yes 42 (47.8%) vs. No 41 (46.5%) (5 (5.7%) non-responders). Mean difference (1–5) 0.844 (95% CI 0.36–1.33, p = 0.0008). Previously witness a seizure: Yes 40 (45.4%) vs No 48.9% (5 (5.7%) non-responders). Mean difference (1–5) 0.56. (95% CI 0.06–1.06, p = 0.0274). Previously taught a child with epilepsy: Yes 55 (62.5%) vs No 28 (31.8%) (5 (5.7%) non-responders). Mean difference (1–5) 0.37 (95% CI –0.17 to 0.91, p = 0.1742). Friend/Relative with epilepsy: Yes 32 (36.4%) vs 51 (57.9%) (5 (5.7%) non-responders). Mean difference (1–5) 0.79 (95% CI 0.29–1.30, p = 0.0023).

Conclusion: Significant factors include healthcare staff on site, previous seizure exposure, friend/relatives with epilepsy & epilepsy training. There was no significance of school level or previously having taught a child with epilepsy.

p0363

ASSESSMENT CEREBRAL POSTHYPOXIC STRUCTURAL CHANGES ON BASE OF DETERMINATION TRANSIENT EEG PATTERNS IN PRETERM INFANTS WITH VERY LOW BIRTH WEIGHT

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Electroencephalography (EEG) is irreplaceable method of research in complex diagnostics and evaluation of cerebral status in newborn children. EEG in healthy premature infants of different gestational age are recorded various morphological transient patterns (STOP, PTO, delta-brushes), which characterize morphological and functional development of the brain at different stages of early ontogenesis. Detection of disturbance of formation of bioelectrical activity, based on the data of age-dependent appearance of transient patterns contributes to the early diagnosis of brain injury in premature infants.

Purpose: To identify appearance of age-dependent transient EEG patterns in preterm infants with posthypoxic structural changes in brain on MRI and to determine early marker of structural brain damage in preterm infants with very low birth weight (VLBW).

Study involved 43 preterm infants with VLBW and gestational age 24–29 weeks. Allocated 2 groups of patients: first - preterm infants with posthypoxic structural changes in brain on MRI (n = 21), second - preterm infants without brain pathology on MRI (n = 22).

Results and conclusion: Study found that bioelectrical activity in most part of preterm infants without brain changes on MRI pattern of delta-brushes are recorded in corresponding to physiological brain development. In patients with posthypoxic structural changes in brain on MRI pattern of delta-brushes registered significantly later (only in 2 infants it was determined before 30 weeks). Late appearance of transient delta-brushes (after 30 weeks) is identified as early marker of brain pathology.

Changes in development of spontaneous brain activity in patients with cerebral structural changes in neonatal period identified in present study also included changes in severity and age of onset of registration of transient patterns STOP and PTO. These patterns were registered in less quantity of patients of first group (correspondingly in 94/3% and 8/39%) in comparison to patients of second groupA (correspondingly in 16/71% and 13/58%).

p0364

LONG-TERM NETWORK EFFECTS OF CORPUS CALLOSOTOMY IN PATIENTS WITH LENNOX-GASTAUT SYNDROME

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**p0365**

**CLASSIFICATION OF NEONATAL SEIZURES: THE RESULTS FROM A RECENT TEST OF THE ILAE COMMISSION ON CLASSIFICATION & TERMINOLOGY PROPOSED NEONATAL SEIZURE FRAMEWORK**

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**Purpose:** The objective of this study was to inquire what classification of neonatal seizures is currently being used and to test the proposed system by the ILAE Neonatal Task Force.

**Method:** The Task Force on Neonatal Seizures, established in 2014, proposed a neonatal seizure framework that can be integrated into the ILAE classification of the epilepsies. At the 2016 ILAE European Congress on Epileptology in Prague, neurologists, neurophysiologists, neonatologists, pediatricians, EEG technicians, students, nurses, and fellows participated in a test. They were introduced to the proposed neonatal classification system with a “teaching video,” then asked to apply the proposed framework to rate seizure types for each of five babies presented on a subsequent “clinical video.” Raters additionally provided information about their preferred system for classifying seizures. This information and obtained ratings using the proposed framework were compiled and analyzed.

**Results:** Responses of 100 raters were collected and included adult/pediatric neurologists and epileptologists, pediatricians, neurosurgeons, technicians, residents/fellows, nurses, and students. Most raters reported that they use the current ILAE classification system to classify neonatal seizures. However, 76% of raters judged the proposed classification system as better than the current system. Since the last revision of the ILAE classification system in 2006, neonatal seizures no longer are regarded as a separate entity. Using the proposed framework, 79–92% of raters correctly identified the main seizure type for each baby as presented in the videos.

**Conclusion:** The results of the test of the ILAE Commission on Classification & Terminology Proposed Neonatal Seizure Framework suggested there is a need for a new neonatal seizure classification system. The proposed framework was judged as better than the current system by 76% of raters. Furthermore, 79–92% of raters were able to employ it to correctly identify main seizure types.

**p0368**

**RECESSIVE EARLY ONSET EPILEPTIC ENCEPHALOPATHIES**

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**Background:** Early onset epileptic encephalopathies (EOEE) present a unique diagnostic challenge with variable underlying causes. Advances in genomic technologies are facilitating the discovery of both common and rare genetic mutations causing EOEE. Autosomal recessive inheritance has been reported, but most cases of EOEE are sporadic (de novo mutations).

**Purpose:** To identify the underlying genetic defects in patients with unexplained EOEE in a highly consanguineous population.

**Method:** We performed genetic studies (Whole exome sequencing or genes panel) in a cohort of patients with unexplained EOEE from 2 centers in Riyadh: Prince Sultan Military Medical City and Research Centre in King Faisal Specialist Hospital. We characterized all phenotypes in detail and classified children according to known electroclinical syndromes where possible. Infants with previous genetic diagnoses, causative brain malformations, hypoxic ischemic insult, or inborn errors of metabolism were excluded.

**Results:** 128 patients with unexplained EOEE were included. We identified disease-causing variants in 113 children (88%), including mainly the following genes: SLC13A5 (n = 8), FRRS1L (n = 7), ADAT3 (n = 6), ARV1 (n = 4), PCL2B1 (n = 2), etc. 104 variants were recessive, and only 9 variants were de novo. Phenotypes were broadened for some variants identified.

**Conclusion:** Our study provides for the first time comprehensive epidemiologic information, epilepsy phenotype, and recessive genes on a large cohort of EEOE. Diagnosis of the underlying causes of epileptic encephalopathy is essential for treatment, prognosis and genetic counseling.

**p0369**

**BDNF IN CHILDREN WITH EPILEPSY**

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**Purpose:** Assessment of serum BDNF levels in children with epilepsy.

**Method:** We followed 51 children, aged between 3 month and 12 month old. We assessed serum BDNF levels via immunoenzymatic method (ELISA) in the blood of 26 children, aged 3 months to 12 months, presenting epilepsy, who had CNS perinatal hypoxic-ischemic antecedents, and 25 healthy controls. Also we performed imaging and neurophysiological exams. For statistical analysis of the
obtained results was applied arithmetic mean, standard error, relative frequency, correlation coefficient (Pearson) and test ANOVA.

Results: They found decreased serum BDNF at 3 months of age in children who developed epilepsy as compared to the control group (p<0.001). BDNF levels were much lower as the neuropsychological changes (rxy = −0.72, p<0.05) and imaging (rxy = −0.68, p<0.05) were severe. Also appreciated a significant increase in BDNF levels in children with epilepsy at the age of 1 year (25.3%) compared with healthy children (1.5%), but lower compared to this lot (rxy = 0.876, p<0.001).

Conclusion: Serum BDNF levels were significantly lower in children with structure epilepsy (aged 3 months to 12 months) in comparison to controls, which increased immaturity of brain tissue notify them. This could suggest a delayed increase of BDNF levels during those children’s development. With parental serum BDNF increases, notifying immature intracellular axonal networks in 26 infants and children, 2 mos to 17 yrs: 10 FCDI; 6 FCDII; 3 FCD III; 4 hemimegalencephaly (HME); 3 TSC. Bielschowsky impregnations also were prepared. Eight normal age-matched brains provided controls. Frozen section histochecmistry demonstrated mitochondrial enzymatic changes.

Results: The U-fibre layer at gyral bases and depths of sulci exhibited neuronal dispersion and elaborate synaptic plexi; many axons projected into cortex. Deep white matter in FCDII, HME, TSC also showed excessive synapses, often forming clusters. Their axons formed local plexi but did not penetrate the U-fibre layer to extend to cortex; an exception was transmantle dysplasias continuous with cortex. Most subcortical neurons reacted to NeuN, rarely to calretinin. Synaptophysin demonstrated elaborate white matter axonal plexi better than NFP or Bielschowsky. Many subcortical neurons in all cases exhibited intense mitochondrial activity. Regional glia expressed cytoplasmic α-B-crystallin.

Conclusions: U-fibres neurons beneath FCD have complex synaptic plexi that contribute to epileptic circuitry. They are not calretinin-reactive, hence excitatory rather than inhibitory. Frequently depolarizing heterotopic white matter neurons are hypermetabolic; pre- and intra-operative ECoG may demonstrate their discharge. FCD resections that include U-fibres may prevent epileptic spread to adjacent gyri. Neuropathology reports of epilepsy resections should describe dispersed white matter neurons and their synaptic plexi. U-fibre plexi, but not deep white matter heterotopia, are an integral component of epileptic networks.
more severe fatigue. In particular, children in the UCE group had significantly more severe fatigue than those in the WCE group (p < 0.0001).

**Conclusion:** Seizure frequency may be associated with fatigue in children with epilepsy, namely, children with uncontrolled seizures may have more severe fatigue than healthy, seizure-free children.

**p0379**

**FAST (40–150 Hz) OSCILLATIONS ARE ASSOCIATED WITH POSITIVE SLOW WAVES IN THE SCALP Ictal EEGS OF EPILEPTIC SPAEMS IN WEST SYNDROME**


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**Purpose:** To elucidate the generative mechanisms of epileptic spasms (ESs) in West syndrome, we investigated the temporal relationship between scalp fast (40–150 Hz) oscillations (FOs) and slow waves in the ictal electroencephalograms (EEGs) of ESs.

**Methods:** In 11 infants with WS, ictal FOs were detected in a bipolar montage based on spectral and waveform criteria. Their temporal distribution was analyzed in terms of the positive peaks (tough point, T1) of identical EEG data in a referential montage. Among six EEG data sections defined according to T1, the number of FOs, peak power values, and peak frequencies were compared.

**Results:** We identified a total of 1014 FOs (946 gamma and 68 ripple oscillations), which clustered closely at T1. The number of gamma oscillations in the 1 s epoch including T1 was significantly higher than those in the prior and subsequent phases. Peak power values and frequencies tended to be higher in these positive phase sections.

**Conclusions:** The temporal association of FO clustering and positive slow waves in the ictal EEGs of ES indicated that active neuronal firing related to FOs underlies the generation of ESs and their ictal slow waves.

**p0384**

**KETOCNIC VERSUS MODIFIED ATKINS DIET FOR PAEDIATRIC EPILEPSY: A SINGLE CENTRE EXPERIENCE FROM SINGAPORE**


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**Purpose:** To evaluate the efficacy and tolerability between ketogenic diet (KD) and modified Atkins diet (MAD) for paediatric patients with epilepsy.

**Method:** This is a retrospective study of 46 children with epilepsy receiving KD and MAD from year 2004 to 2016 inclusive. Patient demographics, epilepsy history and the diet type initiated were collated. The reasons for diet cessation were obtained.

**Results:** The age ranges for KD (31 patients) and MAD (15 patients) initiation were from 1 to 15 years old and 1 to 22 years old respectively. All the patients in the KD group and the majority in the MAD group have pharmacoresistant epilepsy with developmental delay or mental disability. At 6 months, 25% and 20% achieved seizure freedom on KD and MAD respectively, with the difference being not statistically significant. In our series, 68% of the patients in both groups (KD and MAD) tolerated the diet well. However, 2 patients in the MAD group did not achieve adequate ketosis. Reasons for diet cessation for KD group before 6 months were lack of efficacy in seizure control (6 patients), refusal of KD meals (5 patients), and increased irritability (1 patient). Reasons for diet cessation for MAD group before 6 months were refusal of MAD meals (2 patients) and lack of efficacy in seizure control (1 patient).

**Conclusion:** At 6 months, both the ketogenic diet and modified Atkins diet were comparably effective in seizure control and generally well tolerated. The main reasons for diet cessation regardless of diet type were lack of efficacy in improving seizure control and food refusal. The results of the efficacy and tolerability of these diets are similar to those obtained from other Asian countries.

**p0385**

**THE IMPACT OF SEIZURE ONSET AGE ON COGNITIVE OUTCOME IN CHILDREN WITH STURGE-WEBER SYNDROME**

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**Purpose:** Most children with Sturge-Weber syndrome (WS) develop seizures that may contribute to their neuro-cognitive decline (Bosnyak et al., Ped Neurol, 2016: 61:38–45). Pre-symptomatic treatment with anti-seizure medication may delay seizure onset (Ville et al., Seizure, 2002;11: 145–50) but its potential effect on cognitive outcome is unknown. In this study, we analyzed the impact of seizure onset age on cognitive outcome in WS.

**Method:** Subjects participated in our prospective longitudinal clinical and neuroimaging WS study at the Children’s Hospital of Michigan, Detroit. Inclusion criteria were

a) unilateral SWS on brain MRI,
b) history of epilepsy,
c) age of<13 years,
d) age at neurocognitive assessment>2.5 years,
e) at least one year follow-up.

None of the children had epilepsy surgery. Cognitive functioning (IQ) assessed by WPPSI-III or WISC-III was correlated with age at seizure onset, extent of MRI involvement and epilepsy duration at IQ testing.

**Results:** Thirty-four children (22 girls) were included. Mean age at seizure onset and IQ test were 1.3 years (0.1–6 years) and 6.1 years (2.6–12.5 years), respectively. The mean IQ was 86 (45–118). IQ showed a strong positive correlation with seizure onset age (Spearman’s rho [r] = 0.59, p < 0.001) and negative correlation with epilepsy duration (r = -0.51, p = 0.002) and extent of MRI involvement (r = -0.36, p = 0.04). The effect of seizure onset age on IQ was non-linear, showing the maximum impact below age 1 year. In a multivariate analysis, low age at seizure onset and long duration of epilepsy contributed to low IQ independently.

**Conclusion:** Young age at seizure onset, particularly below age 1 year, is a strong, independent risk factor for poor cognitive outcome in children with SWS. The findings suggest that even a moderate delay of seizure onset by prophylactic anti-seizure medication in children < 1 year of age could have a positive impact on their cognitive outcome.

**p0386**

**SEIZURE OUTCOMES OF CHILDHOOD EPILEPSY**

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**Purpose:** Seizure outcomes of childhood epilepsy range from remission to drug-resistant epilepsy (DRE). Recent diagnostic and therapeutic...
improvements may have improved outcomes, but contemporary population-based data examining this are limited. From the Norwegian Mother and Child Cohort Study (MoBa), the largest prospective pregnancy cohort worldwide, we report seizure outcomes in children with epilepsy (CWE), and associations with clinical and socio-demographic characteristics.

Method: CWE were identified among the 112,744 MoBa participants through registry linkages and sequential MoBa parental questionnaires. Clinical characteristics, seizure outcomes, medication, and investigation results were obtained through medical record reviews and/or parental telephone interviews. Socio-demographic data were obtained from MoBa questionnaires. DRE was defined as not seizure-free at end of follow-up despite having tried ≥2 antiepileptic drugs. 1-year and 2-year-remission were defined as seizure-free at end of follow-up for at least 1 and 2 years, respectively. Only CWE with ≥2 years of follow-up were included.

Results: We identified 475 CWE with ≥2 years follow-up (mean 5.3 years). Of these, 170 CWE (36%, 95%CI 32–40%) had DRE. 247 CWE (52%, 95%CI 47–56%) had achieved 1-year remission (144 medication-free), 178 (37%, 95%CI 33–42%) had achieved 2-year remission (127 medication-free). DRE was positively associated with a number of epilepsy characteristics, all with p < 0.01: a history of neonatal seizures, early age of onset, symptomatic (including structural) etiology, ≥2 seizure types, previous status epilepticus, comorbid neurological/developmental disorders, abnormal neurological examination findings, pathological EEGs, pathological MRIs, and use of ≥2 antiepileptic drugs. These factors were all inversely associated with 2-year remission mediation-free at end of follow-up. Parental age, education and marital status were not predictive of seizure outcomes.

Conclusion: Despite advances in diagnostics and therapeutics, a third of CWE have DRE. Seizure outcomes in CWE in this population were influenced by epilepsy characteristics but not by examined socio-demographic factors.

p0395
ATYPICAL PRESENTATION OF PYRIDOXINE-DEPENDENT EPILEPSY VISITED
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Purpose: Pyridoxine-dependent epilepsy is an autosomal recessive epileptic encephalopathy caused by antiquitin (ALDH7A1) deficiency. Beside the classical presentation in form of early refractory epileptic encephalopathy, numerous neurological manifestations and metabolic/biochemical findings have been reported.

Method: Case series.

Results: We report 5 patients with atypical presentation of PDE: all presented with early onset seizures (<3 months), associated with non-immune hydrops fetalis (1 patient), obstructive hydrocephalus (1 patient), extreme prematurity with intra-ventricular hemorrhage (1 patient), regression of milestones not related to the severity of seizures (1 patient), and benign epilepsy (1 patient).

Conclusion: Since the description of the biomarkers, and the genetic background of PDE, the phenotypic spectrum of PDE expanded. It includes persistent hypoglycemia, lactic acidosis, CNS malformations, or perinatal asphyxia. These atypical presentation may mask the diagnosis, and delay the treatment. All infants presenting with unexplained seizures should be screened for antiquitin deficiency by determination of alpha-aminoacidic semialdehyde and ALDH7A1 molecular analysis. Early treatment with pyridoxine/folinic acid with L-arginine or lysine restricted diet provide good prognosis.

p0396
WEST SYNDROME IN DOWN SYNDROME INFANTS
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Purpose: To determine the prevalence, clinical characteristics and response to treatment in a cohort of Down syndrome (DS) patients with West syndrome (WS) amongst treated in a tertiary hospital in Curitiba-PR, Brazil.

Method: Cross-sectional, retrospective study of 1212 patients with DS followed at a tertiary hospital in Curitiba-PR. All data were collected from medical records: peri and neonatal characteristics, genetics, associated diseases, psychomotor development and mother’s age at child’s birth. Data on gender, genetics, age of onset, treatment response and neuromotor developmental and autistic outcomes in patients with DS and WS were extracted. Statistical analysis was performed by Student t test, Mann-Whitney test, Fisher exact test and chi-square test, with significance level of 5%.

Results: The prevalence of WS in the DS cohort was 1.9%. 22 patients were identified. Male to female ratio was 1:1. Onset of spasms occurred at a median of 7 months (3–57). Patients received Vigabatrin as first line treatment with total control of spasms in 81.8%. All patients displayed neurodevelopmental delay. Five patients (22.7%) developed epilepsy. One of the patients developed Lennox-Gastaut syndrome. There was no significant difference between the groups regarding the general characteristics of the patients (peri and neonatal characteristics, genetics, associated diseases, psychomotor development and mother’s age at child’s birth). A higher frequency of mosaicism (11.8% versus 2.2%, p = 0.02), autism (29.4% versus 5.9%, p < 0.001), seizures (17.6% versus 2.8%, p < 0.001) and clubfoot (11.8% versus 2.3%, p = 0.08) were observed in DS patients with WS than in DS patients without WS.

Conclusion: Pediatricians and pediatric neurologists with better knowl-edge about this association would reduce the time to diagnosis and delay to treatment in order to improve neurodevelopmental outcomes and quality of life of these infants. Vigabatrin therapy was effective with good control of seizures.

p0400
REDUCED STERIODGENESIS IN PATIENTS WITH PCDH19-FEMALE LIMITED EPILEPSY
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Purpose: Patients affected by protocadherin 19 (PCDH19)-female limited epilepsy (PCDH19-FE) present a remarkable reduction in allopregnanolone blood levels. However, no information is available on other neuroactive steroids and the steroidogenic response to hormonal stimulation.

Method: We evaluated allopregnanolone, pregnanolone and pregnenolone sulfate by liquid chromatographic procedures coupled with electrospay tandem mass spectrometry in 12 unrelated patients and 15 age matched controls. We also tested cortisol, progesterone and 17OH-progesterone by standard immunoassays. These hormones were evaluated in basal condition and after stimulation with adrenocorticotropic hormone (ACTH).
Results: A generalized decrease in blood levels of almost all measured neuroactive steroids was found. While administration of ACTH increased neuroactive steroid levels in the PCDH19-FE girls, these fell short of the level of the age matched controls.

Conclusion: Our findings point to multiple defects in steroidogenesis associated with and potentially relevant to PCDH19-FE.

p0402

ADJUNCTIVE TREATMENT WITH PREGABALIN FOR PARTIAL ONSET SEIZURES IN PAEDIATRIC PATIENTS: A RANDOMIZED CONTROLLED TRIAL

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Purpose: Pregabalin is approved as adjunctive therapy for partial onset seizures (POS) in adults in the US and EU. This placebo-controlled study evaluated pregabalin’s efficacy and safety (2 dose levels) as adjunctive treatment for paediatric patients with POS.

Methods: This double-blind, international study had 3 periods:
1) an 8-week baseline,
2) a 12-week double-blind (2-week dose escalation and 10-week fixed-dose), and
3) a 1-week taper. Subjects were selected for being 4–16 years of age, experiencing POS, and being treated with 1–3 antiepileptic drugs (stable regimen).

Study treatments were pregabalin 10-mg/kg/day (maximum 600 mg/day) or 2.5-mg/kg/day (maximum 150 mg/day). The primary efficacy endpoint was log(28-day seizure rate) during the double-blind period, which was analyzed with a linear model with fixed-effect terms for baseline log(28-day seizure rate), geographic region, treatment, and weight (<30 kg, ≥30 kg). Achieving a ≥50% responder rate and safety and tolerability were also evaluated.

Results: The study enrolled 295 patients who were mean age 10.2 years, 55% male, and 69% white. These patients were randomized to 10-mg/kg/ day pregabalin (n = 97), 2.5-mg/kg/day (n = 104), and placebo (n = 94). The placebo-adjusted percent improvement in log(28-day seizure rate) was statistically significant with 10-mg/kg/day pregabalin (−19.9%, p = 0.0185) and was numerically but not statistically significant with 2.5-mg/kg/day (−9.9%, p = 0.2577). Compared with placebo (22.6%), the 50% responder rate significantly favored 10-mg/kg/day pregabalin (40.6%, p = 0.0092) and was higher (but not significantly) with 2.5-mg/kg/day (29.1%, p = 0.8024). Adverse events occurring in ≥10% of any treatment group included somnolence (10-mg/kg/day 25.8%, 2.5-mg/kg/day 17.3%, placebo 13.8%), increased weight (10-mg/kg/day 13.4%, 2.5-mg/kg/day 3.8%, placebo 4.3%), and increased appetite (10-mg/kg/day 10.3%, 2.5-mg/kg/day 6.7%, placebo 4.3%). These were consistent with the known safety profile observed in adults treated with pregabalin.

Conclusions: Relative to placebo, 10-mg/kg/day pregabalin demonstrated efficacy for seizure frequency reduction, and both 10-mg/kg/day and 2.5-mg/kg/day were well tolerated. www.clinicaltrials.gov identifier NCT01389596

p0405

FAMILIAL PREDISPOSITION IN EPILEPTIC ENCEPHALOPATHY WITH CONTINUOUS SPIKE AND WAVE DURING SLEEP: TWO CASES FROM THE SAME FAMILY

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Purpose: Epileptic encephalopathy with continuous spike and wave during sleep is a syndrome characterized by almost continuous slow (typical 1.5–2 Hz) spike and wave during slow sleep (CSWS), different type of seizures and progressive decline in cognitive, behavioral and psychiatric functions. The pathogenesis of CSWS remains unknown. On the basis of few recently published cases related to gene abnormalities, a familial predisposition gains gradual importance. In this study we present two patients with CSWS from the same family.

Case: An eleven-year-old girl with normal mental and motor development until 7 years was admitted to our Epilepsy Outpatient Clinic because of intractable seizures. She was suffering from complex partial seizures characterized by staring, unresponsiveness, vocalization, repetitive stereotypic movement of hand clapping and body shaking. Seizures were lasting a few minutes and repeating a few times weekly. Six months later the frequency and the duration of seizures increased and cognitive decline developed. The repeated sleep EEG’s showed generalized spike-wave discharges compatible with CSWS. Her MRI was normal. Her neuropsychological assessment revealed global cognitive decline in all domains particularly in language function. Despite corticosteroid therapy and various combinations of different antiepileptic drugs she still has seizures almost every day. Her school performance improved a little bit. We found out that her brother also has decline in school performance but no seizure. Like his sister, CSWS was detected in his sleep EEG.

Conclusion: The pathophysiology of CSWS is not completely understood, but corticothalamic neuronal network related to sleep patterns is thought to be involved. Our patient has intractable epilepsy and her prognosis is poor. In the context of this case we want to draw attention to the familial predisposition in CSWS patients and poor outcome. Further studies are required to confirm this relation.

p0407

DISCUSSING SUDEP AS PART OF STANDARD PAEDIATRIC EPILEPSY CARE: PAEDIATRIC HEALTHCARE PROFESSIONAL SURVEY AND LITERATURE REVIEW

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Purpose: To determine compliance with UK national guidelines recommending tailored provision of information on Sudden Unexpected Death in Epilepsy (SUDEP) to all children and families diagnosed with epilepsy.

Method: UK healthcare professionals (HCPs) were contacted via regional epilepsy networks and the British Paediatric Neurology Association and asked to complete an online survey. A systematic literature review was performed on 3rd January 2017, searching MEDLINE for physician practices in discussing SUDEP.

Results: One hundred and seventy-six HCPs responded, including paediatricians (n = 78, 44%), paediatric neurologists (n = 42, 24%), and epilepsy-nurse specialists (n = 19, 11%). Respondents provided information on SUDEP: to all patients with epilepsy (n = 49, 28%), selected patients only (n = 106, 60%), or not at all (n = 20, 11%). Of those who give information only to selected patients, selection criteria include intractable or nocturnal seizures, symptomatic epilepsies, surgical candidates, medication non-compliance, and adolescents. Most discussions take place around the time of diagnosis. Common challenges and barriers to discussing SUDEP were worry about frightening the family, misinterpretation of risk by families, uncertainty of facts and figures, lack of confidence, time constraints, and in childhood absence epilepsy. Sixty-five per cent of respondents wanted more guidance, including specific training, peer discussion and/or standardised written information for families. We found 9 similar surveys in the literature, all published within the last 11 years, featuring mostly adult and paediatric neurologists in the UK and worldwide. Of 2607 respondents, 189 (7%) discuss SUDEP with all patients, 971 (37%) rarely discuss, and 331 (13%) never discuss it.
Abstracts

p0412
EPILEPSY IN AUTISM SPECTRUM DISORDER: A LONG-TERM ELECTROCLINICAL ANALYSIS OF 36 CASES
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Purpose: To analyze the electroclinical features of epilepsy in a population of patients affected by autism spectrum disorder (ASD), in order to verify if precise electroclinical syndromic entities can be identified.

Methods: In a population of 207 patients with initial diagnosis of ASD admitted to our Unit of Child Neuropsychiatry between 1988 and 2012 (genetic epileptic encephalopathies and cases in which the autistic features appeared after the epileptic encephalopathy onset were excluded), 36 patients fulfilled the following criteria: (1) diagnosis of Autism Spectrum Disorder following the DSM-5 (Autistic Disorder or Asperger Syndrome or Pervasive Developmental Disease Non Otherwise Specified, following the DSM-IV criteria) and (2) diagnosis of Epilepsy.

Clinical data, EEG, MRI findings, genetic analysis, ASD-features, and cognitive profile were reviewed. We analyzed particularly the clinical characteristics of seizures and the EEG features. We further analyzed the possible correlation between electroclinical picture, ASD-type and cognitive outcome.

Results: The mean age at follow-up was 13.2 years (from 4 to 22 years). We could identify 3 groups:

- “Self-limited Focal Epilepsies-like” (n = 7): age-dependent forms similar to the one previously known as benign childhood epilepsy with centrotemporal spikes.
- "Structural or unknown etiology Focal Epilepsies” (n = 13): forms otherwise called Symptomatic or Cryptogenic Focal Epilepsy (mainly temporal lobe epilepsy) which tend to persist in time.
- Unclassified Epilepsies (n = 16): forms characterized by electroclinical and evolutative pattern variable and difficult to define. In the majority of cases both seizure types and etiology are unknown.

Conclusion: We confirmed that Epilepsy in ASD patient is a frequent comorbidity (17.3% of our ASD population). In the majority of cases (44.4%) epilepsy is unclassified and prognosis is not predictable. However we found two relatively homogenus groups in the remaining cases: a group of focal epilepsies (36.1%), mostly temporal, with variable prognosis, and the second of self-limited focal epilepsy (19.5%).

p0413
apolipoprotein E – POTENTIAL BIOMARKER IN EPILEPSY
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Purpose: To determine a role of particular apolipoprotein E alleles and as well as the blood lipid profile in presentation of different types of epilepsy in children.

Methods: Alleles of apolipoprotein E gene, blood cholesterol (total cholesterol, HDL, and LDL), triglycerides and HDL levels were analysed from blood samples obtained from 111 children with epilepsy and 118 children of the same age as the control group. After PCR amplification, APOE fragments were genotyped by melting curve analysis using allele-specific probes.

Results: The distribution of APOE alleles was the same in both the experimental and the control group. Significantly increased values of the total cholesterol (p = 0.00039) and the low-density lipoprotein (LDL; p = 0.00034) were observed in the control group compared to the experimental group.

No statistically significant difference was found between the genotype of children with idiopathic and symptomatic epilepsy. However, in regard to the type of epilepsy, patients with symptomatic epilepsy showed significantly higher plasma levels of the total cholesterol (p = 0.014) and LDL cholesterol (p = 0.0009). Surprisingly, genotype showed a correlation to plasma LDL levels (p = 0.02).

Conclusion: Although this study confirmed no connection between APOE and the type of epilepsy in children, it showed that the children with epilepsy have lower total cholesterol and LDL levels, as well as those with idiopathic epilepsy compared to patients with symptomatic condition.

p0414
efficacy and tolerability of perampanel (PER) add-on therapy in children with refractory focal epilepsies
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Purpose: To assess the clinical efficacy and tolerability of PER in children with refractory focal epilepsies.

Method: The study population comprised 68 children (34 boys, 34 girls, aged between 4–17 years) with refractory focal and multifocal epilepsies. PER was given as add-on therapy at the doses 4–12 mg/day. Prior to PER treatment the patients have tried 4–12 antiepileptic drugs. The treatment duration varied between 3 and 46 months. PER clinical efficacy was analyzed in the whole group and dependent on the seizure types and patient’s age. PER tolerability was evaluated during the course and at the end of follow-up.

Results: The complete seizure control and reduction of seizure frequency for >50% were observed in 9 (13.2%) and 31 (45.6%) patients respectively. PER efficacy did not vary significantly in the young (4–12 years) and elder children (13–17 years). PER was mostly effective in patients with focal motor, secondary generalized and tonic seizures while in children with focal hypomotor seizures and epileptic spasms its efficacy was not significant. The adverse events (aggressiveness, restlessness, apathy, nausea, dizziness) occurred in 11/68 patients (16.2%), and in 7 of them PER therapy was stopped after 3–4 months since treatment initiation.

Conclusion: PER showed 50–100% seizure reduction in 58.8% of patients with refractory focal multifocal epilepsy with the highest efficacy against focal hypermotor, secondary generalized and tonic seizures. PER was equally effective in the younger and elder age groups. Adverse events were not frequently observed and led to earlier therapy termination in 7/68 (10.3%) of patients.

p0415
ictal and peri-ictal cardiorespiratory abnormalities in paediatric seizures: possible relation with sudep?
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Purpose: Autonomic and cardiopulmonary regulation play an important role in the cascade of events which results in SUDEP (Sudden Unexpected Death in Epilepsy). Our objective was to assess the frequency of ictal cardiorespiratory abnormalities in a large cohort of paediatric epileptic patients, with the final aim of early detection of potential risk factors for SUDEP.

Method: We retrospectively analysed seizures recorded with video-poligraphic-EEG between 2013 and 2015, in two third level epilepsy centres. Inferential analysis, crude odds ratios and logistic regression were
performed to evaluate association of ictal cardiorespiratory findings with seizures characteristics, demographics and peri-ictal cardiorespiratory abnormalities.

**Results:** The inclusion criteria were valid for 193 seizures in 163 children. Heart rate (HR) variation was found in 70% of seizures (90% tachycardia, 12% bradycardia); breath rate (BR) abnormalities in 80% (58% tachypnea/hyperpnea, 39% bradypnea, 12% apnoea). The risk of ictal tachycardia/bradycardia increased with age (OR = 1.01, p = 0.012), seizures during sleep (OR = 7.91, p < 0.0001) and related with pre-ictal tachycardia (OR = 8.93, p = 0.05) and post-ictal tachycardia (OR = 11.5, p = 0.001). Compared to patients with age-related epilepsy, the risk of HR abnormalities increased in infantile cerebral palsy/acquired cerebropathies and malformative/diagnostic/developmental abnormalities.

**Conclusion:** In paediatric epileptic seizures there is high rate of cardiorespiratory abnormalities, that relate to age, early onset epilepsy, sleep, infantile cerebral palsy/acquired cerebropathies and malformative/genetic syndromes. These data help in the early detection of patients potentially more at risk of SUDEP, with a significant implication in terms of prevention.

**p0419**

**CHILDHOOD ABSENCE EPILEPSY, COGNITIVE OUTCOME**

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**Purpose:** A high risk of academic failures and attention deficit was found out in children suffering from childhood absence epilepsy.

**Aim:** To estimate the peculiarities of CAE course in two groups:

1. With criteria C.P. Panayiotopoulos, 2005;
2. Patients with absence seizures, not included in group 1.

**Method:** Retrospective analysis of 186 cases of patients with CAE, observed in Morozov State Children’s Clinical Hospital, EEG, AED response, neuropsychological assessment by GMDS-ER (2–8).

**Results:**

- 1st group consisted of 124 patients, average age 8.7 years, 2nd group - 64 patients, average age 11.2 years.
- 70.8% patients from the 1st group achieved remission, there were no cases of GTCS or myoclonic seizures, the average duration of therapy was 2.8 years (2.5–3.3), more than one AED was prescribed in 10.4% of cases.
- 51.6% of patients from the 2nd group achieved remission, 30.6% had myoclonic seizures, 51.6% - GTCS; the average duration of therapy was 4.2 years (3.6–5.1), polytherapy was needed in 48.3% of cases.
- Neuropsychological assessment (GMDS-ER 2–8) revealed impaired mental function of varying severity in both groups. In the 1st group 60% of patients had mild or moderate deviation (max. 15.5 months), especially in locomotor, personal-social, eye and hand co-ordination subscales; 40% had more severe (max. 33.5 months) delay, especially in personal-social, performance and practical reasoning subscales.

**Conclusion:** GTCS and myoclonic seizures in combination with absences do not always determine unfavorable prognosis of comorbid cognitive and psycho-emotional disorders. The delay of neuropsychological development in patients with CAE may vary widely. Apparently, CAE is genetically heterogeneous, which may determine the course and outcome peculiarities.

**p0418**

**ELECTROENCEPHALOGRAPHIC AND DIFFUSION TENSOR IMAGING CHANGES IN IDIOPATHIC EPILEPTIC CHILDREN IMANE**

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**Purpose:** Neurocognitive impairment represent one of the most common co-morbidities occurring in school-aged children with idiopathic epilepsy. Diagnosis of the idiopathic form of epilepsy requires absence of any macrostructural abnormality in the conventional MRI, though changes can be found at the microstructural level using advanced imaging techniques as Diffusion tensor imaging (DTI). The purpose of the current study is to assess the correlation between the microstructural white matter DTI abnormalities, the electroencephalographic changes and the cognitive dysfunction in children with idiopathic active epilepsy.

**Method:** Comparative cross sectional study included 60 children with idiopathic active epilepsy. Based on the Stanford binet 5th edition scores, patients were equally allocated to normal cognitive functions or cognitive dysfunction group. History of the epileptic condition was gathered by personal interview. All patients underwent brain EEG and DTI which was interpreted using FSL.

**Results:** Fractional anisotropy (FA) was significantly higher while mean diffusivity (MD) was significantly lower in the normal cognitive functions than in the cognitive dysfunction group. This altered microstructure was related to the degree of the cognitive performance of the studied epileptic children. The microstructural alterations of the neural fibers in the epileptic patients with cognitive dysfunction were significantly related to younger age of onset of epilepsy, poor control of the clinical seizures and the use of multiple antiepileptic medications.

**Conclusion:** Epileptic children with normal cognitive functions differ in the white matter integrity as measured by DTI compared to those with cognitive dysfunction. Individual tract integrity is linked to the type of cognitive dysfunction in the epileptic brain. These changes have important cognitive consequences.

**p0421**

**RISK OF SUICIDE, AFFECTIVE DYSPHORIC DISORDERS AND QUALITY OF LIFE PERCEPTION IN PATIENTS WITH FOCAL REFRACTORY EPILEPSY**

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**Purpose:** To find the frequency of the risk of suicide in patients with focal refractory epilepsy and its possible association with factors like perceived QOL (quality of life) and AsDD (affective-somatoform dysphoric disorder), using the 2007 ILAE’s proposal to classify affective disorders of epilepsy.

**Method:** A total sample of 82 patients was divided into two groups depending on the presence of suicidal risk: study group (A) with suicidal risk and control group (B) without suicidal risk. Questionnaires, scales, interviews and clinical charts were evaluated by professionals with expertise in Neurology and Epileptology (RAM, AGA), Psychiatry (AGE) and Neuropsychology (FGR). Suicidal risk was evaluated with...
the M.E.P.I (International Psychiatry Mini-interview) suicidal module that specifies the current suicidal risk based on scores. QOL was evaluated with the Quality of Life in Epilepsy Inventory-31 survey (QOLIE-31). Logistic regression was conducted to ascertain if ASDD and QOL significantly predicted suicidal risk were considered statistically significant when p value was <0.05.

**Results:** Suicidal risk was present in 40.3% (33 patients). It was classified as severe in 31.7%, and it was only present in temporal lobe epilepsy cases p = 0.002. More than half of patients with ASDD had risk of suicide (52%) (p = 0.006). The presence of ASDD was found to be a risk factor for suicidal risk (OR 3.86; IC 1.3–12.2). Patients with suicidal risk had a worse QOL score than patients without risk of suicide (57.8 ± 16.9 vs 46.0 ± 18.2; p < 0.05) and an affected QOL significantly increased suicidal risk (OR 2.9; CI 1.3–7.8). Multivariate analysis demonstrated that an impaired QOL (OR 2.2) and the presence of ASDD (OR 4.1) significantly increased the probability of having suicidal risk (χ² = 13.6; OR 5.2, p = 0.009).

**Conclusion:** ASDD and low QOL perception increase, independently, the risk of suicide.

**p0423**

STUDY OF PERSONALITY TRAITS OF JAPANESE PATIENTS WITH EPILEPSY USING NEO-PI-R AND BDI-II

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**Purpose:** NEO-PI-R, a widely used self-completed questionnaire method for character research, evaluates character with a five-domain scale (N: Neuroticism, E: Extraversion, O: Openness, A: Agreeableness, C: Conscientiousness) and 30 subclassification facets. We assessed subjective character traits of patients with epilepsy (PWE) using NEO-PI-R and then examined the relation between each NEO-PI-R item and BDI-II (self-completed questionnaire of depressive symptoms) score.

**Method:** One hundred forty-five outpatients (77 women, 68 men; age 33.8 ± 10.2 years; focal epilepsy [n = 116], IGE [n = 27], inherited epilepsy [n = 21]) completed the NEO-PI-R (Japanese version). Scales were scored with the T-score normalized by gender and age group in a general population. The average T-score was “high” when >55 and “low” when <45. The last 41 patients (22 women, 19 men; age 32.4 ± 10.1 years; all focal epilepsy) simultaneously completed the BDI-II.

**Results:** In the five domain scales, we found the “high” trait in N (average age ± SD: 57.5 ± 12.0). In the facet scales, we found “high” traits in N1 (Anxiety, 57.4 ± 10.7), N3 (Depression, 57.8 ± 12.1), and N6 (Vulnerability, 58.0 ± 11.2) and a “low” trait in C1 (Competence, 44.8 ± 10.5). Differences between left (n = 21) and right (n = 25) temporal lobe epilepsy (TLE) or between TLE (n = 52) and extra TLE (n = 26) were not significant (Mann-Whitney U test, p < 0.05). BDI-II scores in the 41 patients correlated highly positively with N, N1, N2 (Angry Hostility), N3, N4 (Self-Consciousness), N5 (Impulsiveness), N6, and O1 (Fantasy) and highly negatively with A and C1 (Spearman’s rank correlation coefficient, rS = 0.4, p < 0.01).

**Conclusion:** No consistent personality trait in PWE or clear difference provided for the personality trait by lateralization or focus localization. However, comorbid depression must be addressed when discussing patients’ personality traits because of the high prevalence of depression in PWE and the possibility that their depression may affect the scales assessing personality traits.

**p0424**

A STUDY ON BIDIRECTIONAL RELATIONSHIP BETWEEN EPILEPSY AND DEPRESSION

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**Purpose:** It is well known that depression is observed more frequently in patients with epilepsy (PWE) than in the general population with the suggested reasoning being that pathophysiological mechanisms common with idiopathic depression may be responsible because of their similar clinical symptoms and the bi-directional relationship between both disorders. To investigate shared pathophysiological mechanisms with depression and epilepsy, clinical characteristics between epilepsy patients with and without depression were compared and identified the risk factors for developing depression in PWE.

**Method:** Subjects consisted of 72 PWE with depressive disorder or a history of depressive disorder. For control, 300 other PWE without psychiatric disorder were studied. Demographic and clinical items were reviewed through direct interview or medical records. Secondly, the subjects were examined the depression related factors including age of onset, duration from onset of epilepsy to that of depression, subtype of depression, triggering factors for depression and comorbid psychiatric disorder.

**Results:** Women and family histories of psychiatric disorder were seen more frequently in patients with depression than without. Significant differences in epilepsy related factors were not observed between both groups. Onset of depression was relatively young (<20 years) and depression preceded epilepsy onset in 20%. Comorbid psychiatric disorders existed in approximately 40% of patients with direct seizure distress rarely inducing depression.

**Conclusion:** Depression may develop more on a basis of biological than psychosocial factors in PWE due to the existence of a bidirectional relationship. The frequent existence of a family history of psychiatric or comorbid psychiatric disorders may indicate a predisposition to depression. With seizures themselves proved of little influence on the occurrence of depression, we suggest that patients with biological vulnerabilities may develop depression when the psychosocial disturbances associated with epilepsy are added.

**p0426**

PSYCHOTIC STATES IN LENNOX-GASTAUT SYNDROME

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**Purpose:** Although psychotic states often occur in patients with epilepsy, there are few reports about psychosis with symptomatic/cryptogenic generalized epilepsy (SGE). We investigated the characteristics of four cases of psychoses with Lennox-Gastaut syndrome (LGS).

**Method:** We selected 984 patients with epilepsy treated in the Neuropsychiatry Department of Kurume University Hospital from April 2010 to March 2016. Four of 37 (10.8%) patients with SGE presented interictal psychosis (IIP). All of them were diagnosed with LGS. We investigated medical records retrospectively and obtained the clinical data from 4 IIP patients with LGS.

**Results:** All patients had schizophrenia-like psychosis. Although positive symptoms, such as auditory hallucinations and delusions, were remarkable in all four patients, negative symptoms, such as blunted affect and emotional withdrawal, were less common. Three patients had transient psychotic periods about within one year, and their psychotic states remitted completely. Only one patient demonstrated a persistent chronic psychotic state for 2 years.

Three patient showed psychoses that correlated with improvement in seizure frequency.

All patients showed frequent epileptic discharges on EEG, such as diffuse spike-wave bursts and diffuse rapid rhythms, during the remission of
psychosis. Two patients showed the disappearance of epileptic discharges during the development of psychosis that correlated with inhibition of seizures.

SPECT was performed in three cases and they all showed hyperperfusion of the frontal lobe. SPECT was performed during both the psychotic and remitted states in only one case. An increase in blood flow to the bilateral frontal lobes was found during the psychotic state compared to that seen during remitted states.

**Conclusion:** These results suggest that changes in epileptic activities may tend to cause the development of psychosis in LGS. Furthermore, SPECT findings suggested an association between psychosis and disturbance of frontal lobe blood flow.

**p0432**

**SCHOOL-AGED CHILDREN AND PARENTS’ EXPERIENCES OF EPILEPSY AND CARE: A QUALITATIVE STUDY**

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**Purpose:** Epilepsy holds a variety of implications for the child and their family beyond seizures, including intricate and multidimensional care arrangements. Despite recognition of the importance of listening to and consulting with children regarding their healthcare, children’s accounts regarding their epilepsy and their involvement in associated care is under examined.

We present data from a study exploring everyday experiences of children with active epilepsy (CWE) (on anti-epileptic drug(s) and or has had a seizure in the last year) and their involvement in their own healthcare in formal clinical and informal home contexts.

**Method:** CWE and their parent(s) were interviewed separately twice. Semi-structured interviews were used to examine, in detail, themes associated with everyday and care experiences of epilepsy. Observation of clinical consultations guided the second interview, generating deeper discussions. Participatory tools were used in child interviews to facilitate conversation. Interviews were recorded and transcribed using NVivo; inductive thematic data analysis was conducted. The study was approved by two Scottish NHS Research Ethics Committees.

**Results:** 23 children (12F; 7–14 years) with different types of epilepsy (e.g. Childhood Absence and Rolandic Epilepsy) and 31 of their parents’ (25F) from varied socioeconomic backgrounds were interviewed.

Taking medication was a major aspect of epilepsy for CWE, often considered burdensome. Parent’s discussions of medication taking included emotional turmoil and complex negotiation strategies. Many CWE reported epilepsy did not interfere with daily life, although some did have restrictions on activities by parents due to perceived risks. CWE differed in their desire for and comfort with involvement in their care. Age was a major factor in how parents determined their child’s autonomy and competence of self-care. Parents saw themselves as gatekeepers of epilepsy information, being selective in what they told their child. CWE and their parents have unmet support and information needs regarding the future of their epilepsy.

**p0436**

**EPILEPSY, STIGMA AND FAMILY**

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**Purpose:** Epilepsy is surrounded by prejudice and stigma. Little is known about the perception of stigma in family members.

**Objective:** To study how consecutive adult patients with epilepsy (PWE) and cohabiting relatives (CR) perceive the stigma of epilepsy and its correlations with the clinical aspects of epilepsy and quality of life (QoL).

**Method:** The study investigated possible associations of the Stigma Scale of Epilepsy (SSE) of 148 consecutive PWE with the SSE of 90 CR (Pearson = 0.214; p = 0.01). SSE scores were significantly higher in PWE with exclusively generalized seizures. Higher SSE scores in PWE were correlated with longer epilepsy duration (0.385; p = 0.001). The CR of PWE with depressive disorder had higher SSE scores (46.3 ± 14.1 x 37.6 ± 12.8; t-test; p = 0.004). Higher stigma (PWE and CR) was correlated with worse QoL in PWE.

**Conclusion:** Perceived stigma was high. Stigma perceived by PWE and CR are correlated. The clinical aspects of epilepsy are related to perceived stigma (PWE and CR). Worse QoL of PWE is associated with higher perceived stigma (PWE and CR).

**p0434**

**THE STIGMA OF EPILEPSY FROM THE PERSPECTIVE OF PATIENTS WITH EPILEPSY AND PEOPLE FROM THE ITALIAN COMMUNITY**

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**Purpose:** To assess the stigma related to epilepsy from the perspective of both epileptic patients and people from the Italian community; moreover, the impact of the perceived stigma on the mood and quality of life of patients was also addressed.

**Method:** We enrolled 53 patients with epilepsy (21 males, mean age 50.3 ± 17.9 years; 30 patients seizure free/23 with refractory epilepsy) and 205 non-epileptic subjects (71 males, mean age 35.4 ± 15.3 years). Both epileptic (ES) and non-epileptic subjects (NES) were interviewed on an individual basis and completed the Stigma Scale of Epilepsy (SSE), a 24-items questionnaire that has been demonstrated to allow the quantification of the perception of stigma by patients and people from community. Moreover, the ES fulfilled a 3-items stigma scale, QUOLIE-31 (Q31) and Beck Depression Inventory 2 (BDI-2) questionnaires for the evaluation of quality of life and depressive symptoms. The results of SSE were correlated with clinical and demographic details of both ES and NES, as well as the Q31 and BDI-2 scores in ES.

**Results:** The SSE scores were significantly higher in NES with respect to ES (respectively 59.6 vs 44.8). Fifty percent of ES reported feeling stigmatised, with 8% reporting feeling highly stigmatised. SSE scores in ES were highly correlated with depressive symptoms and perceived stigma, as measure by SSE, had a negative impact on the overall score of the Q31, as well as on all subscales of Q31, except for the seizure worry.

**Conclusion:** Our study evidenced higher levels in the perception of stigma in NES than in ES. The people with epilepsy still experience feelings of high stigmatisation, strongly correlated with depressive symptoms and lower scores of quality of life. Finally, all aspects of the quality of life of ES, except the seizure worry, correlated negatively with the severity of perceived stigma.
p0437
HYPOCAPNEA WITH MECHANICAL VENTILATION AND POOR OUTCOME OF REFRACTORY STATUS EPILEPTICUS
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Purpose: To determine optimal protocol of mechanical ventilation during intravenous anesthetics to control refractory status epilepticus (RSE). RSE represents a life-threatening condition, requiring anesthetic treatment and neurointensive care with respiratory support. However, it is unknown which protocol of mechanical ventilator was better in case of RSE. Hyperventilation is a well-established procedure for seizure provocation during performance of EEG whereas CO2 has long been known for its anticonvulsant properties in several experimental studies. In theory, initial hypocapnea during mechanical ventilation in case of RSE could be associated with worse outcome.

Method: The status epilepticus (SE) cohort consisted of patients from the epilepsy centers of eight academic tertiary medical centers in South Korea. The clinical data including pCO2 level for all adults with SE from January 2013 to February 2016 were derived from a prospective SE database. The cases with RSE who underwent anesthetic therapy with mechanical ventilation were included. The primary outcome variable was defined as in-hospital death. The secondary outcome variable was defined as a poor functional outcome, i.e., a score of 1–3 on the Glasgow Outcome Scale (GOS) at discharge.

Results: Among the 31 patients with RSE recruited into the study, and excluding those who need ICP control, 11 (35.5%) died in the hospital and 23 (74.2%) were discharges with a poor functional outcome. In 12 patients, initial level of arterial carbon dioxide was below 32 mmHg (hypocapnea). The initial hypocapnea was not associated with in hospital death (33.3% in hypocapnea versus 36.8% in non-hypocapnea, p > 0.99), but a trend toward poor functional outcome at discharge (84.2% of hypocapnea versus 58.3% of non-hypocapnea, p = 0.206).

Conclusion: Hypocapnea with hyperventilation might be avoided in cases with intravenous anesthetic treatment and mechanical ventilation to control RSE.

Results: Significantly lower AP levels were found in CSF of patients affected by SE (−30%; p < 0.05, Mann-Whitney test). Notably, AP was not detectable in 28 out of 41 patients affected by SE (p < 0.01 vs controls, Fisher’s exact test). In serum, AP levels did not differ in the two considered groups. Conversely, PS was present at similar levels in the investigated groups. Finally, differences in AP levels could not be explained by a variation in CSF albumin content. These findings indicate that AP is defective in the CSF of patients affected by SE. This phenomenon was not dependent on carriers for steroids, such as albumin.

Conclusions: AP reduction in CSF of patients with SE may contribute to support the epileptic activity. In such a case, to re-establish the level of this steroid may be an important therapeutic target in patients affected by SE, to avoid refractory evolution. Indeed, the limited, but encouraging evidence obtained in paediatric patients treated with AP to stop super-refractory SE is in agreement with our hypothesis.

p0444
EFFICACY AND SAFETY OF PERAMPANEL ORAL LOADING IN POST-ANOXIC SUPER-REFRACTORY STATUS EPILEPTICUS: A CASE SERIES
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Purpose: Super-refractory non convulsive status epilepticus (NCSE) occurs in 20–25% of patients with post-anoxic encephalopathy following cardiac arrest. In selected patients with favorable multimodal prognostic indicators, treatment of super-refractory NCSE may lead to good neurological outcome.

Method: We analyzed acute EEG changes, neurological outcome and adverse effects in consecutive post-anoxic patients with super-refractory NCSE treated with add-on oral loading of perampanel. Efficacy was defined when Perampanel was the last antiepileptic drug introduced into the antiepileptic therapy within 72 h before the cessation of NCSE and without changes in the comedication.

Results: Eight post-anoxic patients with super-refractory NCSE were treated with perampanel (median initial dose 6 mg, range 6–12 mg) administered via nasogastric tube. Median age was 52 years (range 20–71). All patients had continuous EEG monitoring showing definite generalized NCSE with coma, diagnosed according to the Salzburg criteria. All patients had favorable multimodal prognostic indicators (presence of brainstem reflexes; presence of bilateral N20 responses; absence of periodic discharges/GPEs). Perampanel was given after a median number of 3 antiepileptic drugs (range 2–5) and 3 anesthetic drugs (range 1–4), after a median time of 9.5 days (range 4–35). In 6 patients (75%), status epilepticus resolved within 72 hours after administration of Perampanel, without changing the comedication. Neurological outcomes at 3 months were return to normal or minimal disability in 4 patients (CPC 1–2, 50%), minimally conscious state in 1 patient (CPC 4, 12.5%) and death in 3 patients (CPC 5, 37.5%). No cardiorespiratory or cutaneous adverse effects was reported. A reversible cholostasis, which required no specific treatment, was observed in 5 patients (62.5%).

Conclusion: Perampanel 6–12 mg oral loading appeared an effective and safe option in selected patients with post-anoxic super-refractory NCSE with good prognostic indicators.

p0447
SEXUAL DISORDERS IN WOMEN WITH EPILEPSY
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Most women with epilepsy maintain normal reproductive cycles and sexual lives. However, a significant minority, approximately 20–30%, have
some degree of sexual dysfunction, including problems with seizure exacerbation, libido, arousal, and orgasm. Fluctuating hormone levels may contribute to an array of reproductive cycling abnormalities. With regard to sexual dysfunction, there is some evidence of reduced genital blood flow in women with temporal lobe epilepsy. Other studies suggest that psychosocial factors, such as depression, feeling stigmatized, and being anxious about having seizures during sex, may contribute to the higher rates of sexual dysfunction in this patient population. Some antiepileptic drugs may adversely affect normal reproductive cycling and sexual function, particularly drugs that increase serotoninergic transmis-

sion. Conversely, resective epilepsy surgery has been shown to restore sexual function. Treatments for sexual dysfunction include testosterone replacement, although transdermal testosterone replacement is not yet approved by the Food and Drug Administration for women. Given the possibility that women with epilepsy may experience inadequate vasoco-

gensation during arousal, sildenafil may have a useful role, though it has not proved effective for women in general. This review focuses on potential sexual problems that are faced by women with epilepsy, with the sug-

gestion that proper treatment may alleviate these problems.

p0449

PHARMACOKINETIC VARIABILITY OF VALPROATE IN WOMEN WITH EPILEPSY DURING PREGNANCY


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Purpose: Use of valproate in women of child-bearing age is currently controversial. The risk of teratogenicity is dose-dependent, and recommendations based on dose-event relationships. The purpose was to elucidate pharmacokinetic variability of valproate during pregnancy for improved insight and patient safety.

Method: Anonymized retrospective data from a therapeutic drug monitoring (TDM)-database (2006–2015) and pregnancy data from Oppland Perinatal Database (1994–2015) were used. Included samples were trough total concentrations of valproate at assumed steady-state. The study was approved by the Regional Ethics Committee.

Results: Data from 51 pregnancies in 33 women with epilepsy was used (1–4 pregnancies per woman), mean age 29 years (range 19–40). There were 1–7 TDM samples per woman. Mean dose and serum concentration of valproate before pregnancy was 938 (SD = 342) mg/day and 427 (SD = 97) µmol/L, respectively. In total, 58% had serum concentrations within the reference range (300–600 µmol/L). The variability in concentration/dose (C/D)-ratios between women was 13-fold, and mean inter-patient variability 2.3-fold (up to 5-fold). 17 (52%) women used <700 mg/day, with 5-fold variability in C/D-ratio. There was a significant 46% reduction in C/D-ratios, 0.53–0.29 µmol/L mg, before pregnancy to third trimester, reflecting increased clearance. Unfortunately, free valproate concentrations were only measured in three patients. Additional clinical data was available in 21 women/38 pregnancies: 13 generalised epilepsies, 6 seizure free during pregnancy, and 1 major malformation noted.

Conclusion: Pharmacokinetic variability of valproate during pregnancy was pronounced, demonstrating that dose is a poor approximation of fetal drug exposure. Implementation of TDM and measurement of free valproate concentrations should be aimed at during pregnancy and in further studies.

p0451

MISCARRIAGES IN PREGNANT WOMEN WITH EPILEPSY: FINDINGS FROM THE MONEAD STUDY


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Purpose: Many miscarriages go undetected when early in pregnancy. In recognized pregnancies, miscarriages range 8–25% for the general popu-

lation. In women with epilepsy or treated with antiepileptic drug (AED), some studies have reported slightly higher spontaneous miscarriage rates than comparison groups. Here, we report the occurrence of miscarriages in the Maternal Outcomes and Neurodevelopmental Effects of Antiepileptic Drugs (MONEAD) study, which is an NIH-funded, prospective, observational, multi-center investigation of pregnancy outcomes for both mother and child.

Methods: Women were enrolled across 20 USA sites (2012–2016). Inclusion criteria for PWWE included ages 14–45 years and ≤20 weeks gestational age. Exclusion criteria included history of psychogenic non-epileptic spells, expected IQ < 70, other major medical illness, progressive cerebral disease, and switching AED in pregnancy prior to enrollment.

Results: 351 pregnant women with epilepsy (PWWE), 105 pregnant women without epilepsy (PWWoE), and 109 non-pregnant women with epilepsy were enrolled. For PWWE at enrollment, 74% were on monotherapy, 22% on polytherapy, and 4% on no AEDs. The most common AED monotherapies were lamotrigine (42%), levetiracetam (38%), carbamazepine (5%), zonisamide (5%), oxcarbazepine (5%), and topira-

mate (3%). This analysis is limited to spontaneous miscarriages; which occurred in 3.3% of pregnancies in PWWE and 0% in PWWoE. Mean gestational ages at enrollment were 13.7 weeks in PWWE and 15.4 weeks in PWWoE. Rates did not appear to differ significantly across different antiepileptic drugs. No major congenital malformations were reported in the miscarriages.

Conclusion: Miscarriage rates were low in both PWWE and PWWoE. These low rates are likely related to the advanced gestational ages at enrollment. Future analyses will examine other pregnancy outcomes in the mothers and children. Study supported by: NIH NINDS, NICHD #U01-NS038455.

p0452

THE INFLUENCE OF ETHNIC BACKGROUND ON PARTICIPATION AND PREGNANCY OUTCOMES IN THE AUSTRALIAN PREGNANCY REGISTER

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SURVEY IN GERMAN SPEAKING COUNTRIES
KNOWLEDGE. RESULTS FROM AN INTERNET BASED SURVEY IN GERMAN SPEAKING COUNTRIES
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Purpose: We tried to determine the influence of consulting by a neurologist on the level of pregnancy-related knowledge of women with epilepsy in German speaking countries.

Method: A questionnaire was placed on the internet platform of a patient’s organisation from 4th August 2015 to 31st to December 2015. The questionnaire consisted of 18 questions addressing the characteristics of the syndromes of epilepsy, the patients experience with pregnancy and the sources of their pregnancy-related knowledge. Another 20 items addressed the level of pregnancy-related knowledge. Each of these items consisted of a 5-point Likert scale. We considered Likert scale answers of 1 and 2 as equivalent to disagreement and of 4 and 5 as agreement with the statement in question.

Results: 192 women (179 patients, 13 relatives) aged 30.5 years on average (SD 10.8) participated. Most women got information and advice concerning the treatment of epilepsy from a neurologist (80.73%). Majority of women obtained information concerning driving licence (71.88%) followed by information about pregnancy and delivery (60.42%). On the average only 45.7% of the questions addressing pregnancy-related knowledge were answered correctly. Women, who were counselled by a neurologist gave more correct answers than the others (49% SD 19% vs. 33% SD 24%, p < 0.0002). Women, who remembered being counselled about pregnancy related matters gave more correct answers than the others (51% SD 17% vs. 38% SD 24%, p < 0.011).

Conclusion: Counselling about pregnancy related matters proved to be effective. But even after this huge information needs concerning pregnancy related issues remained.

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p0457
JUVENILE MYOCLONIC EPILEPSY: LONG-TERM PROGNOSIS AND TREATMENT WITHDRAWAL
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Introduction: Juvenile myoclonic epilepsy (JME) is a well-known epileptic syndrome, but there are still doubts about its long-term therapeutic management.

Method: Single centre retrospective study reviewing medical records of patients with JME diagnosis more than 20 years after onset.

Results: A sample of 20 patients with a diagnosis of JME with a mean follow-up time of almost 30 years (29.95, 21–47 years) was obtained. The mean age was 44.1 years and 55% were men. The most common subtype of JME was classic JME in 75% of the cases, with myoclonus plus generalized tonic-clonic seizures (GTCS) being the most common seizure presentation in 70%. 55% of the patients were in monotherapy, 25% were drug-resistant, and 60% had been seizure-free for more than five years. The presence of psychiatric comorbidity and GTCS preceded by myoclonus have been observed as factors associated with drug resistance (p < 0.05). Four patients (20%) had been tried to withdraw the antiepileptic drugs (AEDs) at some point in their evolution; two of them were seizure-free off AEDs, they had a mean age of 44.5 years and carried an average of 5.5 years without treatment; the mean age at which treatment was discontinued was 39 (36 and 42 years), unlike the two patients who relapsed in whom the mean withdrawal age was 23 years.

Conclusion: JME is an epileptic syndrome with a good long-term clinical prognosis. In spite of being a small sample, in our opinion our work supports the possibility of remission off AEDs in patients with seizure freedom maintained over time, highlighting some factors to consider such as psychiatric comorbidity, type of seizures and age of withdrawal.

p0459
SEIZURE SEMIOLOGY VERSUS SUBJECTIVITY: A LINGUISTIC APPROACH TO UNDERSTANDING FOCAL AWARE SEIZURES
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Purpose: Diagnosing some types of epilepsy can be a long and difficult process. Tests can be inconclusive and may not reveal any abnormalities or seizure activity, meaning that the practitioner must often rely on the patient’s articulation of the symptoms and also witness accounts. Focal aware seizures are known for their subjective nature and their wide range of symptoms, often making them difficult to describe. These symptoms can easily be misinterpreted resulting in a prolonged diagnosis or even misdiagnosis. This calls for research to investigate whether it is possible for these types of seizures to be attributed a linguistic profile, with the long-term goal of contributing a referential resource for both practitioners and patients.

Method: Using corpus linguistic methods (a computer-aided method of linguistic analysis), this paper analyses a sample of first-person narratives from the Epilepsy Foundation’s online forum where persons with epilepsy describe their experiences of these seizures. The analysis is conducted in comparison to the symptomatic description provided on the United Kingdom’s National Health Service’s website, ‘NHS Choices’, to identify any discrepancies between the two sources.

Results: The description of focal aware seizures provided by the NHS Choices website is a very general, symptomatic list, which describes a ‘classic’ focal aware seizure. The subjectivity and variability of these seizures means that capturing their nature in a condensed, decontextualised, and atemporal list can run the risk of neglecting important information. However, the qualitative computer-aided analysis of the patient narratives provides a richer, experience-based overview of these seizures.
Conclusion: This paper demonstrates how patient/practitioner commu-
nication in cases concerning focal aware seizures can be enhanced in the
long-term through linguistic research. The analysis demonstrates how the
subjective accounts offered in these online forums are an invaluable asset
which can be systematically analysed and fed back into professional
healthcare.

p0460
SEIZURE AS A STROKE MIMIC: FREQUENCY,
CHARACTERISTICS AND RESULTS OF
NEUROIMAGING
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Purpose: Widespread use of thrombolytic agents in acute stroke necessi-
tates the early differentiation of acute stroke from other ‘stroke mimics’.
Brain perfusion imaging is commonly used in emergency setting to eval-
uate patients presenting with stroke-like symptoms, and seizure is one of
the most commonly encountered diagnosis among the stroke mimics,
because epilepsy patients frequently show focal neurological deficits
with perfusion changes in neuroimaging. The aim of this study was to
analyze the frequency, characteristics and results radiological evalua-
tions including CT perfusion in patients with seizure who initially pre-
sented as a stroke mimic.

Methods: We retrospectively reviewed the medical records of patients
who presented to the emergency room and undertook the CT perfusion
scan under the suspicion of acute stroke between 2008 and 2016. We
studied the frequency and characteristics of patients with seizure who
presented as stroke mimics and the results of neuroimaging including CT
perfusion were further analyzed in correlation with the clinical features.

Result: Among the 4691 patients with stroke-like symptoms at the emer-
gency department, seizure was the second common diagnosis (171
patients, 4.1%) as a stroke mimics followed only by vertigo. Additional
24 patients suffered from symptomatic seizure from acute stroke. Seizure
occurred in previously diagnosed epilepsy or epileptogenic lesions in 162
patients, while nine patients suffered from acute symptomatic seizure
other than acute stroke. Thrombolytic therapy was applied in only 1
patient. CT perfusion showed increased perfusion in 14 patients,
decreased perfusion in 15 patients.

Discussion: Epilepsy is one of the common causes of stroke mimics and
its diagnosis may be complicated when the patients had no previous his-
tory of epilepsy. Because patients with epilepsy may show changes in
perfusion imaging, careful interpretation of results of neuroimaging is
necessary for the accurate differentiation of patients with epilepsy from
stroke.

p0461
NEURONAL ANTIBodies IN EPILEPSY PATIENTS
WITH REFRACTORY SEIZURES
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Purpose: Over recent years, it has been detected that neuronal autoanti-
bodies were associated with many neurological disorders. The presence
of various autoantibodies have been discussed in autoimmune epilepsies.
Our aim was to investigate the presence of neuronal antibodies in patients
with epilepsy resistant to antiepileptic drugs (AEDs) with normal brain
Magnetic Resonance Imaging (MRI).

Method: AEDs-resistant epilepsy patients with normal brain MRI, who
followed in our epilepsy clinic between January 2015 and October 2016
were included in the study. Antibodies against GAD, VGKC, LGI1,
Casp2, NMDAR, AMPAR and GABAR proteins were analyzed by
immunofluorescence, RIA or ELISA methods in all serum samples.

Results: Fifty epilepsy patients, 27 (54%) were female, and 50 healty
volunteers were included in this study. The mean age of the patients was
30.54 ± 9.41 years. The mean age at onset of seizure was
12.37 ± 8.54 years. Thirty seven of the patients (74%) were diagnosed
focal epilepsy and 7 of them (14%) were generalized epilepsy. Other six
patients (12%) could not be classified as having either generalized or
central epilepsy. Eight patients (16%) were positive for neuronal autoanti-
bodies. One patient had antibody against GAD and seven patients had
antibodies against VGKC-complex antigens. Depression was signifi-
cantly more frequent in the patients with VGKC complex antibodies
(p = 0.048). However, although the percentage was higher in the anti-
body-positive group, there was no significant difference between the
groups in terms of the results such as autoimmune disease, psychiatric
disease, febrile convulsion, status epilepticus.

Conclusion: Although the clinical significance of neuronal autoanti-
bodies is not fully understood, recent studies have shown that epileptic
patients with autoimmune etiology are more resistant to treatment. So,
we think that it is important to investigate autoantibodies in patients with
resistant epilepsy even if patients have normal MRI.
p0468
EEG FEATURES OF TYPICAL ABSENCE SEIZURES IN PATIENTS WITH IDIOPATHIC GENERALIZED EPILEPSY
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Purpose: We investigated EEG features of absence seizures in newly presenting patients with idiopathic generalized epilepsy. We examined whether the features of generalized spike and wave discharges (GSW) during absence seizures were determined by specific factors such as epilepsy syndrome, sleep and hyperventilation (HV) or intermittent photic stimulation (IPS).

Method: Patients with typical absence seizures were studied using video-EEG recording prior to the initiation of antiepileptic drug treatment. Forty patients were classified into IGE syndromes. The impact of level of arousal, provocation, and epilepsy syndrome on the EEG features of typical absence seizures was evaluated.

Results: Forty patients with idiopathic generalized epilepsy with typical absence seizures were evaluated. Childhood absence epilepsy (CAE) was found in 12 patients, juvenile absence epilepsy (JAE) in 8, juvenile myoclonic epilepsy (JME) in 14 and eyelid myoclonia with absences (EMA) in 6 patients. Polyspikes were seen only during sleep in patients with CAE, while they were seen during wakefulness, sleep, hyperventilation and photic stimulation in patients with JME and EMA. The duration of ictal discharge during absence seizures was shorter in patients with JME and EMA than in other syndromes. Polyspikes and disorganized discharges were more likely to occur in patients with JME and EMA compared to those with CAE and JAE. In patients with absence seizures during photic stimulation, the number of spikes per wave was significantly higher than that of waking, sleeping and hyperventilation. Disorganized discharges were most commonly seen during sleep and during photic stimulation. In patients with EMA, generalized discharges were disorganized in all states.

Conclusion: EEG features of typical absence seizures are affected by epilepsy syndrome, the level of arousal, hyperventilation and photic stimulation. JME and EMA are more frequently associated with polyspikes and disorganization of generalized discharges.

p0470
PERFORMANCE COGNITIVE POTENTIAL P300 IN IDIOPATHIC AND SYMPTOMATIC FORMS OF EPILEPSY IN TASHKENT
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Purpose: To study features of cognitive evoked potentials in symptomatic and idiopathic forms of epilepsy.

Method: The research is based on data from a survey of 72 patients with epilepsy, including 38 patients with symptomatic epilepsy (SE) and 34 patients with idiopathic epilepsy (IE). The average age of the surveyed patients was 48.0 ± 25.3 years. The control group consisted of 10 healthy individuals matched by age.

Results: In patients with symptomatic and idiopathic epilepsy observed characteristic changes in parameters P300, accompanied by a gross change in idiopathic epilepsy. This is probably due to a higher frequency of epileptic seizures, longer duration of the disease and, consequently, a longer taking anticonvulsants. When idiopathic and symptomatic forms revealed the absence of inter-hemispheric asymmetry of the P300 wave amplitude, which indicates that dysfunctional disorders. Indicators of increased latency of P300 in symptomatic epilepsy, unlike idiopathic and reflect slowing of cognitive processes.

Conclusion: Thus, in patients with epilepsy neuropsychological cognitive evoked potentials indicators objectively reflect the status of higher brain function in epilepsy and depend on its form.

p0476
CAN WE PREDICT DRUG RESPONSE BY GLOBAL CONNECTIVITY IN NEWLY DIAGNOSED EPILEPSY?
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Purpose: The aim of this study was to investigate whether global connectivity could predict a response to antiepileptic drugs in patients with newly diagnosed partial epilepsy.

Method: Fifty-three patients with newly diagnosed partial epilepsy of unknown etiology and healthy subjects were enrolled in this study. First, we conducted correlation analyses between the volumes of the corpus callosum and mean diffusion measures in healthy subjects. Second, we analyzed the differences in the volumes of the corpus callosum between patients with epilepsy and healthy subjects. Third, we divided patients with epilepsy into antiepileptic drug responders and drug non-responders groups, according to their seizure controls, and evaluated the differences in the volumes of the corpus callosum between the groups.

Results: We found that the volumes of the corpus callosum were significantly correlated with the mean diffusion measures (fractional anisotropy, r = 0.408, p = 0.0027; mean diffusivity, r = -0.403, p = 0.0026). The volumes of the corpus callosum in patients with epilepsy were significantly lower than those in normal controls (p = 0.0001). Among epilepsy patients, the volumes of the corpus callosum were significantly lower in antiepileptic drug responders compared with non-responders (p = 0.0481), which was the only independent variable for predicting antiepileptic drug response (OR = 10.07, p = 0.0454).

Conclusion: We found that the volumes of the corpus callosum reflected global connectivity. In addition, we demonstrated that the volumes of the corpus callosum were different according to antiepileptic drug responses in patients with newly diagnosed partial epilepsy, which may suggest that global connectivity could be a biomarker for predicting responses to antiepileptic drugs.

p0478
EFFECTS OF STATIN THERAPY ON THE CIRCULARATORY MARKERS FOR VASCULAR RISK IN EPILEPSY PATIENTS
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Purpose: While it is well documented that long-term therapy with antiepileptic drugs (AEDs) leads to an increase in risk for atherosclerosis, there has been only a few attempts to reduce the increased vascular risk in epilepsy patients.

Method: We conducted a prospective longitudinal study to assess the effects of HMG-CoA reductase (statin) therapy on the increased circulatory markers for vascular risk in epilepsy patients. We recruited adult epilepsy patients with increased vascular risk such as diabetes mellitus, a previous history of cardiovascular/cerebrovascular diseases, and high in total cholesterol or low-density lipoprotein (LDL) cholesterol. With the use of statistical methods, we analyzed the mean difference in the changes of the arterial markers for vascular risk in epilepsy patients.

Results: In the intervention group, the mean change in the arterial markers for vascular risk in epilepsy patients was 9.0% (p = 0.0001). In the control group, the mean change in the arterial markers for vascular risk in epilepsy patients was 2.0% (p = 0.0001). The mean change in the arterial markers for vascular risk in epilepsy patients was significantly lower in the intervention group compared to the control group (p = 0.0001).

Conclusion: Our study suggests that statin therapy can significantly reduce the increased vascular risk in epilepsy patients. Therefore, statin therapy may be an effective option in patients who have increased circulatory markers of vascular risk.
p0479
ONLINE HYDROGEN PEROXIDE MEASUREMENT DURING OXIDATIVE STRESS GENERATED BY SEIZURE ACTIVITY USING A HIGH TEMPORAL RESOLUTION TECHNIQUE
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Purpose: The objective of this work was to detect the hydrogen peroxide (H2O2) during oxidative stress produced by seizures using an online technique with high a temporal resolution in rats treated with intra-ventricular pilocarpine. Additionally to H2O2 measurement, the electrophysiological activity was simultaneously recorded to relate changes in H2O2 concentrations during epileptiform activity.

Method: Male Wistar rats weighing 200–250 gms were used to induce status epilepticus (SE) by pilocarpine. Rats were implanted with a guide cannula for the pilocarpine administration in the right lateral ventricle (2.4 mg / 2 µl); another cannula having an electrode was placed into the hippocampus to place further a microdialysis probe to obtain the dialysate and record the epileptic activity. This technique consists in mixing the microdialysate with an enzymatic reactor that produces a fluorescent compound. The reactor are composed by Amplex Ultra-Red which in presence of horse radish peroxidase generates resorufin that fluoresces at 590 nm, the fluorescence intensity was measured every second with a photomultiplier, and was proportional to the H2O2 concentration.

Results: It was possible to detect the temporal course in H2O2 concentrations during pilocarpine administration and its subsequent epileptic effects, obtaining an increase of 13.5% with respect to its baseline observing progressive changes in epileptic behavior until the SE was established the H2O2 concentration reached 84.6%. Regarding the electrical activity to understand better the role of H2O2 during epileptogenesis.

Conclusion: These results show that with the use of this technique can detect with an improved temporal resolution the oxidative stress that occurs during the seizures and simultaneously relate the changes with the electrical activity to understand better the role of H2O2 during epileptogenesis.

p0481
DIFFERENT PHYSICAL EXERCISE MODELS ALTER THE CYTOKINES LEVELS IN THE HIPPOCAMPUS OF RATS WITH EPILEPSY
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Purpose: The contribution of inflammatory processes in epileptogenesis and establishment of a chronic epilepsy has been increasingly recognized. Altered expression of cytokines has been observed in patients with epilepsy and in animal models. Beneficial effects of physical exercise for people with epilepsy have increasingly been reported. However, the mechanisms responsible for this occurrence are not totally clear. Considering that exercise programs can attenuate neuroinflammation in neurological diseases, we evaluated the hippocampal levels of cytokines in rats with epilepsy submitted to voluntary or forced exercise.

Method: Thirty-seven Wistar rats were divided into the following groups: control (C; n = 9), epilepsy (E; n = 9), epilepsy voluntary exercise (EV; n = 10) and epilepsy forced exercise (EF; n = 9). Exercise groups were submitted to wheel (EV) or treadmill (EF) running during 30 consecutive days. Twenty-four hours after the last exercise session, rats were decapitated, hippocampi dissected and pro (IL-1β, IL-6 and TNFα) and anti (IL-4 and IL-10) inflammatory cytokines were quantified by multiplex microbead immunoassay. Non-parametric tests were used by compare the results.

Results: IL-1β levels increased in E group when compared to C group (p < 0.05) and both exercise models (EV and EF) reduced IL-1β levels compared to C and E groups (p < 0.05). IL-1β/IL10 ratio increased in E group when compared to C group and both exercise models reduced this ratio to C levels (p < 0.05). Thus, forced exercise (EF) reduced IL-1β/IL10 ratio compared to E group. Reduced IL-6 levels were observed in EF group compared to C and E groups (p < 0.01). Increased TNFα/IL-10 ratio was observed in EF group compared to C and E groups (p < 0.01). No significant alterations were observed in IL-4, IL-10 and TNFα levels between groups (p > 0.05).

Conclusion: Our findings suggest that voluntary and forced exercise can attenuate neuroinflammation in rats with epilepsy.

p0482
THE EFFECT OF CANNABIDIOL (CBD) ON HUMAN CNS-EXPRESSED VOLTAGE-GATED SODIUM CHANNELS
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Purpose: The anticonvulsant mechanism of action of CBD has not been fully elucidated and a systematic examination of the effect of CBD on human voltage gated sodium channel (Nav) function has yet to be described. The purpose of this study was to determine the effect of physiologically relevant concentrations of CBD on CNS-expressed human voltage-gated sodium channel (Nav) function.

Method: Human recombiant Nav channel-expressing HEK-293 cells were cultured in standard conditions. Functional selectivity was tested using a pulse train protocol to examine use-dependent block by automated patch clamp electrophysiology (IonWorks). Tetracaine, a non-selective use-dependent Nav channel blocker was used as a positive control. Concentration response curves for CBD (0.6 nM - 33 µM) were constructed describing inhibition of 1st and final pulse of each train. Data were analyzed using IonWork’s Quattro and GraphPad Prism software and fitted to a 4-parameter logistic equation for the determination of IC50.

Results: CBD inhibited the peak transient sodium current with an IC50 > 33 µM for all Na+ subtypes tested (human Na+ 1.1, 1.2, 1.3, 1.6 and 1.7). The positive control Na+ channel inhibitor tetracaine inhibited all Na+ subtype currents elicited by sequential depolarizing pulses in a concentration and use-dependent fashion. In contrast, no such inhibition was observed in the presence of 0.6 nM to 33 µM CBD at Na+ 1.1, 1.2, 1.3, 1.6 and 1.7.

Conclusion: The data presented confirm that CBD does not inhibit peak transient current of wild-type CNS-expressed human Nav channels at physiologically relevant concentrations. Previously, the anti-epileptiform activity of CBD at ≥10 nM was demonstrated using classic in vitro models of epileptiform activity. Thus, the mechanism by which CBD is able to confer its anti-convulsant activity is unlikely to be mediated by inhibition of peak transient voltage-gated sodium channel current. (Funded by GW Research, Ltd).

p0483
AN INTEGRATIVE ANALYSIS OF GENOME-WIDE PROFILING OF DNA METHYLATION AND GENE EXPRESSION IN FOCAL CORTICAL DYSPLASIA
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Purpose: In an attempt to decipher the molecular basis of the pathologic modifications in neuronal circuits in Epilepsy, studies have revealed a remarkably diverse pattern of gene expression resulting from epigenetic changes. DNA methylation is a pertinent type of epigenetic modification which influences brain development, function, and aging. Here Microarray profiling of methylated DNA and RNA sequencing have been used to investigate gene expression in the human tissue samples of Focal Cortical

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Dysplasia (FCD), with the aim of identifying functional pathways which are significantly activated or repressed during epileptogenesis.

**Method:** Methylated DNA was immunoprecipitated using anti-5-methyl cytidine antibody from surgically resected tissues of FCD patients and controls from Autopsy. Whole Genome Amplification and Microarray Hybridization was then carried out using Agilent ChIP on ChIP kit G4495A. RNA sequencing was performed using standard protocols on Illumina HiSeq 2500 platform. Differential gene expression analysis was done using Cuffdiff. Gene Spring Software was used for quantification of methylation and its co-relation with RNA Sequencing data. qPCR was used for validation of the gene expression.

**Results:** A total of 918 genes were identified to be differentially expressed, whose gene expression directly correlated with methylation status. Out of these, 604 genes were hypermethylated and their gene expression depressed. 314 genes were overexpressed and hypomethylated. 176 of these genes were present in the promoter region. Gene Ontology and pathways analysis revealed important pathways like PDGF signaling, mTOR pathway among others, involving aberrantly expressed genes. Gene expression of 9 of these genes was further validated by qPCR. Our results showed significant alteration in BRCA1, EGFR, RP56K3A, PRKAA1.

**Conclusion:** These may prove to be potential prognostic and diagnostic biomarkers in FCD. Hence a better understanding of the mechanism may provide new avenues for therapeutic intervention.

**p0488**

**POST-STATUS EPILEPTICUS BEHAVIORAL ALTERATIONS IN RATS: ASSOCIATION WITH CHRONIC EPILEPSY AND MODULATION BY ENDOCANNABINOID RECEPTOR ACTIVATION**

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**Purpose:** Temporal lobe epilepsy (TLE) is associated with behavioral disorders and cognitive deficit. Lithium-pilocarpine model in rodents reproduces many features of human status epilepticus (SE) and subsequent TLE. In this model, behavioral abnormalities could be consequences of either developed chronic epilepsy or SE-induced damage. Our purpose was to investigate behavior in rats developing spontaneous seizures and in seizure-free rats 5 months after SE.

**Method:** The study was carried out on the lithium-pilocarpine model of SE. SE continued for 90 min and was terminated by pentobarbital; 4 h after SE rats were treated with endocannabinoid receptor agonist WIN-55,212-2 or vehicle. 5 months after SE rats were videomonitored for spontaneous seizures; then behavioral tests were performed: elevated plus-maze, light-dark box, open field test, and Morris water maze.

**Results:** Five months after SE, 54% of rats developed spontaneous seizures, the rest were seizure-free. Presence of spontaneous seizures correlated with hyperactivity in the open field; rats with seizures were hyperactive while no difference was found between seizure-free animals and controls. No signs of anxiety-like behavior were found in rats experienced SE, but they spent more time in the open arms of the plus-maze, the light compartment of the light-dark box, and the center of the open field arena in comparison with controls (no SE). Morris water maze test showed that rats after SE had severely impaired spatial memory, irrespective of spontaneous seizure development. Administration of endocannabinoid receptor agonist early after SE did not prevent seizure development, but reduced behavioral impairment in the elevated plus-maze but not in the other tests.

**Conclusion:** Different behavioral impairments found in the chronic period after SE can result from the initial impact of SE or accompany the development of epilepsy, suggesting that different mechanisms can underlie even seemingly close types of behavioral comorbidities.

**p0492**

**MULTIFACETED ROLE OF INTERICTAL DISCHARGES IN ITCGENESIS**

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**Purpose:** Interictal epileptiform discharges (IEDs) display multiple roles in icogenesis. It has been demonstrated that IEDs can have either pro-ictogenic or anti-ictogenic effects, while certain studies claim that IEDs do not interfere with the transition to seizure. In this study, we have explored the multifaceted role of IEDs from a dynamical perspective.

**Method:** The experiments were performed in vitro in intact hippocampal and isolated CA1 slices perfused with artificial CSF containing high potassium (>8 mM). Field potentials from the hippocampal CA1 and CA3 regions were recorded using extracellular electrodes.

**Results:** In both preparations, seizures originated in the CA1 region. In isolated CA1 slices, the duration of inter-seizure period was 50.3 ± 2.4 s and the seizure onset pattern was characterized by the slow spread of ictal activity to adjacent electrodes (63.9 ± 63.2 ms). In intact slices, the presence of IEDs was associated with a prolonged inter-seizure period (69.5 ± 2.1 s) and with hypersynchronous seizure onset across the entire CA1 area due to an incoming IED (10.4 ± 2.1 ms). To evaluate the relationship between IEDs and the dynamical state of the CA1 network, we have estimated the resilience of the CA1 region from the parameters of high-frequency activity. The results showed that pro-ictogenic effect of IEDs occurred during the dynamical state characterized by low resilience.

**Conclusion:** This study suggests that the pro- or anti-ictogenic effect of IEDs does not have to be determined exclusively by the existence of specific cellular mechanisms. The effect of IEDs can be defined by the dynamical state of the seizure-generating network at the moment of the discharge occurrence. If the CA1 network displays low resilience to perturbations, then the originally anti-ictogenic IEDs develop a capacity to shift the dynamics of the CA1 network into the ictal regime.

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**p0493**

**INHIBITION OF mTOR PATHWAY BY RAPAMYCIN DECREASES P-GLYCOPROTEIN EXPRESSION AND SPONTANEOUS SEIZURES IN PHARMACORESISTANT EPILEPSY**

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**Purpose:** The mammalian target of rapamycin (mTOR) has been demonstrated to mediate multidrug resistance in various tumors by inducing P-glycoprotein (P-gp) overexpression (Potschka, 2010). Here, we investigated the correlation between the mTOR pathway and P-gp expression in pharmacoresistant epilepsy.

**Method:** Temporal cortex specimens were obtained from patients with refractory mesial temporal lobe epilepsy (mTLE) and age-matched controls who underwent surgeries at West China Hospital of Sichuan University between June 2014 and May 2015. We established a rat model of epilepsy kindled by coriaria lactone (CL) and screened pharmacoresistant rats (non-responders) using phenytoin. Non-responders were treated for
4 weeks with vehicle only or with the mTOR pathway inhibitor rapamycin at doses of 1, 3, and 6 mg/kg. Western blotting and immunohistochemistry were used to detect the expression of phospho-S6 (P-S6) and P-gp at different time points (1 h, 8 h, 1 d, 3 d, 1 w, 2 w and 4 w) after the onset of treatment.

**Results:** Overexpression of P-S6 and P-gp was detected in both refractory mTLE patients and non-responders rats. Rapamycin showed an inhibitory effect on P-S6 and P-gp expression 1 week after treatment in rats. In addition, the expression levels of P-S6 and P-gp in the 6 mg/kg group were significantly lower than those in the 1 mg/kg or the 3 mg/kg group at the same time points (all p < 0.05). Moreover, rapamycin decreased the duration and number of CL-induced seizures, as well as the stage of non-responders (all p < 0.05).

**Conclusion:** The current study indicates that the mTOR signaling pathway plays a critical role in P-gp expression in drug-resistant epilepsy. Inhibition of the mTOR pathway by rapamycin may be a potential therapeutic approach for pharmacoresistant epilepsy.

**p0496**

**EVALUATION OF THE VARIATIONS IN REST/NRSF EXPRESSION IN PATIENTS WITH TEMPORAL LOBE EPILEPSY**

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**Purpose:** The aim of this study was to evaluate the variations in the expression of REST/NRSF in hippocampus of patients with pharmacoresistant Mesial Temporal Lobe Epilepsy (MTLE) and investigate if clinical variables, like age, gender, treatments, etc., are associated with the results obtained.

**Method:** Hippocampal tissue was used from patients (n = 28) with temporal lobe epilepsy and as a control, autopsy hippocampus was used (n = 7). The expression of REST/NRSF at the transcriptional (RNA) and translational level (protein) was evaluated by real-time PCR and western blot respectively. Finally, we evaluated the correlation with clinical variables.

**Results:** The results show that expression of mRNA of REST/NRSF in hippocampus of patients with MTLE increasing 141.63% and protein levels increasing 181.2%, both compared to autopsy tissue (p < 0.05). However, this increase in protein was not general, a group of patients did not show changes with respect to autopsy levels. Overexpression of mRNA and protein of this factor did not correlate with clinical data, except with the drugs administered prior to surgery, where valproic acid (VPA), clonazepam (CNZ), levetiracetam (LVT) and topiramate (TPM) may regulate the expression of REST/NRSF at the transcriptional level.

**Conclusion:** We conclude that in patients with TLE, REST/NRSF is overexpressed both at the transcriptional and translational level, regardless of the clinical variables, but treatment with VPA, CNZ, TPM and LVT modify the genic overexpression.
aimed to detect TMT behavioral response of fear, to standardize TMT (time/concentration in the chamber), and to evaluate behavioral and electroencephalographic (EEG) effects on FAK in Wistar rats.

**Method:** Chemical and behavioral responses to different concentrations of TMT (or nanomulsion) were evaluated in male Wistar rats. Another group was submitted to electrical stimulation (FAK protocol), 10 daily electrical stimulations, two days and, at 21st stimulus (third day) testing TMT anticonvulsant activity. Behavior was analyzed with seizure severity index (SSI) and neuroethology. EEG spectral analysis (Fast Fourier Transform, FFT) compared afterdischarges in TMT/control groups at 21st stimulus mean EEG frequency/peak power/frequency at the peak power/total power in amygdala (A), hippocampus (HIP), piriform cortex (PC). EEG basal/seizure periods were analyzed by power spectrum density and total coherence at 20th and 21st stimuli.

**Results:** TMT nanomulsion induced significant reduction of behavioral activity, compared to vehicle. TMT triggered fear reactions and reduced motor activity/grooming behavior. Gas chromatography detected chamber concentrations/time for homogeneous saturation (30 minutes), desaturation. Pure TMT in FAK significantly reduced behavioral seizures (SSI and sequences). FFT EEG analysis (21st stimulus) showed that TMT altered significantly the mean frequency/peak power in (A) in all frequencies, except gamma (p < 0.05; Mann-Whitney-U test). Average frequency (whole spectrum) in PC, also differed between groups (p < 0.05; Mann-Whitney-U test). TMT (21st stimulus) reduced coherence values between PC and HIP on basal period and decreased the HIP power density on seizure period (20th versus 21st stimulus; p < 0.05; paired T-Student test).

**Conclusion:** Chemical/behavioral/EEG data confirm that TMT-induced fear has potent anticonvulsant effects in FAK model.

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**Abstracts**

**p0498**

PHARMACOLOGICAL CHARACTERIZATION OF HAMSTER GASH: SAL. CHRONIC EFFECTS OF ANTI-EPILEPTIC DRUGS IN THE GENETIC AUDIOGENIC SEIZURE


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**Purpose:** The study investigate the anticonvulsant, and potential antiepileptic effects of different antiepileptic drugs (AED) in seizures of the GASH:Sal hamster, an animal model of genetic audiogenic seizure that is in the process of validation. The strain GASH:Sal is a rodent model that exhibits generalized tonic-clonic seizures of genetic origin in response to sound stimulation.

**Method:** We assess the anticonvulsant activity of five AED: Phenobarbital (PB), Valproic acid (VPA), Levetiracetam (LEV), Lamotrigine (LTD) and Retigabine (RTG). The purpose of this study is also to characterize the possible antiepileptic action of AEDs following chronic administration in the hamster.

We used male GASH:Sal hamsters two months old, 5 for each drug and 6 animals untreated for the control group. The AEDs were administered 30 days in the drinking water. The initial dose of the drugs was calculated from the ED50 determined in our model, and was increased every two weeks, according to the response of the animals (PB: 20–60 mg/kg/day; VPA: 150–600 mg/kg/day; LEV: 50–150 mg/kg/day; LTD: 20–25 mg/kg/day; RTG: 6–12 mg/kg/day).

Before starting pharmacological treatment, all animals were stimulated once (0–18 kHz; 115–120 dB) to observe the crisis without influence of the AEDs; then, the audiogenic seizures were recorded every week to see the effect of the AEDs.

**Results:** Drugs that have shown antiepileptic effect after chronic oral administration have been PB and LTD.

**Conclusion:** We can conclude that GASH:Sal is a good model of epilepsy, which will allow a pharmacological study closer to its use in humans.

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**p0499**

PHOTOLYSIS OF RUBI-GABA RAPIDLY TERMINATES SEIZURES IN VIVO: DOSE- AND LIGHT INTENSITY-DEPENDENCE


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**Purpose:** Our previous experimental results have demonstrated that the use of blue light produced by light emitting diode (LED) to uncage ruthenium-bipyridine-triphenylophosphate-c-aminobutyric acid (RuBi-GABA) can rapidly terminate paroxysmal seizure activity both in vitro and in vivo. However, the optimal concentration of RuBi-GABA, and the intensity of illumination to abort seizures, remains unknown. This study aimed to explore the optimal anti-epileptic effects of RuBi-GABA.

**Method:** Focal neocortical seizures of anesthetized rats were induced by microinjection of 4-aminopyridine (4-AP) into the motor cortex. We then investigated the effects of different combinations of RuBi-GABA concentrations and light intensity upon epilepsy by using implantable fibers to introduce blue light into the neocortex of a 4-aminopyridine (4-AP)-induced acute seizure rat model in rat.

**Results:** We first tested the combination of 0.1 mM RuBi-GABA with 15 mW and 20 mW of illumination (30 s). Under these conditions, seizure duration was 61.5 ± 3.57 s and 69.64 ± 10.48 s respectively; there was no significant difference when compared to the control group (p = 0.905 and p = 0.585). However, when the concentration of RuBi-GABA was increased to 0.2 mM with 10 mW and 15 mW of light intensity, the seizure duration was significantly reduced to 25.31 ± 6.05 s and 15.13 ± 7.20 s, respectively. Compared with the control group, these reductions were statistically significant.

**Conclusion:** Our results show that the anti-epileptic effect of RuBi-GABA has obvious RuBi-GABA concentration and light intensity dependence. These results provide important experimental data for future clinical translational studies.
p0502 DIFFERENT MOSSY FIBER SPROUTING PATTERNS IN ILAE HIPPOCAMPAL SCLEROSIS TYPES

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Purpose: Hippocampal sclerosis (HS) is the most prevalent pathology in temporal lobe epilepsy (TLE) and characterized by segmental pyramidal cell loss in the cornu ammonis (CA) 1–4. Migration of granule cells and reorganization of their axons, is observed; known as granule cell dispersion (GCD) and the mossy fiber sprouting (MFS), respectively. The loss of target cells in CA4 and CA3 was considered to be causative for MFS. The ILAE (International League Against Epilepsy) classification of HS identifies three subtypes with different cell loss patterns in CA1-4. We studied the correlation of ILAE HS subtypes with GCD, MFS in a large retrospective single-center series.

Method: Hippocampal specimen of 319 patients were screened, 214 could be analyzed. Immunohistochemistry for semi-quantitative analysis of neuronal cell loss (NeuN) and mossy fiber sprouting (synaptoporin) were used. Presurgical data and seizure outcome was studied and classified according to Engel score Ia-Iv, three, 12 and 24 months after surgery.

Results: In 39 patients (18%) no neuronal cell loss (ILAE no-HS), no GCD and no MFS was observed. In 154 patients (72%) severe neuronal cell loss was seen in CA1, CA4 and CA3 (ILAE HS 1, typical HS); in addition extensive GCD and MFS was observed. In 17 patients (8%), cell loss, predominantly in CA1, was seen (ILAE HS 2), despite the different cell loss pattern, these hippocampi showed also GCD and MFS. In 4 patients (2%) cell loss was seen predominately in CA3 and CA4 (ILAE HS type 3), consecutively GCD and MFS were observed. However, there was no significant correlation of ILAE HS subtypes, patterns of GCD or MFS, with clinical histories; including age at seizure onset, duration of epilepsy before surgery, nor with long-term post-surgical outcome.

Conclusion: Granule cell dispersion and mossy fiber sprouting might develop independently from loss of neuronal target cells.

p0507 POLYSOMNOGRAPHIC SLEEP CHARACTERISTICS OF THE PSYCHOGENIC NON-EPILEPTIC SEIZURES

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Purpose: Psychogenic non-epileptic seizures (PNES) are events resembling an epileptic seizure, but without the characteristic electrical discharges associated with epilepsy. They are one type of non-epileptic seizures. They are a manifestation of psychological distress. Frequently, patients with PNES may look like they are experiencing generalized convulsions similar to tonic clonic seizures with falling and shaking. Less frequently, PNES may mimic absence seizures or complex partial seizures with temporary loss of attention or staring. Little is known about the sleep characteristics (macrostructure and microstructure) of the PNES and we here aimed to describe the polysomnographic sleep characteristics in PNES.

Method: We analyzed video EEG-polysonmographic recordings of 23 patients (9 male and 14 female; mean age: 25 ± 8 years) with a diagnosis of PNES and 25 control cases. Conventional sleep measures (total sleep time, sleep latency, non-rapid eye movement (NREM) and REM sleep, light sleep (N1+ N2), slow wave sleep (N3), latencies of each sleep cycle) were assessed and compared with control group.

Results: Compared to controls, patients with PNES showed that shorted REM onset latency, increased REM density, increased percentage of REM sleep, reduced sleep efficiency, increased awakenings, and decreased slow wave sleep.

Conclusion: The relationship between PNES and sleep is sparse in the currently available literature. Patients with PNES may have a number of psychiatric diagnoses. Our results are similar to sleep characteristics of the major depression. We believe that the detailed clinical and video EEG PSG characteristics of the patients with PNES represents a better understanding of the pathogenic mechanisms and different clinical outcomes of the PNES.

p0504 ANXIETY AND SLEEP DISTURBANCES ARE ASSOCIATED WITH SUBCLINICAL SEIZURES IN ACUTE POSTTRAUMATIC PERIOD IN RATS

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Purpose: To evaluate behavioral and electrophysiological consequences of traumatic brain injury (TBI) with its morphological substrates at the early period of trauma, which may be involved in development of post-traumatic epilepsy with its comorbidity.

Method: We used lateral fluid percussion model (3–4 atm) in adult male Sprague-Dawley and Wistar rats. Immediately after TBI tonic-clonic seizures occurred. To estimate the time course of epileptiform discharges during wake-sleep cycle and global brain function video-electrocorticograms (VECoG) were recorded prior TBI and during acute posttraumatic period - first week after injury. To find epileptiform discharges we developed and used an automatic detection algorithm of EEG events with high value of power spectral density based on wavelet transform. To evaluate symptoms of depression and anxiety light-dark box and elevated plus-maze tests were used. To assess brain damage morphological analysis was performed one week after TBI.

Results: During acute posttraumatic period rats demonstrate symptoms of anxiety and depression associated with reduced percentage of REM-sleep, its decreased frequency and amplitude High voltage rhythmic spikes (HVRS) were detected in background records and after TBI, particularly during the early stage of NREM sleep in several, but not all animals. After TBI, the number of HVRS increased particularly during wakefulness. Histological studies revealed the presence of cortical damage to the ipsilateral hemisphere and to the hippocampus.

Conclusion: So, we at the first time showed anxiety behavior, sleep disturbances accompanying HVRS, which represents a subclinical epileptic form activity, with its morphological substrates in acute period after TBI. Supported by RSF grant # 16-11-10258.

p0508 ROLE OF QUANTITATIVE EEG TO IDENTIFY NONEPILEPTIC EVENTS AT THE BEDSIDE

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Purpose: To evaluate the sensitivity and specificity of quantitative EEG (QEEG) seizure detection trend, and analyses of four spectrograms (asymmetry relative spectrum, FFT spectrum, rhythmicity spectrum, and amplitude EEG), for detecting nonepileptic events.

Method: Hypermotor events captured during EEG monitoring, for thirty adult patients (ages 25–60 years) admitted to Montefiore Medical Centre and associated hospitals from July 2016 to January 2017, were retrospectively assessed using a QEEG seizure detection trend and specific spectrograms. Assessment of raw EEG was employed as the gold standard against which to validate epileptic and nonepileptic events. All EEGs were interpreted by an epileptologist trained in evaluation of QEEG.
Seventeen patients with nonepileptic events were compared to a control group of thirteen patients with epileptic seizures of similar semiology.

**Results:** Eighty two hypermotor events (46 nonepileptic, 36 epileptic) were captured across a duration of 540 hours. QEEG analysis seizure detection trend detected nonepileptic events with a sensitivity of 71% (p = 0.01) and a specificity of 80%. The asymmetry relative spectrogram, FFT spectrogram, rhythmicty spectrogram, and amplitude EEG yielded detection sensitivities of 47% (p = 0.47), 65% (p = 0.09), 60% (p = 0.10), and 58% (p = 0.14) for nonepileptic events. Their specificities were 69%, 69%, 75%, and 75% respectively.

**Conclusion:** High sensitivities and specificities for QEEG seizure detection analyses in detecting nonepileptic events suggest greater utility for its clinical application. QEEG may be employed at bedside to facilitate early identification of nonepileptic events in order to avoid unnecessary administration of antiepileptic drugs (AEDs) and possible iatrogenic consequences.

p0510
**INTERICTAL VERY FAST RIPPLES (500–1000 HZ) AND ULTRA FAST RIPPLES (1–2 KHz): NOVEL BIOMARKERS OF THE EPILEPTOGENIC ZONE**


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**Objective:** In the present study, we aimed to investigate depth EEG recordings in a large cohort of patients with drug resistant epilepsy and to focus on interictal very high frequency oscillations (VHFOs) between 500 Hz and 2 kHz. We hypothesized that interictal VHFOs are more specific biomarkers for epileptogenic zone compared to traditional HFOs.

**Methods:** Forty patients with focal epilepsy who underwent presurgical stereo-electroencephalography (SEEG) were included in the study. SEEG data have been recorded with sampling rate of 25 kHz and 30 minutes of resting period was analyzed for each patient. Ten patients met selected criteria for analyses of correlations with surgical outcome - detection of interictal ripples (R), fast ripples (FR) and VHFOs, resective surgery, and at least one-year post-operative follow-up. Using power envelope computation and visual inspection of power distribution matrices, electrode contacts with HFOs and VHFOs were detected and analyzed.

**Results:** Interictal very fast ripples (VFR; 500–1000 Hz) were detected in 23 out of 40 patients and ultra fast ripples (UFR; 1000–2000 Hz) in almost half of investigated subjects (N = 19). In our study, VFR and UFR were recorded from mesiotemporal structures only. UFR were more spatially restricted in the brain than lower frequency HFOs. When compared to R oscillations, better outcomes were observed in patients with a higher percentages of removed contacts containing FR, VFR, and UFR. The percentage was highest for UFR (95%).

**Conclusion:** Interictal VHFOs are relatively frequent abnormal phenomena in the epileptic brain, and appear to be more specific biomarkers for epileptogenic zone when compared to traditional R and FR HFOs.
p0513
DETECTION OF RECURRENT ACTIVATION PATTERNS IN FOCAL SEIZURES AND APPLICATION TO SEIZURE-ONSET IDENTIFICATION
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Purpose: We introduce a method that quantifies the consistent involvement of intracranially monitored regions in recurrent focal seizures.

Method: We evaluated the consistency of two ictal spectral activation patterns (mean power change and power change onset time) in intracranial recordings across focal seizures from seven patients with well-mapped seizure onset zone (SOZ). We examined SOZ discrimination using both patterns in different frequency bands and periods of interest.

Results: Activation patterns were proved to be consistent across more than 80% of recurrent ictal epochs. In all patients, whole-seizure mean activations were significantly higher for SOZ than non-SOZ regions (p < 0.05) while activation onset times were significantly lower for SOZ than for non-SOZ regions (p < 0.001) in six patients. Alpha-beta bands (8 - 20 Hz) achieved the highest patient-average effect size on the whole-seizure period, while gamma band (20 - 70 Hz) achieved the highest average value near seizure onset (0 - 5s).

Conclusion: Consistent spectral activation patterns in focal epilepsies help identify the SOZ with high levels of accuracy. The present method may be used to improve epileptogenic identification as well as pinpoint additional regions that are functionally altered during ictal events.

p0514
THE ELECTROENCEPHALOGRAPHIC AND ELECTROCARDIOGRAPHIC EFFECT OF INTRAVENOUS LACOSAMIDE IN REFRACTORY FOCAL EPILEPSY
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Purpose: Lacosamide selectively enhances slow inactivation of voltage-gated sodium channels to achieve seizure reduction. Its intravenous formulation has been approved for treatment of acute seizures. We studied the effect of 3 acute parenteral doses of lacosamide on the electroencephalogram (EEG) and electrocardiogram (EKG) as well as its tolerability in patients with refractory epilepsy.

Method: This Canadian, investigator-initiated, multicenter, double-blind study recruited patients with refractory focal epilepsy admitted to a seizure monitoring unit. Participants received a loading dose of either 100 mg, 200 mg or 400 mg over 30 minutes during continuous monitoring by video-EEG and 12-lead EKG. The number of interictal spikes, frequency and quantity of background rhythms, QT, PR interval, heart rate (HR), blood pressure (BP) and respiration rate (RR) during 60 minutes before the administration of lacosamide were compared to 60 minutes starting 30 minutes after the administration. We documented any adverse event during and after the infusion.

Results: 71 patients completed the study. There was a significant decrease in interictal spikes (p = 0.04) and decreased frequency of the alpha rhythm (p = 0.003). No significant difference in beta, theta, and delta frequency or amount was noted. There were significant increases in PR interval (153.4 to 155.8 ms, p = 0.03) and HR (73.4 to 75.3 bpm, p = 0.02) but QT, BP and RR were not affected. 12 patients (16.9%) experienced adverse events, all of them transient and mild, most commonly dizziness and leg tingling. Those who received 400 mg lacosamide had significantly more adverse events (p = 0.048).

Conclusion: Intravenous lacosamide is effective in decreasing interictal spikes. Despite a small dose-related effect on normal EEG and EKG rhythms, the drug is well tolerated when given parenterally with no serious adverse events documented.

p0515
CONSEQUENCE OF TBI – CHRONOTOPOLOGY OF EPILEPTOGENESIS AND SURGICAL TREATMENT FOR POSTTRAUMATIC TEMPORAL EPILEPSY
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Purpose: Traumatic epilepsy is a most severe complication of TBI. The study was aimed at elaboration of diagnostic neurophysiologic biomarkers of postneurotrauma brain structure epileptization to solve principal problems of optimization of epilepsy surgical treatment.

Method: Electroclinical examination and surgical treatment of 276 patients (19–50 aged) with drug-resistant posttraumatic temporal epilepsy. An algorithm of presurgical epilepsy diagnostics comprising neurophysiologic (EEG-ECoG-SEEG) and neuroimaging (MRI, PET) technologies was developed.

Results: Investigation into epileptic syndrome forming in post-neurotrauma patients based on critical chronotopology of electrophographic traits-markers particularities of preclinical (initial), early (temporal) and late (extratemporal) epileptogenesis were established reflecting clinical-neuropsychiologic forms of focal and multifocal temporal epilepsy on different stages of the disease.

Preclinical period revealed a number of critical electrographic EEG-patterns denoting increasing spatial alpha-synchronization and reflecting consecutive stages of brain epileptization before the clinical paroxysmal signs appear. These neurophysiologic criteria help preclinical diagnosis of epilepsy.

In the clinics of temporal epilepsy certain regularities of epileptogenesis were revealed at the levels of morphofunctional organization of temporal epileptic foci and EEG-ECoG-SEEG-analysis. A major group of our series (79%) comprised the patients with combined temporal neocortical and deep limbic structure damage (hippocampus, amygdala), thus optimizing the strategy of open surgical treatment (anterior temporal lobectomy).

SEEG-analysis data demonstrated extratemporal structure routes of epileptization: hippocampus and amygdala entered the Papez circuits system via anterior thalamic nuclei, which should be considered during stereotactic intervention.

Conclusion: Special studies of pathogenetic basis of the forming paroxysmal disorders carried out while examining the patients with the history of cranioencephal trauma helped determine neurophysiologic regularities of preclinical and clinical epileptogenesis. Neurophysiologic indicators appear a reliable method to evaluate chronotopology of epileptic focus at the cortical, limbic and brainstem structure levels. Neurophysiologic peculiarities of early and late epileptogenesis found help determining strategy of differentiated surgical treatment of resistant temporal lobe epilepsy.
p0516 EVALUATION OF VISUAL HABITUATION IN JUVENILE MYOCLONIC EPILEPSY PATIENTS
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Purpose: Juvenile myoclonic epilepsy (JME) is one of the most common age-related idiopathic generalised epilepsies and includes about 5%–10% of all of the epilepsies. The main purpose of the present study was to investigate possible changes in visual habituation responses in JME.
Methods: The patients comprised two groups: juvenile myoclonic epilepsy (JME) (n = 15), and IGE with tonic-clonic seizures alone (GTCA) (n = 20) in this study. Twenty-five healthy subjects were included in the control group. The mean age was 28.5 ± 4.04 years for JME group, 26.3 ± 3.40 years for the GTCA and 31.7 ± 5.30 years for the control group. We measured the peak-to-peak amplitude of the N75-P100 and P100-N75 complexes. Habituation was defined as the slope of the linear regression line for the 6 blocks. All recordings were collected by the same investigator, who did not meet the participants before the examination, since they were not involved in recruitment and inclusion of subjects. P100-N145 pattern-reversal visual evoked potential (PR-VEP) inter-peak amplitudes and N75, P100, N145 latencies for the six blocks of 100 responses were measured. The slope of the linear regression line of the N75-P100 and P100-N145 latencies was also analysed.
Results: There was no difference between the groups regarding gender and age (p > 0.05). Statistical analysis revealed significant differences between the three groups in the slope index of N75-P100 PR-VEP amplitude, with increased in the JME group (p = 0.03).
Conclusion: These findings might be the expression of an abnormal sensorimotor pathway in JME patients that probably is the result of a neurotransmitter disorder. We think that this study is important in terms of supporting PR-VEP habituation as a method of distinguishing JME and IGE patients.

p0519 NON-CONTACT VIDEO DETECTION OF TONIC-CLONIC SEIZURES IN A RESIDENTIAL CARE SETTING
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Purpose: To investigate the detection performance of a non-contact tonic-clonic seizure detection algorithm in a residential care setting.
Method: Our earlier described algorithm discerns tonic-clonic seizures (TCs) from normal behavior in video registrations, by calculating relative frequency content (2–6 Hz relative to 0–12 Hz) in the optical flow signal. A detection threshold was found using a learning set and detector performance was studied using a test set. Experienced observers annotated the clonic phase of all TCs, with five-second annotation margins on both sides to allow for slightly earlier or later detections. The learning set consisted of 50 video-EEG recordings of 50 patients with 72 TCs. The detection threshold was set at the third percentile of detection output maxima during clonic phases, obtaining 97% learning set sensitivity. The test set consisted of 36 full night’s recordings (total duration ~362 hours) of 12 patients in a residential care department, with 15 TCs. The algorithm detects a seizure when its output exceeds the threshold during the clonic phase. Remaining detections were categorized as: Other seizures, detections with caregivers present, and false alarms. Detection performance was measured in terms of sensitivity, latency and false alarm rate per night (8 hours).
Results: Using the learning set, a detection threshold of 0.5 was found. TCs were detected in the test set with 87% sensitivity and 4 second median latency. For all but one patient with TCs, all TCs were detected. The median false alarm rate was 1.0 per night. Other detected seizures were hyperkinetic and myoclonic seizures. False alarms were caused by patient behavior (49%) and video disturbances (51%), such as moving objects or fragmentary variations.
Conclusion: Our algorithm may improve patient safety unobtrusively by detecting TCs in video, with acceptable latency and false alarm rate. Algorithm changes could be made to solve fragmentary variation problems.

p0520 TRANSIENT EPILEPTIC AMNESIA: A CHALLENGING DIAGNOSIS, PITFALLS AND KEY FEATURES
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Background and objectives: Differential diagnosis of transient amnesia is challenging in particular, differentiation between transient global amnesia (TGA) and transient epileptic amnesia (TEA) may be difficult on the basis of the clinical features of the episodes. Our aim was to describe clinical and electroencephalographic features of patients affected by TEA compared to patients with TGA, in order to highlight major pitfalls and key features.
Materials and methods: Among 67 patients admitted to our department because of one or more episodes of transient amnesia from 2008 to 2016, 14 patients (20.9%) were diagnosed as affected by TEA. We assessed clinical features and performed neurophysiological and neuroimaging assessment in all patients.
Results: Twelve out of 14 patients with TEA had temporal epilepsy without mesial sclerosis, the remaining two patients showed symptomatic focal epilepsy. The two groups differed significantly for the recurrence of episodes (higher in patients with TEA) and presence of other symptoms than pure amnestic ones. Trigger factors were suggestive of TGA (25/53 cases), while occurrence of amnestic episodes on waking was more frequent in TEA (6/14 cases). EEG recording showed epileptiform abnormalities only in 9 (64.3%) out of 14 patients, whereas the 24-hour ambulatory EEG revealed these abnormalities in all patients studied.
Discussion: TEA is a neurological condition that typically affects older people and mostly represented by cryptogenic temporal epilepsy. TEA episodes are usually frequent, may have additional ictal manifestations, tend to occur on waking and respond well to AEDs. The long duration of the episodes observed in some patients could be due to postictal phenomena. Interictal abnormalities may be absent in routine EEG studies, but have always been detected during EEG sleep recordings.
Conclusion: The differential diagnosis of TEA from TGA may be difficult in the individual patient. Efforts should be made to obtain in these patients an EEG sleep recording.

p0521 LEVETIRACETAM INDUCED MU RHYTHM STATUS AND CYCLIC INSOMNIA
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Mu rhythm is a physiologic EEG finding of no clinical significance mainly seen during resting wakefulness. There has been only two described case where mu rhythm status was observed one being related to levetiracetam (LEV). We report the second case.
We present the case of an 81 years old patient who had been followed for tonic-clonic seizures of undetermined etiology for 9 months with negative workup. Several antiepileptic drugs (valproate, carbamazepine, lamotrigin, clonazepam) were tried unsuccessfully, leading to the addition of LEV. 45 days after introducing LEV and reaching a dosage of 2 g/day, the patient started experiencing, with constant periodicity, every 4 days, a state of insomnia during which he would present certain hours...
of cognitive impairment, lasting around 30 hours, followed by deep sleep and return to basic state after awakening.

On day 3 after admission, EEG(d3), during a normal clinical state, showed brief runs of diffuse theta slowing. On day 5, the patient got into an episode of insomnia that lasted 30 hours and had the same characteristics as the previous events. EEG(d5) showed a continuous mu rhythm, or a mu status, intermixed with delta waves. Incrimination of LEV was suspected and down tapering was started. On day 11, LEV at 500 mg/d, a second similar clinical event was reported; EEG(d11) showed again a mu status. At day 13, after complete withdrawal of LEV, EEG(d13) showed a disappearance of the mu rhythm and of the delta waves with a well organized background of 8 Hz. The patient did not present any new episode of insomnia after being discharged.

The time correlation between LEV administration and mu status leads us to consider levetiracetam as a causal factor. The mu status was clinically correlated with insomnia and cognitive impairment. The underlying mechanisms of this triade remain to be clarified.

### p0524

**USEFULNESS OF VIDEO-EEG (VEEG) MONITORING IN PATIENTS WITH EPILEPTIC ENCEFALOPATHY. RETROSPECTIVE REVIEW OF 72 PATIENTS**

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**Purpose:**
1. To describe the electro-clinical aspects of patients admitted for vEEG monitoring at FLENI Institute since June 2015 to December 2016.
2. To identify seizures and PNE (Paroxysmal Non epileptic Events) frequency.
3. To determine if parent’s seizure frequency report and seizure type is accurate compare with vEEG findings.

**Method:** Retrospective review of a cohort of 82/569 patients admitted to vEEG unit, who met the electro-clinical criteria, during 18-month period. Ten patients were excluded.

**Results:** 72 patients had Epileptic Encephalopathy (EE), from 1 month–25 year old (6 adults). Associated etiologies were: structural n = 36 (49%), genetic-metabolic n = 10 (13%) unknown n = 26 (36%). All patients received AED, ketogenic diet n = 11, VNS n = 5, surgery n = 4, canabidiol n = 6. Neurological exam was abnormal in 77% (n = 56) and 43% (n = 31) corresponded to cerebral palsy patients.

During vEEG a combination of PNE and epileptic seizures were seen in 38.8% (n = 28), epileptic seizures only 58.3% (n = 42).

Seizure frequency parent’s report was not accurately in 59% (n = 39), either in absolute numbers or range. 20/39 (51%) had >3 years of time disease evolution.

Seizure frequency parent’s report could not be compare with seizure frequency during the vEEG due to lack of information previous admission.

50% n = 37 of parents or caregivers did not recognized at least one seizures type or more reported during the vEEG. The seizures type less recognized were: myoclonias 20/27 (74%), absence 11/17 (64%), focal 6/28 (21%), spasm 6/31 (19%), tonic seizures 9/43 (20%), atonic 2/11 (18%).

**Conclusion:** vEEG monitoring is a useful tool in EE, not only to recognize PNE, either seizure frequency or detecting other seizures types for treatment management. Finding a new seizure type during a vEEG not always implies a progression of the disease and need to be carefully analysed.

### p0525

**A STUDY OF TUBEROUS SCLEROSIS WITH NEW HYBRID INTRACRANIAL MICRO-MACROELECTRODES**


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**Purpose:** Tuberous sclerosis complex (TSC) is a rare genetic disorder associated with mutations in one of the two tumor suppressor genes (TSC1/TSC2). TSC leads to multisystem hamartomas, including various neuropathological brain lesions, such as tubers. Up to 90% patients suffer from partial epilepsy, often drug-refractory. Seizures may remit after epilepsy surgery in selected cases, but the exact location of the seizure onset zone (SOZ) in TSC remains controversial. Some studies suggest that seizures play a greater role in seizure genesis than perituberal cortex. But increasing evidence exists for the epileptogenicity of MRI-normal perituberal tissue. Fast-ripples (FR, 200–600 Hz) are supposed to be biomarkers of the SOZ. However, no FR were found in the tubers of a TSC patient explored by stereo-electroencephalography (SEEG) macroelectrodes.

**Method:** We report the case of a patient who suffers from TSC complicated by drug-refractory epilepsy. She underwent a SEEG pre-surgical assessment using classical macroelectrodes but also 4 newly designed hybrid micro-macro-electrodes (micro-macro): one micro-macro was localized in the tuber and another one in the perituberal cortex. Micro-electrodes have a higher sensitivity to FR than macroelectrodes.

**Results:** Our results show for the first time that FR are recorded both in the tuberal and perituberal cortex using the microelectrodes whereas none were recorded using the macroelectrodes. No FR was recorded in the healthy cortex. Moreover single and multi-unit activities were differently modulated in the tuberal and perituberal cortices when interictal spikes occurred, with an interplay between both regions.

**Conclusion:** Our results imply that the perituberal cortex belongs to the SOZ and suggest in fact neuronal interactions between the perituberal and tuberal cortices.

### p0527

**IDENTIFICATION OF HIGH-FREQUENCY OSCILLATIONS (HFOs) IN PAEDIATRIC INTRACRANIAL EEG BY MEANS OF KURTOSIS-BASED TIME-FREQUENCY ANALYSIS**

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**Purpose:** High-Frequency Oscillations (HFOs, ~80 Hz) are biomarkers of the seizure onset zone (SOZ) and their visual identification in multi-electrode intracranial EEG (iEEG) is time-consuming. We implemented a method for the automatic detection of HFOs with preliminary kurtosis-based selection of the most informative channels. Channels with the highest HFO rates (HFOs area) were compared with the post-operatively confirmed SOZ for validation.

**Method:** iEEG data preceding seizure episodes in 6 representative paediatric patients (mean age: 14y) with focal drug-resistant epilepsy and who underwent presurgical assessment at the Birmingham Children’s Hospital were band-pass filtered (80–250 Hz). Wavelet coefficient and their mean kurtosis were computed on segmented signal. A threshold was set on kurtosis distribution and channels were ranked according to the total number of segments having kurtosis over that threshold. The first third of channels was then retained. Candidate HFOs were detected where the power of the wavelet coefficients exceeded the mean power by 5SD and for at least 20 ms. Channels with the highest HFO rates were
marked as HFO area and compared to the SOZ, determining sensitivity and specificity.

Results: Sensitivity of 100% was obtained in 3/6 patients together with specificity of 100%, 95.08% and 93.11%, meaning that all the channels in the HFO area were concordant with those in the SOZ. For 2/6 patients, just one channel in the SOZ was not recognized (sensitivity 66.67%), still with a low number of false positives (specificity 100% and 96.97% respectively). Sensitivity of 60% and specificity of 85.19% were obtained for 1/6 patient.

Conclusion: Preliminary findings show that the method allows identification of the SOZ with high sensitivity (concordant with resected brain area) and specificity (regions not included in the resection are not identified as HFOs area) in a totally blind and time-saving automatic way, thanks to the kurto-sis-based selection of the most informative channels.

**A STUDY OF PRAXIS-INDUCED SEIZURES IN JUVENILE MYOCLONIC EPILEPSY**

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Purpose: Praxis induction (PI) is a reflex trait tightly linked to juvenile myoclonic epilepsy (JME) whose high frequency allows recording of myoclonia during a Video-EEG neuropsychological protocol (VNPP). The purpose of this study is to characterize semiological and EEG features of PI myoclonia describing subjective perception and impact on patients.

Methods: This study enrolled JME patients who presented myoclonia of upper limbs induced by a VNPP. We analyzed semiological features of myoclonia, ictal EEG patterns, and relations among them. A semi-structured interview assessed subjective description of PI myoclonia, temporal evolution of this reflex trait, and psychosocial aspects.

Results: 59 myoclonia in the arms were analyzed in 15 JME patients (8 women, mean age 23.4 years). Seven involved only hands, 24 distal arms, 24 global arms, and 4 proximal arms. Jerks were more frequently asymmetric or focal (32/59); a bilateral symmetric pattern of all myoclonia was observed in only 5 patients. Hand executing motion was predominantly affected in 20 myoclonia. Jerks affecting only hands were accompanied by spike-wave pattern, while polyspike-wave predominated in the remaining. A more extensive distribution of myoclonia tended to show higher frequency (p < 0.10) and amplitude (p < 0.032) of polyspike; two patients presented distal arms and global arms myoclonia without any visible EEG change. Nine patients answered the semi-structured interview. While 2 never perceived PI in daily life, 2 noted it already in the first year of epilepsy and myoclonia were promptly controlled with VPA. Five perceived PI for the first time more than 3 years after epilepsy onset recognizing stress as aggravating factor. In 4 of them, PI persisted despite different AEDs. Myoclonia provoked falls/other injuries in 5/7, and job change/loss in 3/7.

Conclusion: PI myoclonia are valuable for JME diagnosis. Ictal EEG patterns showed differences according to distribution of myoclonia. PI influences negatively patients lives.

**MODELING OF INTRACEREBRAL INTERICTAL EPILEPTIC DISCHARGES: EVIDENCE FOR NETWORK INTERACTIONS**

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Purpose: Stereoelectric EEG (SEEG) recordings are considered to be the best choice for preoperative invasive evaluation when the epilepsy of the patient is suspected to originate in deep-sited anatomical structures and standard electro-clinical examinations are not conclusive. The interictal epileptic discharges (IEDs) occurring in these recordings in general are abundant compared to ictal discharges, but difficult to interpret due to complex underlying network interactions.

Method: A framework is developed to model the spatiotemporal network interactions underlying the IEDs. To identify the highly synchronized neural activity underlying these discharges, the variation in correlation over time of the SEEG signals is related to the occurrence of the IEDs using the general linear model [van Houwt et al., 2012]. Subsequently, it is assessed whether the brain regions that reflect highly synchronized neural activity are either independent or interacting within an epileptic network. Independent component analysis is applied followed by clustering of the spatial distributions of the independent components. The spatial distributions of the spike clusters are visualized together with the estimated time delays against the patients’ brain anatomy [Meesters et al., 2015].

Results: The analysis framework was evaluated for five patients who underwent SEEG recordings prior to successful epilepsy surgery. The spatial distribution of the spike cluster that was related to the MRI-visible brain lesions coincided with the seizure onset zone of these patients. Unraveling of the complex network interactions underlying the IEDs of two more patients without satisfactory surgical outcome indicated that an alternative and plausible resection strategy could have been considered.

Conclusion: The analysis framework applied to IEDs is considered a valuable additional tool to the current seizure assessment approach, which might lead to a more successful outcome of epilepsy surgery.

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**TUNING DECISION THRESHOLDS FOR ACTIVE/REST PERIODS SIGNIFICANTLY IMPROVES SEIZURE DETECTION ALGORITHM PERFORMANCE: AN EVALUATION USING EMBRACE SMARTWATCH ON OUTPATIENT SETTINGS**


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Purpose: Embrace (Empatica, Inc., Boston, Massachusetts) is a wrist-worn device coupled with a smartphone-based alert system using accelerometer and electrodermal activity sensors. A machine learning classifier trained on inpatient and outpatient convulsive seizure data provides real-time alarms; its performances in real life settings have been...
INTROOPERATIVE HIPPOCAMPAL SPIKES AND HFO IN HIPPOCAMPAL SPARING TEMPORAL LOBE LESIONECTOMY FOR DRUG RESISTANT EPILEPSY
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Purpose: Temporal lobe epilepsy (TLE) with extrahippocampal lesion could be benefit from hippocampal sparing lesionectomy (HLP). To improve the seizure outcomes, some authors suggested extended resection if spikes in the hippocampus. High frequency oscillation (HFO) is recently a popular biomarkers for epileptogenic tissue and used in tailored resection during epilepsy surgery. We conducted this study to see if residual spikes and HFO are associated with poor outcomes in this procedure.

Method: Data were drawn from the database of epilepsy surgery in our hospital between 2010 and 2015. Patients who had drug resistant TLE with lesions in the temporal lobe were included. HSL was decided by multidisciplinary conference after comprehensive presurgical evaluation. The hippocampus was preserved when it looked normal on high resolution brain MRI, regardless of the location of the lesion or electroencephalography (ECOG) findings. We only included patients who had hippocampal recording by either depth electrodes or small strips. HFO were analyzed only in recordings of appropriate sampling rate. Postoperative seizure outcomes were followed for at least 2 years. Postoperative seizure outcomes were followed for at least 2 years.

Results: 27 patients were included (14 male and 13 female, age 10–66, left 16, right 11). Pathology included tumor (48.1%), vascular anomaly (40.7%), focal cortical dysplasia (7.4%) and gliosis (3.7%). Among them, 26 (96.3%) patients had excellent outcomes (Engel’s classification I). Hippocampal spikes were noted in the pre-resection and post-resection ECOG, 21/25 (84.0%), and 18/23 (78.3%) respectively. Fast ripples (>250 Hz) were noted in 8/17 (47.1%) and 5/16 (31.3%) before and after resection. Ripples (80–250 Hz) were noted in 13/18 (72.2%) and 12/16 (75.0%) before and after resection.

Conclusion: Hippocampal spikes and HFO were not uncommon in TLE with extrahippocampal lesion. HSL in patients who had a grossly normal hippocampus excellent seizure outcomes in spite of the presence of irritating features on intraoperative ECOG.

NON EVOLVING PERIODIC DISCHARGES AND EXTERNAL STIMULI REACTIVITY RELEVANCE
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Purpose: Nonconvulsive status epilepticus (NCSE) can have nonspecific ictal manifestations, like in confusional states or deeper stages of coma. In these scenarios diagnosis cannot be made reliably without EEG. When EEG presents periodic discharges (PDs), there is currently no consensus about interpretation and need of antiepileptic drugs (AED). In such situations, reactivity to external stimuli (RES) has been underestimated. We reviewed electroclinical data of patients with PDs and RES contributing to characterize EEG reactivity clinical relevance.

Method: This is a retrospective review of 33 consecutive patients from our Unit Database with non evolving periodic discharges in the EEG. All of them underwent video-EEG in the acute phase of CNS disturbances. The revision was mainly focused in the reactivity to external stimuli with discontinuation of periodic discharges (PDs) -lateralized periodic discharges, bilateral independent periodic discharges and generalized periodic discharges- when these are non time locked to clinically apparent symptoms and don’t have an ictal pattern. Patient charts and available neuroradiography studies were also reviewed.

Results: Of the 33 patients included in our study, 20 were men, mean age 66.52 (SD 11.54) years. The presence of PDs with RES was 63.6% (21 of 33 patients). The aetiology of the CNS disturbance was classified as: toxic metabolic -11 patients- (33.3%), vascular -9 patients- (27.3%), multifactor -7 patients- (21.2%), tumour -4 patients- (12.1%) and infectious -2 patients- (6.1%), with no significant RES association (p > 0.05). The PDs with RES included a higher diagnosis rate of encephalopathy (44.4%) vs lesion discharges (33.3%) or non convulsive status epilepticus (11.1%). The association was only significant for the absence of RES in NCSE (p 0.02).

Conclusion: This small series suggests that periodic discharges with absence of reactivity to external stimuli appear to be more frequently associated with NCSE. The reactivity to external stimuli in periodic discharges may contribute to diagnosis and treatment need decisions.

NON-INVASIVE DETECTION OF FAST RIPPLES IN LOW-NOISE EEG RECORDINGS
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Purpose: Ripples (80–250 Hz) and fast ripples (FR, 250–500 Hz) are characterized by poor signal-to-noise ratio, which reduces their visibility in non-invasive recordings. While ripples are observed in scalp EEG, FR detection has been restricted to invasive recordings. We tested the detectability of FR in the scalp EEG of epilepsy patients, recorded with low-noise EEG, and quantified their specificity for the epileptogenic zone (EZ).

Method: Scalp EEG was recorded during one hour of slow wave sleep in six patients with focal lateralized epilepsy. We used a custom-made low-noise 8-channel amplifier (noise level 2.3 nV/Hz). Electrodes were placed symmetrically on the epileptogenic and non-epileptogenic hemisphere (EZ-h, nEZ-h). Ripples and FR were detected by combining automated detection [1] and offline visual validation.

Results: For each patient, mean event rates were computed for EZ-h and nEZ-h. Across patients, FR rates were 0.17 ± 0.03 event/min in EZ-h
and 0.11 ± 0.05 event/min in nEZ-h (p = 0.031). Ripple rates were 0.19 ± 0.34 event/min in EZ-h and 0.22/min ± 0.45 event/min in nEZ-h (n.s.). Across all channels, mean peak-to-peak amplitude FR was 1.02 ± 0.58 μV on a background noise level of 0.33 ± 0.12 μV while mean peak-to-peak ripple amplitude was 2.09 ± 1.15 μV on a background noise level of 0.70 ± 0.37 μV. **Conclusion:** FR could be detected non-invasively on the scalp by using an optimized low-noise EEG. FR were more specific than ripples for the epileptogenic hemisphere. The opportunity to access FR non-invasively represents a substantial advance in scalp EEG recording and could contribute to therapy monitoring.


**SEIZURE ONSET ZONE CONNECTIVITY DURING WAKEFULNESS AND SLEEP STUDIED THROUGH SINGLE PULSE ELECTRICAL STIMULATION DURING SEEG RECORDINGS**

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**Purpose:** Invasive exploration of the epileptogenic network using depth electrodes is usually indicated in refractory epilepsy patients for the accurate delineation of the seizure onset zone (SOZ). Single pulse electrical stimulation (SPES) protocol is often used for obtaining additional information during the presurgical invasive evaluation. Cortico-cortical evoked potentials (CCEP) elicited by SPES during sleep in comparison with wakefulness have been poorly studied.

**Method:** We performed SPES stimulation protocol in a selected group of 7 refractory epilepsy patients, explored by means of SEEG method with intracerebral depth electrodes. All the patients were operated on and are currently seizure-free. The seizure onset zone was located differently in the studied patients and is dependent on the clinical symptoms. The SPES protocol was performed with a constant current stimulator in 7 refractory epilepsy patients. The electrodes were placed in the SOZ and the response was recorded with a 19-channel EEG system. The results were analyzed statistically and compared with the results obtained during awake and sleep studies.

**Results:** The ER amplitudes by SPES stimulation in the SOZ during wakefulness and sleep showed statistically significant differences (p < 0.001). We identified constant, strong connectivity within the SOZ, but also with other brain areas, irrespective of patient status. The ERs obtained by stimulating the SOZ in the areas adjacent to SOZ are significantly inhibited during sleep in comparison with wakefulness. In 4 patients, by stimulating the SOZ (amygdala and hippocampus), a significant response in the temporal pole was observed during sleep, whereas the response was much lower during wakefulness. The local connectivity of the SOZ during sleep is enforced as opposed to a more widespread connectivity with remote structures during wakefulness.

**Conclusion:** We described how sleep altered the connectivity of the SOZ with various cerebral structures. More study is needed to complete these novel observations on the influence of sleep on the epileptogenic network.

**IMPACT OF CANINE EPILEPSY ON COGNITIVE DYSFUNCTION**


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**Purpose:** There is extensive evidence from studies of both children and adults with epilepsy that epilepsy can compromise cognition, ranging from mild learning impairments to severe cognitive decline. A variety of epilepsy-related factors affect cognitive function, including seizure type and frequency, age of onset and anti-epileptic medication. Epilepsy is the most common chronic neurological disorder in dogs, with parallels to human epilepsy in presentation, diagnosis and treatment. This study investigated whether, after accounting for age, dogs with epilepsy manifested increased levels of cognitive dysfunction compared to control dogs.

**Method:** An online cross-sectional study of dogs aged over 3 years old was conducted. Owners were recruited via veterinary practices and social media and asked to complete the Canine Cognitive Dysfunction Rating Scale (CCDR), a validated tool measuring cognitive impairment in dogs including deficits in learning, memory and spatial awareness. Owners reported their dog’s seizure history and dogs were classified as being affected by idiopathic epilepsy (no structural cerebral pathology suspected) if they met the International Veterinary Epilepsy Task Force diagnostic certainty criteria.

**Results:** Valid data were collected for 4051 dogs of 173 breeds, with a median age of 98 months. Dogs with epilepsy (n = 286) had a significantly higher CCDR score than control dogs (n = 3765) and were significantly more likely to score above the CCDR threshold for diagnosis of cognitive dysfunction (3.8% vs. 1.4%). In a linear model with CCDR score as the outcome variable, the factors significantly associated with CCDR were idiopathic epilepsy diagnosis, age (months), weight and neuter status.

**Conclusion:** These findings are the first to demonstrate the negative effects of canine epilepsy on cognitive function. In addition, older dogs, neutered dogs and lighter dogs were at more risk of impaired cognition. Further studies detailing the nature of cognitive impairment in dogs affected by epilepsy are required.
system has been suggested to play an important role for development and spread of seizures in patients with RTLE and there are evidence that is also affected in depression. The aim of this study was to determine a subgroup of GABAergic interneurons which express the calcium binding protein calbindin (CB), in temporal 20 and 21 Brodmann neocortical areas of patients with RTLE and hippocampal sclerosis (HE) with and without comorbid depression, who underwent epilepsy surgery.

**Method:** Patient with RTLE and HE were included. Neurological, neuropsychological, psychiatric (SCID I, DSMIV) and complementary evaluations (VIDEO EEG, RMN) were conducted before surgery (anterior temporal lobectomy). The cortical sections from 20 and 21 Brodmann areas were processed by histopathological routine techniques, and by immunohistochemistry with anti-CB and anti-NeuN. Focal dysplasias were excluded. Post mortem sections were processed simultaneously.

A quantitative morphometric analysis was conducted (ImageJ). ANOVA/Bonferroni test was used.

**Results:** Patients with RTLE and co-morbid depression n = 9 (age 30 ± 10 years) and without depression n = 6 (age 36 ± 9 years) and 5 matched postmortem controls were included. In patients with comorbid depression the total number of CB interneurons and the reactive area in layer II, were significantly reduced (ANOVA F (2.17) = 5.536, p = 0.014). No significant differences in the groups in the number of neuN cells were found in layer II (ANOVA F (2.14) = 0.550 p = 0.588).

**Conclusion:** Comorbid depression in RTLE patients was associated with a reduction in the total number of CB interneurons in temporal areas, which are involved in sensory integration and codification of affective stimuli, suggesting alterations in inhibitory GABAergic system. Further studies should be performed to confirm and extend this preliminary findings.

**p0543 BRAIN ACTIVITY CONTINUES DURING POSTICTAL EEG SUPPRESSION IN INTRACRANIAL AND SCALP RECORDINGS**


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**Purpose:** Postictal generalized EEG suppression (PGES) has been proposed to reflect profound electrical shutdown of the brain, which can be used as a biomarker of SUDEP and potentially a predictor of individual risk. PGES is typically seen only following generalized tonic-clonic seizures, and while it has been associated with clinical and autonomic features considered to be SUDEP precursors, the nature of the relationship between PGES and SUDEP is controversial. We sought to characterize postictal attenuation and evaluate its role as a potential SUDEP risk predictor.

**Method:** We performed a detailed electroclinical evaluation of an intracranial EEG analogue of PGES, which we term postictal diffuse attenuation (PDA), in a series of 31 secondarily generalized seizures recorded from 16 patients. Scalp EEG recordings from the same patient group were assessed separately for PGES.

**Results:** PDA was common, occurring in 84% of seizures from 94% of patients in this study. PGES was seen in 50% of seizures from 44% of patients who had seizures recorded with scalp electrodes. During the PDA period, there was increased power in the infra-delta (<2 Hz) and high frequency (10–41 Hz) ranges observed in intracranial recordings.

Clinical motor manifestations, including oral automatisms, unilateral or bilateral limb posturing, lateralized head and/or eye deviation, non-purposeful unilateral limb movements and focal or generalized myoclonic jerks were observed during the period of EEG attenuation in 26% of seizures.

**Conclusion:** Our clinical and electrographic findings indicate that brain activity during postictal EEG attenuation is not universally suppressed. Further, our study suggests that a phenomenon as common as postictal EEG attenuation could not serve as a useful predictor of a rare event such as SUDEP, although it does not preclude an association with SUDEP mechanisms. We propose instead that PDA/PGES is a distinct phase of generalized seizures.

**p0546 PACES-V: ADAPTING CONSUMER-DRIVEN EPILEPSY SELF-MANAGEMENT FOR UNITED STATES MILITARY VETERANS**

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**Purpose:** Self-management needs of adults with epilepsy are relevant to addressing co-morbidity and adjustment to disability. The Program for Active Consumer Engagement in Self-management (PACES) in Epilepsy was developed in an adult civilian sample. RCT data showed immediate and long-term effects on depression, epilepsy self-management, epilepsy self-efficacy, and quality of life. Minimal self-management work to date has included U.S. Veterans.

**Method:** PACES developed in 3 phases:
1. Mail survey to patients (n = 200) to identify medical and psychosocial problems, and rank self-management intervention format preferences (location, length, time of day, leadership model). Response rate 61%.
2. Focus groups (4 groups; n = 24) validated survey content and identified requisite changes to PACES, for extension of program beyond academic epilepsy centers.
3. RCT of PACES (n = 108). Based on data from (1) and (2), the 8-week groups are co-lead by a psychologist and trained peer with epilepsy; comprised of 6–8 patients, and meet weekly at hospital or by teleconference for 75 minutes. Cognitive-behavioral psychoeducation and goal setting/attainment scaling is used. Outcome measures: Epilepsy S-M Scale, Epilepsy Self-Efficacy Scale, QOLIE-31, PHQ-9, and GAD-7; administered at baseline, 8 weeks, and 6 months.

This presentation details the results of U.S. Veteran-specific focus group research on program adaptations for this unique sub-population. Additional content relevant to co-morbid traumatic brain injury, PTSD, and PNES is hypothesized, along with location and composition of self-management groups.

**Results:** Quantitative and qualitative Data collection occurs at a VA Epilepsy Center of Excellence, with up 3 focus groups (n = 30) to reach content saturation. Data for PACES content changes and outcomes measures is presented, along with an implementation model for a Veteran-specific RCT.

**Conclusion:** PACES is a consumer-driven, psychoeducational intervention for epilepsy self-management, and promising regarding disability management. Top-down approaches have been less successful at participant engagement and lack longer-term follow-up relevant to sustained cognitive-behavioral change.

**p0547 PROGRAM FOR ACTIVE CONSUMER ENGAGEMENT IN SELF-MANAGEMENT: FINDINGS AND NEW DIRECTIONS**

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**Purpose:** Self-management needs of adults with epilepsy are relevant to addressing co-morbidity and adjustment to disability. The Program for Active Consumer Engagement in Self-management (PACES) in Epilepsy was developed in an adult civilian sample. RCT data showed immediate and long-term effects on depression, epilepsy self-management, epilepsy self-efficacy, and quality of life. Minimal self-management work to date has included U.S. Veterans.

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The PACES in Epilepsy program is a partnership between patients and providers, incorporating the patient’s preferences and goals. Initial literature review indicated issues in some existing self-management programs relative to the derivation of program material and elevated dropout rates. We developed a mail survey on desired content and program design and sent it to 225 patients with epilepsy. The response rate was 61%, with findings that respondents wanted in-person individual or group sessions co-led by an epilepsy professional and a person with epilepsy, eight sessions of one hour each on a weekday or night, with a mixture of education and coping strategies.

In Phase II of the study, PACES was modeled on survey findings and delivered in RCT format. Subjects (n = 42) had significantly improvements vs. controls (n = 42) on depression, epilepsy self-management, epilepsy self-efficacy, and the QOLIE-31. At six months, significant differences remained on a number of measures except depression and self-efficacy. Results also showed high satisfaction with the material and mode of delivery (all ratings >4/5). The highest three rated modules were Epilepsy and Assertive Communication, Dealing with Cognitive Issues, and Managing Epilepsy Care.

In the current third phase of the study, the sponsoring U.S. CDC has encouraged a larger sample (n = 200), with patients from multiple sites including Veterans Affairs, examination of a longer duration of impact, and the use of multiple formats (on-site, telephone, and webinar). This presentation will discuss the issues to be faced in the training and dissemination (e.g., choice of personnel to be trained, a certification process, and fidelity to the model) as well as PACES’ ultimate sustainability (e.g., partnering, financial reimbursement, and collaboration with members of the U.S. Managing Epilepsy Well Provider Network). The above are issues generally confronted by self-management program providers as they seek stability of their programs.

**p0550**
THE Efficacy of Perampanel in Refractory Status Epilepticus
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Perampanel (PER) is a novel drug recently introduced as an add-on therapy for the treatment and prevention of epileptic seizures in patients aged 12 years or over with partial-onset seizures, with or without secondary generalization.

**Purpose:** To determine efficacy of PER as adjunctive treatment, we report on 11 patients admitted to our hospital between 2013 and 2015 with refractory status epilepticus.

**Methods:** Patient records were investigated retrospectively to determine treatment response to PER, measured as cessation of status epilepticus and return to baseline consciousness.

Eleven patients were included, seven females, one child. Median age of the adults 70 years (range 33–90 years). All patients had a symptomatic etiology, and all but four patients had a pre-existing epilepsy. PER was the terminating drug in all cases. However, two patients had a pre-existing status epilepticus and all but four patients had a pre-existing epilepsy.

**Conclusion:** During the maintenance period of eight weeks, we registered cessation of SE in eight of the eleven patients (73%). Six patients responded within two weeks and two patients within four weeks.

**Conclusion:** In terms of the efficacy criteria we have chosen, PER is likely to be effective as an add-on treatment in difficult to treat status epileptics in the majority of patients. Early initiation with PER possibly with a faster titration could be appropriate in patients with refractory status epileptics. The oral administration makes it unlikely that PER will ever play a role in first line and early second line treatment.

**p0552**
REAL-WORLD DATA ON ANTI-EPILEPTIC DRUGS USED IN EPILEPSY TREATMENT IN 2010 AND 2014
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**Purpose:** Antiepileptic drugs (AEDs) are among the most commonly prescribed centrally active agents. This study describes prescription and utilization of AEDs among affiliates of the third Belgian health insurer (MOLOZ - Mutualités Libres - Onafhankelijke Ziekenfondsen) in 2010 and 2014.

**Method:** A detailed descriptive analysis was performed for pharmacological and behavioural features of about 20,000 patients using AEDs during at least 3 months per year (ATC Class: N03) from a retrospectively collected database.

**Results:** We identified 18,045 and 21,865 AED users for 2010 and 2014, respectively. The prevalence of AED consumption increased from 9.2% (95% CI 7.8–10.6) to 10.8 (9.5–12.2)/1000 persons during the study period. According to the age, the proportion of AED users in monotherapy ranged from 58% (0–11 years) to 82% (>65 years) and the average number of different AEDs used varied between 1.6 (0–11 years) and 1.2 (>65 years). Valproic acid was the most common AED (35% of epileptic patients in 2014 vs. 39% in 2010), followed by levetiracetam (19% vs. 14%), lamotrigine (18% vs. 16%) and carbamazepine (15% vs. 19%). Two out of three AEDs were prescribed by GPs (67%), 15% by neurologists and 10% by psychiatrists. Prescription of AEDs by GPs increased with aging (31% for 0–11 years and 82% for >65 years).

**Conclusion:** The use of administrative databases provides interesting findings about the prescription of AEDs in real-world. This study identified prescribing trends in a cohort of patients with epilepsy in Belgium. Results regarding demographic findings and selection of drug therapy are comparable to findings from studies in other countries. The strong positive correlation between monotherapy, prescription by GPs and age of patients seems to show that the elderly or long-time users are less likely to have their treatment changed by the prescriber or more likely to have just prescription renewals.

**p0553**
IMPACT OF EVEROLIMUS TREATMENT ON QUALITY OF LIFE (QOL) IN PATIENTS WITH TUBEROUS SCLEROSIS COMPLEX (TSC) WHO HAVE REFRACTORY PARTIAL-ONSET SEIZURES IN THE CONTEXT OF AN INTERVENTIONAL CLINICAL TRIAL (EXIST-3)
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**Purpose:** Three age-specific QoL measures were included as secondary endpoints in EXIST-3 (NCT01713946), a three-arm, randomized, double-blind, placebo-controlled phase III study to assess the efficacy/safety of two trough exposure ranges of everolimus (Low exposure, LE: 3–7 ng/mL and high exposure, HE: 9–15 ng/mL), as adjunctive therapy in patients with TSC with partial-onset refractory seizures (N = 366). The

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aim of this work was to evaluate QoL alongside clinically relevant and statistically significant reductions in seizure frequency in everolimus-treated patients.

**Method:** QoL measures included QoL in Childhood Epilepsy (QOLCE; caregiver-report for aged 2–<11), QoL in Epilepsy Inventory for Adolescents (QOLIE-AD-48; self-report, aged ≥11–<18), and QoL in Epilepsy Inventory-31-Problems (QOLIE-31-P; self-report, aged ≥18).

**Results:** Primary results showed statistically significant improvements both in the response rate and percentage reduction of TSC-associated seizures from baseline to end of Core phase (Week 18), for both exposure groups of everolimus, relative to placebo. At the end of Core phase, the completion rate for the QOLCE was high across treatment arms (84%, N = 197). The overall QoL score, as measured by the QOLCE, was associated with minimal changes from baseline (LE, +3.1; HE, +4.0; Placebo, +1.7). In everolimus HE arm, improvements were observed for selected QOLCE subscales versus placebo: single QoL item (+1.1), physical restrictions (+5.9) and self-esteem (+9.4). The end of core phase completion rates for the QOLIE-AD-48 (36%, N = 102) and QOLIE-31-P (49%, N = 67) were low, limiting the conclusions that can be drawn. The QOLIE-AD-48 overall QoL score marginally improved for all treatment arms. The QOLIE-31-P overall QoL score was maintained in the LE treatment arm and placebo, while minimal negative change from baseline was observed in the HE arm.

**Conclusion:** Results provide evidence that efficacy gains with respect to significant reduction in seizure frequency were achieved without detriment to patients’ QoL while receiving active treatment for 18 weeks.

**p0557**

**COMPARISON OF SEIZURE OUTCOME IN PATIENTS WITH WEST SYNDROME AFTER EXTREMELY LOW-DOSE ADRENOCORTICOTROPIC HORMONE THERAPY**

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**Purpose:** The daily dose of synthesized adrenocorticotropic hormone (ACTH) for West syndrome varies widely among hospitals, and a dose of 0.005–0.025 mg/kg/day (equivalent to 0.2–1.0 IU/kg/day of natural ACTH) is selected in Japan. We selected 0.005 mg/kg/day for patients <1 year old and 0.025 mg/kg/day for patients >1 year old, with some modifications based on the underlying condition. Here, we compare the seizure outcome among 0.005 mg/kg/day, 0.025 mg/kg/day, and “step-up” (0.005→0.025 mg/kg/day) doses.

**Method:** We retrospectively reviewed the medical charts of patients with West syndrome who underwent ACTH therapy at <3 years of age and were admitted to our hospital between 2005 and 2016.

**Results:** Forty-three patients were included (20 with 0.005 mg/kg/day [group A; median 8 months], 13 with 0.025 mg/kg/day [group B; median 19 months], and 10 with “step-up” [group C; median 8 months]). The seizure-free rate among the 3 groups was not significantly different; it was 85% in A, 85% in B, and 80% in C at the end of ACTH therapy; and 65% in A (median follow-up 42 months), 54% in B (median follow-up 68 months), and 50% in C (median follow-up 88 months) at the final follow-up.

**Conclusion:** Based on our criteria, the short and long-term seizure outcomes were not different among the 0.005 mg/kg/day, 0.025 mg/kg/day, and “step-up” groups. This study indicates that 0.005 mg/kg/day of ACTH therapy for West syndrome, especially in patients <1 year old, might provide the same efficacy as that of 0.025 mg/kg/day.

**p0555**

**THE EFFECT AFTER GOVERNMENT-GUIDING INTRODUCTION OF HLA-B*1502 SCREENING TEST IN TAIWAN**

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**Purpose:** To study the incidence rate of carbamazepine induced Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) after government-guiding introduction of HLA-B*1502 screening test in Taiwan.

**Method:** Patients who received newly prescribed carbamazepine (ATC code N03AF01) between January 1, 2007 and December 31, 2013 (n = 9,838) were identified from Taiwan National Health Insurance Research Database. The dataset was divided into comparison groups and study groups according to the prescription date, before or after June 1, 2010, respectively. Each subject was traced for 60 days from carbamazepine prescription to observe the occurrence of SJS (ICD-9-CM code 695.1). In the study group, whether HLA-B*1502 test was ordered prior to carbamazepine prescription was examined. The demographic characteristics of patients and specialty of prescribing physicians were recorded. The amount of carbamazepine prescription was compared between study and comparison groups. HLA-B*1502 test order rate was calculated in every specialty.

**Results:** There were 2,494 subjects in the study group and 7,344 in the comparison group. The incidence rate of SJS was 0.24% (6 of 2494) in the study group and 0.27% (20 of 7344) in the comparison group. P-value was 0.7896. In the study group, 204 (8.2%) patients received HLA-B*1502 test and one SJS was observed. Five SJS (0.22%, 5 of 2290) were identified in those without HLA-B*1502 test. The top three specialists that reduced carbamazepine prescription were Orthopedics (80%), Rehabilitation (79%), Neurology and Neurosurgery (73%) physicians. Pediatricians, Neurologists, and Psychiatrists were more willingly to test HLA-B*1502 prior to prescribing carbamazepine. The rates of these 3 specialties were 33%, 27%, and 17%, respectively.

**Conclusion:** The government-guiding introduction of HLA-B*1502 screening test in Taiwan only decreased total number of carbamazepine-induced SJS and TEN patients but not the incidence rate. Further investigation is needed to find out why the incidence rate did not decrease as expected.

**p0558**

**BEHAVIORAL EFFECTS OF LEVETIRACETAM IN PATIENTS WITH EPILEPSY. WHO IS LIKELY TO HAVE THEM AND HOW MUCH**

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**Purpose:** Levetiracetam is a broad spectrum antiepileptic drug. There have been concerns regarding its behavioral side effects, but the pattern or risk factors are not yet clearly defined. This study was conducted to assess these effects in our setting.

**Method:** This prospective observational study was undertaken on 157 epilepsy patients who were started on levetiracetam for the first time. Patients having clear psychiatric syndrome were excluded. Behavior symptoms were assessed at baseline; and 4, 8 and 12 weeks according to neuropsychiatry inventory (NPI) which includes ten behavior symptoms. They were rated according to frequency, severity and caregiver distress.

**Results:** Behavioral side effects attributable to levetiracetam were found in 16/157 (10.2%) patients. New onset symptoms were noticed in 10/157 (6.3%) patients while 6/157 patients (3.8%) had exaggeration of baseline symptoms. Agitation was the most common behavioral symptom. Symptoms were severe enough to stop levetiracetam in 9/16 (56.2%) of these patients. After stopping levetiracetam, symptoms significantly decreased in severity and frequency in 8/9 (88.8%) of these patients and completely resolved in 1/9 (11.1%) patient. Suicidal thoughts were present in 2/157 (1.27%) patients. 37/157 (23.5%) patients had baseline behavioral symptoms, of which 19/37 (51.3%) had resolution of symptoms after starting levetiracetam. All of these patients had fully controlled seizures. 12/37

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(32.4%) patients had persistence of symptoms and 6/57 (16.2%) patients had exaggeration of symptoms. We found significant association of behavioral side effects with three variables - abnormal MRI brain, higher doses of levetiracetam at 4 weeks, and unmarried status.

Conclusion: These results show that behavioral side effects are not uncommon in patients on levetiracetam, and may be dose dependent. The incidence may be low if patients with clear psychiatric disorders are excluded. Mild baseline behavioral symptoms may even improve on levetiracetam; which may partly be due to good seizure control.

p0560
THE IMPACT OF PERAMPANEL TREATMENT ON QUALITY OF LIFE AND PSYCHIATRIC SYMPTOMS IN PATIENTS WITH DRUG-REFRACTORY FOCAL EPILEPSY
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Purpose: Perampanel (PER) adverse effects (AE), such as depressive symptoms and behavioural changes have been reported. The aim of the study is to assess prospectively the effect of PER on psychological functioning and Quality of Life (QoL) in a group of patients with drug-refractory focal epilepsy (DRE), before and during PER adjunctive treatment.

Method: Patients with DRE have been enrolled in this 18-months duration study. Socio-demographic and clinical information have been collected. QoL levels, irritability, depressive symptoms and anxiety have been assessed using the QoLIE-31, the Irritability Questionnaire, the BD-II, and the STAI Y-1 and Y-2 questionnaires, at three time points (before PER, after 3 and 6 months).

Results: Data from 45 patients (females 40%, mean age 40.4 yrs SD 12.17) was collected. Before PER, QoL levels are slightly lower in our sample compared to normative data in overall QoLIE-31 score (mean 61.14 SD 15.72), emotional well-being score (mean 65.53 SD 12.17), while anxiety and irritability scores were found not pathological according to normative data. Comparing T0 and T2 assessments, a slight increase in QoL scores were found for all scales (except for social functioning: 56.71 SD 20.50), irritability scores become pathological (mean 15.36 SD 3.35), ataxia (4.42% vs. 3.70%) and increased gamma-glutamyltransferringase (3.3% vs. 0.6%) were more frequent in elderly population (vs. non-elderly). In non-elderly patients (vs. elderly), besides dizziness and somnolence, headache (8.2% vs. 5.8%), nausea (8.0% vs. 5.0%) and diplopia (6.8% vs. 2.5%) and vertigo (3.5% vs. 2.5%) had higher incidence. Concerning hyponatremia, 1.7% serious TEAEs were reported in elderly patients (vs. 0.2% non-elderly).

Conclusion: Overall TEAEs data collected indicate that no specific safety issue was identified for the elderly compared with non-elderly patients.

Purpose: Limited safety data are available in the scientific community concerning the use of eslicarbazepine acetate (ESL) in elderly population. Therefore, a pooled analysis of seven clinical trials (CTs) was conducted to assess the ESL safety/tolerability in elderly patients (≥65-years-old) diagnosed with partial-onset seizures (POS). The incidence of treatment-emergent adverse events (TEAEs) was used to assess this issue and for comparison purposes with non-elderly patients (18 to 64-years-old).

Methods: Data from double-blind, open-label phase II/III CTs in POS (BIA-2093-201,-301 (Part I-IV),-302 (Part I-II),-303 (Part I-III),-304 (Part I-III),-305 (Part I-III),-401) were pooled and analysed by age categories (18-64 and ≥65-years-old). For study -311, only data collected up to September 24th 2015 were included.

Results: The elderly patients treated with ESL (n = 120) showed a similar safety profile to non-elderly patients (n = 1863). At least one TEAE occurred in 75.8% of elderly patients (vs.74.9% non-elderly), with 51.7% reported as possibly-related TEAEs (vs.53.9% non-elderly). Overall, 20% of elderly patients discontinued treatment prematurely due to TEAEs (vs.16.8% non-elderly). Serious TEAEs reported were higher in elderly patients (21.7%) than in non-elderly (7.6%).

For both age categories, dizziness and somnolence were the most frequently reported TEAEs representing 20.2% and 12.6% in the non-elderly group and 10.8% and 9.2% in the elderly group, respectively. Moreover, the incidences of at least possibly-related individual TEAEs differed in both categories: hyponatremia (6.7% vs.1.5%), fatigue (5.8% vs.3.5%), ataxia (4.2% vs.3.7%) and increased gamma-glutamyltransferringase (3.3% vs.0.6%) were more frequent in elderly population (vs. non-elderly).

Conclusion: Overall TEAEs data collected indicate that no specific safety issue was identified for the elderly compared with non-elderly patients.

p0563
EFFICACY AND TOLERABILITY OF LACOSAMIDE AS ADD-ON TREATMENT IN PATIENTS WITH DRUG-REFRACTORY EPILEPSY AND INTELLECTUAL DISABILITY
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Purpose: To assess the efficacy and tolerability of lacosamide (LCM) in patients with difficult-to-treat epilepsy and learning disability.

Methods: In the TDM-registry at the Norwegian Center for Epilepsy in the period 2013–16, 277 patients using LCM were identified. By going through the patients’ medical records, 74 (33%) patients appeared to have refractory epilepsy and learning disability. The efficacy and tolerability of LCM in these 74 patients were analysed.

Results: The study population consisted of 37 females and 37 males. The average age was 31 years, and the median duration of epilepsy was 19 years. The average number of previously tried AEDs was 7.4. In addition to LCM, they used 1–4 other AEDs.

Improved seizure control (>50% reduction of seizure frequency) was obtained in 51 patients (69%), of whom two (2.7%) became seizure free. In 22 patients (31%), LCM had no seizure reducing effect. The drug had been withdrawn in 21 patients, in 7 due to lack of efficacy, 6 due to adverse effects and 6 due to a combination of these. The retention rate after 1 year was 83%. 32 of the patients (43%) had used LCM for more than 3 years.
The mean daily dose of LCM was 321 mg (25 - 600 mg), and mean serum concentration was 20 mmol/L (~10-50).

Adverse effects were reported in 27 patients (37%). There were no serious adverse events. The most commonly reported side effects were gastrointestinal discomfort, headache, dizziness, sedation, psychiatric symptoms.

**Conclusion:** The present study shows that LCM given as add-on drug appears to be favorable in treating patients with difficult-to-treat seizures and learning disability. Improved seizure control was achieved in about 2/3 of patients, and in most cases the drug was well tolerated.

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**p0564**

**DE NOVO MULTIFOCAL MYOCLONUS INDUCED BY LAMOTRIGINE IN A TEMPORAL LOBE EPILEPSY CASE**

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**Introduction:** Exacerbation or de novo LTG-induced myoclonus has been reported in patients with various types of epilepsy. We report the first case of de novo LTG-induced multifocal myoclonus in a patient affected by temporal lobe epilepsy.

**Description:** A 34-year old man came to our attention because of frequent complex partial seizures resistant to antiepileptic drugs. He was treated with valproic acid (VPA) up to 1000 mg/day, with only partial control of seizures; thus, at the age of 17, LTG was progressively titrated. Clinical and electroencephalographic data were consistent with a diagnosis of TLE without mesial sclerosis. Afterwards the patient showed a complex partial seizure with verbal automatisms, followed by confusion and drowsiness. During the following video-EEG monitoring he showed myoclonic jerks and frequent spikes and sharp waves in the left frontotemporal regions. The level of VPA was normal, while the level of LTG was slightly above the therapeutic range.

**Discussion:** We hypothesized that LTG induced a de novo myoclonus, possibly in a dose-dependent manner. The myoclonus induced by LTG has been usually reported in generalized epilepsies. In most of these cases, LTG was added to a pre-existing VPA therapy, leading to synergistic pharmacodynamic interactions. The myoclonus onset or aggravation induced by LTG can also depend on genetic susceptibility. To our knowledge, this is the first report of a de novo multifocal myoclonus induced by LTG toxicity in an adult with TLE.

**Conclusion:** Probably, different factors contribute to generation of the myoclonic phenomenon, including type of epilepsy (focal/generalized), etiology (symptomatic/idiothetic), genetic predisposition (i.e. SCN1A mutations), as well as the LTG plasmatic concentration. Furthermore, on the basis of the EEG NREM pattern of our patient we hypothesize a potential role of the cyclic alternating pattern (CAP) during NREM sleep as a facilitating factor in the development of myoclonus in our patient.

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**p0565**

**ADJUNCTIVE PERAMPANEL IN PATIENTS WITH DRUG-RESISTANT PARTIAL SEIZURES WITH AND WITHOUT CONCURRENT VNS THERAPY IN PHASE III STUDIES**

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**Purpose:** Perampanel is approved for adjunctive treatment of partial seizures with or without secondarily generalized seizures and for primary generalized tonic-clonic seizures in patients with epilepsy aged ≥12 yrs. This post-hoc analysis reports efficacy and safety of perampanel in subjects with drug-resistant partial seizures with and without concurrent VNS therapy from Phase III clinical studies.

**Method:** Subjects with drug-resistant partial seizures were aged ≥12 yrs and receiving 1–3 concomitant AEDs. VNS must have been implanted ≥5 mos before Visit 1; stimulator parameters were to remain stable. After a 6-wk baseline, subjects were randomized to once-daily double-blind treatment (6-wk titration, 13-wk maintenance) with placebo or perampanel 2, 4, 8, or 12 mg. Data were pooled for this post-hoc analysis, and efficacy and safety were analyzed by concurrent VNS status.

**Results:** The full intent-to-treat population included: +VNS = 130 and -VNS = 1348. Number of concomitant AEDs at baseline and baseline characteristics were generally similar between VNS subgroups. Median baseline seizure frequency was higher in +VNS subjects (placebo = 18.1, perampanel 2 mg = 29.2, 4 mg = 28.0, 8 mg = 17.7, 12 mg = 27.3) vs -VNS (placebo = 10.2, perampanel 2 mg = 9.8, 4 mg = 9.8, 8 mg = 11.6, 12 mg = 12.1). During the double-blind phase, reductions in seizure frequency/28 days and responder rates were similar in +VNS and -VNS subjects. Higher total rates of TEAEs, SAEs, and TEAEs leading to withdrawal were observed for perampanel- and placebo-treated +VNS vs -VNS subjects. Most TEAEs in both VNS subgroups were considered mild or moderate; no deaths were reported. Limitations are the small number of subjects with VNS in this post-hoc analysis, which is not powered to show significance between VNS subgroups.

**Conclusion:** In patients with drug-resistant epilepsy, adjunctive perampanel 4, 8, and 12 mg reduced the occurrence of seizures, regardless of subjects’ use of concurrent VNS therapy. Safety data are consistent with and without VNS, with somewhat higher event occurrences for both perampanel and placebo with VNS.

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**p0566**

**ESLICARBAZEPINE ACETATE (ESL) IN TREATMENT OF CHILDHOOD FOCAL EPILEPSY**

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**Purpose:** To evaluate the clinical efficacy and tolerability of ESL in children with focal epilepsies and to compare those of CBZ and OXC.

**Method:** 45 children (28 boys, 17 girls; age 4–17 years) with focal epilepsies treated with ESL at the Danish Epilepsy Centre between 01.01.2012 and 31.12.2016 were included. Therapy duration varied from six to 48 months. Thirty patients received ESL as add-on treatment and 15 as monotherapy. Treatment response was assessed as seizure-free, >50% seizure reduction, <50% and non-responders. Fifteen patients were earlier treated with CBZ, seven with OXC, 12 patients tried both drugs. The clinical effect and tolerability of ESL, CBZ and OXC were evaluated.

**Results:** ESL showed 50–100% seizure reduction in 61.4% of patients, in 38.6% of cases its efficacy was lacking. ESL was well tolerated by all but one patient (withdrawal due to skin rash). None of the children previously treated with CBZ and OXC were seizure-free. After ESL initiation the complete seizure control was achieved in 6/27 patients in CBZ-group, and 4/19 patients in OXB-group. ESL had much better side effect profile compared with CBZ. CBZ was withdrawn in six patients while ESL only in one.

**Conclusion:** ESL if effective and well tolerated drug in children with refractory focal epilepsy. It was equally effective in focal hypomotor, hypermotor and secondary generalized seizures. ESL showed higher efficacy and better tolerability compared with CBZ and OXC.

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**p0570**

**EFFICACY AND TOLERABILITY OF PERAMPANEL IN ADULTS WITH EPILEPSY FROM A MEDICAL CENTER IN TAIWAN: AN INITIAL REAL WORLD EXPERIENCE**

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Purpose: To evaluate the safety and efficacy of Perampanel in epilepsy in adults in real life settings and understand the efficacy and safety of a drug outside clinical trials. Here we report a data from a large series of patients treated with perampanel in Taiwanese population over a period of 6 months.

Method: Patients were retrospectively observed for 6 months. At the end of 6 months, seizure freedom, median percentage seizure reduction, responder rate, retention rate and patients with adverse events (AEs) were evaluated.

Results: Of 232 patients on perampanel, 223 patients were as add on therapy, 92 completed 6 months of evaluation, 57 were continuing and 74 patients discontinued because of lack of efficacy/AEs/lost to follow up or subject choice. The mean age was 39 years and mean duration of epilepsy was 20.8 years. 91.3% patients had focal epilepsy with or without SGTC, 6.5% had PTCG. Number of concomitant AEDs at baseline, majority were on 2–4 AEDs. 82.6% patients were on enzyme inducers. Responder rate at 6 months was 56.7% and seizure freedom was 24.4%. Majority of the patients were on 4–6 mg of Perampanel. The seizure frequency reduction with 2–4 mg was 66.7% and 82.1% with 6 mg. The retention rate at end of 3 months and 6 months were 79.5 & 62.3% respectively. 45.7% had TEAEs and 13% of patients discontinued medication. Most common TEAEs were diziness, somnolence, irritability, respectively. 45.7% had TEAEs and 13% of patients discontinued medication. Majority of the patients were on 4 mg of Perampanel. The seizure frequency reduction with 2–4 mg was 66.7% and 82.1% with 6 mg. The retention rate at end of 3 months and 6 months were 79.5 & 62.3% respectively. 45.7% had TEAEs and 13% of patients discontinued medication. Most common TEAEs were diziness, somnolence, irritability, respectively.

Conclusion: Perampanel is effective and well tolerated in patients with epilepsy. Seizure freedom was 24.4% at end of 6 months with a retention rate of 62.3%. It is important to understand the efficacy and safety outside the clinical trial setting and results are similar to other published real world data on Perampanel.

p0572

GENDER DIFFERENCES IN SAFETY OF ANTI-EPILEPTIC DRUGS

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Purpose: To assess the gender differences in safety of most commonly used antiepileptic drugs (AED) in the treatment of epilepsy.

Method: We conducted a retrospective analysis of medical records of 392 epileptic outpatients (174 males - 44%, mean age = 11 years; 218 females - 56%, mean age = 14 years), who used monotherapy of valproates, carbamazepine, or topiramate, or oxcarbazepine, or levetiracetam, or lamotrigine in 2015–2016. We calculated risk ratios (RR) and 95% confidence intervals (95% CI) for unfavorable outcome (assessment of the safety): the number of patients with adverse effects using software package RevMan 5.3. We compared the unfavorable outcome between male and female patients. The results were considered significant when a P-value was less than 0.05.

Results: Valproates were used in monotherapy in 58%, carbamazepine - in 18%, topiramate - in 14%, oxcarbazepine - in 5%, levetiracetam - in 3%, lamotrigine - in 2% of cases. The risk ratio for the number of males versus females, who had adverse reactions during monotherapy of valproates was as follows: RR = 0.85 95% CI [0.64 to 1.13], of carbamazepine - RR = 1.15 95% CI [0.82 to 1.61], of topiramate - RR = 1.13 95% CI [0.75 to 1.62], of oxcarbazepine - RR = 1.13 95% CI [0.34 to 3.74], of levetiracetam - RR = 0.50 95% CI [0.06 to 4.15], of lamotrigine - RR = 1.33 95% CI [0.13 to 13.74], respectively.

Conclusion: No significant gender differences were found for the safety of monotherapy of valproates, carbamazepine, topiramate, oxcarbazepine, levetiracetam and lamotrigine using as unfavorable outcome the number of patients with adverse effects.

The authors report no conflict of interest in this work.

p0573

SOCIAL COGNITION OF CHILDREN EXPOSED TO ANTI-EPILEPTIC DRUGS IN UTERO

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Purpose: Children exposed to antiepileptic drugs in utero are at higher risk for congenital malformations. Long-term effects on child neurocognitive and behavioral outcome are however hardly known. As a higher risk for autistic spectrum disorders appears, the aim of this study is to investigate emotion recognition ability and social perception of children of mothers with epilepsy who were exposed to anti-epileptic drugs in utero by measuring ‘Affect Recognition’ and ‘Theory of Mind’.

Abstracts
Methods: Children exposed in utero to antiepileptic drugs (monotherapy: VPA, CBZ, LTG, LEV), 6/7 years of age at testing, their mothers and fathers were asked to participate in a longitudinal study by conducting neuropsychological tests (NEPSY-II-NL). Inclusion was on the basis of an earlier inclusion of the mothers with epilepsy in the European Registry of Antiepileptic Drugs in Pregnancy (EURAP-NL) database. Analyses MANOVA will be conducted to evaluate differences between children exposed to the four types of antiepileptic drugs, and to compare the children exposed to AEDs to children from the general population.

Results: Results of the approximately first 125 children will be presented on the basis of the first wave assessment.

Conclusion: Social cognition will be discussed in relation to the risk for autism in this group of children.

p0574 NEUROCOGNITIVE DEVELOPMENT OF CHILDREN PRENATAL EXPOSED TO ANTI EPILEPTIC DRUGS: PRELIMINARY RESULTS OF THE DUTCH PROSPECTIVE OBSERVATIONAL STUDY EURAP & DEVELOPMENT (NL) Y. Huber-Mollenaer*, H. Ro. Rodenburg**, D. Lindhout*, F.J. Oort*, EURAP Development *Stichting Epilepsie Instellingen Nederland (SEIN), Heemstede, Netherlands, **University of Amsterdam, Amsterdam, Netherlands

Rationale: In the past years, there has been increasing attention for the long-term effects of exposure to antiepileptic drugs during pregnancy. For future mothers with epilepsy, it is important to further clarify the effects of prenatal exposure to antiepileptic drugs on neurocognitive development as to make a weighted choice between the risks for the mother with epilepsy and for the unborn child.

Objective: EURAP & Development (NL) is a prospective longitudinal study of children of mothers with epilepsy who were exposed to antiepileptic drugs in utero in which neurocognitive and behavioral development, and parenting is investigated. The current study aims to examine the neurocognitive abilities. The research question is: What are the long-term effects of exposure to monotherapy VPA, CBZ, LTG or LEV during pregnancy on neurocognitive development of children of 6/7 years of age?

Methods: Children born between 2007–2010 and their mothers and fathers were asked to participate by conducting neuropsychological tests (e.g., WISC-III-NL, NEPSY-II-NL), and by completing questionnaires. Inclusion was on the basis of an earlier inclusion of the mothers with epilepsy in the European Registry of Antiepileptic Drugs in Pregnancy (EURAP-NL) database.

Analyses: MANOVA will be conducted to evaluate differences between children exposed to the four types of antiepileptic drugs. Child IQ is the primary outcome variable. Secondary outcomes are more specific cognitive abilities.

Results: In anticipation of the upcoming report, preliminary results of the approximately first 125 children will be presented.

Conclusion: On basis of the results neurocognitive effects of prenatal exposure to antiepileptic drugs will be discussed.

p0575 EFFECTS OF ESLICARB AZEPINE ACETATE ON LIPID METABOLISM PROFILE AND SODIUM VALUES: A RETROSPECTIVE STUDY IN OUR PATIENTS P. Pulitano*, M. Brienda†, C. Davassi†, E. Vicenzini*, O. Mecarelli* *Neurology and Psychiatry, Sapienza University of Rome, Rome, Italy, †Medico-Surgical Science and Biotechnologies, Sapienza University of Rome, Rome, Italy

Purpose: To characterize the association among eslicarbazepine acetate (EGL), plasma lipid levels and sodium values and to compare it with previous effects of traditional dibenzazepine drugs.

Method: This is a retrospective cohort study. We considered 36 adult patients suffering from focal onset epilepsy with and without tonic-clonic bilateral evolution, in add-on treatment with ESL (800–1200 mg/die). In 8/36 patients, ESL was begun by switching from carbamazepine (CBZ) or oxcarbazepine (OXC). The average time of treatment was 10.5 months (range 6–18), 7 patients (19.4%) were already affected by dyslipidemia, nobody by hyponatremia. The lab values assessed prior and after 6 and 12 months of treatment were natremia, total cholesterol, low and high density lipoproteins (LDL and HDL), triglycerides (TGC).

Results: After 6 months of treatment with ESL, we compared the mean total cholesterol and LDL values before and during ESL therapy (total cholesterol values 191.3 ± 29.6 vs 179.7 ± 29.2 mg/dl, p < 0.0001; LDL 114.58 ± 22.7 vs 103.11 ± 19.46 mg/dl, p < 0.0001). Furthermore, we evaluated HDL values before and during ESL (57.5 ± 9.1 vs 63.9 ± 8.3 mg/dl; p < 0.0001). No statistically significant changes were detected in TGC values. ESL was interrupted in 2 patients, after 6 months, because of serious hyponatremia whereas in the other patients, we didn’t observe significant changes of sodium values.

Conclusion: Severe hyponatremia occurred in 6% of patients. The mean total cholesterol and LDL values decreased significantly and HDL increased during treatment with ESL: this suggests that ESL is possibly a safe drug that doesn’t affect negatively the lipid metabolism profile. This represents a difference from CBZ and OXC maybe because ESL binds plasmatic proteins with lower affinity and it is a weaker inducer of liver metabolism. However, a greater number of cases and a more prolonged period of observation are necessary to confirm the results.

Abstracts
Methods: Patient-level data from 46 centres across Europe were merged into a single dataset. Pre-specified outcomes were: 1-year retention rate, 1-year seizure-freedom rate, incidence of adverse events (AEs). Relationships were also explored with cumulative logistic regression analyses.

Results: We included 2372 people with epilepsy treated with perampanel. Median epilepsy duration was 27.0 years; 30.5% had previous psychiatric history; median previously used AEDs was 6; and median concomitant AEDs at baseline was 2 (including enzyme-inducers in 71%). Most had focal seizures (79%; 5% generalized; 16% focal and generalized). At 12 months, 49.5% were still taking perampanel, and 6.2% discontinued due to intolerability. Median time on perampanel was 11.1 months and median dose was 8 mg. Seizure freedom (≥6 months) was seen in 9.2% at 1 year (74/803 in whom data were available), and ≥50% reduction in seizure frequency in 45.6%. During the first year, AEs were reported in 59.0% (1067/1808 in whom data were available), and were more frequent in those titrated every 2 weeks or quicker than in those in whom titration was slower. The most common AE categories were somnolence/sleepiness (15.4%), dizziness/vertigo (13.4%), and behavioural AEs (12.0%). Logistic regression found no factors to be associated with AE rates. Six-month seizure freedom at 1 year was associated with higher age at perampanel initiation, use of non-enzyme-inducing AEDs, and lower number of previously failed AEDs.

Conclusion: Across a large European population, add-on perampanel was retained for ≥1 year in about 50% of patients and 9.2% were seizure free for ≥6 months. AEs were in line with previous reports.

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p0578
USE OF ESLICARB AZEPINE IN CHILDREN AND ADOLESCENTS WITH REFRACTORY EPILEPSY AT TWO NATIONAL EPILEPSY CENTERS, DENMARK AND NORWAY
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Purpose: Eslicarbazepine acetate (ESL) is a novel antiepileptic drug (AED) approved for treatment of focal seizures as add-on in adults, adolescents and children ≥6 years, but in the first years of marketing only for use in adults. Data on use in children and adolescents are scarce. The purpose of this study is to investigate the use of ESL in these two groups in relation to age, comedication and duration of treatment.

Method: Retrospective anonymous data regarding children/adolescents (<17 years) from the therapeutic drug monitoring (TDM)-databases at the National Center for Epilepsy (SSE), Oslo University Hospital Oslo, Norway, and The Danish Epilepsy Center, Filadelphia, Denmark, and clinical data from medical records during 2010–15 were collected.

Results: Data from 50 children and adolescents were included (in- and out-patients), 21 girls/29 boys. Median age was 13 years (3–16), median dose of ESL was 800 mg/day (400–1600) and serum concentration 58 μmol/L (10–100) (n = 17). TDM-data were lacking for the other patients. Median concentration/dose-ratio was 0.07 (0.01–0.1). Only 4 children were <6 years. Polytheraphy with eslicarbazepine was applied in 34 patients (combination with 1–2 other AEDs), most common combinations: levetiracetam (14), topiramate (10) and clobazam (8). Thirteen discontinued the treatment, on average after 137 days (0–1155).

Conclusion: The present study shows that ESL was mostly used in adolescents, although off-label use was observed. Combination with other AEDs was common. 26% of the patients discontinued the treatment. There should be increased focus on documentation of use and pharmacokinetic variability by use of TDM of new AEDs in children and adolescents in a clinical setting.

p0580
TREATMENT WITH ANESTHETIC ANTICONVULSIVE DRUGS IN STATUS EPILEPTICUS: BENEFICIAL OR HARMFUL?
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Purpose: Nowadays there is an ongoing discussion about the risks and benefits of anesthetic treatment of status epilepticus (SE), especially concerning the outcome. Therefore, we performed a retrospective database analysis to examine the influence of treatment with anesthetic drugs and narcosis in SE on mortality and disability.

Method: In a retrospective databank analysis all treatment episodes of a NCSE between January 2010 and June 2013 in the department of Neurology at Rostock University Hospital were identified and evaluated. SE severity before treatment, mortality and disability at discharge were taken into account.

Results: In 24 of 145 treatment episodes anesthesia was used. Although the status epilepticus severity score (STESS) was higher in the anesthesia group (3.5 SD 1.5 vs. 2.2 SD 1.4, U-test p < 0.0007), no patient treated with anesthesia died while in the hospital. In the group not treated with anesthesia 13 patients died (chi-square p = 0.09). For the majority of these patients respiratory failure after pneumonia was the cause of death. By the point of hospital-discharge, the patients who were treated with anesthesia were more often diagnosed with a new neurological deficit than the others (54.2% vs. 18.2%, chi-square p < 0.0002). Consequently, excluding the patients who died, the patients who did not receive a treatment with anesthesia had a smaller deterioration in the modified rankin scale (mRS) at the date of their discharge compared to the estimated mRS before occurrence of SE than the others (p = 0.03).

Conclusion: In this sample of patients there was a trend to lower mortality in the group of patients treated with anesthesia for SE. But preventing death may result in new neurological deficits.

p0585
COMPARATIVE STUDY ABOUT EFFECTS OF DIBENZAZEPINES OVER LIPID METABOLISM PROFILE, SODIUM VALUES, LIVER FUNCTION TESTS AND BLOOD CELL COUNT
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Purpose: Older dibenzazepines with a carboxamide substitution had been demonstrated to cause deleterious effects over lipid metabolism profile, frequent hyponatremia as well as changes in liver function tests and blood cell counts. However some of these adverse effects are more evident with carbamazepine (CBZ) than with oxcarbazepine (OXC) or eslicarbazepine acetate (ESL). The aim of this study was to compare the effects of these 3 antiepileptic drugs over the previously mentioned variables.

Method: Retrospective study of consecutive patients attended in our center between 1998 and 2016 and treated with CBZ, OXC or ESL. Variability and evolution lipid metabolism profiles, sodium, blood cell count and liver function tests was studied and compared between the 3 groups. Patients whose treatment for dyslipidemia was modified during the study period or with medical conditions that could modify the mentioned variables were withdrawn from the analysis.

Results: 303 patients were analyzed. 53% were males; average age was 44; 167 patients were under treatment with CBZ, 55 under treatment with OXC and 81 under treatment with ESL. Average follow up of the entire sample was 48 months. Patients under treatment with CBZ suffered a
statistically significant greater impact over lipid metabolism profile when compared with patients under treatment with OXC or ESL. Patients under treatment with CBZ showed a statistically significant higher frequency of hyponatremia than patients under treatment with CBZ or ESL. No statistical differences were detected in patients related to liver function tests or blood cell count.

Conclusions: In our sample CBZ showed a greater impact than OXC or ESL over lipid metabolism profile, while OXC showed a higher frequency of hyponatremia. No other clinically relevant or statistically significant changes were detected.

p0586
OLIGOHYDROSIS AS ADVERSE EFFECT OF ZONISAMIDE

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Purpose: Zonisamide is classified as a sulfonamide and is characterized having multiple antiepileptic action-mechanisms including inhibiting carbonic anhydrase, which may lead to the oligohydrosis. The purpose of this study is including the followings: (1) to determine the incidence and (2) to reveal the risk factor of oligohydrosis-related symptoms in epileptic patients treated with zonisamide

Method: I prospectively studied 153 patients under 20 ages who was newly diagnosed with epilepsy or referred from other hospitals for controlling a seizure. The patients were treated with zonisamide as a monotherapy or adjuvant therapy. The data was collected by direct interview at least 3 months after taking zonisamide. Facial flushing, lethargy, itching sensation, irritability with hyperthermia, heat sensation and heat intolerance were considered as a oligohydrosis-related symptom.

Results: 24.8% of patients were treated by zonisamide as a monotherapy, and the other patients were treated by zonisamide as an adjuvant therapy. The oligohydrosis-related symptoms were observed in 11.1% of patients, and 2% of the patients have stopping taking zonisamide due to the symptoms. The oligohydrosis-related symptoms were observed more frequently in the patients between 15 and 20 years old than younger ages, and more frequently in the patients who had taken topiramate.

Conclusion: The frequency was significantly higher than the results from previous studies. Clinicians should monitor the patients who are taking zonisamide regarding the oligohydrosis-related symptoms. Especially, the patients between 15 and 20 years old ages and the patients who have a drug history of topiramate should be observed carefully.

p0590
EFFECT OF ADJUNCTIVE PERAMANEL ON MYOCLONIC AND ABSENCE SEIZURES: A POST HOC ANALYSIS

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Purpose: Perampanel is a selective, non-competitive AMPA receptor antagonist, approved for adjunctive treatment of focal seizures, with or without secondarily generalized seizures, and for primary generalized tonic-clonic (PGTCS) seizures in patients with epilepsy aged ≥12 years. Approval for PGTCS seizures was based on the placebo-controlled Phase III Study 332 in patients with PGTCS seizures and idiopathic generalized epilepsy (IGE). Since some antiepileptic drugs can aggravate seizures in IGE, this post hoc analysis assessed myoclonic and absence seizure outcomes for patients receiving adjunctive perampanel in the Extension Phase of Study 332.

Method: Study 332 methodology has been published (French et al. Neurology 2015;85:950–957). Patients completing the Double-blind study could receive perampanel during an Extension Phase: a 6-week blinded Conversion Period (dose optimized to maximum of 12 mg/day) and up to 136 weeks’ unblinded Maintenance. For this post hoc analysis, the following endpoints were assessed for absence and myoclonic seizures across the Extension Phase: median percent changes in seizure frequency per 28 days, and proportions of patients achieving reductions in seizure frequency of ≥50% (50% responder rate) or 100% (seizure-freedom rate).

Results: Of 138 patients entering the Extension Phase, 76 experienced myoclonic (n = 46) and/or absence (n = 52) seizures at Pre-perampanel Baseline. At Weeks 40–52 of perampanel treatment, data were available for 65 patients (myoclonic, n = 40, absence, n = 25). At this time window, median percent changes in seizure frequency were –100.0% for both seizure types, 50% responder rates were 82.5% for myoclonic and 76.7% for absence seizures, and seizure-freedom rates were 57.5% for myoclonic and 55.8% for absence seizures.

Conclusion: In this small, post hoc analysis, changes in seizure frequency did not indicate any overall worsening of myoclonic or absence seizures in patients with IGE who were receiving adjunctive perampanel.

Funding: Eisai Inc.
p0592
LONG-TERM EFFICACY AND SAFETY OF ADJUNCTIVE PERAMPELAN IN OPEN-LABEL EXTENSION (OLEX) STUDIES: A POST HOC ANALYSIS
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Purpose: Perampanel is approved for adjunctive treatment of partial seizures, with or without secondarily generalized (SG) seizures, and for primary generalized tonic-clonic (PGTC) seizures in patients with epilepsy aged ≥12 years. Adjuvantive perampanel was evaluated in Phase II-III randomized, double-blind, placebo-controlled studies in patients with partial seizures with or without SG seizures (Studies 206, 208, 304, 305, 306, 335), or PGTC seizures and idiopathic generalized epilepsy (Study 332). Here, we report post hoc analyses of efficacy and safety for patients with SG or PGTC seizures across the OLEX Studies 207 (complete studies of Studies 206 and 208; NCT00368472) and 307 (completers of Studies 304, 305, 306; NCT00735397), and the OLEX Phases of Studies 335 (NCT01618695) and 332 (NCT01393743).

Method: In the four OLEX studies, patients received perampanel (maximum 12 mg/day) during a blinded Conversion Period (6–16 weeks) and a Maintenance Phase (32–42 weeks) ≤1 to ≤8 years’ exposure).

Results: Mean cumulative exposure to perampanel was 102.3 weeks for patients with SG seizures (n = 720) and 83.9 weeks for patients with PGTC seizures (n = 138), median percent reductions in seizure frequency were 66.7% and 86.6%, respectively. Corresponding 50%, 75%, and 100% responder rates were 59.5%, 45.3%, and 18.4% for SG seizures, and 72.5%, 51.5%, and 16.7% for PGTC seizures. For each seizure type, efficacy was observed irrespective of prior treatment during the Double-blind Phase. Treatment-emergent adverse events affected 90.3% and 87.0% of patients with SG and PGTC seizures, respectively.

Conclusion: Long-term adjunctive perampanel demonstrated efficacy for SG or PGTC seizures. Safety outcomes were consistent with the known safety profile of perampanel.

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p0593
BRIVARACETAM: THE LEEDS EXPERIENCE
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Purpose: Brivaracetam (BVM) was approved in the EU in Jan 2016 as an adjunctive treatment of focal-onset seizures with or without secondary generalised seizures in patients with epilepsy aged 16 years and older. The aim of the study was to assess the efficacy and tolerability of BVM in clinical practice. BVM was also used off licence to treat those with idiopathic generalised epilepsy (IGE).

Method: Preliminary data from 52 patients are presented. Data was collected prospectively from patients experiencing focal and/or secondary generalised tonic clonic seizures and primary generalised seizures.

Results: An overall ≥50% reduction in seizure frequency was achieved in 28% of patients. In those with IGE 45% had a ≥50% reduction in seizure frequency and one patient was rendered seizure free. In those with focal onset epilepsy the overall ≥50% reduction in seizure frequency was 22%. 28% of those with secondary generalised tonic clonic seizures had a ≥50% reduction in seizure frequency. 23% of those with focal seizures had a ≥50% reduction in seizure frequency. The most common adverse events were irritability 17% and sedation 15%.

Conclusion: Patients were taking a median of 2 antiepileptic drugs when BVM was commenced and had previously tried a median of 9 antiepileptic drugs. This was therefore a very difficult to treat group of patients with refractory epilepsy. The overall percentage of patients with a ≥50% responder rate was slightly lower than clinical studies however this may be reflected in the cohort of patients. Reported adverse events varied from clinical trials with irritability being the most common. The evidence suggests that BVM may be a useful adjunctive therapy for those with refractory epilepsy. Interestingly those with IGE had a higher responder rate than those with focal onset epilepsy which requires further investigation.

p0596
ESLIRA: A PROSPECTIVE STUDY TO ASSESS THE BEHAVIOR IN PATIENTS WITH EPILEPSY TREATED WITH ESLICARBAZEPINE ACETATE
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Purpose: This study aims to evaluate changes in the anger status in patients with focal epilepsy who start treatment with Eslicarbazepine acetate (ESL).

Method: Prospective study of patients with focal epilepsy from 6 different hospitals, who met the following criteria: ≥ 18 years old, certain diagnostic of focal epilepsy and ≤2 antiepileptic drugs at baseline visit. All patients completed the State-Trait Anger with the Expression Inventory 2TM (Staxi-2ª), hospital Anxiety and Depression Scale (HADS) and Quality of Life in epilepsy inventory (QOLIE-10) at baseline before starting ESL and in the final follow-up 3 months later.

Results: From 59 patients screened, 42 completed the study. Demographics: Mean age 30.6 years old (range 26–78); Females 45.2%. Half of them were temporal lobe epilepsy and 45.2% cryptogenic. Mean monthly seizure frequency was 3.1, which decreased to 0.7 in the follow-up (p < 0.001). Main reason to start ESL was the presence of baseline adverse events (47.6%) or lack of efficacy (40.5%). In the follow-up 59.5% were on ESL monotherapy and 40.5% bitherapy; levetiracetam and ESL. A significant improvement in anger status was seen. The anger expression index improved significantly in the whole group (p = 0.036), the anger trait was more likely to improve in the bitherapy patients (p = 0.029) and the state of anger showed better performances in patients <50 years old (p = 0.005). A global improvement in anxiety (p = 0.011) and QOLIE-10 (p = 0.023) was seen.

Conclusion: The treatment with ESL, alongside with a good seizure control and tolerability may improve the anger status in patients with epilepsy.

p0597
EFFECTIVENESS AND TOLERABILITY OF PERAMPELAN IN PATIENTS WITH INTELLECTUAL DISABILITY AND REFRACTORY EPILEPSY
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Purpose: Epilepsy is more prevalent in adults and children with intellectual disabilities (ID). Many require life-long antiepileptic drugs for adequate seizure control. Registration and ‘clinical’ studies confirmed efficacy and safety of Perampanel (PER) in refractory epilepsy (RE). Experience on the use of PER among patients with ID is still limited.

The purpose of this study is to extend our knowledge with respect to the relevance of PER for patients with both ID and RE, and furthermore to specify the behavioral adverse reactions (ADRs) of PER in this specific population.

Method: Retrospective, open label, single-center study. Inclusion criteria: 1) follow-up of at least 3 months; 2) presence of ID. Efficacy endpoints included responder rate and percentage of patients with some reduction in seizure frequency. To assess tolerability, we evaluated the incidence and severity of ADRs and the percentage of patients withdrawn due to ADRs.

Results: 46 patients (23 female) were included (age range 8–55 years). Follow-up range: 4–21 months, median: 13 months. Level of ID varied from borderline to profound, and severe ID (moderate-severe-profound) was most common (65%). The mean daily dosage of PER was 5.6 mg (range 2–12 mg). Seizure reduction was achieved in 67% of patients. Responders were 58% and seizure free 7%. 22 patients (48%) experienced ADRs. Behavioral ADRs were present in 10 patients (22%, severe in 4%). Most common were aggression, agitation, and mood symptoms. In 13 patients PER was discontinued (lack of efficacy in 69% and intolerable ADRs in 31%).

Conclusion: The use of PER might lead to an effective seizure reduction without ADRs in 52% of patients with both RE and ID. Pre-existing behavioral problems or polypharmacy do not predict the occurrence of additional behavioral ADRs, implying that these patients need not be excluded from the introduction of PER when clinically indicated.

p0598
PSYCHOGENIC NONEPILEPTIC SEIZURES IN CANADA: A SURVEY DESCRIBING CURRENT PRACTICES
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Purpose: Psychogenic Non-epileptic Seizures (PNES) is one of the commonest differential diagnoses of epilepsy, and have limited access to management. An international task force (ILAE PNES project) has been recently created to address this issue. Our objective is to describe current management in Canada, identify styles of practice and service gaps.

Method: In 2016 a 35-question survey was sent, via email, to the 131 members of the Canadian League Against Epilepsy. The questions were separated into 5 sections:

1) the role of the respondent and their exposure to PNES,
2) diagnostic methods,
3) management of PNES,
4) etiological factors, and
5) problems accessing health care.

This survey was validated in the UK and has been applied in different international populations.

Results: Sixty-two questionnaires were analyzed (response rate: 47%). Responses were received from seven provinces of Canada. Most respondents were epileptologists (76%). 77% respondents diagnose between 1 to 20 new cases of PNES annually. The majority personally diagnoses and communicates the diagnosis of PNES to the patient, but only 55% provide follow-up within their practice and approximately 50% recommend or arrange treatment. A large minority (35%) are either unfamiliar with the diagnosis or treatment of PNES, or are inexperienced in arranging and offering treatment. Most (79%) provide follow-up to those patients with concomitant epilepsy, but otherwise follow-up rates are low. Although 84% of respondents feel that individualized psychological therapy is the most effective treatment, 40% of patients are not referred to psychotherapy.

Conclusion: Though Canadian Health epileptologists’ understanding of PNES mostly reflected current international expert opinion, once the diagnosis is made patients are discharged from the neurological service without appropriate psychological referral in place. This may lead to “bounce-back” and repeated ER visits.

p0600
THE EPIDEMIOLOGY OF FEBRILE SEIZURES IN SOUTH KOREA BASED ON THE NATIONAL HEALTH INSURANCE SERVICE-NATIONAL SAMPLE COHORT, 2002–2013
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Purpose: Febrile seizures are the most common type of seizure in children. We performed a large population-based epidemiologic study of febrile seizures in South Korea.

Method: Data of 54,234 children, born in 2002–2007, was retrieved from the Korean National Health Insurance Service - National Sample Cohort covering 2002–2013 (representing 2% of the total population) until their age five. The primary outcome was the prevalence and incidence of febrile seizures in South Korea. The secondary outcomes were the risk factors of febrile seizures and the probability of being diagnosed with epilepsy after the events. A mixed effects logistic regression model was used to analyze the risk of having febrile seizures.

Results: The prevalence of febrile seizures in children under age five in South Korea was 11.3%, and the incidence during the study period was 3.8%. There was no difference between genders and the highest incidence was in the second year of life (p < 0.001). The risk of febrile seizure was higher for those who had a history of preterm, cerebral birth injury or cerebral palsy (p < 0.001). Children with febrile seizure has an increasing risk of being diagnosed with epilepsy within a year up to 4.7% in cumulative analysis compared to 0.3% in children without febrile seizure (p < 0.001).

Conclusion: As the frequency of febrile seizure increased, the probability of being diagnosed with epilepsy within a year after the events increased in South Korea.

p0603
UTILISATION OF VALPROATE IN WOMEN WITH EPILEPSY AND OTHER DISORDERS IN NORWAY, 2004–2015
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Purpose: The use of valproate in women of childbearing age is under debate with regard to risk of teratogenicity, and also long-term effects on the offspring. The purpose of this study was to document changes in use of valproate in Norway the last decade.

Method: Anonymised data from the Norwegian Prescription Database (2004–2015) were used, including data of antiepileptic drugs (AEDs) from the whole population with detailed information of indication-related reimbursement codes. The study was approved by the National Institute of Public Health.

Results: In 2004, 49% of the total valproate users were women. In 2015 this number was reduced to 44%. There was a total increase in the use of valproate between 2004 and 2015 from 12662 to 18226 users (+44%), and an increase in use of 2.6–3.2 DDDs/1000day (+23%), which was
mainly due to an increase in male users (68% of total) (6425 to 10222 men / 6237 to 8004 women). For women of child-bearing age (15–45 years) there was a total decrease of 12.5% in the use of valproate in Norway from 2010–15. In 2010 there were 4488 women who used valproate for epilepsy, while in 2015 there were 4216 (–6%). The drug utilisation was more reduced, from 0.79 down to 0.72 DDDs/1000 women/day (–9%), which indicate a slight decrease in the daily prescribed dose. Thus, recommendations of careful/restrictive use of valproate in women in recent years have possibly been followed.

**Conclusion:** The present results demonstrate that the use of valproate in women in Norway is decreasing for the indication epilepsy, but not to the same degree in other indications. Recommendations of careful/restrictive use of valproate in women, and especially of childbearing age, in recent years are possibly followed. Documentation of changes in utilisation of AEDs contributes to improved pharmacovigilance and safer treatment.

**p0608**

**DELINEATION OF THE GENETIC CAUSES OF EPILEPTIC ENCEPHALOPATHY IN SOUTH AFRICAN PAEDIATRIC PATIENTS**


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**Purpose:** Sub-Saharan Africa bears the highest burden of epilepsy in the world as a consequence of high incidence of CNS infections, perinatal insults and traumatic brain injury. Genetic epilepsy is underdiagnosed due to lack of awareness and unavailability of genetic testing for epilepsy. In this study we aim to describe the genetic architecture of severe infantile seizure disorders in South African patients and establish a framework for genetic testing in South Africa and Africa more broadly.

**Method:** We recruited 92 South African children diagnosed with epileptic encephalopathy (EE), on the basis of clinical semiology and neuro-physiological studies: 46 Indigenous Black, 35 Mixed Ancestry and 11 Caucasian South African children. Of these, 21 were clinically suspected to have Dravet Syndrome (DS). Targeted resequencing of 71 known EE genes and chromosomal microarrays were deemed appropriate, was performed. Patient recruitment is ongoing and we aim to recruit and test 200 patients.

**Results:** Pathogenic *de novo* mutations were identified in 35 patients. *SCN1A* mutations were found in 9/21 (43%) of the Dravet group, which was markedly less than the published frequency of *SCN1A* mutations in DS. Clinical reassessment with the screening test by Hattori et al., (2008) resulted in a changed working diagnosis of 5 *SCN1A*-negative patients in the Dravet group. *SCN1A* variants were also found in 2 patients of the remaining cohort, who are undergoing clinical reassessment emphasising the value of a genetic diagnosis. In the larger cohort, likely pathogenic changes were detected in 18 genes. A 16p13.11 deletion was detected in 1 patient, additional microarray analysis is ongoing.

**Conclusion:** These results carry implication for patient management and present valuable insights into disease presentation, motivating translation into diagnostic practice even in the resource-limited African setting. This is the first genetic research study of epilepsy in South African patients.

**p0610**

**TERTIARY EPILEPSY CENTRE IN RESOURCE RESTRICTED COUNTRY – LUXURY OR NECESSITY**

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**Purpose:** Up to 40 000 people in Georgia have active epilepsy, 2/3 of them being inappropriately treated or having wrong diagnosis, treatment gap – 71% (G.Lomidze et al 2012). Aim of our study was to evaluate role of a tertiary epilepsy centre for improvement of diagnostic and treatment possibilities and reducing treatment gap in country with restricted resources and deficient health care system like Georgia.

**Method:** The study was carried out in SEIN-SKUH Epilepsy and Sleep Centre Tbilisi. One hundred thirty two patients, who attended our Centre in the period of 2014–2016 for reevaluation of diagnosis and treatment possibilities were enrolled into the study. Inclusion criteria: complete clinical workup, video EEG monitoring 12–48 hr, 1.5–3TL MRI with epilepsy protocol, as well as sleep workup (diaries, actigraphy, PSG) upon requirement.

**Results:** Final diagnosis was made in 98 cases out of 132 (75%). In 28 patients (21%) non-epileptic events were established, including dissociative seizures, syncope and migraine. Seven patients with dissociative seizures previously have undergone treatment in the intensive care unit with diagnosis “convulsive status epilepticus”. Seven patients appeared to have combined clinical course with epileptic seizures together with dissociative ones, this situation severely affecting their treatment outcome. In 21 patients severe sleep disorders were established along with epilepsy (insomnia, OSAS, PLM). In 78 cases epileptic syndrome was established and seizure control, or significant improvement was reached due to elaboration of tailored therapy.

**Conclusion:** Our study showed that tertiary epilepsy centre with “state of the art” special services significantly contributes to reduction of diagnostic and treatment failures, improves quality of life of the patients and decreases social and financial burden of the disease.
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Abstracts

p0614
EPILEPSY IN PRIMARY CARE: A PILOT EXPERIENCE OF ONLINE EDUCATION IN LATIN AMERICA
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Purpose: The aim was to decrease the diagnostic and therapeutic gap in epilepsy, through a virtual course, language and costs-friendly, devoted to primary care physicians in Latin America.

Method: The project was designed by the ILAE Education Commission and submitted to evaluation by ILAE. It included 8 topic-specific modules of 1-week duration each, including epidemiology, clinics, diagnostic procedures, drug treatment, social and legal aspects. A 16-members Latin American teaching team developed the contents. Virtual platform and formal accreditation were obtained through international University collaboration. Repositories and discussion forums were developed. Approval required passing the final exam. Initially developed as a Spanish course, during 2016 all the platform and didactic material can be accessed either in Spanish or Portuguese, and Brazilian tutors were included in every module.

Results: Overall, 95 professionals from 15 countries registered and started the course; 77 completed all modules and approved the final examination. Approximately 20% (11–27%) felt confident on epilepsy patients’ management before the course, increasing to a mean of 71% (64–84%) after the course. Financial support from ILAE for the 3 courses (2015–2016) was USD 13.000, with a total revenue from registrations of USD 5700 (Net ILAE investment: USD 7300).

Conclusion: A cost effective and qualified online course on epilepsy is a simple tool to educate primary care holders worldwide.

p0615
NATIONAL EPILEPSY PROGRAM OF THE MINISTRY OF HEALTH OF CHILE
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Purpose: In the last two years, in Chile a National Epilepsy Care Program was designed, including processes, structure and results measurement, with improvements at all levels of complexity, following the WHO model in relation to the importance of the Health Network. The objective is demonstrate that it is possible to work in Public Health with an Epilepsy Program design for the whole country and in the three levels of complexity of care.

Method: It was selected one Health Service as a pilot observatory, of the 29 existing in Chile. The strategies of the Program are applied: Design of the Health Assistance Network with Regional Centers and Reference Centers in epilepsy, design of “Model of chronic care in primary care”, creation of special polyclinics at the secondary and tertiary levels in epilepsy; On-line and presence-based courses training is provided to professionals, across the country and at the various levels of complexity.

Results: In Primary Care the attention was started based on the “Model of care of chronic patients”. In primary care, the number of people diagnosed and treated as epilepsy in the Pilot Center is doubled. It was performed non invasive surgery in a new center, in addition to one existent. Invasive surgery is performed in a pre-existing single center.

Conclusion: It is possible to give better care to epilepsy patients based on the implementation of a National Epilepsy Program, with an emphasis on network care and the training of professionals in a Latin American country such as Chile.

p0617
THE USE AND ABUSE OF EEG INTERPRETATION IN A DEVELOPING MEDICAL SOCIETY
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Purpose: To study the effects of unnecessary EEG or miss interpreted EEG on patient management.

Method: This was a part of an audit looking at why physicians ask for an EEG. It took place in Mansoura University Children Hospital, Egypt, and run between August 2016 to Feb 2017. We included here only the patients referred to repeat an EEG, whether they were epileptic or non-epileptic, on treatment or not, from 1 month to 17 years. We excluded first time EEG patients.

We collected: demographic data (age, sex, residence), reason for EEG, number of previous EEG done before, who asked for it (private doctor, general hospital, or referred from our hospital), any diagnosis given to the patient, current medication, imaging studies, and basic information about socioeconomic level of parents. Two neurologist with experience in interpretation of EEG, reviewed the previous EEG (whenever accepted or available)

Results: 509 patients were referred for EEG, 249 patients were included in this study. Our preliminary results shows that EEG was performed for unrecognized indications (behavior problems, cochlear implants, delayed speech), treatment with AEDs was started in a significant number of patients without having any clinical seizures and only based on EEG results. There were a number of epileptic patients who were maintained on AEDs for years because of presumed abnormal EEG, and patients who received unsuitable AEDs for their condition.

Conclusion: There is no clear understanding of the indications and interpretation of the EEG and its results in the practice of physicians, and this adversely affect the management of epileptic and unfortunately non epileptic patients as well.

p0618
COMPREHENSIVE EPILEPSY CARE: EMPOWERING HEALTH CARE PROFESSIONALS AND CARE GIVERS IN RESOURCE CONSTRAINED SETTINGS
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Purpose: Around 10 million people are effected with epilepsy in India. In resource constrained settings like India, there is skewed specialist-patient ratio with further accentuation in rural compared to urban settings. This is a description of initiatives by a tertiary care centre in north India to empower health care providers and caregivers.

Method: To facilitate early diagnosis and management of epilepsy, a diagnostic instrument has been developed, validated, and converted into a mobile application. Studies have been conducted to evaluate telephonic consultation against face to face evaluation in children with Neurocysticercosis, West Syndrome and Lennox Gestaut syndrome. Currently, a study is underway in which telephonic consultation by a specialty Nurse is being compared to the same by a Pediatric Neurology resident doctor against face to face evaluation. The longterm vision is to minimize unnecessary hospital visits and decompress the healthcare system. A web-based platform has been launched on epilepsy, along with an interactive platform for parents and physicians. Bilingual patient information booklets on epilepsy, seizure card and seizure diary have been developed to educate and assist care givers.

Results: The mobile application based on the diagnostic tool was launched in December 2015, and has been downloaded on 854 mobile phones. It is being used by nearly 800 physicians across the country. The webpage that was launched in December 2014 gets an average of 20 hits per week. On an average, 200 to 250 children and their families per week
are getting benefitted by the patient information booklets, seizure card and seizure diaries.

Conclusion: Conventional as well as technology aided, affordable and innovative modes of health education can help empower care givers and health care providers in a significant way, particularly in resource constrained settings.

p0619 IMPROVEMENT OF EXECUTIVE FUNCTION AFTER EPILEPSY SURGERY
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Purpose: Executive function means a series of cognitive activities to effectively achieve a purpose, and the impairment is caused by frontal lobe dysfunction. Epilepsy is also known to be associated with impaired executive function. Changes of executive functions after epilepsy surgery were examined using the Wisconsin Card Sorting Test (WCST).

Method: Thirty-eight patients (16 male, 23 female; average age 30 years old) who underwent neuropsychological evaluation including WCST before and 2 years after surgery among patients who underwent surgical treatment since 2007. And the categories achieved (CA), total errors (TE), and perseverative error of Milner/Nelson sustainability (PEM/PEN) was evaluated.

Results: In the seizure type, there were 29 (18 right, 11 left) and 5 of temporal lobe epilepsy (TLE) and temporal lobe neocortical epilepsy (NCE), respectively who underwent resection. There were 4 suspected focal seizures which underwent vagal nerve stimulation (VNS). CA and TE at 2 years after operation were improved at 58% (22/38) and 61% (23/38) respectively, and decreased at 18% (9/34) and 32% (12/38) respectively. PEM/PEN was improved or maintained, except for cases where CA and TE both decreased. Improvement rate by seizure type is 73% (8/11) in left TLE, 50% (9/18) in right TLE, 60% (3/5) in NCE, 25% (1/4). By outcome, improvements in executive functions were obtained at 64% (16/26) in Engel outcome scale class I, 67% (2/3) in class II, and 33% (7/21) in class III at 75% (3/4), and 20% (1/5) in class III/IV of VNS. Correlation with improvement of WAIS-R / III and WMS-R was not strong.

Conclusion: In the cases of resection surgery, 64% of patients obtained improvement of executive function after surgery. On the other hand, the improvement rate was only 20% in the VNS cases. Seizure improvement after resection surgery would contribute the improvement of executive function.

p0620 HIGH FREQUENCY OSCILLATIONS IN TUMOR RELATED EPILEPSY
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Purpose: Epilepsy can be a first sign of a low-grade brain tumor. Gross total resection is not always advised for tumor treatment, but surgery might treat the epilepsy. The epileptic focus can be located around the lesion, for which electrocorticography (ECoG) might help. High frequency oscillations (HFOs) in ECoG are a better biomarker for epileptic tissue than spikes. We investigated the relation between HFOs and low grade brain tumors and their potential value for epilepsy surgery.

Method: We retrospectively analyzed pre- and postresection intra-operative ECoG recorded at 2048 Hz in patients with refractory epilepsy and a low grade brain tumor. We automatically detected ripples (R, 80–250 Hz) and fast ripples (FR, 250–500 Hz), and checked them visually with two reviewers. Presurgical and postsurgical MRIs were coregistered, the tumor and resected volume were marked and locations of the ECoG electrodes were matched. Electrodes on the tumor, in resected tissue that was not tumor, and outside the resection area were identified. Engel I was considered seizure freedom.

Results: We included 43 patients of whom 21 had mesiotemporal tumors, and 22 neocortical tumors. Twenty-two patients had gangliogliomas. Four patients were not seizure free (>1 year after surgery). Mesiotemporal tumors showed more ripples and fast ripples than neocortical tumors (R: p < 0.001. FR: p = 0.05). Tumor plus resected tissue showed more ripples and fast ripples than tissue outside the resection (R: 18.1/min vs. 6.2/min, p = 0.05. FR: 3.8/min vs. 0.1/min, p < 0.001). Three patients showed fast ripples after resection, who were all seizure free and no tumor residual was reported. The rate of ripples and fast ripples after surgery was not higher for patients with residual tumor tissue.

Conclusion: HFOs were a good indicator for the tumor and the surrounding epileptic tissue before surgery. HFOs after resection did not discriminate patients with recurrent seizures or patients with tumor residual.

p0621 GROSS TOTAL RESECTION AS A PREDICTOR OF SEIZURE-FREE OUTCOME IN CHILDREN WITH CORTICAL MALFORMATIONS
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Purpose: To evaluate seizure outcome in children with cortical malformations included focal cortical dysplasia, polymicrogyria, hemimegalencephaly due to volume of resection (gross total or subtotal).

Method: We performed a retrospective analysis of MRI data of children ≤ 18 years who underwent the epilepsy surgery from October 19, 2010 through October 26, 2016 and had one-sided cortical malformations. Surgical outcome was classified as seizure freedom (Engel class I) or seizure recurrence (Engel class II-IV).

Results: Twenty-five patients with cortical malformations included focal cortical dysplasia (18), polymicrogyria (6), hemimegalencephaly (1) were performed 33 operations (8 reoperations). Mean follow-up was 20 months (ranging from 3 to 64 months). Twenty patients (80%) were seizure-free at last follow-up. Five patients (20%) had seizure recurrence (Engel class II-IV). Sixteen patients with seizure-free outcome had gross total resection and six of them patients had undergone reoperations.

Conclusions: Our study shows that gross total resection determine seizure-free outcome in children with cortical malformations.

p0623 EPILEPSY SURGERY OF THE TEMPORAL LOBE IN AN EPILEPSY CENTER IN VENEZUELA. SIX YEARS OF EXPERIENCE
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Purpose: The surgical treatment of epilepsy is currently an effective and safe therapeutic modality. The results depend on an adequate study algorithm, a multidisciplinary approach of the patient, an appropriate selection of the surgical technique and the experience of the neurosurgeon. We describe our experience of six years in surgery of temporal lobe epilepsy in an Epilepsy Surgery Center in a developing country.

Method: This is a retrospective study. We evaluated medical records of patients with drug-resistant temporal lobe epilepsy who underwent epilepsy surgery in our center from May 2009 to Dec 2015.
**Results:** In our study 73 temporal lobectomies were performed. Patients older than 20 years accounted for 82%. The most important personal background in our patients was; history of febrile seizures in 11%, and encephalocranial trauma with loss of consciousness in 9% of cases. Regarding the delay time between the diagnosis of epilepsy and the performance of surgery, similar percentages (30%) shared the patients operated in a range of 1 to 5 years, and those in a time greater than 20 years. All patients were followed for at least one year. 84.5% of patients with temporal lobe resection are in Engel class I, 12.3% in class II. One patient was re-operated due to poor control of their seizures. Four patients presented postoperative complications (psychiatric illness). MRI 60% had hippocampal sclerosis and 13.7% were normal, 12.3% were tumors, 6.9% double lesion, 4.1% hig focial signal in the temporal lobe. Pathology showed: 54.8% with hippocampal sclerosis, 13.7% with dual pathology, 2.7% with dysplasia/heterotopias.

**Conclusion:** In this study epilepsy surgery in selected patients, has minimal morbidity and offers high probability of significant reduction of the seizures. Our results and our percentage of seizure free patients after performing epilepsy surgery are comparable to those reported by other centers in the literature.

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**p0625**

**STEREO ELECTROENCEPHALOGRAPHY-GUIDED RADIOFREQUENCY THERMOCOAGULATION IN DRUG-RESISTANT FOCAL EPILEPSY: A NEW PEDIATRIC TECHNIQUE TO GUIDE THE SURGERY**

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**Purpose:** In case of focal drug-resistant epilepsy, the presurgical evaluation may include intracranial electroencephalogram (EEG), to delineate cortical resection. Depth electrodes allow to realize radiofrequency thermocoagulations, inside the epileptic focus, to reduce the seizure frequency. The improvement is often transient, 2 to 4 months, and is a diagnosis test confirming the limits of the cortical resection defined during stereoEEG. This technique is well-known in adults, for the last 10 years, but unused in pediatrics.

**Method:** We report clinical data and outcome of 26 children eligible for thermocoagulations during phase II invasive investigation by stereoEEG since 2014. Thermocoagulations were performed with bipolar 100 mA current during 10–50 seconds. The diameter of each lesion measure 5–7 mm.

**Results:** 3 to 57 lesions were provoked, with a mean of 18 lesions. We reported 65% of responders at 1 month, including 42% of seizure-free domin. The mean efficacy duration was 3 months. For one patient, we decided to perform thermocoagulations inside the postcentral gyrus, he experienced hemiainesthesia during few days. No side-effect was reported in other patients. When surgery followed an SEEG-guided RF-TC, the positive predictive value of being a responder and to be Engel’s class I after surgery was 71%.

**Conclusion:** Stereo electroencephalography-guided radiofrequency thermocoagulation is a safe technique in children, efficient in many cases. The goal is to confirm the ictal onset zone and the limits of cortical resection as defined after stereoEEG. They could also be used as palliative technique when ictal onset zone is within functional areas, which cannot be operated on without sequellae.
p0632 PROGRESSION OF MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS
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Purpose: To evaluate correlations between epilepsy duration and hippocampal histopathology, electrophysiological findings and volumes of temporal lobe structures in MRI in patients with mesial temporal lobe epilepsy and hippocampal sclerosis (MTLE/HS).

Method: Seventy-seven patients with refractory MTLE/HS submitted to surgery were included. Histopathological analysis:

1) quantitative: hippocampal subfields and total estimated hippocampal cell density (HCD), thickness of the dentate gyrus - normal, thinning or dispersion;
2) qualitative analyses: type of HS and granule cells pathology in the dentate gyrus (normal, neuronal cell loss, dispersion and bilamination).

Ictal and interictal EEG were analysed:

1) ictal EEG: number of localized, lateralized and non-lateralized seizures, switch of lateralization, seizures evolving to tonic-clonic and seizure onset contralateral to HS;
2) Interictal EEG: interictal epileptiform discharges (IEDs) were considered bilateral when ≥ 20% of independent IEDs were contralateral to HS. Fifty-eight patients also had FreeSurfer volumetric analyses of bilateral temporal structures (hippocampus, amygdala, parahippocampal gyrus, temporal pole, entorhinal cortex). Histopathological and imaging findings were compared to normal age-paired controls and the data were adjusted to the age at epilepsy onset.

Results: Forty-two (54.5%) patients presented right HS. A longer epilepsy duration was correlated to a smaller estimated HCD (r = -0.253, p = 0.027). Patients with ≥ 20 years of epilepsy presented a lower probability of having a normal granule cells distribution (p = 0.035) and epilepsy duration of patients with a normal thickness of granule cell layer was shorter compared to the ones with dispersion (p = 0.025) and thinning (p = 0.032). FreeSurfer processing showed that a longer epilepsy duration was correlated to a lower isipsilateral hippocampal volume (r = -0.321, p = 0.015).

Conclusion: MTLE/HS is a progressive disease in histopathological and imaging aspects.

p0633 SUCCESSFUL SEEG-INFORMED LASER ABLATIVE THERAPY OF CINGULATE EPILEPSY WITH DEPDC5 MUTATION
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Purpose: In the past 10 years epilepsy surgery has increasingly been recognized as a viable treatment for patients with medically refractory seizures. Here we present a 17 years old right-handed Caucasian female with MR-negative intractable frontal lobe epilepsy since the age of 8 who had stereotactic electrode encephalogram (SEEG) in order to identify the epileptogenic focus.

Method: Our patient's seizures were characterized by a fearful aura with arousal from sleep, sitting up in panic with nonspecific hypermotor movements of the lower extremities followed by urinary urgency or incontinence. Seizures were 3–6 per night with each lasting 10–45 seconds. She had a positive family history of epilepsy. Scalp video electroencephalogram had no localizing findings at seizure onset with bifrontal slowing and recurrent epileptiform discharges. 1.5 & 3 tesla MRI brain and interictal PET were normal. Functional MRI for language showed bilateral activation. Magnetoencephalography (MEG) demonstrated 2 spike clusters, 90% originating in the right superior frontal gyrus and 10% originating from the left frontal operculum. Neuropsychological testing did not reveal any cognitive deficits. Prior to surgery, an epilepsy gene panel was done given the positive family history for epilepsy which identified a mutation in DEPDC5, a gene associated with autosomal dominant familial focal epilepsy with variable foci and cortical dysplasia.

Results: SEEG implantation and recording, guided by clinical semiology and MEG, identified the right anterior-mid cingulate gyrus as the epileptogenic zone. Patient was counseled on lower chance of seizure freedom given location and genetic findings. Stereotactic laser ablation of the right anterior-mid cingulate gyrus was performed. She has been seizure free for 8 months with no post op deficits.

Conclusion: DEPDC5 mutation should not be considered a contraindication to proceeding with SEEG implantation as it can identify the epileptogenic focus. Laser cingulotomy is safe and should be considered as an option.
p0637
HIGH FREQUENCY OSCILLATIONS IN THE PRE-OPERATIVE ECoG RECORDED AT MACRO- AND MICRO-SCALE
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Purpose: High frequency oscillations (HFOs) in the pre-operative ECoG are a promising biomarker of the epileptogenic zone (EZ). While HFOs are recorded in epilepsy patients by implanted depth electrodes with macro-contacts, little is known about the concomitant neural activity at the micro-scale.

Method: We recorded ECoG during slow wave sleep from three mesial temporal lobe epilepsy patients implanted with depth electrodes. Each macro electrode (8 contacts of 1.3 mm diameter and 1.6 mm length) had nine microwires protruding from its tip, including one low-impedance wire with stripped insulation (1 kΩ). This wire was used as a reference also for macro contacts in order to record from the same brain volume at macro and micro scale. Macro HFO (mHFO) and micro HFO (µHFO) for ripples (80–250 Hz) and fast ripples (FRs, 250–500 Hz) frequency ranges were detected automatically [1]. For each electrode location, we defined the co-occurrence Cm-µ as the percentage µHFO occurring during a mHFO, and Cµ-m as the percentage mHFO occurring during a µHFO.

Results: Across sampled sites, µFR rates were higher than mFR rates (p < 1e-4). We observed a similar spatial distribution for µFR and mFRs rates (Spearman, p < 0.05). The Cµ-m was higher than Cm-µ for FR (p < 1e-4), while Cµ-m was lower than Cm-µ for ripples (p < 0.005). For the two patients where the combined setup covered the EZ, mFR and µFR were higher in the EZ than outside.

Conclusion: Higher µFR rates and the higher co-occurrence with a FR at macroscale is consistent with the more localized nature of FR generators. While mFR confirmed to be a reliable biomarker of the EZ, µFR offer a similar picture on a smaller spatial scale.

p0643
POST-SURGICAL PROGNOSIS OF HEMISPHERECTOMY AND HEMISPHEROTOMY PROCEDURES ON CHILDREN WITH REFRACTORY EPILEPSY
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Purpose: To evaluate the results of epileptic surgery on children operated with Functional Hemispherectomy (FH) and Hemispherotomy (H) techniques at Instituto de Neurocirugía Asenjo (INCA), Chilean public hospital which has operated children with refractory epilepsy since 1990.

Method: A database of 400 children undergoing epileptic surgery at INCA was reviewed. 21 were operated with FH and 24 with H. 5 children were removed for less than 1-year follow-up. We then analyzed the evolution of 40 cases with controlled seizures using the Engel’s Scale, the variation in the Antiepileptic Drugs (AEDs) intake, and the complications presented after surgery.

Results: From 40 children reviewed, an average age of 21 month at the onset of seizure, (11 cases experienced onset at neonatal period). All cases presented Epilepsy secondary to hemispheric structural anomalies. The mean follow-up time was 55 month. 84% of patients (32/40) evolved with Engel Ia at one-year follow-up. 28 cases (70%) evolved with Engel Ia in the last control. Only 6 cases were in Engel III or IV, there were no differences achieved at follow-up between the two surgical techniques. 28/40 children were able to reduce the number of AEDs post-surgery, 19 (67.8%) of which experienced H. In 5 cases AEDs were removed time after surgery. In post-surgery complications, infections were equally found using both techniques. Other complications were only seen in children with FH: 3 hydrocephalus, 3 subdural collections and 1 transitory endocrinological disorder.

Conclusion: Both surgical techniques were equally effective in reducing epileptic seizures. More cases with H reduced the number of AEDs. Infectious events were seen equally in both groups. Hydrocephalus, subdural collections and transient endocrinological alteration were observed only in cases with FH, thus it is a technique that presented a higher frequency of complications.
p0645
DETERMINANTS OF INTELLECTUAL OUTCOME AFTER FOCAL EPILEPSY SURGERY IN CHILDREN
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Purpose: Children often show disparate cognitive trajectories following epilepsy surgery. The clinical and structural brain factors impacting on IQ change post surgically are not yet known.

Method: 55 children who underwent presurgical evaluation were reviewed; 41 had undergone focal resections (frontal 10, parietal 7, temporal 18 and multilobar 6) and 14 had not proceeded to surgery. All underwent IQ and structural MRI assessments as a part of routine pre-surgical investigations (baseline), which were repeated at follow-up. Average age at surgery was 13.8 years, and mean duration from baseline to follow-up was 7.5 years (range 3–16 years). Resection volumes were measured by manual tracing and grey and white matter volumes were extracted from segmentation analyses.

Results: At follow-up, 71% of the surgical group was seizure-free compared to 14% in the non-surgical group; 47.5% and 93% remained on antiepileptic drugs (AEDs), respectively. An overall increase in IQ was seen in surgery patients at follow-up in comparison with non-surgical controls (group x time effect: F_{1,10} = 7.1, p < 0.01). IQ improvement was associated with cessation of AED use (T = 2.7, p = 0.01) but not with seizure freedom (p = 0.2). There was neither a significant impact of the resection location (e.g. frontal, temporal, parietal) nor volume of resection (p > 0.15). However, improved IQ was seen after longer follow-up (r = 0.4, p = 0.02) and was associated with more positive ipsi- and contra-lesional hemispheric grey matter volume changes (ipsi: r = 0.63, p < 0.001; contra: r = 0.55, p = 0.002).

Conclusion: We find positive cognitive outcomes for children who had focal surgery for epilepsy, regardless of the extent or location of the resection. Longer follow-up and cessation of anti-epileptic medication were associated with positive IQ change. Improvements in intellectual functioning were correlated with brain volume change in regions proximal and remote to the resection.

p0647
ENDOSCOPIC DISCONNECTION OF HYPOTHALAMIC HAMARTOMA IN CHILDREN AND ADULTS WITH DRUG RESISTANT EPILEPSY: TECHNIQUE AND RESULTS REGARDING A POPULATION OF 126 PATIENTS
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Purpose: Hypothalamic hamartomas (HH) may induce drug resistant epilepsy (DRE) requiring surgical treatment. Disconnective procedures have been shown to be safe and as effective as removal of the lesion. We report on a large surgical series of 126 patients from our institution, with emphasis on the surgical technique and seizures outcomes.

Method: 126 patients with HH and DRE operated on between 1998 and 2015 were retrospectively reviewed. Hamartoma disconnection was performed using either monopolar coagulation, thulium laser or ultrasonic dissection through a Robot-guided transventricular endoscopic route. Few patients were operated through an open pterional approach. Results in terms of safety and outcome of epilepsy were analysed.

Results: Mean age at surgery in all patients was 14.6 years. Mean age at seizure onset was 31 months; 84% of the patients experienced gelastic or dacrystic seizures as seizure type. Mental retardation was present in 41%. According to the Delalande’s classification, 3.2% of the patients had a hamartoma of type 1, 59.5% of type 2, 27% of type 3 and 10.3% of type 4. Endoscopic transventricular disconnection was performed in 96% of the patients: in a single procedure in 60% and in more than one procedure (2 to 5) in 40%. With a mean follow-up of 3.6 years, 72% of all the patients and 81% of the patients with type 2 hamartoma had an excellent seizure outcome (Engel 1 and 2). 28 patients presented post-operative complications which consisted in recent memory deficit (6), hemiparesis (4), hormonal dysfunction (12), third nerve palsy (5), meningitis (2), and hydrocephalus (1).

Conclusion: Transventricular endoscopic HH disconnection is well tolerated, with an acceptable morbidity, and can easily be repeated in case of large lesions or seizure persistence. Overall seizure outcome is excellent, particularly for type 2 hamartomas.

p0656
CAN GENE PANEL TESTING IN EPILEPSY SAVE MONEY?
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Purpose: next generation genetic testing is being introduced to epilepsy practice in many industrialized countries, but few evaluations of its implementation have been reported, especially in the area of cost-effectiveness. We evaluated our epilepsy genetic diagnostic and counseling services for a UK region of 3.5 million.

Methods: We set up a regional specialist outpatients clinic for suspected genetic epilepsy staffed by an epilepsy geneticist, genetic counselor and research fellow, in parallel with a gene panel diagnostic service using gene panels ranging from 45–102 genes. We calculated diagnostic yield, estimated clinical impact, surveyed referring clinicians and families who used the outpatients service, and reconstructed investigational costs.

Results: 96 patients were referred for panel testing and 44 for outpatient consultation. A genetic diagnosis was made in 40% when seizure onset was <2 years, with average turnaround 21 days. Almost half the pathogenic variants were in SCN2A, SCN8A, SCN1A and KCNQ2; half of the results had implications for antiepileptic medication, including experimental therapies. Clinical prediction was poor. Referrers rated the service highly (83%) and 100% of families would recommend us to family and friends. Among 15 tested neonates, the average investigation cost was £1,200 on zero yield array CGH, single gene and metabolic testing.

Conclusion: Diagnostic yield of gene panel in <2 year onset group is excellent, and a specialist multidisciplinary clinic well received by referrers and families. Clinical impact ranged from AED guidance to recurrence risk, prenatal and extended pedigree counseling, and will broaden clinical prediction was poor. Referrers rated the service highly (83%) and 100% of families would recommend us to family and friends. Among 15 tested neonates, the average investigation cost was £1,200 on zero yield array CGH, single gene and metabolic testing.

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Conclusion: Diagnostic yield of gene panel in <2 year onset group is excellent, and a specialist multidisciplinary clinic well received by referrers and families. Clinical impact ranged from AED guidance to recurrence risk, prenatal and extended pedigree counseling, and will broaden new clinical trials open. The introduction of NGS technology mandates the revision of conventional clinical diagnostic pathways in an effort to at least achieve cost neutrality; in the neonatal group, we show possible savings of £1,200 on zero yield array CGH, single gene and metabolic testing.

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p0658
EXPRESSION OF SERUM MIR-21 IN EPILEPSY: A PRELIMINARY STUDY
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Purpose: MicroRNAs are short non-coding RNAs that regulate gene expression post-transcriptionally, being able to modulate diverse biological processes. The influence of MicroRNAs (miRs) in epileptogenesis represents a growing field of research. MiR-21 is strongly associated to immune cell differentiation and proliferation and has been shown to be upregulated in epilepsy animal and human tissues (Peng, J. et al. 2012; Roncon, P. et al. 0.2015). Knowing that miR expression is very stable in biological fluids such as plasma or serum our aim was to analyse circulating serum miR-21 expression in Genetic Generalized Epilepsy (GGE) and Mesial Temporal Lobe Epilepsy (MTLE).

Method: Expression levels of miR-21 were quantified by Real-Time PCR in sera from 48 GGE and 36 MTLE Patients. Forty-six healthy individuals were used as control. Relative expression values were calculated by the 2^-ΔΔCt method.

Results: Serum expression levels of miR-21 were decreased in GGE patients vs controls. However, no statistically significant differences were observed. MTLE patients and controls had similar miR-21 expression levels.

Conclusion: Our study is the first to evaluate serum miR-21 expression levels on GGE and MTLE patients. These results are not concordant with the previously reported miR-21 up-regulation in epilepsy. This may result from differences in clinical features and cohort size. This is a preliminary study that requires further investigation on a larger cohort.

Our primary interest within the consortium was the pharmacoresponse of specific AEDs or groups of AEDs. For idiopathic generalized epilepsy (IGE) we included 850 subjects, for focal epilepsies we included 3650 subjects. We performed genome wide association studies (GWAS) for 9 different AEDs or groups of AEDs. In the next step, we conceived a list of 406 ADME genes that were likely involved in pharmacoresponse and performed a gene set analysis based on the GWAS analyses.

Results and outlook: We could not observe any significant genetic associations (p < 5x10^-8) in the 17 GWAS subsets. Although, we detected some promising association signals, the total number of cases might have been too low to retrieve significant results. The gene set analysis for ADME genes revealed no significant results. For 4 AEDs (levetiracetam, valproate, lamotrigine and lacosamide) exome sequencing data has been obtained to extend this study to include rare coding variants. Results are still pending.

p0661
MALE PATIENTS AFFECTED BY MOSAIC PCDH19 MUTATIONS: 5 NEW CASES
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Purpose: Mutations in the PCDH19 gene are associated with epilepsy, intellectual disability (ID) and behavioral disturbances. Only heterozygous females and mosaic males are affected, likely due to a disease mechanism named cellular interference. Until now, only four affected mosaic male patients have been described in literature. Here, we report five additional male patients, of which four are older than the oldest patient reported so far.

Method: All reported patients were selected for genetic testing because of developmental delay and/or epilepsy. Custom targeted next generation sequencing gene panels for epilepsy genes were used. Clinical data were collected from medical records.

Results: All patients were mosaic for mutations in the PCDH19 gene. In most, clinical features were very similar to the female phenotype, with normal development before seizure onset, which occurred between 5 and 10 months of age, clustering of seizures and sensitivity to fever. Four out of five patients had mild to severe ID and behavioral problems.

Conclusion: In five male patients, mosaic PCHD19 mutations were identified by Next Generation Sequencing. We reaffirm the similarity between male and female PCDH19-related phenotypes, now also for male patients of ages 10–14 years. The fact that mosaic males and heterozygous females for a PCDH19 mutation show identical clinical phenotypes weakens the hypothesis of a compensating effect by a non-paralogous gene in hemizygous males.
p0662
PCDH19 MOSAIC MUTATION IN A MALE PATIENT WITH LENNOX-GASTAUT SYNDROME
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Purpose: Variants in the gene encoding protocadherin-19 (PCDH19), which are associated with epilepsy and mental retardation limited to females (EFMR) and epileptic encephalopathies resembling Dravet syndrome. This study aimed to supplement the phenotypic spectrum associated with PCDH19 mutations in epilepsy patients.

Method: We selected 90 patients with epilepsy, and collected their clinical data on age at seizure onset, seizure types, seizure frequency, seizure offset, results of EEG, psychomotor development, and behavioral features. Mutations were detected by targeted next generation sequencing (NGS) approach, and all the pathogenic mutations were confirmed by Sanger sequencing. Functional impact of all variants was inspected by three different in silico tools (sift http://sift.jcvi.org/; polyphen http://genetics.bwh.harvard.edu/pph2/; mutation taster http://www.mutationtaster.org/). Meanwhile, SNP Array test was used to check PCDH19 for gene number.

Results:
1. Sequencing analysis showed a de novo heterozygous mutation in the PCDH19 gene (NM_001184880) c.1091delC and no mutation in the SCN1A gene.
2. One male patient was diagnosed as LGS based on his typical clinical features, and the PCDH19 mosaic mutation (p.P364fs) was identified in this patient by de novo pattern.
3. The mutation, p.P364fs, is predicted to result in functional disturbance of EC4 of PCDH19.

Conclusion: In this study, we report the first PCDH19-related Lennox-Gastaut syndrome in a mosaic male patient. This finding suggests a possible role for PCDH19 in the etiology of Lennox-Gastaut syndrome. The molecular genetic screening for PCDH19 gene should be addressed to male patients with early onset epilepsy and mental retardation.

p0663
USE OF EPILEPSY GENE PANELS FOR EARLY DIAGNOSIS OF EPILEPSY IN CHILDREN 2–4 YEARS OF AGE: EXPERT CONSIDERATIONS ON CURRENT AND FUTURE PRACTICES IN EUROPE
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Purpose: The epilepsy gene panel is a molecular test increasingly used in clinical practice for the genetic diagnosis of epilepsy. A delay from clinical onset to molecular diagnosis may occur due to variability in referral criteria, regional variability in gene panel content, test availability/awareness and cost.

Methods: In December 2016, eight European experts in the genetic diagnosis of epilepsy completed a survey and met to discuss current and future application of epilepsy gene panels in the diagnosis of children aged 2–4 years. The meeting was sponsored by BioMarin Pharmaceutical Inc.

Results: Upon first presentation of unprovoked seizures in children aged 2–4 years, molecular testing is usually ordered only after several clinical examinations (e.g. metabolic investigations, EEG, MRI), seizure worsening, manifestation of additional symptoms, and/or resistance to anti-epileptic drugs (AEDs).

Key considerations offered:
1. To shorten the time to genetic diagnosis of epilepsy, a gene panel test performed during initiation of AEDs may be warranted before worsening of symptoms, when an additional symptom is present;
2. all epilepsy gene panels should include a core set of genes linked to epilepsy syndromes/diseases presenting with epilepsy and with clinically actionable potential;
3. a gene panel is the first-tier choice in contrast to whole-exome/genome, due to higher gene coverage and lower cost.

Conclusions: Early use of an epilepsy gene panel provides a cost-effective diagnostic approach for timely identification of genetic causes of pediatric epilepsy which informs: clinical management, genetic counseling, prognosis and, when available, targeted therapy.

p0664
A NOVEL CENTROMERE PROTEIN F MUTATION IN A PEDIATRIC PATIENT WITH PRESENTATION OF MOTOR AND MENTAL RETARDATION, MICROCEPHALY AND DRUG-RESISTANT EPILEPSY
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Purpose: Centrioles are microtubule derived cylindrical structures that play an important role in the formation of centrosomes, cilia and flagella. Mutations in centrosomal and microtubule-regulating genes can lead to disorders of neuronal migration and microcephaly. Centriole length regulation has recently been described in the pathogenesis of the ciliopathy disorders. Mutations in centrormere protein F (CENPF) gene are associated with disorders of severe ciliopathy and microcephaly. Herein, we report a novel CENPF mutation in a 3-year-old female with presentation of motor and mental retardation, microcephaly, and drug-resistant epilepsy.

Method: A 3-year-old girl presented with motor and mental retardation, microcephaly, and drug-resistant epilepsy. In family history of patient, it was learned that her sister had lost with diagnosis of Lennox-gastaut syndrome. The eye examination revealed bilateral chorioretinal atrophy. All laboratory findings, including cerebrospinal fluid neurotransmitter analysis and metabolic tests, were within normal limits. Electroencephalography was compatible with epileptic encephalopathy. Brain magnetic resonance imaging demonstrated generalized cerebral atrophy.

Results: Molecular analysis revealed a novel homozygous nonsense mutation (R3063X) in CENPF gene.

Conclusion: CENPF gene mutations should be considered in patients with neuronal migration disorders and microcephaly. CENPF gene mutations could also be implicated in drug-resistant epilepsy related phenotypes. Further studies will provide knowledge regarding the development of heterogeneity of phenotypic characteristics of CENPF gene mutations.
Abstracts

p0665
A NOVEL MUTATION OF THE INOSITOL 1,4,5-TRIPHOSPHATE RECEPTOR TYPE 1 GENE IN DIZYGOTIC TWIN BROTHERS WITH REFRACTORY EPILEPSY
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Purpose: The inositol 1,4,5-triphosphate receptor type 1 (ITPR1) is a gene that encodes the inositol 1,4,5-triphosphate (IP3) receptor. This receptor modulates intracellular calcium signaling over an intracellular IP3-gated calcium channel. IP-3 is one of the intracellular secondary messengers, causing Ca2+ release from the endoplasmic reticulum that are involved in various cellular processes. ITPR1 is the most plentiful in the central nervous system, highly enriched in the cerebellum, particularly in Purkinje cells. Herein, we report a novel mutation of the ITPR1 gene in dizygotic twin brothers with refractory epilepsy.

Method: Both siblings were born to consanguinous, unaffected Turkish parents. The first patient s a 16-year-old girl who presented with motor and mental retardation, microcephaly, and intractable epilepsy. The pregnancy and neonatal periods were unremarkable. The physical examination revealed microcephaly, muscle hypotonia, joint hypermobility, skin hypertextennsibility, osteoporosis, and scoliosis. Nystagmus and bilateral optic atrophy were detected on ophthalmic examination. Brain MRI demonstrated brainstem and cerebellar atrophy. MR spectroscopy demonstrated an increase in brain myo-inositol. Phenotypic features, radiologic findings and clinical course of the second patient are similar to first patient except for the male gender.


Conclusion: ITPR1-dependent pathways have been implicated in the development and maintenance of the normal functions of cerebellum. ITPR1-dependent pathways may be responsible for the development of cerebellar atrophy. Our study showed that ITPR1 gene mutations may be responsible for the development of cerebellar atrophy. The hypothesis is that reduced expression in heterozygous controls (p = 0.031). In a concurrent analysis of 20 healthy postmortem brains, we also showed that 75% of the variation in ME2 expression is explained by 3 SNPs in the ME2 gene (p < 0.005). Using the genotypes at these 3 SNPs, we predicted ME2 expression levels in 125 GGE cases and 81 controls. We found that predicted ME2 expression was significantly lower in cases than controls (p < 7x10^-7).

Conclusion: Thus there is very strong evidence for ME2’s role in GGE; and the accumulation of evidence from the original findings, our replication results, and preliminary expression studies, continues to support ME2 as a major susceptibility gene for GGE.

p0667
ME2 GENE INFLUENCES SUSCEPTIBILITY TO GENETIC GENERALIZED EPILEPSY: EVIDENCE FROM COSEGREGATION, GENETIC ASSOCIATION AND GENE EXPRESSION STUDIES IS COMPPELLING
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Purpose: Based on previous cosegregation (HLOD 4.50; Durner et al. 2001) and genetic association (p < 4x10^-5; Greenberg et al. 2005) analyses, we showed that malic enzyme 2 (ME2) is one of several major susceptibility genes for GGE (genetic generalized epilepsy).

Method: Now, we have replicated the original cosegregation result (HLOD = 3.1), and the original association result (p < 2x10^-5) using an entirely new sample. Our most recent work points directly and unambiguously to ME2, and it continues to support a recessive mode of inheritance, which is the most common form of inheritance for enzymatic disorders.

Results: In the original genetic association analysis, we identified a 9-SNP-risk haplotype of ME2 (OR = 6.1) that is present homozygously in 35% of GGE cases and only 8% of controls (p < 0.025). This led us to hypothesize that reduced ME2 expression may play a causal role in GGE susceptibility. By testing lymphocytes, we found that ME2 expression in homozygous carriers of the 9-SNP-risk haplotype is 11% lower than expression in heterozygous controls (p < 0.031). In a concurrent analysis of 20 healthy postmortem brains, we also showed that 75% of the variation in ME2 expression is explained by 3 SNPs in the ME2 gene (p < 0.005). Using the genotypes at these 3 SNPs, we predicted ME2 expression levels in 125 GGE cases and 81 controls. We found that predicted ME2 expression was significantly lower in cases than controls (p < 7x10^-7).

Conclusion: Thus there is very strong evidence for ME2’s role in GGE; and the accumulation of evidence from the original findings, our replication results, and preliminary expression studies, continues to support ME2 as a major susceptibility gene for GGE.

p0668
PET-ANALYSIS: A NEW USER-FRIENDLY TOOLBOX FOR EPILEPTIC SEIZURE ONSET ZONE LOCALIZATION. VALIDATION AND COMPARISON WITH STATISTICAL PARAMETRIC MAPPING
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Purpose: To validate PET-Analysis, a new user-friendly application for seizure onset zone (SOZ) localization from 11F-FDG PET in refractory epilepsy and compare the results with visual assessment and Statistical Parametric Mapping (SPM).

Method: Thirty patients with treatment-refractory epilepsy who underwent presurgical 11F-FDG PET and had a good postoperative outcome (Engel I-II) were included. Two observers evaluated the studies by visual assessment, with SPMs and PET-Analysis. In statistical methods, a voxel-based two-sample T-test was performed between each patient and a control database. In SPM, T-maps were thresholded at p < 0.05 and cluster size k > 50, when FWE correction for multiple comparisons was
ICTAL BRAIN PERFUSION SPECT SUBTRACTED WITH INTERICTAL FDG-PET FOR SEIZURE ONSET FOCUS LOCALIZATION

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Purpose: To develop and validate a new processing nuclear imaging procedure consisting of ictal perfusion SPECT studies subtracted with interictal FDG-PET images coregistered to MRI (PISCOM) for seizure onset focus (SOF) localization in patients with intractable complex partial seizures.

Method: A retrospective selection from our clinical practice included 23 patients (13 male and 12 female, from 4 to 61 years - mean age: 31 years) who had been diagnosed of medically refractory epilepsy, studied with MRI, ictal SPECT, interictal FDG-PET and also that remained seizure free for at least two years after surgical resection of the SOF. To perform PISCOM analysis, interictal FDG-PET images were resampled and filtered to obtain a same matrix, voxel size and a similar degradation to that of 99mTc-interictal perfusion SPECT. PISCOM and SISCOM images coregistered with MRI were obtained using Focus-DET software and SOF localization in both techniques was determined blinded for clinical data by two nuclear medicine experts. Results of both studies were compared with each other and with the known surgical site of resection (10 temporal and 8 extratemporal).

Results: PISCOM and SISCOM showed equivalent results in 17/23 cases with a good concordance among them (global agreement of 74% - CI 56-87%). The SF was correctly identified as compared to surgical resection brain area and post-surgical outcome in 15/23 (65%) patients by both PISCOM and SISCOM. PISCOM successfully identified SF in 19/23 (83%) subjects and SISCOM in 17/23 (74%). In two cases both modalities failed to correctly identify SOF.

Conclusion: Preliminary findings of this new procedure are promising as a high rate of PISCOM/SISCOM concordance and correct seizure onset focus localization has been found. Possibly, with further development of the PISCOM technique, the need to obtain interictal SPECT images could be minimized or even be avoided and replaced by interictal FDG-PET images.

MAPPING OF TEMPORAL LOBE LANGUAGE REGIONS USING VISUAL AND AUDITORY NAMING STIMULI: A LANGUAGE FMRI STUDY IN TEMPORAL LOBE EPILEPSY

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Purpose: Verbal fluency functional MRI (fMRI) is used for predicting language deficits after anterior temporal lobe resection (ATLR) for temporal lobe epilepsy (TLE), but primarily engages frontal lobe areas. In this observational study, we investigated fMRI paradigms using visual and auditory stimuli, which predominately involve language areas resected during ATLR.

Method: Thirty-three controls and 60 patients (36 left (L-TLE), 24 right (R-TLE)) were assessed using three fMRI paradigms: verbal fluency, auditory naming with a contrast of auditory reversed speech, and picture naming with a contrast of scrambled pictures and blurred faces.

Results: Auditory naming and picture naming showed bilateral temporal lobe activations. Correcting for auditory and visual input (by subtracting activations resulting from auditory reversed speech and blurred pictures/scrambled faces respectively) resulted in left-lateralised activations in posterior temporal lobe regions for patients and controls. These activations were correlated with clinical naming performance outside of the scanner (McKenna Graded Naming Test Score). Verbal fluency primarily activated frontal lobe areas.

Conclusion: While verbal fluency primarily activated frontal lobe language regions, auditory and picture naming activated temporal lobe structures, which are resected during ATLR. Controlling for auditory and visual input resulted in more left-lateralised activations. Temporal lobe activations correlated with clinical naming performance. We hypothesise that these paradigms may be more predictive of naming decline following ATLR than verbal fluency fMRI.

Semantic Verbal Memory Outcome After Surgery in Drug Refractory Epilepsy: An FMRI Based Study

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Purpose: The surgical planning in DRE patients is usually associated memory deficit. The aim of study was to measure BOLD activation during semantic verbal memory task and correlation with clinical parameters (age of seizure onset, duration and PGI memory evaluation) in cases (pre and 6 month of post-surgery) and controls.

Method: After obtaining the institute ethics approval, 20 TLE (mean age: 25.1 ± 5.7; M/F: 13/7) and 10 ETLE (mean age: 20.1 ± 4.6; Seizure onset: 4.2 ± 1.9; Seizure duration: 15.9 ± 5.7; M/F: 5/5) and 24 (mean age: 27 ± 6.7; M/F: 18/6) healthy controls were recruited in this study. Auditory cue of a standardized story in Hindi, using Super Lab presentation software was provided to the subjects using MR compatible auditory interface system (Nordic NeuroLab, Norway). After the story, patients were instructed to speak the answers in this story based questions during
fMRI scan. The fMRI sessions were carried out using 1.5T MR scanner (Avanto, Siemens, Germany).

Results: The intra group comparison analysis (pre-surgery with respect to post-surgery group) of BOLD activation in TLE subjects during the memory task, using paired t-test (p<0.001, cluster threshold 10) elicited significant BOLD activation in left MTG. Whereas post-surgery compared to pre-surgery group revealed, greater activation in right MTG along with hippocampal gyrus. In ETLE group significant BOLD activation was observed in bilateral MTG along with hippocampal gyrus in pre-surgical than post-surgical group. Clinical memory assessment was declined in TLE compared ETLE after 6 months of surgery. Negative correlation was found in LMTG (r = -0.5; p < 0.05) in patients with higher seizure duration. Greater activation in hippocampus and LMTG correlated (r = 0.6; p < 0.05) with lower seizure duration.

Conclusion: Decreased PGI memory rating and changes of BOLD activation in MTL region suggest memory (mild to moderate) impairment in TLE subjects post ATLR.

p0673
SPECIFIC MR-IMAGING PATTERNS OF NEURONAL-GLIAL TUMORS ASSOCIATED WITH FOCAL EPILEPSY IN CHILDREN
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Purpose: To analyze the specificity of MRI patterns encountered during visualization of neuronal-glial tumors associated with epilepsy in children.

Method: Were analyzed MR-images of 33 epileptic children with neuronal-glial tumors who underwent examination and treatment at the RCCH at 2007–2016 years with 1–8 years catamnesis. High resolution MRI scans was done before and after surgery on the GE Signa infinity 1.5 Tesla device.

Results: Dysembryoplastic neuroepithelial tumor (DNET) was observed in 18 patients and ganglioglioma (GG) in 15 cases. A combination with FCD IIb revealed in 4 patients and the presence of histological signs of DNET and GG in one tumor substrate in two patients. Verification of the neoplastic process on the MRI was difficult in 12 patients. Predominantly temporal localization of the tumor substrate was observed in 16 cases, rarely parietal - 7, frontal - 5 and 5 cases of multilobar localization. In one case of DNET in mass effect perifocal edema was not detected. In 12 patients with DNET and 7 with GG were revealed the specific characteristics of neuronal-glial tumors such as cortical localization, triangular configuration, “comet tail” symptom and “soap bubble” pattern. The presence of 3 or more specific patterns were present in 7 patients with DNET and in 5 with GG. Hyperintensity of the peritumoral signal, the violation of gray-white matter differentiation and cortical organization suggested FCD-associates in 9 patients which was confirmed by histology in 6 cases. Contrast-positive effect was seen in 1 DNET cases and in 4 GG.

Conclusion: MRI-patterns described in the literature as specific for DNET could also occur with high probability in GG and some other tumors. We were able to assume neuronal-glial tumors in 21 patients according to MRI, however, conclusively differentiation between DNET/OG/FCD IIb type on the results of standard MRI is not possible.

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**p0675** BRAIN FUNCTIONAL CONNECTIVITY IN SLEEP-RELATED HYPERMOTOR EPILEPSY

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**Purpose:** Sleep-related hypermotor epilepsy (SHE) is a form of focal epilepsy in which hypermotor seizures appear almost exclusively during sleep. Orbito-frontal and mesial involvement is necessary for ictal motor manifestation, however a wider network involving thalamus, basal ganglia and extra-frontal areas participate in SHE pathophysiology.

We evaluated the resting state functional connectivity (FC) in a group of SHE patients compared to healthy controls, in order to detect any resting state network (RSN) abnormalities and to assess a possible topographical organization.

**Method:** Resting-state fMRI was acquired in 13 SHE patients (age = 38.3 ± 11.8 years, 6M) and 13 matched healthy controls (age = 38.5 ± 10.8 y, 6M). Independent component analysis (ICA) and graph theoretical approach were applied. We evaluated node degree (ND), betweenness centrality (BC), clustering coefficient (CC), local efficiency (LE) and global efficiency (GE).

**Results:** ICA. At the group level, we distinguished 16 RSNs. SHE patients showed mainly significantly increased FC in a sensorimotor-thalamo-cortical network. Compared to controls, SHE patients showed no significant differences in network global efficiency, while ND and BC were increased in the limbic system regions and decreased in the occipital cortex, while CC and LE were increased in basal ganglia regions and decreased in the same limbic zones.

**Conclusion:** The increased FC of the sensorimotor-thalamo network may be in agreement with the hypothesis of altered excitability of the arousal regulatory system in SHE patients. An altered topology has been found in structures like basal ganglia and the limbic system, which have been hypothesized to be responsible for the hypermotor manifestations observed during the seizures. These data support the idea that it is an oversimplification to consider SHE as just a focal epilepsy.

**p0676** PARTIAL VOLUME CORRECTED PET SHOWS PROGRESSIVE FOCAL HYPOMETABOLISM ASSOCIATED WITH TEMPORAL LOBECTOMY OUTCOME

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**Rationale:** It is unclear if progressive fluorine 18-2-deoxyglucose positron emission tomography (FDG-PET) mesial temporal hypometabolism in temporal lobe epilepsy (TLE) is independent of hippocampal volume loss, and has independent clinical significance.

**Method:** We used FDG PET and MRI to study patients with TLE confirmed on ictal video electroencephalography. An automated MRI-registered partial volume correction (PVC) algorithm was applied. Metabolic activity in congruent regions of interest was used to calculate asymmetry indices (AI): 2/(C+C/1-C). We used ANOVA and Mann-Whitney test to compare onset age, epilepsy duration, and post surgical outcome on PVC hippocampal asymmetry index (HAI), and AI between patients seizure-free (SF) or not seizure-free (NSF) after surgery.

**Results:** 38 patients (17 females) had minimum 1 year anterior temporal lobectomy follow up. Mean onset age was 14.3 years (range 1–43) and epilepsy duration prior to imaging 19.7 years (range 2–45). MRI was normal in 13 patients. 23 had mesial temporal sclerosis, one a lateral temporal lesion and one callosal dysgenesis. PVC PET showed gradually increasing asymmetry index with increased epilepsy duration of for patients seizure free after surgery (R² 0.32; P 10.9: p < 0.005), but not in patients who continued to have seizures after surgery. Parahippocampal gyrus and amygdala asymmetry were significantly correlated with HAI; increasing asymmetry was not seen in amygdala. For all patients, PVC-PET HAI showed significant correlation with epilepsy duration and post surgical outcome but not MRI findings or epilepsy onset age. Seizure-free patients had significantly higher HAI (p < 0.005).

**Conclusion:** This study shows progressive hippocampal hypometabolism with increasing epilepsy duration, after correction for volume loss, suggesting independent progressive cellular dysfunction in TLE, particularly in patients seizure-free after temporal lobectomy. NSF Patients had lower AI than SF patients, which could be due to an incorrect presurgical hypothesis or more diffuse pathology.

**p0677** ‘IMAGING’ MEMORY IN TEMPORAL LOBE EPILEPSY-VALIDATION OF ‘WITHIN-SCANNER’ MATERIAL SPECIFIC ENCODING-RECALL PARADIGMS DURING MEMORY TASK-BASED FUNCTIONAL MAGNETIC RESONANCE IMAGING (fMRI)


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**Purpose:** To establish efficiency of within-scanner encoding and recognition-memory paradigms for task-based memory fMRI as an objective measure of pre-operative hippocampal reserve (HR) in mesial temporal lobe epilepsy due to hippocampal sclerosis (MTLE-HS).

**Method:** Memory paradigms were designed for three stimuli types - faces, word-pairs and abstract designs. The deep-encoding task was designed as a block design paradigm comprising of a total of 9 cycles run within a 1.5T MRI scanner. The recall session was performed after 1 hour within the scanner using an event related paradigm; the pre-encoded stimuli were randomly combined with distracters following a ratio 10:15. Group analysis was done following post-processing of recognition memory performances, with ‘correct–incorrect’ responses denoted ‘1-0’ applied as parametric modulators on the design specification in Statistical Parametric Mapping version 8 using boot-strap method to enable estimation of laterality indices (LI) with a p-value < 0.05 considered significant.

**Results:** Fifteen subjects with drug-resistant MTLE-HS [10 patients of left MTLE-HS (verbal memory impairment in 6) and 5 patients of right MTLE-HS (1 verbal memory deficits)] and 15 age-matched healthy controls (right handed; age range: 18–45 years) were recruited. Encoding paradigms in both the patient and control groups revealed robust bilateral BOLD activations over the regions of interest. Analysis of delayed-recognition memory BOLD signals in the left MTLE-HS group demonstrated moderate to strong right laterality for faces (LI −0.49 ± 0.16), word-pairs (LI −0.54 ± 0.13) and designs (LI −0.21 ± 0.07). The right MTLE-HS group demonstrated moderate-strong left laterality for word-pairs (LI +0.52 ± 0.19) as well as faces (+0.24 ± 0.13) but not for designs (LI −0.03 ± 0.16).

**Conclusion:** This is the first study validating intra-mural recall efficiency of material-specific memory paradigms equivalent to the widely-practised out-of scanner recall score based post-processing of encoded BOLD signals. Our results provide objective proof of HR for predominantly word-pair and face stimuli in MTLE-HS.
p0678
ASYMMETRICAL VOLUME REDUCTION OF THE HIPPOCAMPAL SUBFIELDS IN DRUG-RESISTANT PATIENTS WITH GENERALIZED TONIC-CLONIC SEIZURES
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Purpose: It has been recognized that the hippocampus participates in the pathophysiology of genetic generalized epilepsy (GGE). Meanwhile, repeated seizures induce neuronal loss in the hippocampus. However, hippocampal atrophy is not entirely understood in GGE patients with drug-resistant epilepsy (DRE). Since the hippocampus is heterogeneous with distinct functions in subfields, we investigated the alteration of subfield volume in drug-resistant patients with GGE characterized by generalized tonic-clonic seizure (GTCS).

Method: A total of 23 patients with GGE-GTCS aged between 14 and 50 were enrolled retrospectively. The subjects having cognitive or psychological impairment were excluded. According to DRE definition of ILAE 2010, 12 individuals were regarded as drug-resistant, and 11 were drug-responsive. MRI data were obtained on a 3T scanner from patients and 17 healthy controls. The volumes of the bilateral hippocampal subregions were measured with the FreeSurfer 5.3 subfield segmentation package employed. Moreover, abnormal volumes were correlated with seizure duration in linear models.

Results: The entire volume of the left hippocampus was significantly smaller in drug-resistant patients than in the healthy controls. The major atrophy was located in the CA2-3, CA4-DG (the dentate gyrus), presubiculum, and subiculum. The drug-responsive individuals showed dramatic atrophy only in the left presubiculum without change in the whole structure when compared to the controls. There were no significant differences in right hippocampal volumes of the whole or all subfields among the controls, the drug-responsive patients, and the subjects with DRE. In addition, the volumes of the whole hippocampus, presubiculum and subiculum in the left side showed strong negative correlation with seizure duration respectively among the drug-resistant group.

Conclusion: Our findings found significantly asymmetrical atrophy among hippocampal subfields in drug-resistant patients, which was more severe than drug-responsive group. Hippocampal subfield volumes may be helpful for identification of DRE, and indicate potential cognitive deficit at a preclinical stage.

p0679
EPIJET: FIRST COMMERCiALLY AVAILABLE AUTOMATED INJECTOR FOR Ictal SPECT
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Purpose: To present the main features of the first remotely controlled automated injector system for ictal SPECT (epiJET, LemerPax, Nantes, France) used in patients with refractory epilepsy. We report the results of injection time (Ti) and seizure focus (SF) localization with ictal SPECT using epiJET.

Method: Ti and SF localization using epiJET in 23 patients were compared with Ti (t-test) and SF localization (X2) of the retrospective database of the historic pool of 126 patients injected manually during 2011–2015. Injection dose error and radiation dosimetry were also compared.

Results: EpiJET injects the full volume of the perfusion radiotracer (3–8 ml) in 3.5s on average (2–6s) and all injections were performed without any problem. Ti with epiJET, using the remote control system and doing the injection from the control-EEG room was 12 ± 12s (p < 0.001). When the manual injection took place with the operator waiting the seizure from the control room (same conditions used in epiJET), the Ti in these group of 54 patients was 24 ± 12s (p = 0.001). When the manual injection took place with the operator waiting the seizure inside the patient room (bedside and worse conditions compared with epiJET), the average Ti in these 72 patients were 13 ± 9.7s (p = 0.6). Ictal SPECT with epiJET localized SF in 18/21 (85%) patients and with manual injection in 89/117 (76%) of patients (p > 0.05). Radiation exposure with epiJET was very low and injection dose error decreased from <12% with manual injection to <5% with epiJET.

Conclusion: EpiJET, the first commercially available dedicated automated injector for ictal SPECT simplify the methodology for injecting radioactive doses during seizure, making ictal SPECT more accessible. First results using epiJET are promising in reducing injection time and improving SPECT accuracy.
p0684
INTERACTIONS BETWEEN DEFAULT MODE NETWORK AND MEMORY PERFORMANCE IN PATIENTS WITH TEMPORAL LOBE EPILEPSY AND CONTROLS
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Purpose: We investigated the Default Mode Network (DMN) during resting-state functional MRI (rs-fMRI) and its relation to cognitive impairment in patients with temporal lobe epilepsy (TLE). It is expected that patients with TLE present cognitive impairments secondary to damaged structures directly involved in memory, such as hippocampus; however, it still essential to better understand the extension and causes of these damages. DMN is known to be active during introspective thoughts that might be related with cognitive processes. Studies suggest that DMN has an altered activation in patients with TLE. Our purpose is to investigate the relationship between DMN and neuropsychological performance in TLE patients and controls.

Method: We scanned (3T-MRI) 69 controls, 42 right-TLE, 49 left-TLE, 31 MRI-Negative TLE patients. We performed seed-based analysis using posterior cingulate cortex to identify the DMN. Images were pre-processed/analyzed on SPM12. Significance was determined at p < 0.01. We analyzed IQ, verbal, visual and delayed memory in all patients and 41 controls. We used SPSS22 for statistical analysis, including chi-square test and GLM.

Results: A MANOVA with Bonferroni correction confirmed that controls had a significant better performance in all tests, while MRI-Negative performed better than right-TLE. Left-TLE performed worst, except on visual memory tests. On rs-fMRI, right-TLE and left-TLE presented similar patterns of increased connectivity, considering the hemispheres ipsilateral and contralateral to the seizure focus. In the ipsilateral hemisphere, frontal lobe was more connected, while temporal lobe, caudate and hippocampus presented reduced connectivity.

Conclusion: Our data suggest that there is a disruption of the normal pattern of DMN in TLE, with reduction of temporal lobe connectivity. Per neuropsychological examination, both right-TLE and left-TLE had a worse performance in verbal memory compared to controls and MR-Neg. The absence of hippocampal atrophy (MRI-Negative) seems to yield a less prominent disruption in both functional connectivity and neuropsychological performance.

p0685
ANTIEPILEPTIC MEDICATIONS MODULATE FUNCTIONAL CONNECTIVITY IN MESIAL TEMPORAL LOBE EPILEPSY
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Purpose: Mesial temporal lobe epilepsy (MTLE) is the most common refractory epilepsy of adulthood and high doses of antiepileptic medications (AEDs) or polytherapy is often required. Functional connectivity is disrupted in MTLE and AEDs affect these networks. The objective of this study was to investigate this interaction between AEDs and the resting state functional connectivity.

Method: 31 patients with MTLE (16 right and 15 left) and 36 controls were included. Patients were grouped into high and low doses according to the drug load calculated as the sum of prescribed daily dose and defined daily dose ratios for each coprescribed AED. T1 volumetric and resting state EPI images were acquired in a 3T scanner. The software CONN was used for the analysis. Structural images were registered into standard space and automatically segmented. Functional images were realigned, normalized, smoothed and corrected for artifactual effects (de-noising). General linear model (GLM) was used to obtain the correlation maps between BOLD timeseries. Statistical analysis was performed using GLM (p < 0.05 FDR corrected). Seed (amygdala and hippocampus ipsilateral to the atrophy) to voxel analysis was performed. Comparisons were made between patients with MTLE (right or left) using high or low doses of AEDs and controls.

Results: Areas of reduced connectivity were observed. For left MTLE with high doses, abnormalities were disclosed in the mesial temporal regions. For low doses, a more extensive involvement was observed encompassing the medial frontal cortex, posterior cingulate and precuneus. For right MTLE with high doses abnormal areas were disclosed in the medial frontal cortex, whereas for low doses in the medial frontal cortex and posterior cingulate region. Positive correlation was observed between the connectivity and AEDs load.

Conclusion: Areas of impaired functional connectivity were observed in patients with MTLE. AEDs doses influenced these observations. Patients receiving higher doses showed less abnormalities.

p0686
CHARACTERISTICS OF SEIZURE-INDUCED SIGNAL CHANGES ON MRI IN PATIENTS WITH FIRST SEIZURES
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Purpose: The aim of this study was to investigate the predictive factors and identify the characteristics of the seizure-induced signal changes on MRI (SCM) in patients with first seizures.

Method: We conducted a retrospective study of patients with first seizures from March 2010 to August 2014. The inclusion criteria for this study were patients with 1) first seizures, and 2) MRI and EEG performed within 24 hours of the first seizures. The definition of SCM was hyperintensities in the brain not applying to cerebral arterial territories. Multivariate logistic regression was performed with or without SCM as a dependent variable.

Results: Of 431 patients with seizures visiting the ER, 69 patients met the inclusion criteria. Of 69 patients, 11 patients (15.9%) had SCM. Epileptiform discharge on EEG (OR 29.7, 95% CI 1.79–493.37, p = 0.018) was a independently significant variable predicting the presence of SCM in patients with first seizures. In addition, the topography of SCM was as follows: i) ipsilateral hippocampus, thalamus and cerebral cortex (5/11), ii) unilateral cortex (4/11), iii) ipsilateral thalamus and cerebral cortex (1/11), iv) bilateral hippocampus (1/11). Moreover, 6 out of 7 patients who underwent both perfusion CT and MRI exhibited unilateral cortical hyperperfusion with ipsilateral thalamic involvement reflecting unrestricted vascular territories.

Conclusion: Epileptiform activities may contribute to the possible mechanism of SCM in patients with first seizures. Additionally, the involvement of the unilateral cortex and ipsilateral thalamus in SCM and its hyperperfusion state could be helpful in differentiating the consequences of epileptic seizures from other pathologies.
**Purpose:** The European Union funded E-PILEPSY project was launched to develop guidelines and recommendations for epilepsy surgery across Europe. In this systematic review we aimed to assess the predictive value of fMRI, selective / super-selective WADA-Test, MEG and fTCD for memory and language outcome after surgery.

**Method:** An extensive literature search was conducted using PubMed, Embase and CENTRAL. The predicted value was expressed in terms of sensitivity and specificity for postoperative language or memory decline, as determined by pre- and postoperative neuropsychological assessment.

**Results:** 29 papers met the inclusion criteria and data was extracted for further analysis. All tests for heterogeneity were highly significant indicating large between-study variability (p < 0.001). For memory outcomes, meta-analyses were conducted for WADA-Tests (n = 17) using both, memory and language Laterality Quotients (LQs). If two or more estimates of sensitivity or specificity were extracted from a study, two meta-analyses were conducted indicating the maximum (“best case”) and the minimum (“worst case”) of all estimates. In the “best case”, meta-analyses yielded a sensitivity estimate of 0.79 (95% CI: 0.67–0.92) and a specificity estimate of 0.65 (95% CI: 0.47–0.83). Though, in the “worst case”, meta-analyses yielded a sensitivity estimate of 0.65 (95% CI: 0.48–0.82) and a specificity estimate of 0.46 (95% CI: 0.28–0.65). Meta-analyses concerning the diagnostic accuracy of fMRI and fTCD for memory changes were not feasible due to small numbers of studies (fMRI: n = 4; fTCD: n = 1). For language outcomes, meta-analyses were again not possible due to small numbers of studies eligible for respective analyses (WADA-Test: n = 6; fMRI: n = 2; fTCD: n = 1).

**Conclusion:** Only in a few subgroups, meta-analyses could be conducted. This underscores the necessity for more evidence for certain methods regarding our research question. Moreover, the large between-study heterogeneity also indicates the need for more homogeneous and thus more comparable studies in future research.

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**p0690**

**AN EMERGING NEUROPSYCHOLOGICAL ISSUE OF TEMPORAL LOBE EPILEPSY: SOCIAL COGNITION**


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**Purpose:** Patients with epilepsy may experience communication interpersonal difficulties, with poor social adjustment. Social cognition includes theory of mind (ToM), perception of social situations, empathy, and sensitivity to conventional and moral rules, allowing to predict other’s behaviour and to interact with social environments and relations. This study characterized social cognition and its relationship to psychopathological symptoms in patients with temporal lobe epilepsy (TLE).

**Method:** Fifty TLE patients enrolled in eight Italian credited epilepsy centres and 50 healthy controls were evaluated using standardized neuropsychological tests for ToM, empathy, recognition of behaviour appropriateness in social situations, and sensitivity to moral and conventional rules. The Symptoms Check List 90R (SCL 90R) assessed the psychopathological aspects.
Abstracts

**p0695**

**LONG-TERM FORGETTING IN CHILDREN WITH GENETIC GENERALISED EPILEPSY: THE TEMPORAL TRAJECTORY AND CONTRIBUTION OF EXECUTIVE SKILLS**

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**Purpose:** Long-term memory, which is critical for day to day life, social interaction, and academic learning, is impaired in children with genetic generalised epilepsy (GGE). In this study, we examined the relationship between the temporal pattern of long-term forgetting and executive skills of children with GGE, which has not been previously reported.

**Method:** Ten children with GGE and 47 typically developing control children, completed standardised tests of executive skills and two experimental long-term memory tasks (one verbal and visual). The verbal task involved the recall of words after short (2- and 30-min) and long (1-day, 2-weeks) delays. The visual task involved the selection and placement of objects into a previously shown scene at two long delays (1 day, 2 weeks).

**Results:** On the visual task, analyses revealed that children with GGE obtained lower object placement accuracy score ($p = 0.029$) and selected fewer correct objects ($p = 0.021$) at 2 weeks, but not at 1 day relative to typically developing control children. On the verbal task, the between group difference was not significant at any delay. In the GGE group, visual working memory (WM) was correlated with lower object placement accuracy ($r = -0.648$, $p = 0.043$), but not with the number of correctly selected objects at the 2 weeks delay.

**Conclusion:** This study provided several novel findings. For the first time, deficits were found in long-term visual memory in children with GGE. The study revealed that deficits in long-term visual memory emerge gradually and relate to reduced executive skills. Our findings can be used to inform the development of interventions for remediation of long-term forgetting of visual information.

**p0696**

**LANGUAGE OUTCOME FOLLOWING DOMINANT HEMISPHERIC LASER ABLATION SURGERY FOR THE TREATMENT OF MEDICALLY REFRACTORY EPILEPSY**


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**Purpose:** To examine post-surgical language outcome in a consecutive series of adult patients undergoing dominant hemisphere mesio-temporal laser ablation for the treatment of pharmaco-resistant epilepsy.

**Method:** 10 consecutive patients with documented hemispheric language dominance (confirmed with fMR and/or WADA) that underwent laser ablation surgery for the treatment of intractable seizures were included in the study. Comprehensive neuropsychological examination was conducted 6–12 months pre- and post-procedure. Evaluation of language skills included measures of confrontation naming, and semantic and phonemic fluency. Eight of the subjects were male and the group had a mean age of 41.70 (SD = 16.37), 13.33 (SD = 3.61) years of education, and a mean duration of seizure disorder of 29.60 (SD = 15.58) years. Correlation analysis was performed to examine the relation between language scores and demographic and clinical variables. Repeated measures analysis was conducted to assess changes in language post-surgically.

**Results:** Demographic and clinical variables were not correlated with scores of the three measures of language examined. Repeated measures analysis did not reveal significant differences between pre- and post-surgical language performance. However, two patients exhibited clinically significant decline (>1 SD) in naming and phonemic fluency, while one subject deteriorated significantly in the measure of semantic fluency.

**Conclusion:** Preliminary analysis suggests that, as a group, no significant language morbidity occurs following dominant hemisphere laser ablation for the treatment of medically refractory temporal lobe epilepsy. However, individual differences may exist and further studies with a larger sample size are necessary to understand clinical and/or demographic factors mediating potential changes in language capacities.

**p0700**

**SAFETY AND EFFICACY OF VNS THERAPY® IN A POPULATION BASED STUDY IN FRANCE**

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**Purpose:** In order to assess long-term safety and effectiveness of VNS Therapy in patients with drug resistant epilepsy in France, consecutive patients from 15 out of 32 implanting centers were followed. This post-market evaluation, requested by the French Health Authorities (HAS: Haute Autorité de Santé), provides a comprehensive evaluation of patients treated with VNS Therapy in France.

**Method:** (ISRCTN #72921325) 15 sites were selected for participation based on geographic location and experience with VNS Therapy. 174 of the 181 enrolled patients were implanted for the first time with a VNS Therapy system between February 2013 and March 2015. Long-term data through 2 years post-implant were collected on seizure frequency, seizure severity (NHS3), quality of life (QOLIE-31P / QOLIE-48-AD), general health status (EQ-5D-3L/EQ-5D-Y), and safety.
Results: [Based on an interim analysis of ~100 patients. Data on all patients will be available at the time of the conference.] Of the 181 enrolled patients, 53% were female with an average age of 35.6 years (range 6–59 years), 53.3% of all patients had focal epilepsy, while 43.3% had generalized epilepsy. Patients failed an average of 7 anti-epileptic drugs (range 0–18) prior to treatment with VNS Therapy. Following 24 months of VNS Therapy, 47.3% (n = 44/93) of patients were responders (≥50% reduction in seizure frequency). Statistical significant improvements in seizure severity and quality of life were also observed. The most common adverse events were cough (n = 10; 10%) and dysphonia (n = 9; 9%).

Conclusions: Treatment with VNS Therapy was well tolerated. In this refractory epilepsy population, nearly half of all patients had ≥50% reduction in seizure frequency following 2 years of treatment. Improvement in quality of life and seizure severity were reported in the long-term.

p0701
HIGH-FREQUENCY BURST VAGAL NERVE SIMULATION THERAPY IN A NATURAL PRIMATE MODEL OF GENETIC GENERALIZED EPILEPSY
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Purpose: Since the approval of Vagal Nerve Stimulation (VNS) Therapy for medically refractory focal epilepsies, it has been also reported to be effective in idiopathic generalized epilepsies. Instead of conventional VNS Therapy delivered at 20–30 Hz signal frequencies, this study evaluates efficacy and tolerability of high-frequency burst stimulation (300 Hz) with varying interburst intervals in the epileptic baboons, representing a natural animal model for genetic generalized epilepsy (GGE).

Method: Two female baboons had at least weekly generalized tonic-clonic seizures (GTCS) prior to VNS implantation. VNS Therapy was initiated after 4–5 weeks, and different VNS settings (0.25, 2 or 2.5 mA, 300 Hz, 4 vs 7 pulses, 0.5–2.5 sec interburst interval, stimulation intermittently for 1–2 hours/day vs continuously) were tested over the subsequent fifteen weeks, including a 4–6-week wash-out period. GTCS frequencies were quantified for each setting, while seizure duration and postictal recovery times were compared to baseline. Scalp EEG studies were performed at most settings, including intermittent light stimulation (ILS) to evaluate photosensitivity, interictal discharge (IED) rates and ILS responses were compared between trials. Finally, treatment-related behavioral effects were also evaluated.

Results: High-frequency burst VNS therapy successfully reduced GTCS frequencies at most treatment settings, except when output currents were reduced (0.25 mA) or intermittent stimulation was restricted to 1–2 hours/day. Scalp EEG studies did not demonstrate treatment-related decrease of IED rates or photosensitivity, but continuous treatment during ILS did reduce photoparoxysmal responses. VNS Therapy was well-tolerated, without cardiac or behavioral changes. Repetitive muscle contractions involving the neck and left shoulder girdle were observed intermittently in both baboons, most commonly at 0.5 interburst intervals.

Conclusion: This study demonstrates efficacy and tolerability of high-frequency VNS therapy in the baboon model of GGE. The twitching artifact may be due to aberrant propagation of the stimulus along the vagal nerve or ansa cervicalis.

p0704
CLINICAL OUTCOMES OF VNS THERAPY WITH ASPIRESR AT A LARGE UK COMPLEX EPILEPSY AND SURGERY CENTRE
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Purpose: Vagal nerve stimulation (VNS) emerged in 1988 as a treatment alternative for medically refractory epilepsy which is not amenable to resective surgery. Device models have evolved over time with the latest being the AspireSR (model #106). This latest generation model has been shown to have the ability to detect a rapid-onset tachycardia as a proxy to an epileptic seizure and deliver on-demand closed-loop electrical stimulation. The traditionally held view is that one-third of the implanted patients will have significant benefit of ≥50% seizure burden reduction, one-third of patients will have less meaningful benefit, and the final third will have little benefit. More recent large series have suggested about two-thirds of patient will have a significant benefit. The aim of this study is to compare the seizure control effect of the AspireSR at a large complex epilepsy and surgery centre in the UK with preceding VNS battery models.

Method: We retrospectively analysed the records for 55 patients who had battery change to the AspireSR implants over a period of 3 years using our electronic patient database. Supplemental telephone interviews were used to trace patients whose follow-up details were not available electronically. Seizure frequency and severity pre and post AspireSR were compared to pre-VNS therapy. Results are presented aligned to the McHugh classification of VNS outcomes.

Results: Pre-Aspire follow-up was for a mean of 7.6 years and post-Aspire added a further 1 year of mean follow-up. The ≥50%-responder cohort increased from 53% to 80% with AspireSR. Within this cohort, the >80% group increased from 22% to 38%. In contrast, the <50%-responder cohort decreased from 47% to 20% with AspireSR.

Conclusion: With four-fifths of the patients having more than 50% reduction in seizure frequency, the AspireSR has shown promising outcomes, which often translates into better quality of life.

p0705
CATHODAL TRANSCRANIAL DIRECT CURRENT STIMULATION REDUCES SEIZURE FREQUENCY AND MODULATES BRAIN FUNCTIONAL CONNECTIVITY IN DRUG-RESISTANT TEMPORAL LOBE EPILEPSY: A SHAM CONTROLLED STUDY
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Purpose: One-third of epilepsy patients develop drug resistance epilepsy (DRE), and half of them can benefit from the surgical removal of epileptic foci. Cathodal transcranial direct current stimulation (ctDCS) is a techniques able to non-invasively inhibit cortical excitability, which is abnormally increased in epilepsy, but its efficacy in reducing seizures and in modulating epileptic network is still under debate.

We evaluated the efficacy of 20-minutes 1 mA ctDCS vs sham-ctDCS in reducing seizure frequency and in modulating the functional...
connectivity (FC) between EF and the other cortical areas, in temporal DRE patients.

**Methods:** After 7 days of seizure diary, patients were randomized to either first-ctDCS or first-sham-ctDCS treatment. On day 8, patients underwent the assigned stimulation. On day 38, patients underwent the single-session opposite stimulation. 7 days after the second session, the study was concluded.

The ctDCS cathode was placed over the EF and the anode over the contralateral homologous region. Immediately before and after stimulation, a one-hour resting state closed-eyes 19-electrodes video-EEG recording was acquired.

We enrolled ten patients affected by temporal lobe DRE (4 males; 42 ± 15.7 years old; 4 symptomatic and 6 cryptogenic;5 right EF).

**Results:** ctDCS reduced the percent weekly SF more than sham stimulation (–71 ± 33% ctDCS vs 25 ± 125% sham; Z = –2.201, p = 0.028). EA changes did not differ between ctDCS respect to sham-ctDCS (p > 0.200 consistently). No patients reported worsening of SF or of seizure intensity.

FC changed after real stimulation in all patients and involved the focus in 71% of the new connections. No FC change was found after sham.

**Conclusions:** we demonstrated that an individualized ctDCS reduced seizure frequency in temporal DRE without any safety concern. FC changes may help to explain ctDCS effects on DRE patients.

### Abstracts

**p0707**

**AN EVALUATION OF SEIZURES REDUCTION OUTCOMES IN VARIOUS DUTY CYCLES IN VAGAL NERVE STIMULATION (VNS) THERAPY IN LEEDS GENERAL INFIRMARY**

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**Purpose:** VNS is an adjunctive treatment for people with intractable generalised or focal epilepsy where resective surgery is not suitable or desired (NICE Guidelines 2016). This study aims to evaluate seizure reduction in patients with a VNS in Leeds and establish any features of the patient group that may influence effectiveness of the VNS.

**Method:** Data was collected retrospectively from 68 patients with intractable epilepsy and VNS therapy at therapeutic range (1.0 mA to 2.25 mA). Overall seizure reduction rates and effect of VNS were analysed at varying duty cycles (on/off times of the VNS).

**Results:** An overall reduction in seizure frequency from baseline was achieved in 53% of patients throughout all seizure types. Patients with generalised seizures achieved an overall seizure reduction of 57% (19 patients), patients with focal seizures achieved an overall seizure reduction of 52%. 75% of patients had an improvement in mood and 78% noted an effect on seizures (aborted a seizure, reduced seizure severity, shortened a seizure and/or improved recovery time) when using the VNS magnet. 27 patients on 8–19% duty cycles achieved 61% seizure reduction (range 0–100%), 13 patients on 20–29% duty cycles achieved 58% seizure reduction (range 0–100%). 18 patients on 30–39% duty cycles achieved a 45% seizure reduction (range 0–100%) and 9 patients on 40–49% duty cycle achieved a 59% seizure reduction (range 0–92%).

**Conclusion:** These were a very refractory group of patients having tried a median of 7 anti-epileptic drugs (AEDs) (range 4–13) and taking a median of 3 AEDs (range 1–5) concomitantly with VNS therapy. The responder rates were similar to other studies, however, there are few studies that examine the effect of VNS duty cycles on seizure frequency. This study demonstrates that VNS therapy is effective at multiple VNS duty cycles in both focal and generalised epilepsy.

**p0706**

**A SINGLE CENTRE STUDY COMPARING THE EFFECTIVENESS OF THE ASPIRESR® 106 VAGUS NERVE STIMULATOR MODEL TO OLDER MODELS IN DRUG RESISTANT EPILEPSY**

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**Purpose:** One third of patients with epilepsy are drug resistant. A vagus nerve stimulator (VNS) demonstrates sustained efficacy with around 50–60% achieving a 50% seizure reduction after two years of treatment in patients not suitable for resective surgery. The Livanova AspireSR® VNS106 is the newest model with an additional auto-activation upon detection of tachycardia. The effectiveness of this additional feature in clinical practice requires further evaluation.

**Method:** We retrospectively compared the seizure efficacy for the new Livanova AspireSR® model 106 device to previous models in patients who had undergone VNS replacement or de novo insertions for drug resistant epilepsy at Leeds Teaching Hospitals NHS Trust (LTHT). We also examined the adverse effect profile and tolerance of the new AspireSR® model 106.

**Results:** We examined 19 patients who had AspireSR® model 106 device inserted at LTHT. Nine patients had a replacement VNS106 and ten patients underwent a de novo VNS106 insertion. At a mean follow-up of 6 months (3–12 months), there was an 68% mean reduction in seizure frequency with AspireSR® VNS 106. This compared to a 33% mean seizure frequency reduction over a similar period of follow-up prior to initiation of battery depletion with previous models. Over half the sample reported improvement in seizure severity and 90% reported an improvement in quality of life with AspireSR® VNS 106 device. 80% of participants subjectively reported an improvement in mood with the 106 model. Further analyses will report on long-term efficacy and tolerability for both treatment groups.

**Conclusion:** Preliminary results suggest that AspireSR® VNS 106 may exhibit greater efficacy in seizure control when compared to older models. Whilst further data is to be reported on this cohort, the results are encouraging with high percentage seizure reductions and improvement in mood quality of life outcomes. Available data would also suggest that the VNS106 is well tolerated.

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motor seizures (4) and others (4). Location of FCD: frontal (18), temporal (13), parietal (11), multilobar (5) and occipital (2). MRI abnormalities were identified at mean age 7.14 years (range 0–19.7 years) using epilepsy protocol at 1.5T (19 patients) or 3T (30 patients). The mean volume of focal cortical dysplasia was 22.5 cm³ (range 0.87–167.4 cm³). Mean age at surgery was 9.5 years (range 2 months–21 years old). There was no significant correlation between age of seizure onset and location of FCD (p = 0.433). Age of seizure onset before one month was found in patients with large lesions (r = 0.24). There was a trend for temporal tip abnormalities to have later seizure onset (p < 0.06).

Conclusion: Larger FCD is associated with earlier age of seizure onset. The trend for location of FCD and age of onset may reflect myelin maturation and capacity for seizure propagation.

**p0712**

**BLOOD LEVELS OF KYNURENINE DERIVATIVES IN CHILDREN FED KETOGENIC DIET**

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**Purpose:** The aim of the present study was to measure blood levels of tryptophan (TRP) and its kynurenine derivatives and to correlate them with clinical efficacy of the KD used therapeutically in children suffering from refractory epilepsy and autism.

**Material and methods:** 16 children (9 F, 7 M), with refractory epilepsy (12) or autism (4) were enrolled into the study in the Department of Child Neurology, Medical University, Lublin, Poland. Patients were fed the classical ketogenic diet or modified Atkins diet. After reaching ketosis of >2 mM of β-hydroxybutyrate, patients’ blood levels of TRP, kynurenine (KYN), KYNA, and 3-OH-kynurenine (3-OH-KYN) were measured chromatographically after 3 months, 6 months, and 12 months on the diet; pre-KD levels served as base-line controls.

**Results:** TRP levels remained unchanged at 3, 6, and 12 months on the diet (95%, 107%, 87%, respectively; p > 0.05). KYN blood levels increased 152% at 3 months (p < 0.001), 206% at 6 months (p < 0.001), and 273% at 12 months (p < 0.05) compared to the pre-KD controls. Of 16 patients, 8 attained high level of compliance and consequently had the best clinical outcome. In those patients, KYN levels increased were also the least variable and the highest in magnitude, consequently had the best clinical outcome. In these patients, KYNA levels increases were also the least variable and the highest in magnitude, ranging from 314 to 327% at 6 months and 12 months compared to the pre-KD control levels, respectively. KYNA levels decreased compared to the pre-KD control levels (83%, 79%, and 77%, at 3, 6, and 12 months, respectively; p > 0.05) while 3-OH-KYN levels increased 126%, 171%, and 130%, respectively; p > 0.05). Conclusions: Blood levels of KYNA were significantly elevated in KD-fed patients. These elevations appeared even more pronounced in patients with better compliance to the diet regimen, which was also associated with a better clinical outcome.

**p0716**

**ACQUIRED EPILEPTIFORM OPERCULAR SYNDROME WITHOUT ROLANDIC EPILEPSY? A VARIANT OF LKS**

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Landau-Kleffner syndrome (LKS) is a rare epilepsy syndrome characterized by regression in speech and language in association with frequent sleep-activated epileptiform discharges +/- seizures. The most common associated language disorder is verbal auditory agnosia, with severe deficits in language comprehension and expression. There are rare reports of omotor and speech disturbances in children with rolandic epilepsy, labeled acquired epileptiform opercular syndrome. Most have sleep activated EEG abnormalities, typically CSWS. We report a case of severe speech impairment without deficits in expressive language or comprehension, who does not have rolandic epilepsy, centro-temporal spikes or CSWS.

R.F. is a 3 year old female with previously normal development, who awoke from a nap with slurred speech, followed by progressive deterioration in her articulation and increasing difficulty producing words over the ensuing 3 weeks. There was deterioration in language comprehension. About 2 weeks into the course of her illness she developed gaggling while eating. Three weeks after the onset of symptoms her exam was remarkable for a youngster with severe verbal dyspraxia, which worsened as mean length of utterance increased and fluctuated during the exam. Language comprehension was intact, and the rest of her neurologic examination was normal. Non-contrast brain MRI was normal. Video-EEG monitoring at this time was remarkable for rare paroxysmal bursts of high amplitude delta activity, with intermixed spikes in the left frontal-central region. She was started on a course of high dose steroids.

This case is unique because prior cases of oral apraxia without structural lesion have been associated with frequent seizures or, often with continuous or near continuous epileptiform discharges, usually activated by non-REM sleep (CSWS). Our patient has a marked verbal dyspraxia, but relatively infrequent discharges. We postulate that this may be due to performing VEEG assessment so early in the course of her illness.

**p0717**

**KETOGENIC DIET IN PYRUVATE DEHYDROGENASE COMPLEX DEFICIENCY**

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**Purpose:** To assess the clinical characteristics and efficacy of ketogenic diet therapy in a case of pyruvate dehydrogenase complex (PDHC) deficiency, which is a major inborn error of oxidative metabolism of pyruvate in the mitochondria causing congenital lactic acidosis and brain dysgenesis. PDHC provides the link between glycolysis and the tricarboxylic acid cycle by catalyzing the conversion of pyruvate into acetyl-CoA.

**Method:** A 9-year-old female patient with PDHC deficiency was evaluated. At 24 weeks of gestation a fetal ultrasonography revealed enlargement of the lateral ventricles and hypoplasia of the cerebellum. Immediately after birth the patient developed fatal lactic acidosis and hypoglycemia. The patient was diagnosed as having PDHC deficiency based on normal ratio of lactate/pyruvate and improvement of lactic acidosis by ketogenic diet. Currently she is bed-ridden and treated with ketogenic diet (ketone ratio 1:1), vitamin B1, and L-carnitine. We evaluated the seizure semiology and EEG findings.

**Results:** Her seizures comprised of abrupt breath holding and brief hiccup-like movement of mouth and upper trunk, once in several minutes. EEG showed continuous fluctuating periodic epileptiform discharges, generalized and multifocal, bilaterally independently.

**Conclusion:** Ketogenic diet can be effective to PDHC deficiency not only to provide an alternate source of acetyl-CoA derived from ketone bodies to the developing brain but also to suppress seizures.

**p0721**

**AGGRAVATION OF EPILEPSY IN A PATIENT WITH ATYPICAL BENIGN PARTIAL EPILEPSY OF CHILDHOOD AFTER ADMINISTRATION OF SULTHIAME**

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**Purpose:** To describe our own experience of treatment with sultiamine that led to worsening of epilepsy.
Abstracts

Method: A 6 years old patient, male, with atypical benign partial epilepsy of childhood debuted at 4 years and 6 months. The diagnosis was proved by typical seizures and changes in EEG. The Patient was suffered from several types of seizures: focal motor seizures with Todd paralysis, atypical absences, atomic seizures, jerks, secondarily generalised tonic-clonic seizures. EEG changes: awake EEG showed bilateral centromedial spikes and there was CSWS during sleep. After the start of seizures, ADHD and speech disorders were developed. Administration of VPA, levetiracetam, ethosuximide gained a few therapeutic effect.

Results: Sulthiame is one of the most effective drug used for the treatment of benign childhood focal epilepsies with regard to its effect in suppressing seizures and EEG abnormalities. After administration of sulthiame in a dose of 5 mg/kg there was improvement in behavioral and mental sphere, decrease of seizures and improvement of EEG changes. Further treatment with sulthiame in a 10 mg/kg dose resulted in severe aggravation of all types of seizures, even absence status epilepticus was developed. This negative clinical changes were proved by EEG.

Conclusion: In rare cases, in the treatment of children with atypical benign partial epilepsy it’s important to keep in mind the possibility that the treatment with sulthiame may make them worse.

p0725
TOLERABILITY OF ADJUNCTIVE LACOSAMIDE IN PAEDIATRIC PATIENTS AGED 4 TO <16 YEARS WITH FOCAL SEIZURES: AN INTERIM POOLED ANALYSIS OF DATA FROM OPEN-LABEL TRIALS

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Purpose: To assess long-term tolerability of adjunctive lacosamide in children (4 to <16 years) with focal seizures.

Method: Interim data (cut-off: 02 May 2016) were pooled from three open-label trials (SP0847/NCT00938431, SP848/NCT00938912, EP0034/NCT019064560) investigating adjunctive lacosamide in children with focal seizures. Weight-based dosing regimens of 2–12 mg/kg/day were used (oral solution/tablets; maximum dose: 600 mg/day). Safety data are presented for patients aged 4 to <16 years.

Results: Data from 294 patients were analysed (45.9% female; mean ± SD age: 10.25 ± 3.34 years; mean epilepsy duration: 6.46 ± 3.64 years). 109 (37.1%) had 1–3 previous antiepileptic drugs (AEDs) and 93 (31.6%) had ≥4. At cut-off date, 174 (59.2%) had ongoing lacosamide, 45 (15.3%) had completed, and 75 (25.5%) had discontinued prematurely. Most common primary reasons for discontinuation were lack of efficacy (33 [11.2%]) and adverse events (AEs) (17 [5.8%]). Mean duration of lacosamide exposure was 351 ± 236.7 days; 216 (73.5%) patients received treatment for >6 months, 135 (45.9%) for >12 months, and 55 (18.7%) for >24 months. Mean modal daily lacosamide dose was 7.79 ± 2.83 mg/kg/day. Most patients had 2 (50.7%) or 3 (31.6%) concomitant AEDs at lacosamide initiation. Levetiracetam, valproate, and lamotrigine were most common concomitant AEDs during exposure period. Treatment-emergent AEs occurred in 240 (81.6%) patients, most commonly nasopharyngitis (19.4%), vomiting (17.0%), dizziness (16.3%), pyrexia (14.6%), upper respiratory tract infection (12.2%), somnolence (11.9%) and headache (11.6%). 128 (43.5%) patients had drug-related TEAEs (most common: dizziness [12.2%]; somnolence [10.2%]) and 7 (2.4%) had drug-related serious TEAEs. TEAEs leading to discontinuation in ≥1% patients were dizziness (1.7%) and convulsion (1.4%). One patient died due to unknown causes (not considered lacosamide-related).

Conclusion: Long-term adjunctive lacosamide was generally well tolerated in children (4 to <16 years) with focal seizures. Tolerability of adjunctive lacosamide in children was consistent with well-established tolerability profile in adults. No new safety concerns were identified.

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p0730
HYPSARRHYTHMIA MAY INDICATES THE PATIENT’S NONCOMPLIANCE – OBSERVATION IN TWO TSC PATIENTS FROM EPISTOP PROJECT

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Purpose: EPISTOP project is a large, 7th FP EU multicenter study aimed to identify the risk factors and biomarkers of epileptogenesis in a genetic model of focal epilepsy - tuberous sclerosis complex. The clinical part of the project is based on prospective study on infants with the diagnosis of TSC prior to epileptic seizures. The children are followed with video EEG, brain MRI and blood samples analysis (genetic protein, immunological and other studies) up to the age of 2 years. At the point of epileptic discharges seen on EEG patients are randomized to early treatment group (before the clinical seizures) or standard group (after clinical seizures) group in order to establish the clinical benefit of early intervention in TSC children.

Method: We present 2 children -a girl and a boy, participating in a randomized part of the study. Video EEG was being registered in 6 weeks intervals and analyzed according to EPISTOP EEG score form. Both
infants were randomized to early treatment group based on video EEG results at the age of 5 and 3 months, respectively.

**Results:** In both children, follow-up EEG after treatment initiation revealed hypsarrhythmia pattern. They still present no clinical seizures. Detailed review with the family showed that both children didn’t get the recommended treatment. After treatment re-start, in both children EEG improved, hypsarrhythmia disappeared.

**Conclusion:** Currently hypsarrhythmia is a very rare pattern observed in TSC patients before clinical seizures. Its presence in patients on antiepileptic medication may result from noncompliance.

**p0731**

**DEMOGRAPHIC AND CLINICAL PROFILE OF CHILDREN WITH EPILEPSY IN DEVELOPING ECONOMY**

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**Purpose:** All India Institute of Medical Sciences (AIIMS) Patna is one of the newly established institutes of national importance in India. Analysis of clinical and demographic profile of newly established Pediatric epilepsy Clinic is likely to help in making health policies for similar economies.

**Method:** Retrospective analysis of demographic and clinical profile of the children registered at Pediatric Seizure Clinic. Children having seizures with developmental issues are part of Neurodevelopment clinic and they are not included in this analysis.

**Results:** Out of 243 registrations, 148 files with sufficient information were analyzed. The most common type of seizure is GTCS noted in 92 (62.2%), and focal in 41 (27.7%) children. Neuroimaging was found normal in 48 (38.7%) out of 124 children screened so far. Inflammatory granuloma is most common CT finding noted in 26 (21%) children. NCC was detected in 19 children (46.3%) out of 41 presenting with focal epilepsy. Thyroid function was found abnormal in 7 out of 29 children screened for it. First line AEDs for GTCS and focal seizures are valproate and carbamazepine respectively. Common add-on drugs include levetiracetam, clobazam, clonazepam and vigabatrin. 101 (68.2%) children have well controlled seizures while 47 (31.7%) have partial control.

**Conclusion:** Inflammatory granuloma is most common CT finding in children with focal seizures. Incidence of thyroid dysfunction in these children was found more than the background incidence in the population. Most of the cases had good control on first line AEDs.

**p0732**

**REVIEW OF DRUG RESISTANT EPILEPSY CHILDREN: FOCUS ON THE DISCLOSURE OF UNNOTICED EPILEPSY-SURGERY CANDIDATES**

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**Purpose:** To reveal the unnoticed non-pharmacological therapy (especially epilepsy-surgery) candidates among the children with epilepsy, being in the long-term care of the Clinic of Paediatric Neurology of University Hospital and Epilepsy Center of Brno, The Czech Republic.

**Method:** A single-center retrospective, outpatient trial, realized in following methodological steps: In the first step, 1032 patients, ranging age 0–19 years, with diagnosis epilepsy and/or epileptic status were examined. In the second step, 141 drug resistant epilepsy children (excluding patients with benign age-dependent epilepsies and patients, who have been seizure-free more than 6 months since the last visit) were selected. In the third step, 12 patients with low seizure frequency were excluded. In the fourth step, in October 2016, remaining 129 patients were re-examined by two independent paediatric epileptologists, who made an effort to select eligible candidates for non-pharmacological treatment. Finally, descriptive statistics was used for complete assessment.

**Results:** From a total of 1032 patients, only 141 (13.67%) were classified as drug resistant and 129 of them were subsequently enrolled into the next evaluation - 39 (30.2%) patients were assessed as potential eligible candidates for non-pharmacology therapy by both of epileptologists. In 33 cases the vagal nerve stimulation was recommended as a choice of option by both epileptologists. From 82 (63.6%) patients, considered to be unsuitable for non-pharmacological treatment, 51 (39.5%) became seizure-free and 10 (7.8%) were already clearly targeted to epilepsy-surgery or ketogenic diet treatment.

**Conclusion:** Revaluation of patients as a form of self-control in the scope of one epilepsy center can be helpful in registration unnoticed epilepsy-surgery candidates. In our experience, in majority of 39 detected candidates, the parent’s refusal of non-pharmacological therapy was the main reason of its providing failure.

**p0735**

**CLINICAL, ELECTROENCEPHALOGRAFICAL AND FAMILIAR CHARACTERIZATION OF ROLANDIC EPILEPSY IN PEDIATRIC POPULATION OF TWO CENTERS FROM MEDELLÍN, COLOMBIA, FROM 2011 TO 2016**

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**Purpose:** Rolandic epilepsy is the commonest epileptic syndrome in pediatric population. We don’t have any data of this epilepsy in our country. The aim of this study was to describe clinical, electroencephalographic and familiar characteristic in our population and with this data orientate future investigations.

**Method:** Descriptive, retrospective, cross-sectional study.

**Results:** We enrolled 39 patients, 53% male, 47% female. The first seizure was at 6.5 years old (2.28 SD). Most crisis presented in the awake state (46%) and the most frequent symptom was sialorrhea in 5.1%. There was chronic generalization in 66.6% of patients.

In the EEG we had left irritative activity in 38.4% and bilateral irritative activity in 23%. All patients had spike wave complexes. The maximum irritative activity presented in N2 sleep stage in 82%. There was extra centro-temporal irritative activity in 23%.

Patients had family history of epilepsy in 33.3% and personal history of academic difficulties in 38.5%. This was the most frequent comorbidity in the group, follow by attention deficit hyperactivity disorder in 23%. The aim of this study was to describe clinical, electroencephalographic and familiar characteristic in our population and with this data orientate future investigations.

**Conclusion:** Of notice the big prevalence of academic difficulties in this population. This is an important issue to be aware of in the following of this patients.
p0737
THE ROLE OF AN AGE APPROPRIATE FDG-PET DATABASE IN PEDIATRIC CLINICAL PATHWAYS OF PRE-SURGICAL PLANNING FOR THE TREATMENT OF EPILEPSY
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Purpose: Evaluation of paediatric F-18-deoxyglucose positron emission tomography (FDG-PET) images as part of pre-surgical planning is currently a subjective procedure, based on visual assessment only. Conversely, voxel-wise statistics is an objective and user independent analysis to automatically identify areas of significant hypometabolism associated to the epileptogenic zone. This analysis is implemented in commercially available software packages like Scenium (Siemens). The main limitation of this software is the use of an in-built adult control dataset which differs from children in both brain size and metabolism. In this work, we present a semi-quantitative processing pipeline to improve the accuracy in localising the epileptic focus on FDG-PET data and aid clinical diagnosis.

Methods: We developed a flexible pipeline based on SPM8, allowing the use of in-house FDG-PET templates in paediatric standard space and age-matched control dataset (6–20y). We retrospectively collated the FDG-PET scans of 20 patients (6–17y) with focal and generalised epilepsy, which reflects what is normally found in the clinical setting. We compared their clinical diagnosis, established on the basis of clinical information and imaging findings, with the results of the semi-quantitative analysis from Scenium (an automated FDA-approved software which relies only on adult dataset, 19–44y) and our pipeline.

Results: We report agreement with clinical diagnosis in 90% of cases for younger patients (6–9y) and 80% for older ones (10–17y), compared to 60% in both cases, with Scenium. In the younger (older) patient group, we report a sensitivity of 90% (89%), while Scenium achieves 80% (67%). The average percentage of false positives is found to be 33% (17% for the older patients) with our pipeline as compared to 58% (33%) of Scenium.

Conclusions: Our initial results show that the use of a more appropriately matched image database can lead to a more accurate detection of the epileptogenic zone on paediatric FDG-PET scans.

p0738
IRON SUPPLEMENTATION ON PAROXYSMAL NON-EPILEPTIC EVENTS
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Purpose: Paroxysmal nonepileptic event (PNE) is a common seizure-like symptom in children, resulting in sudden changes in behavior or consciousness. In contrast to the common incidence, there are few known therapies. It is important that the PNE be separated from the epileptic seizures as well as being careful not to be misdiagnosed so that the anticonvulsant is not used improperly. In relation to therapy, a reduction in iron was reported in breath-holding spells, but not in other PNEs. We investigated the effects of iron supplementation on various PNEs.

Method: We retrospectively reviewed the medical records of patients who visited the Chungnam National University Hospital between January, 2013 and February, 2016.

Results: A total of 46 patients were analyzed. Seventeen patients were male and 29 patients were female. The mean gestational age was 39.3 weeks, and birth weight was 3,000 g. The mean age at the time of visit was 3.6 years. Among 11 cases of brain MRI, 10 cases were normal and 1 case was subdural hemorrhage. All 2 cases underwent brain ultrasound were normal. EEG was performed in 33 patients, 24 patients were normal (72.7%), slow background waves were 4 (12.1%), and spikes were observed in 5 patients. 31 patients (67.4%) had less than 80 μg/dL iron. Except for 2 patients who were not followed for 3 months or more, 24 of the 44 patients had iron supplementation, and 91.7% of them showed improvement. In 20 patients without iron supplementation, 65.0% showed improvement in symptoms, it was statistically significant (p = 0.035).

Conclusion: PNE improved near 80%, and the rate of symptom improvement can be expected through iron administration.

p0742
SCN8A MUTATION-RELATED EPILEPSY RESPONSIVE TO LOW DOSE PHENYTOIN
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Purpose: Some SCN8A mutation patients were recently reported to have a paradoxical good response to sodium channel blocker drugs. We report a kid with SCN8A mutation who became seizure free under low-dose phenytoin therapy.

Method: A 3 years-old boy presented with seizures since the age of 8 months; neurological and developmental milestones were normal until that age. By the age of 8 months he developed infanile spasms associated to an hypsarrhythmic EEG partially treated with ACTH, vigabatrin, multiple anti-epileptic drugs and immunoglobulin. Developmental delay was noted after seizure onset. By the age of 2 years he presented with refractory unaccountable daily atypical absences, generalized tonic-clonic, tonic, and myoclonic seizures. Exome evaluation disclosed SCN8A mutations. He was unable to sit or speak, presented with sequential upper respiratory tract infections, and underwent gastrostomy. EEG showed multifocal epileptic discharges and frequent secondary bilateral synchrony. MRI was normal. At admission, he was taking valproate, lacosamide and steroids.

Results: Oxcarbazepine led to a marked reduction in tonic, myoclonic and generalized tonic-clonic seizures. He was submitted to VNS which led to additional seizure frequency reduction (especially atypical absences) and cognitive improvement; there were still frequent daily seizures. He was started on phenytoin 7 mg/kg daily (50 mg bid); phenytoin plasma level under this regimen was 3 μg/ml. Seizures disappeared almost immediately after phenytoin was started; cognitive, motor and behavior improvement were also noted. EEG showed independent bitemporal spiking; no generalized activity or secondary bilateral synchrony was noted. He remained seizure-free for the last 6 months.

Conclusion: Contrary to SCN1A mutations’ patients, SCN8A patients might benefit from the use of sodium channel blocker drugs. The dosage and plasma levels needed to ensure seizure control might be lower than the traditionally accepted ones in this patient population.
p0744 PAROXYSMAL NON EPILEPTIC EVENTS IN PEDIATRIC EPILEPSY CLINIC: A DESCRIPTIVE STUDY OF ETIOLOGY, PROPORTION AND THERAPEUTIC IMPLICATIONS AT A TERTIARY HEALTH CARE CENTRE
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Purpose: To retrospectively evaluate atypical MR images in three cases of Rasmussen’s encephalitis (RE) with clinical and histopathology findings fulfilling Part B diagnostic criteria of the disease as proposed by the European consensus (2005). We present MR findings that may assist radiologist to consider RE in the differential diagnosis of epilepsy patients and eventually aid in the early recognitions of this condition.

Method: All patients underwent at least one contrast enhanced brain MRI at 1.5T including T1, T2, FLAIR and DWI sequences. Diagnosis was established based on clinical features and histology findings after brain biopsy or surgery samples.

Results: Age at onset was 9 years (7-13y), all patients showed ictal semiology of focal origin before the development of epilepsy paroxysmal continua (EPC). Two patients presented with unilateral, transitory and isolated clonic movement of limbs and absent gaze. One patient evidenced ictal hypersalivation, absent gaze, ocular and head version with further development of behavior disturbances and hallucinations. EEG during clinical episodes was characterized by unilateral fast activity spikes, acute waves or spike-waves without hemispheric slowing in all cases. Average time to EPC was 9 months in all patients (3-12 m). All patients had histo-pathology findings compatible with active RE. During the acute stage all patient had subcortical FLAIR/T2 hyper-intensities with partial collapse of subarachnoid spaces. Lesions were initially unilateral in all cases (one or two lobes affected) with further involvement of the contralateral hemisphere in one patient. Two patients had five follow-up MRI during 18 and 7 months respectively. Lesions progressed in both cases after brain biopsy involving previously unaffected regions (within 3 months). Patient showed no evidence of brain atrophy.

Conclusion: MRI evidence of brain atrophy is not required for the definitive diagnosis of RE. Non typical initial neuro-imaging or unusual progression are not sufficient to exclude the diagnosis.

p0751 EARLY ELECTROCLINICAL FEATURES AND OUTCOME AT 6 YEARS OF AGE OF 61 SUBJECTS WITH DRAVET SYNDROME BORN BETWEEN 1972 AND 2010
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Purpose: The correlations in DS between type of mutation and phenotype are unknown and the definition of the early electroclinical features having a prognostic meaning remains debated. In order to evaluate which findings can be predicting and/or conditioning the outcome and if it has modified during the years we analyzed comparatively the electroclinical features of 61 DS cases (aged 7 to 55 years) born between 1972-1990 (Group 1: 20), 1991-2000 (group 2: 22), 2001-2010 (Group 3: 19).

Method: They have been analyzed demographic and electroclinical findings at onset and during the evolution, age at diagnosis, kind of genetic disorder, treatment and the epilepsy, neurological and cognitive outcome at the age of 6 years. According to the cognitive outcome the received unnecessary AEDs. The change in treatment with correct diagnosis was statistically significant (p = 0.0001).

Conclusion: Mimickers of epilepsy are common in pediatric practice and are often a cause of drug refractoriness and side effects of antiepileptic drugs (AEDs) and mental and financial burden to entire family. Correct diagnosis leads to correct management, commencing new treatment for the specific diagnosis if needed and appropriate referrals to other health care providers as indicated.
Abstracts

subjects have been divided into two groups: Normal/Mild ID (18), Moderate/Severe ID (43).

Results: The incidence of cases showing a moderate/severe ID is greater (80%) in group 3 than in group 1, 2 (53%). The findings statistically related with a worse neurological and cognitive outcome are: age at onset < 6 months, significant and persistent myoclonic manifestations (absences with myoclonias and massive myoclonias), photosensitivity, self-induction. No correlations have been found according to type of genetic disorder, first seizure semiology, partial or generalized seizures occurrence and frequency. Diagnosis in the first year is more frequent in group 3 and long-lasting treatment with phenobarbital and phenytoin more frequent in groups 1, 2 without reaching statistical significance.

Conclusion: The electroclinical features observing during the first years constitute the only significant prognostic factors, having myoclonic manifestations, photosensitivity and self-induction a poorer significance. The relatively lower incidence of subjects with a poorer outcome in group 3 is only related to the expanded phenotypic spectrum of DS. Only future long-term studies concerning cases born in the last years can evidence if earlier diagnosis and different treatments can modify the prognosis.

p0754
INTERICTAL DYSPHORIC DISORDER AND QUALITY OF LIFE IN PATIENTS WITH EPILEPSY
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Purpose: Intercital dysphoric disorder (IDD) is described in patients with epilepsy (PWE), but the associated factors remain controversial.

Objective: To analyze the occurrence of IDD in PWE and its relationship with the clinical and cognitive aspects of epilepsy and quality of life (QoL).

Method: The study included 117 consecutive PWE from the neurology outpatient clinic of PUC-Campinas. Possible associations of Intercital Dysphoric Disorder Inventory (IDDI) data with the clinical aspects of epilepsy and QOLIE-31 were investigated at a significance level of 5% (p < 0.05).

Results: The patients had a mean age of 42.9 (±16.2) years; mean education level of 6.4 years; mean age at first seizure (ES) of 19.5 (±14.5) years; 45.7% of the patients were female; and 40.2% of the PWE had psychiatric disorders. Twenty-five (21.4%) patients had idiopathic generalized epilepsy, 29 (24.8%) had symptomatic focal epilepsy, and 63 (53.8%) had probably symptomatic focal epilepsy. IDD was found in 25 (21.4%) PWE. IDD was significantly more common in patients with psychiatric disorders (χ²; p = 0.021) and those with Neurological Disorders Depression Inventory for Epilepsy (NDDE-E) scores >15 (χ²; p = 0.039).

The presence of IDD did not vary significantly by epileptic syndrome, hemispheric lateralization, seizure frequency, and type of seizure. PWE with IDD had significantly lower QOLIE-31 scores (dimensions and total score). The total QOLIE-31 score was negatively correlated (Spearman’s correlation; p < 0.05) with total symptomatology, labile depressive symptoms, labile affective symptoms, and specific IDDI symptoms.

Conclusion: IDD was found in 21.4% of the cases and occurred in different epileptic syndromes. Worse QoL (dimensions and total score) was associated with the presence of IDD.

p0755
EMOTION RECOGNITION OF AUDITORY AND VISUAL STIMULI IN PATIENTS WITH RESISTANT TEMPORAL LOBE EPILEPSY
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Purpose: Temporal lobe epilepsy (TLE) is the most common form of epilepsy. The hippocampus-amygdala complex, along with others structures of the limbic system, plays a central role in emotional recognition (ER) and this function plays an essential role in social cognition and behavior. The aim of this study was to determine the performance in ER in patients with drug-resistant TLE (RTLE) using visual and auditory stimuli.

Methods: Patients with RTLE were diagnosed according to the following protocol: neurological, neuropsychological, and psychiatric evaluations; EEG, VEEG and MRI studies. Healthy controls were matched according to age and gender. The ER was determined using visual stimuli from the Set “Pictures of facial affect” (POFA) - (Ekman and Friesen, 1976) and auditory stimuli from the Set “Montreal Affective Voices” (Belin, Fillon-Bilodeau and Gosselin, 2008). In both cases, the emotional categories of the stimuli sets were seven: Happiness, Anger, Sadness, Fear, Disgust, Surprise and Neutral. Statistical analysis performed: normality test, Student’s test and Mann-Whitney test were applied for the statistical analysis.

Results: We included 53 subjects; 29 patients with RTLE (13 women, 16 men, mean age: 32.09 ± 13 years) and 24 healthy controls (13 women, 11 men, mean age: 37.21 ± 13 years). The RTLE patients presented a lower performance in the ER with both, auditory (a-) and visual (v-) stimuli in the general performance (p < 0.01) and in the following stimuli categories: v-Happiness, a & v-Anger, a- Fear, a & v-Surprise, a & v-Neutral (p < 0.01) and in a-Happiness, v-Fear, a-Asco, a & v-Sadness (p < 0.05).

Conclusion: Patients with RTLE presented a marked alteration in ER for both visual and auditory stimuli, which may explain at least partially the behavioral and social cognition alterations observed in these patients.

p0756
DIAGNOSTIC AND TREATMENT SERVICES FOR PATIENTS WITH PSYCHOGENIC NONEPILEPTIC SEIZURES (PNES): A SURVEY OF HEALTH PROFESSIONALS IN URBAN CHINA
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Purpose: The Psychogenic Nonepileptic Seizures (PNES) Task Force of International League Against Epilepsy (ILAE) neuropsychiatric committee devised a questionnaire for health professionals to investigate how they diagnose and treat PNES. Using this questionnaire, we conducted a survey among Chinese health professionals to gain an overview of diagnostic and treatment services for PNES.

Method: The survey was conducted at the Sixth Advanced International Course: Clinical Epileptology. We distributed the questionnaires to the health professionals attending the course. Descriptive analysis was performed upon the reclaimed questionnaires.

Results: One hundred and two eligible questionnaires were analysed. Responses were received from urban areas in 20 provinces /
municipalities all around China. Most respondents were neurologists. The results showed that hospitals in urban China were mostly well-equipped to diagnose patients with PNES, and that health professionals understanding of PNES mostly reflected current international expert opinion. However, although more than half of the participants knew how to diagnose PNES, many of them would not actually make the diagnosis, and most provided neither follow-up nor treatment (especially psychotherapy) for patients with PNES. Only about one third of the patients diagnosed with PNES were estimated to have at least one appointment for psychological treatment. In the opinion of the respondents, tacit trauma (neglect and stress) play a particularly important role in the development of PNES. The main obstacles to patients with PNES accessing health services for their condition were considered to be lack of knowledge or awareness among health professionals, patients and society at large.

**Conclusion:** Despite good access to equipment, diagnostic and treatment service for patients with PNES in China are currently deficient. Education programmes about PNES with different target groups, a more effective referral and social security system, and more qualified psychological practitioners emerge from the survey as particular development needs.

**p0763**

**ASSOCIATION OF RELIGIOSITY WITH ANXIETY, DEPRESSIVE SYMPTOMS AND QUALITY OF LIFE IN PATIENTS WITH EPILEPSY**


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**Purpose:** Little is known about the impact of religiosity and spirituality on quality of life in epilepsy patients. This study was designed to analyze the association of religiosity and spirituality with anxiety, depression and quality of life (QoL) in epilepsy patients.

**Method:** We investigated 227 patients with epilepsy (41.9% male, mean age 40.9 years, range 19-70). Anxiety and depressive symptoms were assessed with the Hospital Anxiety and Depression Scale (HADS) and QoL with the WHO Well-being Index. The Duke University Religion Index and the Spirituality Self-Rating Scale were administered to assess religiosity and spirituality of the individuals, respectively. The Duke University Religion Index is a multidimensional measurement of religiosity assessing organizational religiosity, non-organizational religiosity (NOR), and intrinsic religiosity (IR), which were categorized into 2 or 3 subgroups (no-religiosity, low-religiosity, and high-religiosity). The confounding variables included in the multiple linear regression analyses were age, sex, and composite seizure severity.

**Results:** In univariate analyses, the degree of anxiety, depressive symptoms, and QoL were significantly different among NOR and IR subgroups (p < 0.05). After adjusting confounding variables, yes-religiosity NOR subgroup and no- and high-religiosity IR subgroups were still significantly related to the higher QoL and lower HADS than the other subgroups (p < 0.05). Further adjusting HADS for QoL, yes-religiosity NOR and high-religiosity IR subgroups significantly had the higher QoL comparing to the other subgroups. There was no significant association with organizational religiosity and spirituality with anxiety, depressive symptoms, and QoL in patient with epilepsy.

**Conclusion:** Our data suggest that there are significant associations between religiosity and anxiety, depressive symptoms, and QoL in epilepsy patients. Therefore, having religiosity could be a supportive strategy to improve QoL in patients with epilepsy.

**p0764**

**CURATED EPILEPSY CONTENT TO FOSTER SELF-MANAGEMENT: MYEPILEPSYKEY**

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**Purpose:** In a digitally connected world 70% of Australians own either a smartphone, tablet device or both(1) with approximately 98.5% having network coverage(2). Pew reports 72% of people sought health information online in the previous year(3). A Google search on ‘epilepsy’ returns more than twenty million results. The need for reliable, curated epilepsy content was identified. The aim was to test the feasibility of an exclusive service via USB key or QR code accessible micro-site with curated evidence-based epilepsy content to increase client and their family’s understanding of the condition through offerings such as self-management tools, resources and courses to optimise life outcomes.

**Methodology:** Consumer and stakeholder consultation, analysis of support service requests and review of QOL and self-management literature was undertaken. A small reference group was consulted during the development phase. Content was gathered, tailored to the needs of three streams: Adults; Youth; and Parents of children with epilepsy. Content was divided into four sections ‘About Epilepsy’, ‘What’s Available’, ‘Get Connected’ and ‘Your Say’. A cohort of 62 clients piloted and evaluated the concept.
Results: Pilot cohort n = 62, 53% adults, 13% youth and 34% parents of children with epilepsy. 65% reported 'About Epilepsy' was the most useful with 34% finding 'What’s Available' most useful. 78% intended to share the information within the next month while 69% found the site very easy or easy to navigate. 65% reported they now had a better understanding of their or their family member’s epilepsy.

Conclusion: This self-management tool, MyEpilepsyKey, has proven to meet the intended purpose of curated, reliable, evidence-based information for people living with epilepsy. It has emerged through evaluation of general comments that the greatest benefit is gained by those newly diagnosed with epilepsy whilst those with greater life experience of epilepsy requested the addition of specialised information.

p0765
THE EXPERIENCE OF TRANSITION FOR YOUNG PEOPLE WITH EPILEPSY: DEVELOPING AN ANIMATION

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Purpose: Epilepsy affects one in 240 children in the United Kingdom; the majority will transition to adult care. When approaching adulthood, young people with epilepsy (YPWE) experience challenges to successful transition, including knowledge deficits and negative attitudes towards their condition. Our aim was to explore the experience of transition for YPWE to produce accessible resources, increase knowledge and engagement in adult epilepsy services.

Method: A longitudinal mixed-methods study followed 22 YPWE (16-21 years old) and 18 parents/carers through transition to the Walton Centre, Liverpool UK. Each participant attended up to four focus groups; with semi-structured interviews gathering longitudinal data. Quantitative self-reported questionnaires were completed at recruitment and at study completion to assess knowledge, mood, seizure impact, and quality of life. Descriptive statistics and thematic analysis generated key themes to explore the contextual data from interviews and focus groups.

Results: Young people told us they lacked social support during transition, and struggled to locate and access appropriate information at the required times when needed, such as prior to first appointment in adult services or when they experienced changes in their condition. Of interest, participants revealed misconceptions about pregnancy and topics including inheritance, antiepileptic drug risk, and actions to take if experiencing accidental pregnancy. They valued meeting other young people, and felt it should form part of their routine epilepsy care. The opportunity to develop and improve their social and coping skills was achieved through development of an animation for future YPWE first attending adult epilepsy services.

Conclusion: This project builds on previous studies identifying barriers to transition. Working with YPWE we identified key themes about transitional worries, utilized to develop accessible resources: leaflets, animation and group interventions. These resources focus on psycho-social education and coping strategies in order to increase knowledge and resilience and facilitate engagement with adult epilepsy services.

p0766
DRIVING IN NEWLY DIAGNOSED EPILEPSY PATIENTS: RESULTS FROM THE SEISMIC STUDY

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Purpose: To determine the frequency and factors associated with driving before and within 1 year after a diagnosis of epilepsy in adults.

Method: The Sydney Epilepsy Incidence Study to Measure Illness Consequences (SEISMIC) was a prospective, multicenter, community-wide study of people of all ages with newly diagnosed epilepsy in Sydney, Australia. Socioeconomic, clinical, epilepsy-related and demographic characteristics including driving status were obtained. Multivariate logistic regression was used to determine variables associated with driving before the diagnosis of epilepsy and at 12-months assessments.

Results: Before the diagnosis of epilepsy, 181 (76%) adult participants (22-85 years) drove. Being in a relationship, in paid employment, owning accommodation, having better family function and no family history of epilepsy were associated with driving before the diagnosis of epilepsy (C statistics 0.81). Driving status at 12 months was available for 152 participants who drove before the diagnosis of epilepsy, of whom 34 (22%) stopped driving. Driving for reasons other than getting to work or place of education (odds ratio [OR] 4.70, 95% confidence intervals [CI] 1.87 to 11.86), seizure recurrence since diagnosis (OR 5.15, 95% CI 2.07 to 12.82) and being on antiepileptic drug polytherapy (OR 4.54, 95% CI 1.45 to 14.22) were associated with stopping driving (C statistics 0.79). Over half of the participants with recurrent seizures did drive in the same timeframe.

Conclusion: SEISMIC project identified variables associated with driving before and after the diagnosis of epilepsy. Accessible public transportation or home-based employment opportunities should be available for people with epilepsy who have been told they are unable to drive. Individuals with newly diagnosed epilepsy, especially those being seizure free or on fewer AEDs, should be advised about when they are eligible for returning to driving.

p0768
A NEW WIRELESS ACCELEROMETRY DEVICE FOR MOTOR EPILEPSY DETECTION: A WAY TO DECREASE ECONOMIC BURDEN OF EPILEPTIC POPULATION

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Purpose: Epilepsy is a serious neurological condition with different types of manifestations which sometimes are difficult to diagnose accurately. Epileptic status is the failure of seizure termination, which seriously threaten the patients’ life, especially for those suffer generalized tonic clonic seizure when they are alone. Difficulties in diagnosis, especially when no one witnessed the emergence of seizures, and hospitalization due to epileptic status increase the economic burden of epileptic population. In order to monitor the seizures for sake of seeking help from family members timely and help diagnosis, portable epilepsy monitor device is necessary to be invented and widely used in areas where medical resources are limited. The objective of this study was to quantitatively analyze the movement trajectories of temporal lobe seizure and psychogenic non-epileptic seizure.
Method: From movement trajectories obtained from patients, amplitude, frequency, proximal/distal limb amplitude ratios, and shoulder/abdominal amplitude ratios measurements were calculated. One-way ANOVA were used to analyze all the data.

Results: The results revealed statistically significant differences in average amplitude, as well as proximal/distal limb amplitude ratios in supplementary motor area(SMA) seizures when compared with those of temporal lobe seizures and psychogenic non-epileptic seizures. This study proved the feasibility of quantitative analysis of SMA seizures and suggested that it should be further evaluated for its capability to distinguish different seizure manifestations for the diagnosis of epilepsy.

Conclusion: The wireless monitoring device we developed shows a promising perspective for timely recognizing seizures and help to provide information about seizures to the physicians. The use of this device could decrease the economic burden due to hospitalization and ease the patients and family members from the fear of seizures when the patients are alone. 


Purpose: To identify categories concerning the life impact of illness in patients with drug-resistant epilepsy, taking into account the patient’s narratives.

Method: A qualitative method using semistructured interviews -McGill Illness Narrative Interview Schedule- was chosen to gain an in-depth understanding of the perspectives of epilepsy life impact. 32 patients were interviewed. All of them were admitted in the VEEG-Units at two general hospitals in Buenos Aires (Argentina). The interviews were transcribed Verbatim. Analysis involved open coding of the data using a process of constant comparison. The data were organized into themes by sorting codes according to relationships between them.

Results: Several domains emerged from the data: Social commandment, affective reactions, autonomy, prejudice, limitations, epilepsy meanings, explanatory models, seizure unpredictability, doctor-patient communication, among others. These categories were organized into 6 broad themes: Self-perception; External perception; Performance; Illness attributions; Illness characteristics; Health-system features.

Conclusion: Qualitative methods make it possible to identify idiosyncratic meanings about the disease, which are difficult to achieve through self-administered questionnaires. They give access to gaining knowledge on how patients understand their illness, and how they feel like living with epilepsy. The domains presented in this work serve as a basis to develop conceptual models about the impact of drug-resistant epilepsy in the patients’ different life areas -social, cognitive, affective, economic, among others- They also allow focusing on local features of the disease. In fact, some of the domains relate specifically to characteristics of the context of inquiry -i.e., Health system features-, and cultural variables -i.e., Explanatory models, Social commandments. Taking into account the patients’ points of view give place to a better understanding of the patients’ experience and the life impact of the disease. It could also be useful to generate more comprehensive forms of patient care in chronic conditions.

p0773 “INVOLVED – AND YET FEELING OUTSIDE”: A NURSING PERSPECTIVE FROM PEDIATRIC EPILEPSY SURGERY H. Grønvold

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Purpose: At the Danish Epilepsy Center, we have well documented patient courses for our brain surgery patients. This also includes a big awareness of the time-consuming stress and worry it can cause to take part in the complex process towards epilepsy surgery. However, it appears that siblings to the children waiting for epilepsy surgery seem to feel outside when the rest of the family debate all the surgery’s pros and cons. We therefore wanted to pay more attention towards this part of the family in order to prevent feelings of loneliness and worries.

Methods: In a professional framework, we offered, as a pilot project, an individual nurse consultation that was addressed to the individual sister/ brother. The consultation had focus on informing and answering questions regarding the surgery field, but perhaps the most important thing was to pay attention to the feelings and worries described from the sibling.

Results: The consultation proved very beneficial for the child as she could address all her deepest worries and feelings. The consultation highlighted particularly the siblings feeling of loneliness as the parents were occupied with their own worries about the coming surgery.

Conclusion: The outcome from the consultation highlighted the importance of adding more focus and attention to this field. Particularly the siblings seem to have many considerations for the parents as they can feel their worries. The nurses could possibly contribute with more focused psychosocial approaches to these healthy children, as the process is very vulnerable for the whole family. Hence, healthy siblings are described in the literature as an important group to have in mind, it should be highlighted that siblings within this very stressful period needs extra attention.

p0779 THE RESULTS OF DIFFERENCES BETWEEN MOTHERS SELF AND RESEARCHER READING FOR “IMPACT OF PEDIATRIC EPILEPSY SCALE” M. Tanrıverdi, F. Muluay. *Bezmialem Vakıf University, Istanbul, Turkey, †Istanbul Medipol University, Istanbul, Turkey

Purpose: The psychosocial impact of pediatric epilepsy on the family have that 11-item scale was created for parents’ use to evaluate the influence of epilepsy on the major aspects of their family and child’s life by Carol Camfield et all. We investigated interrater reliability (mothers self and researcher reading) of overall assessment of Impact of Pediatric Epilepsy Scale (IPES) in children with epilepsy in Turkey.

Method: Mothers rated their child’s quality of life on a visual analogue scale (1-6) and completed the Impact of Pediatric Epilepsy Scale (IPES), which assesses the impact on academic achievement, participation in activities, health, relationships with family and with peers and siblings, social activities, self-esteem, and the caregiver’s hopes for their child’s future adapted. Simple percentage agreement, the Cohen kappa statistic representing interrater reliability for each item, and overall kappa between examiners were evaluated.

Results: Twenty-eight female (35%), 52 male (65%) 80 patients were included. The mean mothers education level was found 58 (72.5%) primary school, 5 (6.3%) secondary school, 11 (13.8%) high school, 6 (7.5%) college level. The intraclass correlation coefficient for interrater reliability of the IPES was (95% ICC=0.453-0.735). A highly significant correlation was found between the responses of the mothers self and physiotherapist reading to the IPES (r=0.942, p < 0.01).Interrater reliabilities were substantial to almost perfect for each. Considering overall interrater reliability was substantial (Kappa 0.76).

Conclusion: The IPES can be used by the physiotherapists to determine the functional-social changes in children with epilepsy and can help clinicians derive important information from the families about functional of their children. And we think that education level is important to fill in the scales in our country.
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Abstracts

p0781
EFFICACY OF CONTINUOUS MIDAZOLAM INFUSION FOR HYPERTHERMIA-INDUCED SEIZURES IN DRAVET SYNDROME
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Purpose: We investigated the efficacy of continuous intravenous midazolam (cIV-MDL) infusion in patients with Dravet syndrome and hyperthermia-induced seizures.

Method: We retrospectively reviewed the medical charts of patients with Dravet syndrome who were admitted to our hospital and underwent cIV-MDL due to hyperthermia-induced seizures from 2005-2016.

Results: A total of 11 patients, 24 cIV-MDL administration were included. The median age was 4 years 10 months (1 year 2 months-12 years 7 months). Eleven (46%) presented with seizures in clusters and 3 (13%) with status epilepticus immediately before administration. The median dose of initial cIV-MDL was 0.2 mg/kg/h (0.05-0.2 mg/kg/h), and 10/24 (42%) patients had recurring seizures. The median dose of second (increased) cIV-MDL was 0.3 mg/kg/h (0.1-0.3 mg/kg/h), and 1/9 (11%) patients had recurring seizures. The median dose of the recurrence group was 0.15 mg/kg/h (0.05-0.2 mg/kg/h), and of the control group was 0.2 mg/kg/h (0.1-0.3 mg/kg/h) (p = 0.003). In the 0.1 mg/kg/h, 0.2 mg/kg/h, and 0.3 mg/kg/h groups, 2/7 (29%), 15/21 (71%), and 5/5 (100%) patients had the seizures under control, respectively (p = 0.004); however, 1/7 (14%), 3/21 (14%), and 2/5 (40%) patients needed oxygen supplementation.

Conclusion: For hyperthermia-induced seizures, especially in clusters, in Dravet syndrome, cIV-MDL exhibits a dose-dependent efficacy of seizure suppression; however, caution is needed for the emergence of respiratory depression.

p0782
LACOSAMIDE IN STATUS EPILEPTICUS TREATMENT: EXPERIENCE IN AN HOSPITALIZED ADULT POPULATION
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Purpose: To evaluate the efficacy and safety of Lacosamide in Status Epilepticus (SE) treatment.

Method: Adults patients with SE were prospectively collected (period: 2012-2017) at the OCSAE hospital in Modena, Italy. Among them, patients treated with Lacosamide were extracted and separately analyzed.

Results: we collected 306 SE patients. Among them, 32 (10.5%) were treated with Lacosamide either as a first line antiepileptic drug (AED) after benzodiazepine administration or as an add on treatment after other AEDs. 20 patients were female (62.5%), the mean age was 63 (ranging from 18 to 98). The most common etiologies were: cerebrovascular disease (28%), cerebral tumour (19%) and sepsis (15%); overall 41% presented an acute symptomatic etiology. Lacosamide was mainly chosen as a treatment in clearly focal SE manifesting as Non-convulsive SE (NCSE, 28%), Focal motor SE (FMSE, 28%) or FMSE evolving into NCSE (25%). Lacosamide was used as a second choice drug for the treatment of Established SE, after benzodiazepines and after another AED administration in 18 patients (56%); while in 6 patients (19%) was used as first choice immediately after benzodiazepines and in another 3 patients even before the benzodiazepines administration. Lacosamide was administered as an iv bolus in 25 patients (78%) and the dose most frequently used was 200 mg. The SE was interrupted after Lacosamide administration in 17 patients (53%). Among these lacosamide was effective in 2 out of 5 cases of refractory/super-refractory SE. None immediately major complication was seen after Lacosamide infusion, and the drug was well tolerated even in the chronic phase.

Conclusion: These results, even if derived from a single center and a small cohort of patients, confirm the effectiveness and safety of Lacosamide and encourage its use in the treatment of established Status Epilepticus or as an adjunctive therapy in the treatment of Refractory SE.

p0788
NO GROWTH-RELATED LONG-TERM EFFECTS OF PRENATAL EXPOSURE TO TOPIRAMATE
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Purpose: Treatment with topiramate (TPM) during pregnancy has been associated with foetal growth retardation. We aimed to evaluate the postpartum growth in TPM exposed infants up to one year of age.

Method: Pregnancies with use of TPM during pregnancy between 2004 and 2014 in Denmark were identified from the International Registry of Antiepileptic Drug and Pregnancy Registry (EURAP). Data on birth weight, length, and head circumference at delivery were collected from EURAP. The weight, length, and head circumference at five weeks, five months and one year of age were obtained by contacting the children’s general practitioners. All data were compared with an ideal birth weight in relation to the gestational age calculated with a fourth-degree polynomial equation based on Scandinavians birth weights. Growth patterns data were plotted on standardized growth charts based on Danish boys and girls.

Results: 43 pregnancies with TPM exposure were identified. Data from GPs were available in 18 women giving birth to 24 infants (13 boys/11 girls). In the majority of pregnancies (66.7% (16/24)) TPM was prescribed as polytherapy. Four infants (16.6%) were found to be small for gestational age. Two of these showed a spurt in weight gain ending up following a higher growth curve at one year of age, one showed a spurt in weight gain too but data were only available until the 5th month, and one had a spurt in weight gain too but was underneath -2SD at one year. In total, three of 21 children showed a weight-restricted growth pattern at one year. The heights and head circumference at one year were within +/-10% from the mean in all children.

Conclusion: In our small study, infants born to mothers treated with TPM during pregnancy had normal growth patterns regarding to weight, height and head circumference during their first year of life.
P0790 SPONTANEOUS ABORTIONS AMONG WOMEN WITH EPILEPSY

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Purpose: To report on the number of spontaneous abortions among women with epilepsy (WWE). The aim is to evaluate the spontaneous abortions, especially repetitive spontaneous abortions among pregnant WWE.

Method: 114 pregnancies of WWE on AEDs were followed prospectively by obstetricians and neurologists. We analyzed those pregnancies that were interrupted with spontaneous abortions unexpectedly.

Results: Ten pregnancies out of 114 ended with spontaneous abortions. Spontaneous abortions happened in WWE taking AED monotherapy (CBZ) except in two WWE who were on polytherapy (VPA + TPM and CBZ + Pb). Seizure control was not achieved during pregnancy in 3 cases and folinic acid supplementation was not used in one pregnancy during first trimester. Three out of ten pregnancies were twin pregnancies and two ended with only one healthy newborn each. Five spontaneous abortions in two WWE were repetitive. Six spontaneous abortions happened in 3 WWE with GGE. These three WWE were diagnosed before pregnancy erroneously as having focal epilepsy of unknown etiology. Two of them with rare GTCs at seizure onset were treated with CBZ. One of them without seizure control was gradually switched from CBZ and TPM to VPA monotherapy. In this WWE 2 repetitive spontaneous abortions happened while she was on polytherapy VPA and TPM, but she had 3 consecutive pregnancies with healthy newborns with VPA monotherapy.

Conclusion: There are reports that spontaneous abortions in WWE are genetically provoked. There are reports about the greatest teratogenic potential of VPA. There are reports of best seizure control of GGE in WWE with VPA. Proper epilepsy classification, AED selection and management according the EBM guidelines are essential for WWE to have healthy pregnancy and healthy newborn. Personalized approach is recommended to WWE planning pregnancy having in mind not only epileptic (AED) but also genetic factors involved in pregnancy outcome.

P0791 PREGNANCY AND FETAL OUTCOMES IN WOMEN AFTER SURGERY FOR DRUG REFRACTORY EPILEPSY

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Purpose: To determine pregnancy and fetal outcomes in women with epilepsy, after surgery for drug refractory epilepsy.

Method: Study population was selected from Kerala Registry of Epilepsy in Pregnancy. Women with focal epilepsy who underwent epilepsy surgery were included in the “Surgical group”, while who didn’t undergo surgery but managed medically were included in the “Medical group”. Women who underwent surgery prior to the index pregnancy and later were included in the “Surgery first group” and “Pregnancy first group” respectively. Epilepsy course during pregnancy (seizure freedom during pregnancy, increase in AED dosage or number), Pregnancy and fetal outcomes (complications during pregnancy, fetal loss (abortions/intrauterine death/neonatal death), major congenital malformations and development at 1 year of age) were compared. Sub group analysis of surgical first group was done comparing women in whom AEDs could be withdrawn before conceiving (Withdrawal Group) and in whom AEDs had to be continued (Non-withdrawal group).

Results: Among the epilepsy outcomes, surgery first group (n = 76) had prolonged seizure freedom prior to pregnancy (31.8 vs 13.6 months < 0.05) and decreased seizure aggravation during pregnancy (13.2 vs 34.8 %, p < 0.05) as compared to medical group (n = 158). There were no differences in the pregnancy outcomes. Among fetal outcomes, there was no difference in birth weight, APGAR scores, malformations (8.5% vs 11.1%, p 0.79) and normal development at 1 year of age (59% vs 57.1%, p 0.07). All women in the withdrawal group remained seizure free throughout pregnancy without any need for reintroduction of AEDs. There were no complications during pregnancy, fetal loss or malformations as compared to non-withdrawal group (0% vs 9.8%, p 0.355).

Conclusion: Epilepsy surgery before pregnancy is associated with less seizure aggravation during pregnancy. There was trend towards less AED fetal exposure, Major congenital malformations and better development at one year of age.

P0793 PREVALENCE OF CESAREAN SECTION IN PREGNANT CHINESE WOMEN WITH EPILEPSY AND ITS POTENTIAL CORRELATIONS

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Purpose: To investigate the prevalence of cesarean section in Chinese women with epilepsy (WWE) and identify its potential correlations with selected sociodemographic and clinical factors.

Method: A semi-structured questionnaire was administered to 258 WWE in South-West China from December 2013 to July 2015. Data about sociodemographic, obstetric, and epilepsy variables were collected. Univariate and multivariate logistic regression analyses were utilized to examine associations between selected factors and delivery mode.

Results: The cesarean section rate in participants was 70.5% (182/258). Epilepsy was involved as a reason in 77(42.3%) participants who chose to have cesarean section. Of whom, 20.8% (16/77) were of increased seizure frequency (11/16) or status epilepticus (5/16) during the last trimester. The rest of them (61/77) chose cesarean section because they were afraid of seizure onset during delivery although some of them (20/61) had no seizure in their whole pregnant period. About one quarter of the participants had cesarean section because of perinatal obstetric
complications. The most common perinatal indications for C-section were failure to progress and fetal distress in the current study. Enrolled WVE who lived in rural areas or had term delivery were more inclined to have vaginal delivery. Seizure onset during pregnancy and AED polytherapy were positively associated with cesarean section.

**Conclusion:** Chinese WVE in our study have high prevalence of cesarean section. Good seizure control and optimal therapy during gestation were associated with a higher rate of natural delivery.

**p0794**

**VALPROATE USAGE AND PREGNANCY RELATED KNOWLEDGE IN WOMEN WITH EPILEPSY OF CHILDBEARING AGE IN CROATIA**

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**Purpose:** After the FDA and EMA warnings on valproate in 2013 and 2014, the role of this drug in the population of women with epilepsy is being redefined. We made a study among women with epilepsy in Croatia about their knowledge and sources of information regarding pregnancy related issues in epilepsy (PRIE), with special interest in those receiving valproate.

**Method:** An online anonymous questionnaire was offered during August and September 2016 to women with epilepsy aged 15-45 years.

**Results:** Respondents were 225 women aged 29 ± 7.9 years, and in 46% they stated that they have previously discussed PRIE with their neurologist. There were 52 women (25% of total) currently taking valproate, among which 26 (50%) as monotherapy. Valproate therapy was significantly related with earlier epilepsy onset. In the group of women taking valproate, only 41% have previously discussed PRIE with their neurologist. They were planning to have children in 51% of cases, and further 18% were unsure. Forty-nine percent thought that the risk for fetal malformations is similar among all the antiepileptics.

**Conclusion:** In Croatia a quarter of all women with epilepsy of childbearing age are taking valproate, but they have not received proper counseling in the majority of cases, and are largely unaware of the potential harmful consequences.

**p0798**

**MEASURING COGNITION AND COGNITIVE RESERVE IN PATIENTS WITH FIRST SEIZURE OR NEW ONSET EPILEPSY**

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**Purpose:** Up to 80% of people with epilepsy will develop some degree of cognitive impairment. Subtle cognitive dysfunction may be present even before a first seizure (FS), suggesting very early, diffuse changes in brain function. The relationship between cognitive dysfunction and epilepsy progression is poorly understood. Cognitive reserve (CR) is a concept that has been validated as a mediating factor between neuropathology and cognition in several chronic conditions. The concept may be helpful in predicting cognitive changes in FS and new onset epilepsy (NOE), as well as risk of disease progression. This study seeks to elucidate the relationship between early cognitive dysfunction, CR, and indicators of neuropathology in patients with FS and NOE, in a well-controlled prospective cohort.

**Method:** 60 patients with unprovoked FS or NOE are being recruited from the Halifax First Seizure Clinic. We are collecting clinical variables (demographic details, seizure semiology and frequency, family history, medications), neurophysiological and neuroimaging data, and a cognitive screening assessment at the time of initial presentation. We are also deriving composite scores for CR, based on IQ, occupational attainment, and engagement in leisure activities. Patients will be followed for one year, with monitoring for conversion to NOE and for indicators of refractory epilepsy.

**Results:** We present two illustrative cases from ongoing data collection, which demonstrate the interplay between cognitive reserve, cognition, and indicators of neuropathology at the time of the initial clinic visit.

**Conclusion:** We describe a comprehensive system for the evaluation of cognition in FS or NOE. The illustrative cases suggest that CR may mediate between markers of brain pathology and cognitive dysfunction in epilepsy. If this hypothesis is confirmed, then CR and early cognitive dysfunction can be further explored as possible biomarkers for disease trajectory with respect to cognitive decline or even the development of medically refractory seizures.
p0800
FALLS AS A NEW CLINICAL MANIFESTATION OF TEMPORAL LOBE EPILEPSY
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Purpose: Sudden falls are not supposed to be the typical sign of temporal lobe epilepsy (TLE). Despite of this claim, we sometimes meet a patient who report brief fall as a typical seizure type. The main aim of this study was to retrospectively evaluate the presence of a sudden fall as a clinical manifestation of TLE. We suppose that some type of vegetative instability must be responsible for this seizure manifestation, that’s why we analyzed interictal ECG in these patient.

Method: We have retrospectively reviewed the data of all patients investigated in Brno Epilepsy Center since 2000. We included into our study only patients (1) who reported sudden unexpected falls as a typical seizure manifestation; (2) who underwent comprehensive evaluation including long-term ECG monitoring and tilt-table test; (3) who were operated and in whom the seizure, including falls, completely disappeared since surgery. Subsequently the age- and gender-matched control group of operated patients for TLE without falls was created, these two groups were compared in term of 20 minutes long interictal ECG.

Results: We identified 13 patients (7 females, 6 males) who reported sudden falls which completely disappeared after surgery. The median age of epilepsy onset was 13 (minimum-maximum 1-30 years), the median duration of epilepsy was 15 (minimum-maximum 3-20 years), the median age at the surgery was 25 (minimum-maximum 20-47 years). When comparison of interictal ECG between patients with falls and patients without falls was made, patients with falls tend to have significantly higher cardiac frequency (p = 0.006).

Conclusion: It seems that sudden unexpected falls could be associated with TLE as a new clinical sign of this epilepsy.

p0801
EVALUATION OF VENTRICULAR REPOLARIZATION PARAMETERS IN EPILEPSY PATIENTS
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Purpose: Cardiac rhythm abnormalities and autonomic dysfunction are generally associated with TLE. The role of amygdala in cardiovascular autonomic control and insular propagation of the seizure activity are among the possible pathologic mechanisms. In this study, we aimed to evaluate whether vulnerability to ventricular arrhythmias differ between subgroups of epileptic patients and also patients with pure non-epileptic psychogenic seizures (NEPS).

Method: Records of 74 patients followed in the outpatient clinic of NEU Meram Faculty of Medicine-Neurology Department between Oct 15th 2015- Sept 16th 2016 were retrospectively reviewed. A 12-lead electrocardiogram of each patient was examined by a cardiologist and heart rate (HR), PR, QRS, QTc intervals, QT dispersion were calculated. The patients who had a seizure within the last 48 hours were not included so the evaluation was performed in the interictal state.

Results: Fifty four patients (% 73%) were diagnosed with epilepsy according to ILAE criteria. The remaining twenty patients (% 27) had pure NEPS and were medication free. Twenty seven patients had primary generalized epilepsy (PGE) and another 27 were diagnosed with focal epilepsy (FE). Median age was similar between epileptic and non-epileptic subjects (p > 0.05). HR, PR-QRS intervals and QTc were also similar between these groups (p > 0.05); however QT dispersion was significantly longer in the epilepsy group [46.5 ± 6.2 vs 36.9 ± 4, p < 0.001]. In a further step, cardiac parameters were compared between PGE and FE patients. HR, PR-QRS intervals, QTc and QTc dispersion did not differ between PGE and FE patients (p > 0.05).

Conclusion: Our results suggest that QT dispersion is longer in epilepsy patients when compared to patients with pure NEPS. Since there was no difference among epilepsy subgroups; QT dispersion, as well as vulnerability to ventricular arrhythmias could be a consequence of epilepsy regardless of origin. Further studies are needed to clarify the underlying mechanism of increased QT dispersion in the epileptic patients and its prognostic value.

p0802
QUALITY OF LIFE IN ADULT PATIENTS WITH EPILEPSY AND THEIR FAMILY MEMBERS IN TASHKENT
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Purpose: Epilepsy is not only a neurological disorder but may also have negative psychosocial consequences on people with epilepsy (PWE) and their relatives. Epilepsy has a major impact on quality of life (QoL) in PWE and family members. Therefore, the study aimed to investigate factors that influence QoL in hospitalized adult patients with epilepsy and their relatives.

Method: An explorative cross-sectional study has been conducted in a clinic in Uzbekistan. Hospitalized adult patients with epilepsy and their relatives were enrolled in the study. Subjective QoL as well as family support and family functioning were measured with patients and family members. Patients and their relatives assessed the patients’ support need and their satisfaction with the care provided. In addition, patients were administered a disease-related HRQoL measure. Backward stepwise multivariate linear regression analysis was used to explain variances in patients and relatives’ subjective QoL.

Results: One hundred and four dyads of patient and family member participated. Subjective QoL in patients and family members differed significantly, as did satisfaction with care delivery. In both groups family support contributed significantly to QoL. In the models 38% of the variance in QoL in patients and relatives could be explained. While the quality of life of the family members was affected by the patients’ knowledge about the disease and the reason for their current hospitalization, patient QoL scores had no influence on the QoL of family members. The patients’ QoL, however, depended significantly on the QoL of the family members.

Conclusion: Affected by the patients’ knowledge about the disease and the reason for their current hospitalization, patient QoL scores had no influence on the QoL of family members. The patients’ QoL, however, depended significantly on the QoL of the family members.

p0804
EPILEPTIC SEIZURES AS A PREDICTOR OF IN-HOSPITAL MORTALITY IN PATIENTS WITH ACUTE ISCHEMIC STROKE
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Purpose: Aim of this study was to evaluate incidence of epileptic seizures as the first manifestation of acute ischemic stroke (AIS) and in-hospital mortality rate in those patients.

Method: During the six month period we conducted prospectively analysis of 2198 patients (1132 women and 1066 men, aged 20-102 y, mean=71.11) with AIS admitted to our hospital. The diagnosis of AIS was based upon the clinical picture, physical finding and neuroradiological brain examination. Epileptic seizure as the first manifestation of stroke preceding hospital admission were diagnosed according to the clear heteroanamnestic data obtained by the qualified neurologists from eye-witnesses or emergency physicians upon arrival. We compared mortality rate of patients who had epileptic seizures as the initial symptom of AIS with mortality rate of patients without epileptic seizures preceding hospital admission.

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**Abstracts**

**p0805**  
LOW CARDIOVASCULAR FITNESS IN PATIENTS WITH PHARMACORESISTANT TEMPORAL LOBE EPILEPSY  

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**Purpose:** To study autonomic variables and cardiovascular response to exercise of patients with epilepsy (PWE), with no known cardiovascular disease, submitted to maximal treadmill test, comparing them with matched controls.  

**Method:** Thirty consecutive PWE [mean age 37.4 ± standard deviation (SD) 11.2, 18 (60%) males] and sex, and age and body mass index (BMI) matched controls were submitted to clinical assessment, 12-lead electrocardiogram (ECC) and echocardiogram to exclude cardiovascular disease. Maximal/exhaustive treadmill test using the Bruce protocol was then performed.  

**Results:** Clinical-epidemiological features were similar in both groups, regarding known cardiovascular risk factors, such as diabetes, dyslipidemia, hypertension, family history for premature cardiac disease or sedentary lifestyle. Patients with epilepsy achieved a lower peak heart rate (163.8 ± 21.28 bpm x 180.9 ± 12.52 bpm; p = 0.002), which was associated to a lower Bruce protocol stage (4.0 ± 0.91  vs. 4.7 ± 0.91; p = 0.004). Lower duration of exercise (673.6 ± 148.27 seconds x 784.4 ± 155.72 seconds; p = 0.004), lower Duke Score (11.8 ± 2.48 x 13.4 ± 2.28; p = 0.02) and lower achieved metabolic equivalent of task (MET) (12.8 ± 2.49 x 14.5 ± 2.46; p = 0.006). Chronotropic incompetence (measured as peak heart rate ≤ 85% of maximal age predicted heart rate or ≤ 80% of the chronotropic index) was more frequent in PWE. Female gender, age of epilepsy onset, number of secondarily generalized seizures and polytherapy were associated to lower cardiovascular fitness in multiple linear regression.  

**Conclusion:** PWE have a 20 to 40-fold increased risk for sudden unexpected death (SUDEP) compared to the general population. Possible mechanistic explanations include seizure-related autonomic abnormalities associated with respiratory and cardiac dysfunction. This increased risk for SUDEP in PWE may be associated with autonomic disturbances of the cardiovascular system secondary to low cardiovascular fitness.

**p0806**  
ROLE OF EMERGENCY DEPARTMENT (ED) PHYSICIANS IN IDENTIFYING AND MANAGING PATIENTS WHO MAY MEET THE “PRACTICAL CLINICAL” DEFINITION OF EPILEPSY  

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**Purpose:** In 2014, the ILAE re-defined epilepsy as a disease of the brain causing at least two unprovoked or reflex seizures occurring more than 24 hours apart or after one seizure if risk of recurrence are “high” (>60%). Although most patients with a single unprovoked seizure have low to intermediate risks for recurrence (20-50%), some patients such as those with remote symptomatic etiologies, epileptiform discharges on EEG, or an epileptogenic lesion identified on neuroimaging may be at high risk for multiple seizure recurrences. This retrospective study attempts to determine if current practice in a busy emergency department properly addresses the diagnosis of epilepsy based on the new “practical clinical” definition.  

**Method:** All patients seen in a six month period (10/01/2015-03/31/16) at the Spectrum Health Butterworth Hospital ED with a principle diagnostic code of seizure, epilepsy, or status epilepticus were reviewed. Chart review included ED documentation, completed testing (CT brain, EEG), patient disposition (admission, Observation Unit, or discharge home), neurological consultation and evaluation / treatment plan.  

**Results:** 285 patients were identified by primary diagnostic codes (including seizure or epilepsy), and subsequent chart review was completed on 210 patients. Forty-four patients were identified with a clinical presentation consistent with new onset seizure, while 166 patients were excluded with a history of confirmed epilepsy or psychogenic nonepileptic seizures (PNES). No specific evaluation protocol was identified, and disposition included direct admissions (n = 20), admission after initial evaluation in Observation Unit (n = 3), discharge after ED evaluation (n = 19), and discharge after evaluation in Observation Unit (n = 2).  

**Conclusion:** Current practice in the ED may fall short of identifying patients with a diagnosis of epilepsy as risk factors for seizure recurrence are not fully assessed after presentation with a new onset seizure.

**p0808**  
EFFECTS OF CHRONIC ANTI-EPILEPTIC USE ON SERUM 25OH-VITAMIN D LEVELS AND CALCIUM METABOLISM  

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**Purpose:** Chronic antiepileptic use may lead to Ca metabolism derangements and is a well-known cause for secondary osteoporosis. Hepatic microsomal enzyme inducers such as carbamazepine and phenytoin, increase vitamin-D metabolism and cause Vitamin-D deficiency. In this study, we aimed to evaluate Ca metabolism in epilepsy patients and the effects of enzyme inducers on serum Ca, P and 25OH-Vitamin D levels in these patients.  

**Method:** Records of 147 epilepsy patients, who were admitted to outpatient clinics of NEU Meram and Adnan Menderes Faculty of Medicine between December 2015-December 2016 were retrospectively evaluated and 106 patients were enrolled in the study. Age, disease duration, seizure types/frequency, medication history, serum Ca, P and 25OH-Vitamin D levels were recorded. Described parameters were compared between the users and non-users of enzyme inducers with appropriate statistical methods.  

**Results:** Enzyme inducer users consisted of 29.2% of patients. Polytherapy was more common among enzyme inducer users when compared to non-users (64.5% vs. 25.3%, p < 0.001); however serum 25OH-Vitamin D levels did not differ between mono and polytherapy groups (p = 0.365). Likewise, serum 25OH-Vitamin D levels did not differ significantly between enzyme inducer users and non-users (11.27 ± 8.5 ng/mL vs. 11.47 ± 10.5 ng/mL; p = 0.947). Serum Ca and P levels were also similar between two groups (p = 0.135 and p = 0.824, respectively).  

**Conclusion:** Our results indicate that there is no difference between 25OH-Vitamin D levels of enzyme inducer users and non-users. These results may be related to high prevalence of Vitamin-D deficiency in the Turkish population. On the other, it should be noted that Ca and bone metabolism derangements related to conventional antiepileptic use is not always associated with hepatic microsomal enzyme induction and Vitamin D dependent mechanisms.
p0810
AUTOMATIC MEG DATA CLASSIFICATION TO EPILEPTIC AND HEALTHY SUBJECT USING STATISTICAL FEATURES
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Purpose: To have independent predictors of which subject is likely to be Epileptic or not. The diagnosis of Epilepsy up until present day is a clinical diagnosis with supplementary evidence of Electroencephalogram (EEG). In this study we use magnetoencephalogram (MEG) data which is an artifacts free & rich of signals variation to identify a certain features to easily differentiate epileptic from non-epileptic individuals, a process which can help as screening tools for hiring/recruitment or in the future to assert the diagnosis.

Method: These data were collected from real Patients who were seen, assessed & diagnosed with Epilepsy in multiple visits & investigated thoroughly the Control were just normal person matching age without significant past medical History. signal classification method based on statistical features for classifying multi-channel MEG signals into epileptic and health subjects is proposed. The method is composed of two phases: statistical feature extraction and classification. After segmenting the multi-channel signal into 30-second non-overlapping segments, four statistical features are extracted from each segment to form the feature vector. The features are skewness, mean, median, and interquartile range. The feature vectors are used for training a k-nearest neighbor classifier which is then employed in the testing phase.

Results: 4-fold cross validation strategy is adopted in the experiment. The proposed method is evaluated using real MEG data obtained from 32 healthy subjects and 32 epileptic patients and achieved a sensitivity of 96.59%, a specificity of 93.25%, and an accuracy of 94.9%.

Conclusion: These results are largely showing how excellent the test as positive Predictive test. the high detection rate of epileptic Patients.

p0811
EPILEPSY MIMICKING STROKE: CAN WE MANAGE IT BETTER? A PREVALENCE AND CLINICAL FEATURES STUDY
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Purpose: Patients presenting with transient neurological deficit (TND) of epileptic etiology are often misdiagnosed with transient ischemic attack (TIA) even with a normal neurovascular assessment. This frequently implies repeated emergency consultations and tests, as the TND normally reappears. Our aim is to review the prevalence of “epileptic stroke mimics” in our stroke unit and try to identify special electroclinical features that could help prevent misdiagnoses.

Method: We reviewed the clinical records of all patients admitted to our stroke unit between April 2013 and December 2016 with a TIA diagnosis (TND, normal or inespecific MRI features) and analyzed those of patients diagnosed with epilepsy after repeated TND.

Results: We found 301 patients diagnosed with TIA, seven of which (2.3%, mean age 73.5 years old) were finally diagnosed with epilepsy. 100% presented language impairment as part of the TND (median duration of 60 minutes) and suffered 4 episodes on average (range 2-8) before the diagnosis of epilepsy was established (5.5 months on average after the first event). Six patients (85.7%) had stereotypical episodes. Paroxismal auralic fibrillation was found in one patient, being the neurovascular assessment normal in the rest. Interictal EEG showed epileptic features in 28.57% (n = 2). Six patients (85%) were seizure free after starting an antiepileptic drug (AED) treatment.

Conclusion: Seizures presenting with TND are frequently misdiagnosed with TIA, leading to unnecessary repeated neurovascular assessment and treatment delay which could be prevented with a better characterization of common clinical features in this group of patients. Our results suggest that repeated TND involving language impairment could be strongly related to an epileptic etiology when initial neurovascular assessment is normal (even without interictal epileptic activity). Further and prospective studies should be done in order to better identify a clear and reliable electroclinical constellation with consequent earlier diagnosis and management improvement.

p0812
USE OF COMPLEMENTARY AND ALTERNATIVE MEDICINE AMONG ADULT PATIENTS WITH EPILEPSY IN SINGAPORE
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Purpose: Complementary and alternative medicine (CAM) use is prevalent in Asian patients with chronic diseases. Previous studies have reported that healthcare providers were often not informed about CAM use in patients on chronic medications. This study aims to characterize CAM usage and identify predictors of CAM usage in adult patients with epilepsy (PwE) in a multi-ethnic community.

Method: A prospective cross-sectional study was conducted at a tertiary adult neurology clinic in Singapore from September 2016 to January 2017. Patients with epilepsy were recruited to complete an interviewer-administered survey. Those who declined participation, unable to provide informed consent independently or lacked understanding of English or Chinese were excluded.

Results: Of the 113 adult PwEs surveyed (mean age: 43.9 ± 12.6), 46.9% were male and almost 80% were Chinese. Overall CAM use was 80.5%, with the most frequently reported being vitamins and supplements (60.4%), traditional herbs (31.9%) and prayers (31.9%). The main reasons cited for CAM use were for general health (46.4%), seizure control (14.3%), improve mood and relaxation (12.7%), and management of side effects of antiepileptic drugs (12.2%). Among those who indicated CAM use for seizure control, prayers (50%), meditation (18.2%) and traditional herbs (13.2%) were commonly used. Majority (70%) of the oral CAM users did not disclose CAM usage to their healthcare providers and only 16% considered the risk of interactions with antiepileptic drugs. Multivariate analysis showed that patients with tertiary education (OR=4.83, 95% CI 1.43-16.33) and non-Chinese (OR=7.32, 95% CI 1.25-43.01) were more likely to use CAM.

Conclusion: CAM use is prevalent across our adult PwE. There is limited disclosure of CAM usage to healthcare providers and lack of awareness of potential antiepileptic drug interactions risk with oral CAM use. Active enquiry by healthcare providers on CAM use may provide opportunities to discuss safe modalities for unmet needs.

p0814
TREATMENT OF STATUS EPILEPTICUS/SEIZURE CLUSTERS IN TWO PATIENTS WITH MELAS SYNDROME
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Purpose: MELAS syndrome is a hereditary mitochondrial disorder characterized by myopathy, encephalopathy, lactic acidosis and stroke-like episodes. Stroke-like episodes are often triggered by epileptic seizures. Treatment of epileptic seizures may be complicating because anti-epileptic drugs (AED) may interfere with mitochondrial function and thereby provoke life-threatening lactic acidosis. Our knowledge about the feasibility of the modern third and fourth generation AED in these cases is very sparse.

Method: We report two adult patients with genetically confirmed MELAS and refractory seizures, treated for acute seizure clusters with various newer anti-epileptic drugs under monitoring of serum lactate levels, EEG and clinical response.

Results: After the first stroke-like episode, the first patient was treated with levetiracetam and L-arginin with good response. After a severe generalized tonic-clonic seizure, lacosamide was added. No signs of lactic acidosis but she developed a psychosis. Swithing from levetiracetam/lacosamide to perampanel/brivaracetam only slightly improved the psychosis. The other patient suffered from status epilepticus (SE) due to a stroke-like episode. EEG confirmed SE and treatment with levetiracetam, lacosamide and phenytoin was without clinical or EEG improvement. Diazepam improved the EEG but not the clinical symptoms. Lactate levels remained stable. L-arginin was started with rapid improvement of the EEG and almost completely recovered. A new SE due to stroke-like episode despite treatment with levetiracetam and L-arginin was treated with phenytoin with improvement in the EEG but not clinically.

Conclusion: These two patients with MELAS and seizures been treated with a large panel of newer and older anti-epileptic drugs. None of the drugs used induced lactic acidosis or caused other MELAS-related complications. If required, newer and older AED may be used with caution in patients with MELAS and clinical need for rapid AED treatment.

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p0815 THE MODIFIED ATKINS DIET IN PATIENTS WITH REFRACTORY EPILEPSY AND INTELLECTUAL DISABILITY: A RANDOMIZED CONTROLLED TRIAL
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Purpose: The modified Atkins diet (MAD) is an effective dietary treatment for children with epilepsy, and fewer trials have also shown a positive effect on seizure control in adults. However, trials including adult patients with intellectual disability (ID) are lacking. We aimed to establish efficacy, safety and feasibility of the MAD in adult patients with ID and pharmacoresistant epilepsy.

Method: We performed a prospective open-label randomized controlled trial in institutionalized adult epilepsy patients with moderate to severe ID. Antiepileptic drugs were continued during the trial-period. Patients were randomized to receive the MAD or no dietary intervention. Primary outcome was the number of responders (>50% reduction in seizure frequency) at 4 months. Secondary outcome parameters were adverse events and effect on daily functioning. An intention to treat analysis was performed. To obtain a difference with α=5% and a power of 80%, an estimated sample size of 27 per group was computed.

Results: After randomization of 23 patients (11 in the MAD group, 12 in the control group) an interim safety and feasibility analysis was performed. One of the patients randomized for MAD did not start the diet because of withdrawal of support from caregivers, and 5 patients on MAD discontinued before the study end point was reached, because of inefficacy or side effects. At 4 months, the number of responders in the MAD group was 0/11 (0%), and in the control group 1/12(8%). One patient on MAD was reported to recover sooner from seizures and thus have an increased quality of life. Most common reported side effects were fatigue and apathy. The results from the interim analysis led to premature termination of the trial for reasons of non-feasibility.

Conclusion: We could not demonstrate a beneficial effect of the MAD in adult patients with refractory epilepsy and moderate to severe intellectual disability.

p0817 OLFATORY AND GUSTATORY DYSFUNCTION IN EPILEPSY
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Purpose: Neurosensory dysfunction in temporal lobe epilepsy (TLE) usually involve either hallucinations prior to seizures or chronic impairments in odor and taste discrimination and identification. We aim to evaluate the olfactory and gustatory function in TLE patients, but also in the generalized epilepsy and extra-temporal epilepsy patients. We compare the results with age and sex-matched healthy controls.

Method: 165 individuals with epilepsy who had applied to our epilepsy outpatient clinic for last 6 months and 76 healthy volunteers were studied. A questionnaire was applied which included 30 questions, questioning whether the patients were experiencing problems with smell and taste. We correlate chemosensory function with the duration of seizure and the number of drugs used.

Results: Patients showed significantly lower (p < 0.001) olfactory and gustatory scores than the healthy controls. Chemosensory dysfunction was detected mostly in TLE patients, generalized epilepsy and extra-temporal epilepsy patients, respectively.

Conclusion: This study shows the presence of the olfactory and gustatory dysfunction not only in TLE patients but also in generalized epilepsy and extra-temporal epilepsy patients.

p0818 EFFECTIVENESS AND SAFETY OF ESILCARBAZEPINA ACETATE AS ADJUNCTIVE TREATMENT FOR REFRACTORY EPILEPSY: A LONG TERM RETROSPECTIVE STUDY
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Purpose: In refractory epilepsy (RE) newer drugs have improved outcomes mainly due to improved tolerability profile rather than increased seizure freedom rates. The purpose of this study is to assess the long-term efficacy and tolerability of eslicarbazepine acetate (ESL) as an adjunctive treatment in adult patients with refractory epilepsy.

Method: Retrospective, open label, single-center study. Inclusion criteria: (1) refractory epilepsy with focal seizures (2) minimum 12 months of clinical follow-up. The percentage of patients with ≥50% seizures reduction (responders) was estimated. Tolerability was evaluated in relation to incidence and severity of adverse reactions and drop-out due to ADRs.

Results: 27 patients were included (average age 37.7 years). 6 (22%) patients had more than 20 seizures/month, 18 (66%) patients had 2-20 seizures/month. At baseline 22 patients (81%) were taking more than 2 AEDs (range 2-6). None of the patients were treated with concomitant carbamazepine. 8 (30%) patients were on VNS therapy. At 12 months a percentage of responders of 33% (9/27) was observed. 15% (4/27) of patients had a reduction of seizures < 50%. None were seizure free (compare with 15% at 6 months follow up). 7/27 (26%) experienced side effects: 1 irritability, 1 drowsiness, 1 recurrent falls, 1 peptic ulcer, 3 (11%) severe hyponatremia. There was no evidence of a correlation between the appearance of adverse effects and the number of concomitant AEDs (1 to 5). 8/27 (30%) patients dropped-out between 9 and 12 months; 3 due to inefficacy, 5 because of side effects.

Conclusion: The use of ESL was associated with significant seizure reduction without ADRs in approximately 1/3 of our RE sample at 12 months. In contrast to open label extension studies, no long-term seizure-free patients were observed. Considering the severity of epilepsy in our sample, responders rates are still high. Hyponatremia was the most common side effect.
p0819
CO-OCCURRENCE OF ANTI-NMDAR ANTIBODIES IN PATIENTS WITH TLE AND HIPPOCAMPAL SCLEROSIS
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Purpose: Autoantibodies to specific neurologic proteins are associated with subacute onset encephalopathies, which often present with refractory seizures. Previous studies have found specific neurologic antibodies in a small proportion of people with epilepsy. Positive antibody titers appear to be more frequent in patients with focal epilepsies of unknown cause. Studies also suggested a potential role of autoimmunity in the precipitation of adult-onset temporal lobe epilepsy with hippocampal sclerosis (TLE-HS). TLE-HS is considered to be the most frequent of all epileptic syndromes. The prevalence of autoantibodies to neuronal surface proteins in this population is uncertain. We aim to investigate the frequency of neurological autoantibodies in a group of patients with TLE-HS.

Method: We screened neuronal autoantibodies in 47 patients with previous established diagnosis of TLE-HS. Forty-five patients were enrolled randomly and two were included because the symptomatology suggested limbic encephalitis.

Results: The two patients with suggestive symptoms of limbic encephalitis had diagnosis of refractory TLE-HS several years before, with fluctuating psychiatric symptoms. They had acute and severe exacerbation of psychiatric symptoms. No significant change in previous seizure frequency was noted. These two patients tested positive for antibodies against NMDAR. In the group of 45 patients who were tested randomly, two were positive for anti-NMDAR Abs. Age at seizure onset was similar in those with or without positive Abs, initiating in infancy or early childhood. In the group of patients who randomly tested positive for anti-NMDAR, one patient had refractory epilepsy with frequent seizures and mild depression, and the other had familial mesial TLE with infrequent seizures and no psychiatric symptoms.

Conclusion: Among patients with TLE-HS, a significant minority (4.4%) had detectable serum Abs suggesting an autoimmune etiology. Certain clinical features, such as striking psychiatric symptoms, could be used to identify patients with the highest probability of harboring neurological Abs.

p0820
PERI-ICITAL PRONE POSITION IS ASSOCIATED WITH INDEPENDENT RISK FACTORS FOR SUDDEN UNEXPECTED DEATH IN EPILEPSY: A CONTROLLED VIDEO-EEG MONITORING UNIT STUDY
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Purpose: Sudden unexpected death in epilepsy (SUDEP) is the major cause of death in patients with chronic drug-resistant epilepsy and peri-ictal prone position has been proposed as a risk factor for SUDEP. We aimed to investigate the patients with peri-ictal prone position in our video epilepsy monitoring (VEM) unit and compare the patients with and without peri-ictal prone position to emphasize its relationship with other independent risk factors for SUDEP.

Method: We retrospectively screened all patients with peri-ictal prone position who underwent VEM in our epilepsy monitoring unit for a 10-year period and these patients constituted the Prone (+) group. All patients without peri-ictal prone position who underwent VEM in the last two years constituted Prone (-) group. Peri-ictal positions were evaluated in detail in Prone (+) group. Clinical and laboratory features and SUDEP 7 scores were compared between groups.

Results: A total of 21 seizures were identified in peri-ictal prone position from 16 patients. SUDEP 7 scores were significantly higher in Prone (+) group. Longer duration of epilepsy, early age at seizure onset, mental retardation and frequency of seizures of any type (>50 seizures per month for last year) were found significantly different between Prone (+) and Prone (-) groups. A binary logistic regression analysis showed that mental retardation was the differentiating variable between groups.

Conclusion: Peri-ictal prone position in VEM unit may relate with other independent risk factors of SUDEP, especially with mental retardation. Nocturnal supervision becomes important to reduce SUDEP risk especially in patients with mental retardation.

p0821
LONG-TERM FOLLOW-UP OF ICTAL ASYSTOLE IN TEMPORAL LOBE EPILEPSY: IS PERMANENT PACEMAKER THERAPY NEEDED?
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Background: Ictal asystole (IA) is an infrequent complication of temporal lobe epilepsy (TLE), but one that may cause transient loss of consciousness (T-LOC) similar to reflex syncope (particularly the vasovagal faint). Although IA-triggered T-LOC is relatively rare, its recognition is therapeutically important. However, while the need for anti-epileptic drugs (AEDs) is broadly accepted, cardiac pacing in IA is controversial. This study aimed to evaluate the need for cardiac pacing in the follow-up of IA patients being treated with AEDs.

Methods and results: Six patients (2 men, mean age of 66 ± 16 years), with documented prolonged asystole on electrocardiogram (ECG) in association with TLE, were followed for an average of 19.7 (range, 2-37) years; a pacemaker had been implanted in 4 of 6 patients, whereas 2 patients underwent long-term ECG monitoring with an implantable loop recorder (ILR). The longest documented IA pause lasted 12.6 ± 6.2 seconds (range: 3.5-20 seconds). All patients were treated with AEDs. During follow-up, after optimization of AED dosing, none of the patients had T-LOC spells or detected epileptic seizure episodes. During regular device interrogation, there was no evidence of pacing interventions (cumulative ventricular pacing, 0%) in the 4 pacemaker patients, and no symptomatic bradyarrhythmias in the 2 ILR patients.

Conclusions: AED therapy was effective to prevent IA in this cohort of TLE patients with prior IA. Consequently, pacemaker implantation is not immediately indicated for IA prevention, but should be reserved for those cases in which there is documented failure of AED therapy.

p0824
LEVETRACETAM MODIFIES QUANTITATIVE EEG IN EPILEPTIC PATIENTS SHOWING PSYCHIATRIC MANIFESTATIONS
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Purpose: Levetiracetam (LEV) is a widely used second generation antiepileptic drug. It was documented that LEV may induce psychotic disorders, depression, and paroxysmal non-epileptic seizures (PNES). Forced normalization has been hypothesized at the basis of psychiatric symptoms occurring after LEV use. Moreover, LEV significantly reduces epileptiform discharges in epileptic patients and increases the
frontal theta bands in healthy volunteers. This study aimed at evaluating the quantitative EEG changes in a group of epileptic patients who discontinued LEV due to the appearance of psychiatric adverse events, although the significant seizure reduction.

**Method:** We retrospectively evaluated a group of seven epileptic patients visited at our centre from October 2015, who started LEV as monotherapy. We considered for the quantitative analysis the EEG performed before starting treatment in the diagnostic workup and the EEG performed at the follow-up visit, when psychiatric events were reported.

**Results:** Seven patients under LEV monotherapy (range 1000-2000 mg/day) were evaluated (1M2F, aged 18-57). At follow-up, 4 patients (1M2F) showed depressive symptoms, 2 patients (2F) reported aggressiveness, and 1 patient presented PNES (1F). All patients were seizure free. Comparing the quantitative EEG analysis we observed the reduction in the beta1 band in the anterior cortical regions in all patients (Fp1, Fp2, F3, F4, F7, F8, Fz, C3, C4, Cz). No other significant quantitative EEG changes were observed in the other bands and/or cortical regions.

**Conclusions:** This report suggested that forced normalization may be the cause of psychiatric symptoms in epileptic patients treated by LEV. We documented in all patients the pathological slowing of quantitative EEG in the anterior cortical regions, which may underlie the dysfunction of the frontal cortex in patients showing psychiatric adverse events due to LEV. Hence, we supposed that LEV may induce psychiatric symptoms in epileptic patients by altering the frontal networks.

**p0825**

**EVALUATION OF COGNITIVE FUNCTIONS AND DIFFUSION TENSOR MRI IN PATIENTS WITH JUVENILE MYOCLOLIC EPILEPSY**

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**Background:** Frontal lobe dysfunction in juvenile myoclonic epilepsy (JME) patients has been reported with significant impairment on tests of frontal functioning.

**Purpose:** To study the cognitive performance and its relation with the clinical and neuroanatomical/neurophysiological abnormalities in JME patients.

**Methods:** Fifty patients with JME and a sample of healthy controls were assessed using a series of neuropsychological tests as well as diffusion tensor imaging MRI (DTI), tractography and electroencephalography. DTI measures assessed fractional anisotropy within the white matter.

**Results:** Cognitive testing showed subtle dysfunction in verbal learning and memory, phonemic and semantic fluency, attention, speed and mental flexibility in JME patients compared to healthy controls. We also found significant reductions in fractional anisotropy in the left anterior corpus callosum, right supplementary motor area and left anterior cingulate in JME patients.

**Conclusion:** Patients with JME had poorer cognitive performance in verbal learning and memory, attention, speed and mental flexibility, which was associated with white matter cortical/subcortical microstructural alterations.

**p0829**

**RNA-EDITED GLYCINE RECEPTORS ARE A POTENTIAL TARGET FOR ANTI-EPILEPTIC DRUGS IN TEMPORAL LOBE EPILEPSY**

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**Purpose:** Temporal lobe epilepsy (TLE) is one of the most common forms of focal epilepsy. Unfortunately, 70% of TLE patients develop pharmacoresistance and continue to suffer from seizures despite polytherapy with antiepileptic drugs. For these cases, resection of the affected brain region remains the sole therapy option. In resected brain tissue from pharmacoresistant TLE patients with a severe course of disease, expression of RNA-edited glycine receptors was shown to be elevated. C-to-U RNA editing in GlyR mRNA leads to a gain of function due to amino acid recoding, resulting in an increased affinity for glycine.

**Method:** In a corresponding knock-in animal model, these RNA-edited GlyRs facilitate glutamate release of principal neurons, leading to faster onset of epileptiform activity and possible pro-epileptic effects. In contrast, expression of these receptors in parvalbumin-positive interneurons facilitates persistence of contextual fear memory.

**Results:** We recently identified two substances that specifically block the possibly pathogenic RNA-edited GlyRs. We are currently assessing their potential antiepileptic efficacy on RNA-edited GlyR associated changes in human TLE specimen.

**Conclusion:** We propose that our research on TLE-associated modification of GlyR-coding gene transcripts can be useful for the identification of affected neuron types in intractable TLE and possibly provide new treatment options against maladaptive neuronal plasticity in TLE.

**p0830**

**SPATIAL – TEMPORAL CHARACTERISTICS OF THALAMO-CORTICAL OSCILLATIONS AFTER UNILATERAL CORtical SPREADING DEPRESSION IN THE RECOVERY PERIOD IN WAG/RIJ RATS**

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**Purpose:** To investigate cortical pattern and incidence of thalamo-cortical oscillations after transient unilateral physiological cortical inactivation in WAG/Rij rats.

**Method:** A single unilateral cortical spreading depression (SD) was used as a temporal functional inactivation of the cortex by injection of 5% KCl in the occipital cortex of awake WAG/Rij rats (n = 12), control rats received sham microinjections. Rats were equipped with six recording stainless-steel electrodes placed bilaterally over the frontal, somatosensory and parietal cortex. EEG was recorded for one hour before, immediately after, and 24 hours after SD initiation. The successful induction of SD in cortex was verified by spectral analysis of EEG based on a brief slumber of gamma-activity.

**Results:** A significant (p < 0.01) increase in number and mean duration of sleep spindles (SS), spike-wave spindles (SW spindles) and decrease in SWDs in both hemispheres was found in the hour after unilateral single cortical SD. Unilateral SS, SW spindles and SWDs reappeared first in the contralateral somatosensory cortex. SS and SW spindles were also quicker to return than SWDs in the contralateral hemisphere. Bilateral SWDs, SS and SW spindles reappeared later than unilateral SWDs, SS and SW spindles in the same chronological order as in the contralateral hemisphere. Next day all oscillations returned to baseline except SW spindles.
**Conclusion:** Transient changes of functional state even in one hemisphere lead to a suppression of non-convulsive epileptic activity in both hemispheres. This suggests that a functional integrity of interhemispheric cortico-cortical and cortico-thalamo-cortical network for generation of bilateral occurring SWDs is necessary. The appearance of first SWDs in the somatosensory cortex confirms the crucial role of the somatosensory cortex in generation of SWDs. The fast return of sleep spindles might be due to their thalamic origin and that in contrast to SWDs, a complete intact cortex is not a requirement for their presence.

**Purpose:** Changes in platelet-derived growth factor receptor beta expression have been associated to pathophysiological cerebrovascular functions, with a link to pericyte modifications. Perivascular PDGFRβ+ pericyte reactivity was observed in human temporal lobe epilepsy. We asked whether changes in PDGFRα+ cells spatially and temporally match the archetypical parenchymal and perivascular inflammatory response occurring during seizures.

**Method:** We used intra-peritoneal (i.p.) or intra-hippocampal (i.h.) kainic acid (KA) injections in mice to induce status epilepticus (SE) and epileptogenesis, as monitored by video-EEG. Animals were processed at 24 h, 72 h, 1 week after SE (i.p KA) or focal hippocampal seizures (i.h. KA), and during spontaneous EEG activity (i.h. KA: 6-8 weeks).

**Results:** Perivascular PDGFRβ+ reactivity was increased in the hippocampal 72 hours and 1 week after seizures induction. The latter topographically coincided with pockets of IsoB4/IBA1/GFAP inflammation. Z-plane morphological reconstruction indicated PDGFRβ+ vascular reactivity at the pericyte level. PDGFRα+ cells were increased, suggesting an oligodendrocyte response concerted with PDGFRα+ cells. We identified perivascular and parenchymal PDGFRβ+ double positive cells, parallelized by two discrete cell populations in the parenchyma. Accordingly, in vitro epileptiform activity induced PDGFRα+ reactivity proximal to RECA-1+ vessels, with KA exerting greater changes linked to inflammatory changes. The effect of PDGFR activation (PDGF-BB) and inhibition (Imatinib) on perivascular cell remodeling was determined.

**Conclusion:** Our results support PDGFRβ+ pericytes and oligodendrocytes as participants to the inflammatory and vascular remodeling during seizure progression. The possibility of modulating PDGFR signaling to modify these changes is offered.

**Purpose:** Dystonia is closely tied to dysfunction in both the basal ganglia and cerebellum. Recent work has shown that perfusion of ouabain, a selective blocker of the alpha-3 isoform of the NaK-ATPase, into the cerebellar cortex is sufficient to induce dystonia in mice. Cerebellar Purkinje cells (PCs) exclusively express the alpha-3 isoform of the NaK-ATPase, making them particularly sensitive to mutations in the ATP1A3 gene. While not considered sufficient to be the major cause of dystonia, cell death in the cerebellar cortex has been found in one alpha-3 knockdown model of dystonia. This study investigated whether dystonia in a knock-in (E815K) mouse model of Alternating Hemiplegia of Childhood (AHC), which manifests prominent dystonia and is associated with ATP1A3 dysfunction, could result from cerebellar PC loss.

**Method:** Mouse brains were extracted, sectioned, and immunostained using GAD67 to identify GABAergic cells. PCs were identified by stain quality, morphology, and location. Cell numbers were quantified using stereological analysis in the cerebellar vermis and each of the cerebellar hemispheres. Mean cell counts were then compared using Student’s t-test.

**Results:** Vermis PC counts did not show a significant difference between heterozygous E815K mice (HET, N = 4) and wild type littermate controls (WT, N = 4), (12379 ± 3855 vs 112119 ± 18722, p = 0.60543). Similarly, the cerebellar hemispheres, when considered together, showed no significant differences in PC numbers between HET and WT (132886 ± 32817 vs 117176 ± 20214, p = 0.46116). Comparing the hemispheres separately as well as total PC number between HET and WT also yielded no significant results.

**Conclusion:** These results indicate that the pathophysiology in dystonia in the model does not involve reduction in cells in the cerebellar cortex. This is reason to investigate PC physiology as well as other cell types as explanations for dystonia in the E815K model.

**Purpose:** Seizure control remains a clinical issue in 1/3 of the epileptic patients. Variations between anti-epileptic drug plasma levels and efficacy can be observed. We propose the hypothesis that epileptogenesis is sufficient to install changes in brain and hepatic metabolic enzymes (Cyp) expression. We propose the corollary hypothesis that seizure activity impacts the expression of specific nuclear receptors (NR) known to be master controllers of Cyp levels.

**Method:** Cyp and NR expression was determined in two experimental models of seizures, i.e., intra-peritoneal (i.p.) and intra-hippocampal (i.h.) kainic acid (KA) injections in mice inducing status epilepticus and spontaneous chronic seizures monitored using video-EEG. Mice were anesthetized at 24 h, 72 h and 1 week after i.p. or i.h. KA, while chronic epileptic animals were obtained 6-8 weeks after i.h. KA. Hepatic and brain areas were snap frozen for qPCR and Western blot analysis, while additional animals were processed for immunohistochemistry.

**Results:** We found increased hepatic and brain expression of Cyp3a11, Cyp3a13 and Cyp2e1 in chronic epileptic animals. These enzymes are known to metabolize a number of anti-epileptic drugs. Interestingly, acute SE or partial seizures were associated with a decreased Cyp and NR112 or NR113 expression in the liver.

**Conclusion:** Our results indicate dynamic changes of key metabolic enzymes during epileptogenesis in the liver and brain. The functional relevance to drug bio-distribution and resistance is under examination.
Abstracts

p0836 CHANGES IN MICROSEIZURE PROPERTIES ANTICIPATE SEIZURE CLUSTERS IN TETANUS TOXIN MODEL OF TEMPORAL LOBE EPILEPSY

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Purpose: The long-term fluctuations in seizure probability are well documented in both patients and various models of epilepsy. The most frequently observed type of the fluctuation is a seizure clustering. In this study, we show that specific changes in parameters of short seizure-like EEG events (microseizures) anticipate the onset of the clusters.  

Method: TLE was induced in six adult rats by injection of 10 ng of tetanus toxin into the right dorsal hippocampus. Then, the animals were implanted with recording electrodes in the hippocampi and motor cortices. The animals were video-EEG monitored for three weeks. Microseizures were detected using a custom-made detector and its detections were visually confirmed. The inter-cluster periods were equally divided into 5 time segments in which the following parameters of microseizures were analyzed: rate, duration, signal power and cross-correlation between channels.  

Results: In total 6560 microseizures from 6 inter-cluster periods were analyzed. Microseizure rate gradually increased from 99 ± 42 events in the first segment to 305 ± 37 in the fifth segment. Signal power increased from 5.7 ± 0.6 to 6.9 ± 0.9 mV²/s and mean cross-correlation coefficient between channels increased from 0.48 ± 0.02 to 0.62 ± 0.02. Average duration initially decreased, and from the third to the fifth segment it increased from 0.53 ± 0.05 to 1.01 ± 0.09 s. Each parameter in each rat was fitted by a straight line. Slopes of the lines were significantly different (Wilcoxon signed rank test, p < 0.05).  

Conclusion: This study demonstrates that changes in the brain dynamics precede seizure clusters. Initiation of the cluster is not a sudden process but is preceded by an increase in several parameters of microseizures. These results may have implications for understanding of long-term seizure dynamics and mechanisms responsible for seizure clustering.  

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p0837 EFFECT OF SODIUM BROMIDE ON GABAERGIC TRANSMISSION, SYNAPTIC PLASTICITY AND PILOCARPINE-INDUCED SEIZURES

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Purpose: Bromide, even though it has been supplanted by more recent drug developments, is an effective drug for the treatment of refractory epilepsy in pediatric patients, often used as last-line drug. Its mechanism of action is still under debate and our study aims to clarify this issue.  

Method: We tested the effect of sodium bromide in chronically epileptic rats following a pilocarpine-induced status epilepticus using field and intracellular recordings in hippocampal slices to gauge synaptic plasticity (long-term potentiation; LTP), GABAergic responses and membrane properties, as well as behavioural analyses (video monitoring) to quantify seizures.  

Results: Acute application of sodium bromide to hippocampal slices from control and epileptic animals evoked no effect on long-term potentiation (LTP). Moreover, intracellular recordings with sharp microelectrodes from CA1-neurons failed to detect changes in active and passive membrane properties. Furthermore, GABA-A receptor mediated inhibitory post-synaptic potentials and GABA-A receptor reversal potential were equally unaffected by acute application of sodium bromide. We next tested chronic sodium bromide treatment using osmotic pumps inserted subcutaneously during the late phase of epileptogenesis. In marked contrast to the acute bromide application, chronic sodium bromide treatment significantly reduced generalised seizures in epileptic rats. Intriguingly, chronic sodium bromide application was accompanied by a decreased LTP level in slices from pilocarpine treated rats, while this therapy had no effect on LTP in saline treated animals.  

Conclusion: These results indicate that chronic treatment with bromide is an effective anticonvulsant therapy in the pilocarpine model of epilepsy. However, the therapeutic effect of sodium bromide cannot be explained by acute effects on GABAergic transmission or synaptic plasticity. Rather, chronic effects seem to be required for antiseizure efficacy, but the underlying mechanisms during chronic treatment await further investigation.

p0838 CX3CR1 MODULATION ALTERS SYNAPTIC INTEGRATION OF ADULT BORN HIPPOCAMPAL NEURONS FOLLOWING AN EPILEPTOGENIC INSULT

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The fractalkine-CX3CR1 pathway has been shown to regulate neurogenesis in the dentate gyrus (DG). In temporal lobe epilepsy neuronal proliferation in the hippocampus is frequently described and microglia activation is associated with a reduced survival of new adult born neurons. If a reduced inflammatory environment, by CX3CR1 modulation, will alter the synaptic integration of these neurons remains to be studied. These mechanisms might be important in driving hippocampal hyperexcitability after epileptogenic injury and may be targeted for therapeutic intervention. Thus, we investigated the expression of synaptic proteins in neurons born in an acute epileptic environment with an altered neuroinflammatory milieu.  

Adult male rats were implanted with electrodes in the right hippocampus and a brain infusion cannula in the lateral ventricles. Following 1w of recovery temporal status epilepticus (SE) was electrically induced in the hippocampus. Seven days following SE, rats were injected with retroviral vector expressing GFP. Immediately after, brain infusion cannulas were connected with osmotic pumps carrying either anti-CX3CR1 antibody (ab) or vehicle.  

7w following SE, morphological evaluations revealed changes in dendritic morphology with reduced medial dendrites in SE-CX3CR1 rats. Seizure-induced microglia activation was also reduced in the hilus in SE-CX3CR1 animals. Although no changes in the expression of scaffolding proteins ( gephyrin ) and adhesion molecules (NL-2) were detected at inhibitory synapses, there was a strong reduction of scaffolding proteins at excitatory synapses in treated rats. PSD-95 cluster density was decreased in the molecular layer of the DG. No changes were observed in the excitatory adhesion molecule NL-1.  

Here we show a role of fractalkine-CX3CR1 pathway in mediating neuroinflammation on synaptic integration of neurons born in an epileptic environment, confirmed by altered morphological profiles and altered expression of synaptic scaffolding proteins. Future studies need to investigate whether an altered neuroinflammatory environment leads to differences in chronic seizure burden in these animals.

p0839 SELECTIVE, UNILATERAL ABLATION OF HIPPOCAMPAL INTERNEURONS CAUSES ACUTE SEIZURES

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Purpose: The death of GABAergic interneurons has long been hypothesized to contribute importantly to acquired epilepsy. Pharmacological
treatments that block GABA-mediated inhibition produce seizures in normal brain, and evidence from animal models and humans suggests interneuron death often occurs in acquired epilepsy. However, relatively little is known about whether interneuron lesions alone can cause spontaneous recurrent seizures (SRSs, i.e., epilepsy). These experiments aimed to test the hypothesis that focal death of interneurons can cause chronic epilepsy.

**Method:** Gad2-ires-Cre mice were injected unilaterally in the CA1 area of the dorsal hippocampus with an adenovirus-associated virus (AAV) containing the diphtheria toxin receptor (DTR) to selectively ablate interneurons. Simultaneously, an electrode, connected to a miniature telemetry device, was positioned at the injection site for chronic recordings.

**Results:** Two weeks after virus transfection, intraperitoneal injection of diphtheria toxin (DT) caused focal ablation of interneurons (confirmed with immunohistochemistry). Whole cell recordings from CA1 pyramidal cells in ex vivo slices showed that the frequency of miniature inhibitory post-synaptic currents was reduced. Long-term, continuous monitoring revealed that all mice with focal, DT-induced interneuron lesions had SRSs after DT treatment. Sham-control animals had no detectable seizures. The onset of the SRSs was 3-5 days after DT treatment, and for 5 of 6 mice the seizures stopped within several days (in one animal the seizures persisted for at least 34 days post-DT).

**Conclusion:** These data show that selective interneuron ablation can cause SRSs (and not status epilepticus), which appear to have no latent period and generally undergo remission.

**p0840**

**KCNQ1 GENE EXPRESSION IN EPILEPTIC RATS**

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**Purpose:** KCNQ1 gene exhibits expression in heart as well as in brain, in multiple regions including the hippocampus. The aim of our study is to investigate changes in KCNQ1 gene expression both in brain and heart of rats, at different stages of epileptogenesis (latent period, early chronic and late chronic periods), following Status Epilepticus (SE).

**Method:** Lithium-pilocarpine model was used in order to provoke SE in Sprague-Dawley rats. To determine whether expression of KCNQ1 gene is modified at critical stages of epileptogenesis, our study was developed as follows:

1. Five latent period rats (10 days following SE) and 2 controls.
2. Five early chronic epileptogenesis period rats (1 month following SE) and 2 controls.
3. Five late chronic epileptogenesis period rats (2 months following SE) and 2 controls. Total RNA was isolated from hippocampus and heart. Relative changes in gene expression were assessed by quantitative RT-PCR analysis by delta-delta CT method.

**Results:** No differences in the gene expression levels in the heart was found at different stages of epileptogenesis. In the hippocampus, our analysis revealed a significant change in gene expression at the different stages of epileptogenesis. A significant down-regulation was detected at 10 days following SE. Gene expression was up-regulated at 1 month following SE. These findings suggest that the seizure-related changes in gene expression exhibit different patterns that may indicate dynamic reorganization of molecular machinery accompanying structural and functional modifications in epilepsy.

**p0841**

**DOES EARLY-LIFE KINDLING AFFECT THE CHARACTERISTICS OF SWDS IN ADULTHOOD IN RATS WITH GENETIC ABSENCE EPILEPSY?**

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**Purpose:** Genetic Absence Epilepsy Rats from Strasbourg (GAERS) show a resistance to secondary generalization of focal limbic seizures evoked by kindling. These findings indicate a mutual interaction between the limbic seizure circuits and the networks involved in absence epilepsy. In present study, we investigated whether early-life kindling may alter the characteristics and occurrence of spike-and-wave discharges (SWDs) of GAERS in adulthood.

**Method:** Stimulation electrodes were stereotactically implanted into basolateral amygdala and recording electrodes were implanted on the cortices of male GAERS at PN20. After a short recovery period, rat pups in kindling-GAERS group were stimulated until they achieved three stage 5 seizures using fast kindling protocol. Sham-GAERS group did not receive any stimulation. The rats in both groups were allowed to grow until PN75 then the EEG was recorded to analyze SWDs.

**Results:** The mean duration of the SWDs was calculated as the ratio of the cumulative total duration to the number of SWDs over 3-hours period. The cumulative total duration of SWDs decreased in the kindling-GAERS group compared to sham-GAERS group (p < 0.05). The spectral characteristics of first 2 seconds of SWDs were analyzed by computing the power spectra using the Fast Fourier Transform. The peak frequency of SWDs were faster in kindling-GAERS rats than the sham-GAERS group (7.75 ± 0.25 vs. 7.5 ± 0.158 Hz).

**Conclusion:** These findings support the evidence that indicate a mutual interaction between the limbic circuits and the cortico-thalamo-cortical networks involved in absence epilepsy.

**p0843**

**RESVERATROL ATTENUATES OXIDATIVE STRESS AND MITOCHONDRIAL DYSFUNCTION IN IMMATURE BRAIN DURING EPILEPTOGENESIS**

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**Purpose:** We have demonstrated recently existence of oxidative stress and mitochondrial dysfunction in immature brain during the period of epileptogenesis. The aim of the present study was to evaluate potential protective effect of natural polyphenol resveratrol.

**Method:** Status epilepticus (SE) was induced in immature 12-day-old rats by Li-pilocarpine and at selected periods of early epileptogenesis (up to 5 weeks) rat pups were subjected to examinations. Dihydroethidium (Het) method was used for detection of superoxide anion production in brain in situ. Mitochondrial function was evaluated by measuring activity of respiratory chain complex I in isolated mitochondria. Oxidative damage of mitochondrial proteins was assessed by immunoblot analyses of 3-nitrotyrosine (3-NT) and 4-hydroxynonenal (4-HNE). Resveratrol was given i.p. at selected time points both before and after the induction of SE.

**Results:** Increased levels of superoxide anion in all the studied structures (CA1, CA3, dentate granule, cerebral cortex and thalamus), a marked decrease of complex I activity and the increased levels of 3-NT and 4-HNE persisted during the whole period of epileptogenesis studied. Resveratrol either completely prevented or significantly reduced markers both of oxidative stress and mitochondrial dysfunction.
Conclusion: The present findings suggest that compounds with antioxidant properties or ability to promote endogenous antioxidant defence, combined with conventional therapies, could provide a beneficial effect in the treatment of epilepsy.

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p0846
CHARACTERISING EEG CORTICAL DYNAMICS AND CONNECTIVITY WITH RESPONSES TO SINGLE PULSE ELECTRICAL STIMULATION (SPES)
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Purpose: To model cortical connections as control systems in order to characterize their oscillatory behavior and role in the generation of spontaneous electroencephalogram (EEG).

Method: We studied averaged responses to single pulse electrical stimulation (SPES) from the non-epileptogenic hemisphere of five patients assessed with intracranial EEG who became seizure free after contralateral temporal lobectomy. Second order control system equations were modified to characterize the systems generating a given response. SPES responses were modelled as responses to a unit step input. EEG power spectrum was calculated on the 20 seconds preceding SPES.

Results: 121 channels showed responses to thirty-two stimulation sites. A single control system could model the response in 41.3% and two systems were required in 58.7%. Peaks in the frequency response of the models tended to occur within the frequency range of most activity on the spontaneous EEG. Discrepancies were noted between activity predicted by models and activity recorded in the spontaneous EEG. These discrepancies could be explained by the existence of alpha rhythm or interictal epileptiform discharges.

Conclusion: Cortical interactions shown by SPES can be described as control systems which can predict cortical oscillatory behaviour. The method is unique as it describes connectivity as well as dynamic interactions.

p0850
ABERRANT CONNECTIVITY OF HIPPOCAMPAL MOSSY FIBERS IN TEMPORAL LOBE EPILEPSY
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Purpose: The pathoanatomical correlate of temporal lobe epilepsy is hippocampal sclerosis, characterized by a selective neuronal death of mossy cells in the hilus and of pyramidal cells in CA1. Granule cells survive, but loose mossy cell as targets and redirect their axons, the mossy fibers, backwards into the granule cell layer. It has been assumed that this leads to excitatory circuits. Therefore we examined, whether sprouted mossy fibers impinge only excitatory granule cells or also inhibitory interneurons, such as basket cells, which might have survived the neuronal death.

Method: Resected hippocampal specimens of patients with hippocampal sclerosis were compared with controls of patients with extrahippocampal lesions with only mild sclerosis. Mossy fibers were traced with neurobiotin or labeled against synaptophysin, inhibitory interneurons against parvalbumin. Synapses were examined with electron microscopy, labeled in addition with post-embedding GABA-immunogold.

Results: Sprouted mossy fibers of epileptic hippocampi innervate not only excitatory granule cells but also inhibitory parvalbuminergic interneurons. The axonal plexus of inhibitory interneurons, which surrounds the granule cells, is still preserved despite neuronal death in hippocampal sclerosis. Connections of sprouted mossy fibers and inhibitory axon terminals were quantified, showing that the number of inhibitory axon terminals exceeds significantly the number of sprouted excitatory mossy fiber terminals.

Conclusion: This aberrant connectivity might lead to an increased inhibition and synchronization of granule cells because the preserved inhibitory interneurons show an additional innervation through sprouted mossy fibers. This results in instability of a previously balanced network.

p0852
HIGH FREQUENCY OSCILLATIONS DETECTED BY AUTOMATIC KURTOSIS-BASED TIME-FREQUENCY ANALYSIS IN MEG AND INTRACRANIAL EEG IN PAEDIATRIC EPILEPSY
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Purpose: High frequency oscillations (HFOs) in epilepsy have been proposed as electrophysiological biomarkers for localising the seizure onset zone (SOZ). We present an automated approach to detecting HFOs non-invasively in MEG recordings in a group of paediatric patients with refractory epilepsy. HFO detection was validated against intracranial EEG recordings in the same group of patients.

Method: MEG and intracranial EEG data were acquired on six paediatric patients (4 male; mean age 16 years) from Birmingham Children’s Hospital during presurgical evaluation. Atlas-guided beamformer source reconstruction was performed on the filtered (80-250 Hz) MEG data using the automatic anatomical labelling atlas (AAL) to produce time series (virtual electrodes) for 90 regions of interest across the entire brain. An automatic HFO detection algorithm based on the preliminary selection of informative channels by means of kurtosis and time-frequency analysis was applied to the data.

Results: HFOs were detected in the intracranial EEG (iEEG) data of all 6 patients. The source locations of the HFOs identified in iEEG data corresponded with the SOZ with 66% sensitivity and 91% specificity across the 6 patients. HFOs were identified in the MEG virtual electrodes in 5/6 patients, which represents 83% concordance between modalities, and the sources of HFOs coincided with the SOZ at the sub-lobe level.

Conclusion: These results show good concordance between the source locations of HFOs detected in non-invasive MEG data and those identified in intracranial recordings, which were in close proximity to the SOZ. The non-invasive localisation of HFOs using MEG could prove a useful addition to surgical planning in paediatric patients with epilepsy.

p0853
EXPLORING CARDIAC AUTONOMIC FUNCTIONS IN EATING EPILEPSY
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Purpose: Reflex epilepsies are known to be associated with autonomic dysfunction. While this has been characterized in few reflex epilepsies, currently there does not seem to be information of cardiac autonomic function in eating epilepsy. The current study explored possible alteration in cardiac autonomic function parameters in patients of eating epilepsy.

Methods: The study protocol was approved by the Institute Ethics Committee and informed consent was obtained from the participants. Drug naive eating epilepsy patients (n = 10, mean age 24.9 ± 4.51 yrs, male: female 6:4) were recruited from the Neurology Out-patient Department, NIMHANS, India. Age and gender matched healthy volunteers are recruited as controls (n = 20, mean age 20.08 ± 6.04 yrs, male/female 14:6). Resting Heart rate was obtained from continuous Lead II ECG recording for 15 min using Power Lab (AD Instruments, Australia) and Blood pressure was recorded using Finometer (Finapres Medical Systems, The Netherlands). Data was analysed offline to obtain time and frequency domain parameters of Heart Rate variability(HRV) and Blood Pressure Variability (BPV). Baroreflex sensitivity (BRS) was determined by spectral and sequence methods. Mann Whitney U test was used for comparing between the groups; significance was set at p < 0.05.

Results: Significant dysfunction was evidenced in most of the autonomic function parameters in the eating epilepsy patients when compared with controls. In the HRV parameters, parasympathetic activity (Up BRS = 35, Total BRS = 28). The overt cardiovascular autonomic dysfunction observed here may be evidence for other pathways for triggering seizures while eating in these patients in addition to just gastrointestinal activity.

Conclusion: This study probably can further explain why the mesial temporal lobe discharges prefer to propagate to contralateral mesial temporal structures and bilateral neocortical temporal regions.

References:
2. doi: 10.1111/epi.13944

p0859

MULTILOBAR EPILEPTOGENIC ZONES BUT MOTOR AREA: MOSES’S MOTOR AREA SKIPPING PATHOLOGICAL HFO

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Purpose: Subtotal hemispherectomy is characterized by resection of multiple-lobes skipping motor area (MA). We determined the epileptogenicity using occurrence rate (OR) of high frequency oscillations (HFO) and modulation index (MI) demonstrating strength of coupling between HFO and slow wave. We hypothesized that epileptogenicity increased over the multiple-lobes but skipping MA.

Method: We analyzed 23 children(subtotal hemispherectomy, 14; multi-lobe resections, 9). Scalp video-EEG and magnetoencephalography were performed before surgery. We analyzed OR(HFO) and MI(5-phase=0.5-8 Hz) on electrodes of total, resection areas and MA. We divided good (ILAE I) vs. poor (II-VI) seizure outcome groups.

Results: ILAE Class Ia outcome was achieved in 18 children. Among MI(5-phase slow waves, in the resection areas, MI(HFO & 3-4 Hz) was the highest. OR(HFO) and MI(HFO & 3-4 Hz) in both total area and resection areas were significantly higher of good seizure outcome group than those of poor group. OR(HFO) and MI(HFO & 3-4 Hz) in resection areas were significantly higher than those of MA.

Conclusion: Our patient cohort with subtotal hemispherectomy showed evidence of multifocal epileptogenicity specifically skipping MA, as if Moses parted the sea of pathological HFO. This is the first study demonstrating the electrophysiological phenotype of multifocal epilepsy specifically skipping MA, using OR(HFO) and MI(HFO & 3-4 Hz).

p0861

EVENT-RELATED POTENTIALS IN TEMPORAL LOBE EPILEPSY WITH AND WITHOUT HIPPOCAMPAL SCLEROSIS

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Purpose: To investigate the role of event-related potentials in patients suffering from temporal lobe epilepsy with and without hippocampal sclerosis.

Methods: Fourteen patients (6 men and 8 women; mean age: 35.5 years old) suffering from temporal lobe epilepsy with hippocampal sclerosis (TLE-HS) and eleven non-lesional temporal lobe epilepsy (TLE-NL) patients (6 men and 5 women; mean age: 37.1 years old) enrolled in the...
study. P300 was elicited using an auditory two-stimulus oddball paradigm and MMN was elicited using a passive oddball paradigm. The peak latency and amplitude of P300 measured at Pz and the latency and amplitude of MMN measured at Cz.

**Results:** These two groups did not differ significantly in mean age and sex. TLE-HS had a significantly longer duration of epilepsy (14.8 ± 11.1 vs 4.5 ± 4.2 years, p < 0.01), and frequent seizure attacks (29.5/year vs 3.4/year, p < 0.01). The average number of AED was significantly larger in TLE-HS (2.6 ± 1.0) than that of TLE-NL (1.5 ± 0.6, p < 0.01). Among ERP variables, the amplitude of P300 was significantly lower in TLE-HS patients (11.4 ± 5.4 uV) than in TLE-NL patients (16.1 ± 3.5 uV, p < 0.01). Subsequent ANCOVA showed significant P300 amplitude differences even after adjusting for age, duration of epilepsy and seizure frequencies. There was no additive meaningful difference between two groups in the other variables.

**Conclusion:** The scalp-recorded auditory ERPs of patients with TLE varied among studies due to different selective criteria of the methods. A previous study, using intracranial EEG, demonstrated that limbic P300 potentials were selectively reduced by HS compared to other epileptogenic lesions of the temporal lobe. From our results, we might infer that the presence of HS is a major independent precipitate factor for abnormal amplitude of P300 in the TLE patients. Future studies should focus on the association of these P300 with cognition in such patients.

**p0862**

**ALTERNATIVE SEIZURE PROVOKING TECHNIQUES AT THE EPILEPSY MONITORING UNIT**

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**Purpose:** Provocation may be of particular value in patients who have infrequent seizures and would otherwise be unsuitable for telemetry. Routine photic and hyperventilation stimuli are the most common activating procedures. Stress in general and in some cases simple suggestion are very important provoking factor for both epileptic seizures (ES) and psychogenic non epileptic seizures (PNES), as well. In patients with reflex epilepsy, seizure can be elicited by simple or complex triggers. Little is known so far about the evalubility of cognitive stimulation techniques as a seizure provoking technique.

**Methods:** We reviewed the long term video-EEG-recordings at the EMU of the Danish Epilepsy Centre in 2016, selecting patient who underwent a tailored protocol of intensive cognitive and motor stimulation (CMs) as a seizure provoking technique. We evaluated whether CMs (1) was time related with the appearance of a clinical event (ES or PNES) (2) the time latency between CMs the clinical event.

**Results:** 235 patients have been monitored and 45 (31 females, 14 males) of them underwent CMs during the recordings. Patient’s age ranged from 10 - 68 years. Twenty-one patients did not present clinical manifestation in relation to CMs, whilst 24/45 subjects (53%) had one or more typical clinical event (9 had PNES, 15 ES) during or short after stimulation. PNES were typically recorded during (5/9) or short after CMs. Patients with ES in relation to CMs had often a focus involving the temporal region (9/15 patients); the seizure in most cases came (12/15 patients) a few hours after CMs.

**Conclusion:** Cognitive and motor stimulation during intensive video-EEG-monitoring seems to be a valuable non-invasive instrument for the provocation of both epileptic and non-epileptic seizures. On the base of our preliminary data, we estimate we were likely able to reduce the need for prolonged recordings in about one-half of patients.

**p0864**

**INVASIVE AND SCALP EEG IN PRESURGICAL EVALUATION OF MR NEGATIVE DRUG RESISTANT EPILEPSY**

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**Purpose:** To evaluate seizure outcomes in surgically treated patients with magnetic resonance (MR) negative drug-resistant epilepsy who underwent invasive and noninvasive presurgical EEG.

**Method:** Study includes 47 patients with drug-resistant epilepsy without any abnormalities on brain MRI. Patient population was divided to 2 groups. In 17 patients (31%) localization of epileptogenic zone was confirmed by ictal scalp EEG. Invasive EEG (iEEG) monitoring was performed in 30 patients (69%). Both subdural strips and depth electrodes was used. In cases of equivocal ictal epileptiform activity and bilateral electrographic seizure onset iEEG was performed. The patients underwent resective surgery between 01.01.2014 and 01.02.2017. 32 patients were followed up at 12 months after surgery; 9 and 23 patients from scalp and iEEG group respectively. Surgical outcomes, complication rate, MRI results were analyzed in both groups.

**Results:** Temporal lobe epilepsy was diagnosed in 32 (68%) patients, generalized forms - 2 (6%) patients, temporal plus - 11 (23%) patients, partial form - 2 (6%) patient. Average duration of EEG monitoring was 100.42 ± 40.7 hours. In iEEG group 14 patients (61%) became seizure free: 9 patients (39%) - Engel Ia, 5 (22%) - Engel Ib. 7 patients (30%) had Engel II. The unsatisfactory results of treatment were noted at 2 patients (9%) - Engel IVA. Burr hole liquortheria and hemorrhagic impregnation after depth electrode implantation was noted in 5 patients (16%).

In scalp EEG group 6 patients (66%) became seizure free (Engel Ia). 2 patients (11%) had Engel Iib. The unsatisfactory results of treatment were noted at 2 patients (22%) - Engel IIIb and IVa respectively.

**Conclusion:** Scalp EEG in presurgical evaluation of MR negative drug resistant epilepsy showed comparative results with invasive EEG in selected patients with clear clinical and electrographic seizure onset. Invasive EEG monitoring showed low complication rate with good surgical outcome.

**p0868**

**DIFFERENTIAL REACTIVITY OF HFOS TO COGNITIVE STIMULATION WITHIN EPILEPTIC AND NON-EPILEPTIC HIPPOCAMPUS**

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**Purpose:** In the present study, we aimed to investigate deep EEG recordings and to focus on the effect of cognitive stimulation on interictal high frequency oscillations (HFOs) within epileptic (EH) and non-epileptic (NH) hippocampi. We hypothesized differential reactivity of ripples and fast ripples (including their characteristics) to cognitive stimulation within EH and NH.

**Method:** We analyzed stereo-electroencephalography (SEEG) data from 13 patients with drug resistant focal epilepsy, in whom hippocampal activity was recorded during quiet wakefulness and subsequently during a simple cognitive task. Automated detection was used to detect HFOs.
The characteristics (especially rate, relative amplitude, spectral entropy and duration) of HFOs were statistically compared separately in ripple (R; 80-250 Hz) and fast ripple (FR; 250-600 Hz) range.

**Results:** HFOs were significantly more frequent, shorter with higher relative amplitude and spectral entropy in EH than in the NH. Compared to quiet wakefulness we observed a significant reduction of R and FR rate during cognitive stimulation in EH, moreover, R rate was lower also in NH. During cognitive stimulation the relative amplitude and entropy of HFOs were lower and higher respectively in both EH and NH in comparison with wakefulness period.

**Conclusion:** Various HFO parameters differ in epileptic and non-epileptic hippocampi. Our results thus point to differential reactivity especially of fast ripples to cognitive stimulation within EH and NH.

**p0869**

**PREDICTING OUTCOME IN POSTANOXIC ENCEPHALOPATHY: A QUANTITATIVE MODEL-BASED APPROACH (EEG STATE SPACE ANALYSIS)**

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**Purpose:** The majority of comatose patients after cardiac arrest do not regain consciousness due to severe postanoxic encephalopathy. Early and accurate outcome prediction is therefore essential in determining further therapeutic interventions. The electroencephalogram (EEG) provides a standardized and commonly available tool for measuring brain activity and has been used to determine prognosis in postanoxic patients. The identification of pathological EEG patterns with poor prognosis relies however primarily on visual EEG scoring. We introduced a model based approach of EEG analysis (state space model), that allows for a quantitative description of temporal EEG variability.

**Method:** We retrospectively analyzed standard EEG recordings in 83 comatose patients after cardiac arrest between 2005 and 2013 in the intensive care unit of the University Hospital Zurich. Neurological outcome was assessed one month after cardiac arrest using the Cerebral Performance Category. For a dynamic and quantitative EEG analysis, we implemented a model-based approach (state space analysis) to quantify EEG background variability independent from visual scoring of EEG epochs. We then compared state space velocity (i.e. a measure for spectral variability) between groups and correlated mean velocity with clinical outcome parameters and EEG patterns.

**Results:** Quantitative assessment of spectral variability (state space velocity) revealed a significant difference between patients with poor and good outcome after cardiac arrest: Lower mean velocity of temporal electrodes (T4 and T5) was significantly associated with poor prognostic outcome (p < 0.005) and correlated with visual EEG markers such as generalized periodic discharges (p < 0.02) or burst suppression pattern (p < 0.03). Receiver operating characteristic (ROC) analysis confirmed the predictive value of lower state space velocity for poor clinical outcome after cardiac arrest (AUC 80.8, 70% sensitivity, 15% false positive rate).

**Conclusion:** Model-based quantitative EEG analysis (state space analysis) provides a novel, complementary marker for prognosis in postanoxic encephalopathy.

**p0870**

**DURATION OF TACHYCARDIA IN THE POST-ICTAL PERIOD**

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**Purpose:** Continuous recording of electrocardiogram (ECG) during EEG Video Telemetry is common practice in epilepsy monitoring units (EMU). Ictal tachycardia (IT) frequently accompanies and outlasts convulsive seizures which have been identified as a risk factor for sudden unexpected death in epilepsy (SUDEP) however there is little information on the duration of heart rate changes.

The aim of this study was to determine the duration of the heart rate changes following convulsive seizures.

**Method:** We reviewed the ECG of patients recruited into a study on autonomic markers for SUDEP and who had generalised tonic-clonic seizures (GTCS). Recordings were carried out between June 2015 and January 2017 and the majority of these were Phase I or II presurgical investigations. 27 GTCS recorded in 24 patients (18 males, mean age 30.2 years). GTCS were only included if the heart rate (HR) returned to baseline prior to any subsequent seizure. Heart rate was counted over 30 s epochs. Baseline heart rate was counted 1 minute before the first change in either EEG or ECG and IT was defined as a HR >100 bpm. Onset of IT was marked, time when HR<100 bpm and time taken to return to within 10% of baseline.

**Results:** HR was >100 bpm (ictal and postictal) for an average of 52.75 minutes (1.5 mins - 4.5 hrs); peak HR was 134 ± 15.3 bpm (mean±SD). Average time to return to baseline was 153 minutes (2mins - 6 hrs). There was no clear correlation between duration of GTCS (average 116s), the clonic phase (average 38 s), pre-ictal or peak HR to explain the variation in heart rate recovery.

**Conclusion:** This study highlights the prolonged autonomic changes caused by GTCS evidenced by increased heart rate that outlast the ictal and immediate postictal period thus emphasising the importance of maintaining adequate ECG recording at all times in the EMU.

**p0871**

**DYNAMIC PROPAGATION OF INTERICTAL EPILEPTIC SPIKE OF MEDIAL TEMPORAL LOBE EPILEPSY PREDICT SEIZURE NETWORK: A MEG COMBINED WITH SEEG STUDY**

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**Background:** Medial temporal lobe epilepsy (MTLE) is stereotype of focal epilepsy, especially in adults. Interictal spikes (IIS) were recognized as the signatures of epileptogenicity, reflecting brief pathologically synchronous discharges of neuronal populations that are large enough to be manifest as voltage transients. Even IISs occur much more frequently than seizures, the propagation of IISs in MTLE through neural networks is not yet defined well.

**Purpose:** The purpose of current study is to map the epileptic network of interictal status by probing the propagation pattern of IISs in patients with MTLE using magnetoecephalography (MEG) , and to investigate the correlation between interictal and ictal epileptic network.

**Method:** Three patients with refractory MTLE and unilateral hippocampal sclerosis who underwent presurgical evaluation were studied. All the patients were performed MEG with a 306-Channel MEG system. Typical IISs of 15 min continued MEG epoch of each patient were identified by visual inspection. IISs will be further classified if there is more than one pattern based on electrographic waveforms. The initiation, propagation of representative IIS and averaged IISs (the peak of IISs were considered as zero) were tracked by using dynamic magnetic source imaging (dMSI). Since all the patients were implanted SEEG, the magnetoecephalographic pathway of IISs was further compared with intracranial recordings.

**Results:** Significantly, reproduced pathway of MEG IISs along rostral-dorsal axis of hippocampus were identified among all the patients, which is parallel with the spread of ictal discharges recorded by SEEG.
Abstracts

**Conclusion:** IISs propagation patterns are indicative of the hierarchical structure of epileptic network. Our study demonstrated the dynamic propagation of IISs could predict seizure network.

**Methods:** Analysis of infraslow EEG activity (ISA) has shown potential for spikes and waves using a novel algorithm developed in Matlab. 50 TA seizures were analyzed in different vigilance states obtained from overnight-recordings in 10 treatment naïve children (ages 4-10 yrs mean 7.65). Spikes and waves were marked independently as time events in different electrodes. Range of frequencies was measured for the two components of the spike Wave complex, in Wake and Sleep-Non Rem and Rem.

**Results:** Spike-event frequency frontally ranged from 2-45 Hz (mean 11.8 Hz wake, 15 Hz N1, 10.9 Hz N2, 10.2 Hz N3 and 11.7 Hz REM). Wave-event frequency ranged from 1.5-9 Hz (3.5 Hz wake, 2.5 Hz N1, 2.3 Hz N2, 2.3 Hz N3 and 2.5 Hz REM). At Wake spikes and waves tend to manifest themselves as complex while at Rem Sleep at least one spike precedes the wave appearance and terminate themselves one second before the end of the seizure. Time Series of Spike events are different in Wake and in Rem; their distribution is right and left skewed respectively. The more prolonged discharges were observed at N1 and wake and had two phases: during the initial part of the seizure the frequency decreased quickly from 4 to 3 Hz and slower frequency decrease with periodical fluctuations, during the second part of the seizure and a final frequency quick decrease at the end of the discharge.

**Conclusion:** Studies demonstrated substantially reduced connectivity in REM sleep when compared to wakefulness and rare TA. This investigation could elucidate possible parameters involved in the periodical frequency fluctuations of TA in different states of vigilance - and the cortico-thalamo-cortical oscillatory system involved.

**Conclusion:** Epileptic patients sometimes report experiential phenomena related to a previous dream during seizures or cortical stimulations. This has been alluded to as “déjà-rêvé” (“already dreamed”) in the literature, but no neuroscientific evidence supports its existence.

**Purpose:** Intracranial infraslow activity was concordant with the conventionally identified clinical seizures in all the recorded habitual seizures. The identified infraslow activity was concordant with the conventionally identified epileptogenic zone.

**Results:** Focal unilateral infraslow activity was identified in all the cases. The recorded lateralized/focal infraslow activity preceded the onset of the clinical seizures in all the recorded habitual seizures. The identified infraslow activity was concordant with the conventionally identified epileptogenic zone.

**Conclusion:** Focal infraslow activity can be detected prior to the onset of clinical seizures in children with drug-resistant epilepsy. Identification of focal infraslow activity (ISA) can help in determining and localizing the epileptogenic zone in patient with drug-resistant epilepsy.
long and even increasing years of epilepsy duration, despite published guidelines on early referral for epilepsy surgery. Here we analyze the database of our center, draining approximately 2/3 of the Swiss epileptic population, in order to determine if these trends are also observed.

Method: We reviewed our database between 1.4.1995 and 31.12.2016. Patients investigated for other reasons (e.g. differential diagnosis) were excluded from the study. All patients received video-EEG monitoring and structural MRI. Whenever possible, imaging included also PET, SPECT, electrical source imaging and, less frequently, EEG-fMRI. We considered only patients with at least 2 years of follow-up.

Results: A total of 826 patients underwent evaluation. 410 (56%) were operated and 99/410 (24%) were < 16 years. The duration of epilepsy decreased from 1995 to 2016 in adults (on average by 16 to 20 years), but remained stable in children (mean: 5.3 y). Patients with hippocampal sclerosis and benign tumors as epilepsy origin decreased compared to non-lesional and dysplasia cases. Complete seizure control was obtained in 71% undergoing surgery with a curative goal (47% with temporal resection). No major changes of outcome were observed over time, despite an increased number of non-temporal surgeries.

Conclusions: Our retrospective analysis confirmed stable favorable surgical outcome despite an increase in complex surgeries, similar to previous studies. There is now a strong trend to refer adult patients earlier, compared to earlier years, as a result of continuous education. It shows the benefit of national meetings in creating a strong national network and close collaboration within the neurology community.

References

p0883 AN INTERIM ANALYSIS FROM THE MULTI-SITE HOBSCOTCH REPLICA TION TRIAL


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Purpose: This study aims to compare results from the initial randomized controlled trial of the epilepsy self-management intervention, HOME. Based Self-management and COgnitive Training CHanges lives (HOBSCOTCH) to an ongoing pragmatic replication trial of HOBSCOTCH performed at four New England medical centers. An interim analysis was performed to assure fidelity of the program and to compare in-person with virtual delivery.

Method: This analysis (n = 44) compared waitlisted controls (n = 25) against two delivery methods of the intervention: in-person (H-IP, n = 11) and virtual (H-V, n = 8). Quality of life (QOLIE-31), depression (PHQ-9) and self-reported cognitive function (Neuro-QOL - Cognitive Function) were assessed at baseline and after 3 month follow up.

Results: Patients who received H-IP had statistically significant improvements in QOLIE-31 (p < 0.001), Neuro-QOL (p = 0.03), and PHQ-9 (p = 0.02) scores compared to waitlisted controls. For controls, the mean change in score worsened on both the QOLIE-31 (-1.4), and PHQ-9 (+0.6), whereas the mean scores improved for the H-IP group on both measures (QOLIE: +13.7 PHQ-9: -3.5). The treatment effect was greater for H-IP than H-V, as the virtual group did not report significant differences from waitlisted controls on any outcome measures. Differences in total scores between H-IP and H-V were not statistically significant.

Conclusion: Compared with waitlisted controls, patients who received HOBS COTCH in person reported improved quality of life and subjective cognitive function scores, in addition to decreased depression scores 3 months after treatment. This analysis replicated the findings of the initial HOBSCOTCH trial and supports the generalizability of the program across multiple sites and trials. Our findings indicate that the program can enhance patients’ self-reported executive functioning and has fidelity at other health care institutions. Despite a small sample size, it appears that H-IP may be a more effective delivery method than H-V. The trial is ongoing with inclusion of more patients.

p0891 DESIGN AND METHODS OF STUDY 338: A MULTICENTER, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED TRIAL OF PERAMPANEL AS ADJUNCTIVE TREATMENT IN SUBJECTS ≥2 YEARS OF AGE WITH INADEQUATELY CONTROLLED SEIZURES ASSOCIATED WITH LENNOX-GASTAUT SYNDROME

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Purpose: Lennox-Gastaut syndrome (LGS) is a severe form of childhood-onset epilepsy associated with multiple seizure types.* Polytherapy is often required, complicated by pharmacoresistant seizures. * Study 338 explores whether adjunctive perampanel (PER) is superior to placebo in reducing drop seizures during 18-weeks of treatment in subjects with inadequately controlled seizures associated with LGS.

Method: This multicenter, double-blind, randomized, parallel-group study consists of a Core Phase [P]rerandomization Screening and Baseline
**Abstracts**

**p0894**

**ANTIEPILEPTIC DRUGS AND ANTIRETROVIRAL THERAPY USE IN HIV POSITIVE PATIENTS**

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**Introduction:** Antiepileptic drugs (AED) are commonly used in HIV-patients. There are few studies which report the concomitant use of AED in patients on antiretroviral therapy (ART), in Senegal there are no formal AED treatment guidelines currently exist for HIV-patients.

**Purpose:** Identify different indications of AED in the HIV-patients and the virological interactions that may exist between AED and ART.

**Methods:** We conducted a retrospective study from 2013 to 2016 and we’ve collected epidemiological data of patients who are both under ART and AED. We have identified the indications for putting under ART to evaluate the interaction virological between Enzyme-Inducing Antiepileptic Drugs (EI-AED) and Non Enzyme-Inducing Antiepileptic Drugs (NEI-AED) by assay of viral load and CD4 count.

**Results:** Record of 28 patients were analyzed, indications for AED were central nervous system opportunistic infections associated with seizure (n = 16), stroke associated with seizure (n = 2), painful peripheral neuropathy (n = 4), mood disorders (n = 5) and migraine (n = 1). All patients were taking ART for at least 6 months, with episodes of AED and ART overlap by at least 28 days, 12 patients were under EI-AED, and 16 under NEI-AED. The viral load suppression during ART treatment was inferior in patients who were co-administered EI-AED (5/12) compared to NEI-AED (2/16). The EI-AED and NEI-AED did not differ in CD4 count at ART initiation. We did not take into account the interactions with trimethoprim/sulfamethoxazole (used in 18/28 patients for prophylaxis against opportunistic infections) which commonly compete with AED.

**Conclusion:** There are many indications of AED in HIV patients; our study has found virological impact between AED and ART. The measurement of serum levels of both treatment is important to better assess these interactions in order to provide specific recommendations for better management of this drugs-drugs interactions.

**p0895**

**IMPROVEMENTS IN SEIZURE FREQUENCY PARALLEL IMPROVEMENTS IN SEIZURE SEVERITY IN AN OPEN LABEL STUDY OF CANNABIDIOL**


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**Purpose:** To assess the response to pharmaceutical formulation of CBD ( Epidiolex) in patients with treatment-refractory epilepsy enrolled in an open-label safety study.

**Method:** Patients who failed ≥4 different AEDs were enrolled. Pre-CBD seizure frequency was averaged over 3 months prior to initiating CBD at 5 mg/kg/day for seizure control. Adjustments were allowed as tolerated every two weeks by 5 mg/kg/day up to a maximum of 50 mg/kg/day. Baseline and bi-weekly seizure frequency (SF) was monitored via diary and seizure severity was assessed at every visit with the Chalfont Seizure Severity Scale (CSSS). Other AEDs were adjusted as needed. Mixed model analysis allowing fixed (dose) and random (patient) effects with an autoregressive covariance structure was utilized.

**Results:** Seizure severity (N = 115; 59 children): the outcome is the percentage of total CSSS score at baseline. For all patients, the estimated coefficient of CBD dose is significant (t value = -9.51, p < 0.0001); this is significant for adults (t value = -8.15, p < 0.0001) and children (t value = -3.97, p < 0.0001). SF (N = 105; 56 children): the outcome is the percentage of total seizure frequency at baseline. For all patients, the estimated coefficient of CBD dose is significant (t value = -4.44, p < 0.05); this was not significant for adults (t value = -1.82, p > 0.05) and children (t value = 1.68, p > 0.05), separately. Seizure severity and frequency combined: the outcome is the product of the percentage of SF and CSSS at baseline. For all patients, the estimated coefficient of CBD dose is significant (t value = -7.05, p < 0.0001); this is also significant for adults (t value = 6.04, p < 0.0001) and children (t value = -3.87, p < 0.001).

**Conclusion:** For every unit increase in CBD dose there is a decrease of seizure severity and frequency. There is consistency in subgroups though seizure frequency decreases are significant only when data from children and adults are combined. Decreases in seizure frequency and severity occur in parallel.

**p0896**

**PHYSIOLOGICALLY BASED PHARMACOKINETIC (PBPK) MODELING OF DISPOSITION AND DRUG-DRUG INTERACTIONS FOR VALPROIC ACID/ DIVALPROEX**

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**Purpose:** Valproic acid (VPA; Divalproex) is a first-line antiepileptic drug used for treating seizures. This study presents a new physiologically based pharmacokinetic (PBPK) model considering UGT enzyme kinetics and an Advanced Dissolution, Absorption and Metabolism (ADAM) model for extended-release (ER) formulations. Our objective was to predict VPA disposition within adults, and evaluate the model’s predictive performance through drug-drug interactions (DDIs).

**Method:** Our PBPK models for VPA IR–ER formulations were constructed using Simcyp Simulator (Version 15), utilizing the ADAM model for extended-release (ER) formulations. Our objective was to predict VPA disposition within adults, and evaluate the model’s predictive performance through drug-drug interactions (DDIs).

**Results:** Our PBPK models for VPA IR–ER formulations were constructed using Simcyp Simulator (Version 15), utilizing the ADAM model for ER. We applied simulation to observed data from 19 peer-reviewed, published clinical studies. Concentration-time profiles were simulated for IR single-dose (SD) and steady-state (SS) doses (range: 250 to 1000 mg). Similarly, profiles were simulated for ER SD and SS doses of 500 mg and 1000 mg, respectively. Co-administration of VPA as an enzyme-inhibitor of phenytoin and lorazepam was simulated for DDI prediction.

**Results:** Our VPA PBPK model predicted serum concentration-time profiles for IR and ER formulations within 95th and 5th percentile confidence intervals. AUC and Cmax results for IR SD were within 40% and 25% of observed data, respectively; IR SS dosing was within 40% and 30% of observed data, respectively. The ADAM model included a
controlled-release profile for ER where simulated profiles were in good agreement with observed data. AUC and Cmax values for ER SD was within 20% and 30% of observed data, respectively; ER SS dosing was within 40% and 25% of observed data, respectively (see Figures 1 & 2). The ratio of AUC inhibited:AUC control for VPA inhibition of phenytoin metabolism was within 1% of observed data; likewise, the AUC ratio for VPA inhibition of lorazepam was within 1% of observed.

Conclusion: Our novel PBPK model predicted serum VPA concentration-time disposition for ER and IR formulation profiles reasonably well and had substantial accuracy for DDI prediction.

**p0899**

**IMPROVEMENT IN QUALITY OF LIFE RATINGS AFTER ONE YEAR OF TREATMENT WITH PHARMACEUTICAL FORMULATION OF CANNABIDIOL (CBD)**

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**Purpose:** Refractory epilepsy has negative effects on quality of life (QOL). Previously presented data revealed that 6 refractory epilepsy patients enrolled in an open label expanded access CBD program who withdrew from the study due to inefficacy had a clinically significant change in QOLIE-89 scores between enrollment and withdrawal from the study. The aim of this study was to compare QOLIE-89 scores at baseline and after one year of treatment with CBD. We hypothesized that QOLIE-89 scores would improve in patients at one year follow up.

**Method:** The AL state CBD program is an open-label safety study in the use of CBD (pharmaceutical grade; Epidiolex) for treatment-refractory epilepsy, defined here as failing at least 4 anti-epileptic drugs (AEDs), including a trial of 2 concomitant AEDs. We collected QOLIE-89 scores from adult patients with refractory epilepsy on two occasions: at study enrollment (baseline) and after one year of CBD treatment (follow-up). If a patient withdrew from the study before one year follow, a follow-up QOLIE-89 was completed at study termination visit (at which time CBD had been stopped). Two-tailed paired samples T-test was used for analysis. A clinically significant change in QOLIE-89 score has been previously defined as ≥ 10 points.

**Results:** At the time of this analysis, 31 patients had completed baseline and follow-up QOLIE-89 (15 female, ages 19-62). Six of these patients’ follow-up QOLIE-89 were completed at study withdrawal secondary to drug inefficacy. Mean baseline QOLIE-89 score was 48.4 ± 17 points, while mean follow-up score was 53.7 ± 21 points (mean difference +9.9 points). This difference was statistically significant at P = 0.027.

**Conclusion:** A significant improvement in QOL was seen on average in adult epilepsy patients after 1 year of treatment with CBD. Future data will need to be collected to determine if this improvement is sustained over time.

**p0907**

**LACOSAMIDE/LEVETIRACETAM COMBINATION TREATMENT IN EPILEPSY PATIENTS – PERSPECTIVE FROM THE ASIAN REGION**

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**Purpose:** Lacosamide(LCS) is an antiepileptic agent with a unique mechanism of action (slow inactivation of sodium channels). Levetiracetam(LEV) is one of the most widely used AEDs with binding to the synaptic vesicle protein SV2a. The aim of this study is to evaluate the clinical use of LCS/LEV combination in partial-onset seizure patients as compared with patients who are only offered LCS-only treatment.

**Method:** This is a prospective, observational, open-label study to assess the efficacy and tolerability of LCS/LEV combination in Chinese subjects aged 18 years or above. Patients on LEV are screened for a low and slow titration schedule of LCS over 8 weeks. A maintenance phase of 8 weeks will be given. The treatment phase refers to the entire period of treatment beyond 16 weeks. The primary efficacy endpoint was the 50%-responder rate and percentage change from baseline in 28-day total seizure frequency from baseline to maintenance phase or treatment phase. The safety profile is based on the incidence and severity of treatment-emergent adverse events (TEAE).

**Results:** 92 patients were included in this study with 40 patients for the LCS/LEV cohort in whom 9 screening failures occurred. 69 patients were recruited for the LCS-only group in whom 8 were screening failures. The baseline demographics of the two groups did not differ. The 50% responder rate for the LCS/LEV group was 67.7%(21/31) and for the LCS-only group 50.8% (p < 0.05). The percentage reduction of seizure was -57.44 ± -42.32 for the LCS/LEV group and -30.78 ± -81.56 for the LCS-only group. Seizure freedom was achieved in 32.3% (LCS/LEV) and 14.8%(LCS only) respectively. TEAE was reported in 19.4%(LCS/LEV) and 24.4%(LCS only). The withdrawal rates due to TEAE was 9.7%(LCS/LEV) and 13.1%(LCS-only).

**Conclusion:** The LCS/LEV combination offers a higher 50%-responder rate and fewer TEAEs/withdrawals compared with the LCS-only combination for partial epilepsy.

**p0909**

**THE INVESTIGATION OF THE ADVERSE EVENTS DURING INTRA-GROUP REPLACEMENT OF ANTI-EPILEPTIC DRUGS**

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**Purpose:** To describe the clinical types of adverse events at changing the original anti-epileptic drugs to generic drugs in patients with various forms of epilepsy.

**Method:** There were studied 61 cases of unsuccessful transfer of the patients (24 men and 37 women) with epilepsy from an original antiepileptic drug to generic drug. Changing the trade name of prescribed drug was carried out in the following groups: valproate, levetiracetam, topiramate, lamotrigine.

The statement of the fact of the transfer and the development of an adverse event was conducted retrospectively, since the change was carried out due to the changes in the provision of concessional supplementation of patients without participation of treating epileptologist.

**Results:** In 45 of 61 patients at changing of the original drug to a generic appeared failure of remission or marked more frequent attacks. Of these, from group of topiramate there were 16 patients, levetiracetam group had 14, in valproate group there were 10, lamotrigine group had 5. At the time of replace of a drug 16 of 61 patients developed side effects that did not exist before during long-term use of the original form. Of these, a group of lamotrigine had 6 (1 - urticaria, 1 - headache, 4 - dermatitis); levetiracetam had 6 (2 - dermatitis, 2 - angioedema, 1 - urticaria, 1 - depression), valproate had 3 (1 - urticaria, daytime sleepiness, 1 - dyspepsia), topiramate had 1 (dizziness).

**Conclusion:** The presented clinical experience demonstrates the undesirability of intra-group replacement of anti-epileptic drugs. Transfer of patients from the original form to the generics led to the disruption of remission or worsening at the course of epilepsy, or to the development of side effects (mainly allergic reactions) that were not defined previously.
p0912

**IMPACT OF TREATMENT REFRACTORYNESS ON THE EFFECTIVENESS, SAFETY AND TOLERABILITY OF ES LICARB AZEPINE ACETATE IN CLINICAL PRACTICE**

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**Purpose:** Eslicarbazepine acetate (ESL) is approved in Europe as adjunctive therapy for adults, adolescents and children aged >6 years with partial-onset seizures, with or without secondary generalisation. Patients encountered in clinical practice are often less refractory to antiepileptic drug (AED) treatment than those in clinical trials. We investigated the effectiveness, safety and tolerability of ESL in terms of treatment refractoriness (number of concomitant AEDs) using data from a large audit of real-world studies.

**Method:** Data from the Euro-Esli study (pooled analysis of 14 European clinical practice studies) were analysed by the number of baseline AEDs patients were receiving when ESL was initiated (0, 1, 2 or ≥3 AEDs). Effectiveness assessments included responder rate (≥50% seizure frequency reduction) and seizure freedom rate (seizure freedom at least since prior visit), assessed after 3, 6 and 12 months of ESL treatment. Safety and tolerability were assessed by evaluating adverse events (AEs) and ESL discontinuations.

**Results:** At baseline, the numbers of patients treated with 0, 1, 2 and ≥3 concomitant AEDs were 88 (4.3%), 969 (47.4%), 567 (27.7%) and 421 (20.6%), respectively. At 12 months, responder rates for patients receiving 0, 1, 2 and ≥3 concomitant AEDs were 94.1% (48/51), 87.6% (429/490), 69.5% (198/285) and 53.8% (121/225), respectively. Corresponding values for seizure freedom rates were 88.2% (45/51), 59.2% (290/490), 24.2% (69/285) and 13.8% (31/225), respectively. At all timepoints, responder and seizure freedom rates were significantly greater in patients treated with lower versus higher numbers of concomitant AEDs (p < 0.001 for all comparisons). Overall, for patients treated with higher versus lower numbers of concomitant AEDs, there were significantly higher rates of reported AEs (p = 0.004) and AEs leading to ESL discontinuation (p < 0.001).

**Conclusion:** ESL’s effectiveness, safety and tolerability were significantly superior in patients who were less - versus more - refractory to treatment at baseline.

Study supported by Eisai.

p0914

**EFFECTIVENESS AND SAFETY OF ES LICARB AZEPINE ACETATE FOR TREATMENT OF PARTIAL-ONSET SEIZURES IN CLINICAL PRACTICE ACCORDING TO AGE DECADE OF PATIENTS**

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**Purpose:** Eslicarbazepine acetate (ESL) is approved in Europe as adjunctive therapy for adults, adolescents and children aged >6 years with partial-onset seizures, with or without secondary generalisation. We investigated the effectiveness and safety profile of ESL by age decade, using real-world data from the Euro-Esli study.

**Method:** Euro-Esli was an exploratory pooled analysis of real-world data from 14 European clinical practice studies. Assessments of effectiveness included responder rate (≥50% seizure frequency reduction) and seizure freedom rate (seizure freedom at least since prior visit), assessed after 3, 6 and 12 months of ESL treatment. Adverse events (AEs) were evaluated. Data were analysed for cohorts aged < 18, 18-29, 30-39, 40-49, 50-59, 60-69 and ≥70 years.

**Results:** Euro-Esli included 2057 patients aged < 18 (n = 12), 18-29 (n = 404), 30-39 (n = 479), 40-49 (n = 444), 50-59 (n = 360), 60-69 (n = 225) and ≥70 (n = 133) years. After 12 months, responder rates were 100.0%, 71.8%, 77.8%, 67.9%, 76.8%, 80.5% and 90.3% in patients aged < 18, 18-29, 30-39, 40-49, 50-59, 60-69 and ≥70 years, respectively, and corresponding seizure freedom rates were 77.8%, 40.5%, 32.6%, 35.3%, 39.0%, 58.6% and 58.3%, respectively. At 12 months, responder and seizure freedom rates were significantly greater in earlier and more advanced ages versus intermediate ages (responder rate, p = 0.001; seizure freedom rate, p < 0.001). Overall, AEs were reported by 33.3%, 30.5%, 27.9%, 33.6%, 39.4%, 39.5% and 44.4% of patients aged < 18, 18-29, 30-39, 40-49, 50-59, 60-69 and ≥70 years, respectively. Incidence of AEs was significantly greater in more advanced ages than in less advanced ages (p = 0.001).

**Conclusion:** ESL was effective with a generally acceptable safety profile regardless of the age decade of patients. As expected, incidence of AEs was greatest in patients of more advanced age.

Study supported by Eisai.
RUFIPRAT: A RETROSPECTIVE STUDY ON THE EVERYDAY CLINICAL USE OF RUFINAMIDE IN CHILDREN WITH REFRACTORY EPILEPSY

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Purpose: Evaluate efficacy and tolerability of Rufinamide as used in everyday clinical practice by French child Neurologists.

Method: The files of children aged 4 years and above, treated with Rufinamide, between January 2010 and December 2015 at 6 University Hospitals (Grenoble, Lyon, Marseille, Paris-Debré, Paris-Necker, Toulouse) were collected by a per centre principal investigator and pooled for analysis. Data related to the global epilepsy profile (age at onset; underlying aetiology; type(s) of seizures and predominant type of seizures; syndromic diagnosis; concomitant medication and titration attitudes have been recorded.

Results: We analyzed the data from 136 patients (85 males, age range 3–56). Most the patients presented with multiple seizure types (drop attacks; diaphoretic; tonic; generalized tonic-clonic seizures) and suffered from drug-resistant epilepsy of early onset (usually before the age of 12-18 months). Intellectual disability and behavioral or psychotic troubles were often present. Sodium Valproate and Levetiracetam were frequently associated.

Investigators estimated that seizure frequency reduction was recorded in nearly 50% of the children treated. No major adverse event was reported. Weight loss, vomiting, asthenia and somnolence were the most frequent, rarely leading to a discontinuation for adverse event.

Conclusion: Rufinamide can be safely tried for the treatment of a large spectrum of seizure types. The clinical profile of the patients as well as efficacy and tolerability results will be presented in detail.

IMPACT OF INTELECTUAL DISABILITY ON THE EFFECTIVENESS, SAFETY AND TOLERABILITY OF ESLICARBAXEPINE ACETATE AS A TREATMENT FOR PARTIAL-ONSET SEIZURES: THE EURO-ESLI STUDY

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Purpose: Eslicarbazepine acetate (ESL) is approved in Europe as adjunctive therapy for adults, adolescents and children aged ≥6 years with partial-onset seizures, with or without secondary generalisation. Real-world clinical practice data complement evidence from clinical trials by providing information on patients who are more diverse in terms of clinical characteristics than those recruited for clinical trials. The purpose of Euro-ESli was to audit the real-world effectiveness, safety and tolerability of ESL when used in everyday clinical practice.

Method: An exploratory pooled analysis of real-world data from 14 European clinical practice studies was conducted. Retention and effectiveness were assessed after 3,6 and 12 months of ESL treatment. Effectiveness assessments comprised percentage reduction from baseline in monthly seizure frequency, responder rate (≥50% seizure frequency reduction) and seizure freedom rate (seizure freedom at least since prior visit). Safety and tolerability were assessed by evaluating adverse events (AEs) and ESL discontinuations.

Results: Data from 2058 patients (52.1% male; mean age 44 years; mean epilepsy duration 20.9 years) were included. All patients were assessed for safety and 1975 were assessed for effectiveness. At 3, 6 and 12 months, retention rates were 95.4%, 86.6% and 73.4%, responder rates were 60.9%, 70.5% and 75.6%, and seizure freedom rates were 30.6%, 38.3% and 41.3%, respectively. There were significant reductions from baseline to final visit in monthly frequencies of total (mean reduction 44.1%), simple partial (78.8%), complex partial (53.1%) and secondarily generalised (80.0%) seizures (p < 0.001 for all). AEs were reported for 34.0% of patients and led to discontinuation of 13.6% patients. The most frequently reported AEs were dizziness (6.7%), fatigue (5.4%) and somnolence (5.1%).

Conclusion: This large audit demonstrated that ESL was effective and generally well tolerated when used in everyday clinical practice, with approximately three-quarters of patients retained on treatment at 12 months. Study supported by Eisai.
**Abstracts**

**p0919**

**ESLICARBAZEPINE ACETATE AS A TREATMENT FOR PARTIAL-ONSET SEIZURES IN PATIENTS WITH PSYCHIATRIC COMORBIDITIES, INCLUDING DEPRESSION**

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**Purpose:** Psychiatric comorbidities, including depression, are common in epilepsy patients and can influence the effectiveness of antiepileptic treatment. We investigated the effectiveness, safety and tolerability of eslicarbazepine acetate (ESL) in patients with psychiatric comorbidities and those specifically with comorbid depression, using data from a large audit of European real-world studies.

**Method:** Data from patients with psychiatric comorbidities and depression included in the Euro-Esli study (a pooled analysis of 14 European clinical practice studies) were extracted and compared with data from patients without these comorbidities. Effectiveness assessments included responder rate (≥50% seizure frequency reduction) and seizure freedom rate (seizure freedom at least since prior visit), assessed after 3, 6 and 12 months of ESL treatment. Safety and tolerability were assessed by evaluating adverse events (AEs) and ESL discontinuations.

**Results:** At baseline, psychiatric comorbidities and depression were present in 283/1138 (24.9%) and 141/1134 (12.4%) patients, respectively. At 12 months, responder rates for patients with versus without psychiatric comorbidities were 83.1% (128/154) versus 82.5% (326/395) (p<0.01), and seizure freedom rates were 51.3% (79/154) versus 51.4% (203/395) (p=not significant). Corresponding values for patients with versus without depression were 81.0% (51/63) versus 82.9% (402/485) (p<0.01), and 46.0% (29/63) versus 52.0% (252/485) (p<0.01), respectively. Overall, for patients with versus without psychiatric comorbidities, 43.1% (122/283) versus 30.5% (261/855) reported AEs (p<0.01), and 31.9% (88/276) versus 21.2% (178/840) had AEs leading to ESL discontinuation (p<0.01). Corresponding values for patients with versus without depression were 60.1% (32/53) versus 53.5% (64/120) (p=0.17), and 43.4% (48/111) versus 22.2% (21/94) (p<0.01), respectively.

**Conclusion:** ESL’s effectiveness was generally similar in patients with versus without psychiatric comorbidities, and in those with versus without comorbid depression. ESL’s safety and tolerability were less favourable in patients with psychiatric comorbidities and depression, compared with those without these comorbidities.

Study supported by Eisai.

**p0924**

**BRAIN LESIONS IN ELOQUENT AREAS: INTRAOPERATIVE MAPPING, SEIZURES OCCURRENCE AND ANTIPILEPTIC DRUG PROPHYLAXIS: COMPARISON OF PHENYTIN VS LEVETIRACETAM VS LACOSAMIDE USE: EFFICACY AND SAFETY**

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Purpose: Intraoperative mapping and monitoring techniques for eloquent area brain lesions surgery are routinely used worldwide. Very few data are available regarding intraoperative seizures (IS) occurrence and intraoperative antiepileptic drug prophylaxis use. The IS incidence as reported, in literature, ranges from 0% to 24% and seems to be related several variables: parameters of stimulation, anesthetic regimen, the intrinsic epileptogenicity of the tumor. The IS prevention is fundamental to avoid premature interruption of functional mapping as well as premature interruption of tumor resection and consequent postoperative neurological deficits.

Methods: 107 patients undergoing elective craniotomy for brain lesions in eloquent area with intraoperative mapping, received antiepileptic drugs (27 pts levetiracetam, 24 pts phenytoin and 56 pts lacosamide) as intraoperative seizures prophylaxis. The drug was administered intravenously after induction of anaesthesia and approximately two hours before start of surgery. Levetiracetam was administrated at dosage of 20 mg/Kg and lacosamide in a single dose of 200 mg, both given as slow infusion (20 min.); phenytoin was administrated at dosages of 15 mg/Kg a slower infusion rate (40 min.) as recommended to prevent cardiovascular adverse effects. Cortical mapping was performed using short train direct electrostimulation technique (250 Hz, monophasic current, 500 μs, train of 4-5) with motor evoked potentials (MEP) monitoring. The seizure occurrence was evaluated clinically and was reported by neurosurgeon, anesthesiologist or neurophysiologist.

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Results: Seizures were observed in five patients of 27 who received levetiracetam, one seizure was reported in 24 patients who received phenytoin and one seizure in 56 patients who received lacosamide. Categorial ANOVA was used to compare the three groups LCS vs LEV p = 0.02; PHT vs LEV p = 0.05; LCS vs PHT p=ns.

Conclusions: Lacosamide is effective and safe as well as phenytoin in preventing intraoperative seizures without any special precaution.

p0926 PHARMACOKINETIC VARIABILITY OF PHENYTOIN – AN OLD DRUG USED IN NEW COMBINATIONS
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Purpose: Phenytoin is an old antiepileptic drug (AED) with challenging pharmacokinetic properties, mainly prescribed to patients with refractory epilepsy. The purpose of this study was to investigate the impact of age, gender and comedication with a selection of newer AEDs thought to have interaction potential on the pharmacokinetic variability of phenytoin.

Method: Anonymous data from the therapeutic drug monitoring (TDM)-database at the National Center for Epilepsy in Norway were collected for patients who used phenytoin during 2010-15. Variables included age, gender, dose, drug-fasting steady-state serum concentrations and concomitantly prescribed AEDs. The study was approved by the Regional Ethics Committee.

Results: 280 patients were included: Median age 53 years (range 1-96), gender distribution 40/60% women/men, 29% were elderly above 65 years and 7% were under 18 years. Mean dose and serum concentration were 288 mg/day (range 25-900) and 53 µmol/L (observed range 2-170, reference range 40-80), respectively. Mean concentration/dose (C/D)-ratio was 0.19 (SD=0.13) µmol/L/mg, with a 180-fold variability. There were no gender differences in C/D ratio or significant differences between adults and elderly, 0.16 (0.11) and 0.17 (0.12) respectively. Polytherapy (2-4 AEDs) was noted in 182 patients (65%), 108 patients (59%) used at least one newer AED. No significant changes in C/D-ratio were found when phenytoin was combined with newer AEDs, such as the possible inducer topiramate (> 200 mg/day) or the inhibitor oxcarbazepine, compared to monotherapy or combinations with AEDs with no expected interactions (C/D-ratio 0.16 (0.08), 0.20 (0.18) and 0.21 (0.18) (n = 7,14,98) respectively).

Conclusion: The pharmacokinetic variability of phenytoin was extensive and could not be explained by single factors such as age, gender or comedication. One third of the patients were elderly. Polytherapy was common, with combinations with newer AEDs stated in two thirds of the population. Careful monitoring of phenytoin therapy is still important for improved safety.

p0928 GANAXOLONE IN CHILDREN WITH CDKL5-GENE RELATED EPILEPTIC ENCEPHALOPATHY: PRELIMINARY ANALYSIS FROM AN OPEN-LABEL TRIAL
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Purpose: The X-linked CDKL5 gene, which encodes cyclin-dependent kinase-like 5 protein, has been implicated in early-onset encephalopathy and atypical Rett syndrome with early-onset difficult-to-control seizures. An open-label study is being conducted to explore safety, tolerability and possible efficacy of ganaxolone in children with CDKL5 epileptic encephalopathy.

Method: NCT02358538 is an open-label flexible-dose study at 10 Italian and US centers with exploratory objectives of safety, tolerability and efficacy in various epileptic encephalopathy syndromes. Following screening and baseline visit, the patients enroll into a 26-week study during which the investigators can flexibly dose ganaxolone up to 1,800 mg/day (> 30 kg) or 63 mg/kg/day (< 30 kg). Following the 26-week study period eligible patients may enroll into a 52-week extension. The primary efficacy measure is % change from baseline in the 28-day seizure frequency (total seizure count).

Results: Preliminary data were analyzed for the first 4 enrolled subjects with CDKL5 epilepsy (4 girls; average age of 7.5 years; average ganaxolone exposure of 5 months at time of analysis). Three of the 4 patients experienced a seizure reduction ranging from 52% to 88%. CGI-I scores administered by the caregiver or investigator generally correlated with seizure reduction. One subject was discontinued after four months of treatment due to lack of efficacy. All three responders continue to receive treatment. Two patients who completed the 26-week study period have enrolled into the study extension. There have been no SAEs or drug-related AEs reported in this small cohort of patients.

Conclusion: These preliminary results suggest that ganaxolone is safe and well-tolerated, and could have potential in the treatment of CDKL5-related epileptic encephalopathy.
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epilepsy. An updated analysis from an expanded CDKL5 cohort will be presented.

p0930
LACOSAMIDE – A NEW TREATMENT OPTION FOR CHILDREN WITH ELECTRICAL STATUS EPILEPTICUS IN SLEEP (ESES)
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Purpose: ‘Electrical status epilepticus in sleep’ (ESES) is a childhood-onset self-limited sleep-induced EEG pattern characterized by (nearly) continuous focal or generalized spike and waves during non-rapid eye movement sleep. Most patients develop epileptic seizures and they present with variable degrees of regression in different aspects of development related to no other factor than ESES. Treatment has therefore to extend beyond the control of epileptic seizures and should aim to suppress the nocturnal interictal EEG discharges as early as possible. ESES often remains pharmacoresistant, and complete resolution is primarily achieved using steroids, whereas the application of standard antiepileptic drugs (AEDs) is often ineffective. In addition, some AEDs - especially sodium channel blocking agents may aggravate the disorder.

Lacosamide (LCM) - despite the fact that it selectively enhances slow inactivation of voltage-gated sodium channels- has been reported to be effective in 75% of eight children with ESES (1). We evaluated the efficacy and safety of LCM on EEG and language development in children with ESES.

Method: Children with a confirmed diagnosis of ESES and drug-resistant to standard treatment with steroids were included. 24-h EEG recordings and neuropsychological testing were performed before and 12 months after initiation of LCM. The spike-wave index (SWI) and Language quotients (LQs) were calculated.

Results: 20 children (11 boys) were included. 80% of patients responded to treatment (SWI < 25%). In 40% of them the EEG completely normalized. Seizure and/or EEG aggravation was not observed. In addition, marked improvement in LQs was noticed.

Conclusion: LCM seems to be an effective and safe treatment option for children with ESES.

p0932
DYNAMICS OF QUALITY OF LIFE IN EPILEPSY PATIENTS WITH COMPARATIVE ANALYSIS OF EFFICACY ANTI-EPILEPTIC DRUGS MONOTHERAPY
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Purpose: Evaluate the quality of life (QOL) of epilepsy patients with estimating its dynamics on the background of monotherapy with some AEDs.

Method: The study included 52 patients (aged 18-44 years), underwent standard clinical-neurological, electroencephalographic studies. In addition, all patients filled questionnaire QOLIE-31 before beginning AEDs or its correction and after optimization of antiepileptic therapy (4 month later).

Results: Clinical picture of disease was represented by the following types of seizures: simple partial- 25% of all patients, complex partial (automatisms) - 19%, secondary generalized seizures - 56%. From all cases 31% of epilepsy was idiopathic, 54% - symptomatic, 15% - cryptogenic. All patients with epilepsy were on monotherapy with following AEDs: Carbamazepine - 37% of patients, Valproate - 37%, Topiramate - 15, Lamotrigine- 11%.

A comparative analysis of the efficiency of AEDs on QOL of patients with epilepsy showed higher rates for patients receiving Valproate and Lamotrigine, which correlate with higher efficacy and tolerability of therapy. The most significant anti seizure efficiency among all groups of drugs demonstrated Topiramate, frequency of clinically significant side effects and negative impact on QOL weren’t observed, which doesn’t distinguish it from Valproate. Change by subscales “Emotional well-being”, “Cognitive functioning” in course of treatment was significantly higher in Carbamazepine, than in Lamotrigine and Valproate groups. This confirms existing data in the literature about greater negative impact of Topiramate on cognitive function than other AEDs.

Conclusion: Optimized pharmacotherapy reduces incidence of side effects, increases efficiency and improves the emotional, psychological and physical condition of patients. To achieve high QOL remission of seizures is not enough, because QOL is affected by presence or absence of side effects, psycho-emotional disorders, social adaptation. Assessing QOL of epilepsy patients using QOLIE-31 along with clinical, instrumental methods of examination is a reliable criterion for evaluating the additional efficacy and tolerability of therapy.

p0933
PHARMACISTS’ PERCEIVED CONFIDENCE AND KNOWLEDGE ON ANTI-EPILEPTIC DRUGS IN ALBANIA
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Purpose: Antiepileptic drugs (AEDs) are pivotal in epilepsy treatment and pharmacists play a key role in supporting and advising people with epilepsy (PWE). Therefore our aim was to assess pharmacists’ knowledge and attitude about AEDs use in Albania.

Method: Random pharmacists from four different cities were invited to answer to a self-administered questionnaire on demographics, years of practice, distance from the nearest health-care center, and average number of PWE seen per month. Before the test, pharmacists were asked to state their level of confidence and need for training on AEDs. Moreover, a 10-item evidence-based knowledge test created by expert neurologists was administered. These 10 vignettes included real-life situations as emergency situations, drug-drug interactions, valproic acid blood levels and start of lamotrigine therapy, to which pharmacists were asked to act. Each correct action was given 1 point creating a scale of 0-10 points.

Results: Seventy-eight pharmacists, 52 females (66.7%), with a mean age of 35.6 (±10.2) years, were included in our analysis. The level of confidence in AEDs was very high in 19.2%, average in 65.4% and low in 15.4%. Nevertheless, 78.2% admitted that training and update were needed. Knowledge level was impressively low, mean 2.77 ± 1.55. The score was not affected by gender, age, years of practice and number of PWE per month in either t-test, correlation or regression analysis. Importantly, likewise higher confidence level did not statistically predict better knowledge.

Conclusion: Pharmacists’ knowledge on antiepileptic drugs in Albania is very low (2.77 out of 10) warranting their immediate training, regardless their perceived competence or confidence.

p0934
PERAMANEL IN 359 REFRACTORY FOCAL EPILEPSIES: A FRENCH COHORT
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Purpose: Perampanel (PER) was introduced in France in May, 2014 as add-on in drug-resistant focal epilepsies. As of June 28, 2016, all patients newly treated with PER have been prospectively added to an ad hoc database in two tertiary epilepsy clinics (Montpellier and Marseille), in order to assess efficacy and tolerability in a practical setting.

Method: Patients were reviewed at 3 months intervals at least and were encouraged to manifest at shorter intervals in case of problems with their
Treatment. We recorded all personal and epilepsy data, and actively looked for side effects and all parameters of clinical efficacy at each contact.

Results: A total of 359 patients were included in this study (53.5% women; mean age 44.5 years (range 11-83); epilepsy duration 28 ± 15.26 years; symptomatic epilepsy 62% vs cryptogenic 38%). Patients had seizure at least one per day (11%), at least one per week (33%) and at least one per month (47%). They were on two antiepileptic drugs (15%), three (28%), four (41%), more than four (16%). Mean daily dose of PER was 6.3 mg +/- 2.6 mg (range 1-14 mg). Mean exposition to PER was 13.41 ± 4.4 (range 1-25 months). PER was stopped in 23% of the cases mainly for side effects (75%) and also for lack of efficacy (25%). The percentage of patients with a > 50% reduction in seizure frequency was 53% and 15% became seizure free. Side effects were reported by 31% of the patients: drowsiness 21%, dizziness 12%, asthenia 10%, psychiatric disorders 10%, irritability 5%.

Conclusion: In this population, PER appears to be an effective antiepileptic drug and should thus be tried in patients who are not satisfactorily controlled by the usual drugs. Its use can be limited by the occurrence of psychiatric disorders or irritability. We recommend a dose around 6 mg/day.

p0935
PERAM PanEL IN 65 ADULTS WITH THE LENNOX-GASTAUT SYNDROME AND RELATED ENCEPHALOPATHIES
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Purpose: Perampanel (PER) was introduced in France in May, 2014 as add-on in drug-resistant focal epilepsy. The Lennox-Gastaut syndrome (LGS) is a rare, severe epileptic encephalopathy, in which bilateral synchrony plays a major role, and the same consideration applies to related epileptic encephalopathies with diffuse EEG changes that do not fulfill the strict criteria of LGS. All LGS patients newly treated with PER have been prospectively added to a database in two tertiary epilepsy clinics (Montpellier and Marseille) in order to assess efficacy and tolerability.

Method: Patients were reviewed at 3-month intervals at least and were encouraged to manifest at shorter intervals in case of problems with their treatment. We recorded all personal and epilepsy data from patient diaries, and actively looked for side-effects and all parameters of clinical efficacy at each contact. We asked carers to quantify visible seizures, including falls, motor seizures and absences.

Results: As of June 28, 2016, we have treated 43 patients with LGS and 22 with related epileptic encephalopathies (M 51%, F 49%, mean age 37 years, range 18-68). All patients had a history of mixed seizures, moderate to severe mental handicap, and drug resistance. They were receiving an average of 4.5 antiepileptic drugs, 28% also had vagus nerve stimulation. Usual daily dose of PER was 6 mg. The percentage of patients with a > 50% reduction in seizure frequency was 53% including 17% a > 90% reduction. Side effects were reported by 27% of the patients: psychiatric disorders 20%, drowsiness and asthenia 5%, dizziness 2.5% and seizures aggravation 5%.

Conclusion: PER is a new treatment option. More than 50% had worthwhile improvement with a mean daily dose of 6 mg. Its use can be limited by the occurrence of psychiatric disorders or behavioural side effects.
Mean age at epilepsy onset was 43 months ± 43.26 and 10.7 years ± 3.95 (range 0-17) of epilepsy duration with at least three seizure per-month (up to several per-day). 67% (n = 51) had symptomatic focal epilepsy. Mean number of AEDs used in the past was 7.06 and mean number of concomitant AEDs was 2.48. Mean PER dose was 6.96 ± 2.4 mg (2-12 mg). After an average of 14-months of follow-up (12-21 months), 48 patients (77%) continued on PER. The response rate was 54%, 17% with ≥75% seizure frequency reduction and 5% (n = 3) completing completely seizure free. Seizure aggravation was observed in 10.5% (n = 8). Adverse events were experienced in 167 (21%) and resulted in withdrawal in 23 (30.3%). The most common adverse events were behavior disturbance (irritability and aggression), dizziness and sedation.

**Conclusion:** Perampanel is effective in children and adolescents with refractory epilepsy but is associated with a relatively high rate of behavioral adverse events mainly in older.

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**p0937**

**OROMUCOSAL MIDAZOLAM IN PATIENTS WITH PROLONGED ACUTE CONVULSIVE SEIZURES: AN ITALIAN EXPERIENCE**

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**Purpose:** In pediatric age, convulsive seizures lasting more than 5 minutes represent a life-threatening condition. Oromucosal midazolam is a promising first-line treatment option, which is approved in the EU for the treatment of prolonged, acute, convulsive seizures (PACS), in patients aged between 6 months and 18 years. The aim of this study is to evaluate the effectiveness of oromucosal midazolam and, to compare with rectal diazepam efficacy.

**Methods:** We included all consecutive patients followed-up at Bambino Gesù Children’s Hospital in Rome who received oromucosal midazolam treatment between January 2015 and July 2016. A telephone survey was carried out to evaluate effectiveness, tolerability and convenience of the administration route of oromucosal midazolam in terminating PACS. Moreover, when rectal diazepam was previously used, has been asked a comparative effectiveness between the two benzodiazepines.

**Results:** We enrolled 293 patients (149 males), aged between 6 months and 18 years (9 ± 4.61 years old; median: 9 years) at the time of prescription, with a 16-month follow-up in average (16 ± 5.24 months). Most of them (98/203, 48%) had a symptomatic epilepsy and 90% (268/273) received oromucosal midazolam care plan for the first time. We will present the results of the telephone survey.

**Conclusion:** In the previous reported clinical trials, oromucosal midazolam was at least as effective as rectal diazepam in the treatment of PACS in children and was generally well tolerated. The results of this survey showed that oromucosal midazolam has several advantages if compared with rectal diazepam, the previous gold standard of treatment, such as having a more convenient and socially acceptable administration route.

**p0940**

**LAFORA BODY DEGRADATION BY A THERAPEUTIC ENZYME FOR THE TREATMENT OF LAFORA DISEASE**

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Lafora disease (LD) is the most common form of progressive myoclonus epilepsy. LD manifests in adolescence with an initial seizure, followed by rapid development of epilepsy, neurodegeneration and dementia, leading to a vegetative state. Treatments for LD are only palliative; death ensues ten years after initial onset. Insoluble carbohydrate deposits known as Lafora bodies (LBs) are present in all tissues of LD patients and contain an aberrant form of glycogen, a carbohydrate storage molecule normally found in most cells. LD is caused by mutations in EPM2A and EPM2B, genes that respectively encode laforin, the glycogen phosphatase, and malin, an E3 ubiquitin ligase. EPM2A- and EPM2B-deficient mice have LBs, neurodegeneration, and seizures, and multiple groups have shown that the reduction or ablation of glycogen synthesis eliminates LB formation and rescues LD in mice, demonstrating that LBs drive disease progression.

Enzyme therapy is becoming increasingly popular in the treatment of genetic diseases, but delivery to the cytoplasm is problematic. By fusing an enzyme to an anti-DNA autoantibody fragment that penetrate cells via a nuclease transporter, Valerion Therapeutics successfully designed cytosol-deliverable enzymes that are efficacious for the treatment of Pompe disease and myotubular myopathy. We explored this approach to deliver an amylase that would degrade LBs. We isolated LBs from EPM2A-deficient mice and showed that amylase 2A conjugated to an Fab fragment of human IgG1 (Fab-AMY) degrades LBs in vitro, and injected Fab-AMY is active in vivo. We are now testing whether LBs isolated from EPM2B-deficient tissues can be degraded by Fab-AMY, and if Fab-AMY injection reduces LB load in LD mice. Fab-AMY is a promising therapeutic for Lafora epilepsy, potentially the first drug to provide a significant clinical benefit.

**p0941**

**FEBRILE SEIZURES AND RISK OF PSYCHIATRIC DISEASE IN ADULTHOOD**

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**Purpose:** To examine the relationship between febrile seizures and subsequent risk of psychiatric disease in adulthood.

**Method:** This is a population-based cohort, including all children born in Denmark between 1977 and 2002. We assessed the risks of psychiatric disease associated with a history of febrile seizures. We followed the children from their 10th birthday, and assessed the risk of psychiatric disease in adulthood.

**Results:** We followed 1,556,959 children, of which 54,614 (3.5%) had febrile seizures for a total of ~19 million person-years of follow up and identified 101,515 persons who subsequently developed a psychiatric disease. A history of febrile seizures was associated with slightly elevated rates of psychiatric diseases in later life, with the associations being strongest for schizophrenia (HR: 1.25, 95% CI: 1.13-1.37). Recurrent admissions to the hospital for febrile seizures were generally associated with more pronounced effects. Age of onset of febrile seizures (3-14 months/≥15 months) did not seem to affect the strength of the associations.

**Conclusion:** Febrile seizures were associated with a mild to moderate increased risk of psychiatric disease in adulthood. The findings suggest that in some children, febrile seizures may affect the developing brain, resulting in an increased vulnerability to develop psychiatric disease. However, the associations may also be explained by a common underlying genetic susceptibility or by unmeasured or residual confounding.
p0943

INFECTIONS INCREASE THE RISK OF EPILEPSY: A NATIONWIDE REGISTER-BASED COHORT STUDY
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Purpose: The causes of epilepsy are not fully understood. But epilepsy has a high degree of psychiatric comorbidity, and infections increase the risk of psychiatric disorders, while certain infectious diseases also increase the risk of epilepsy. This study investigates whether infectious diseases increase the risk of subsequent epilepsy.

Methods: This is a nationwide, prospective cohort study including all 2,235,490 persons born in Denmark from 1977 to 2012. Patients with infections and epilepsy were identified from the National Patient Register. Vital status was determined from the Danish Civil Registration System and the Danish Medical Birth Register. Persons were individually followed from the day of birth until one of the following endpoints: epilepsy diagnosis, death, emigration, or December 31st 2012, whichever came first.

Results: During 36 years of follow up, 721,460 persons had hospital contacts with infection and 35,112 with epilepsy. The overall risk of epilepsy after a hospital contact with infection was approximately twice that of persons without hospital contacts for infection (aHR = 2.05, 95% CI: 2.00-2.10). The risk of epilepsy increased with the number of contacts with infection: one contact: 1.72 (1.67-1.77), two: 2.18 (2.09-2.28), three: 2.57 (2.41-2.74), four: 3.40 (3.13-3.68), five: 3.70 (3.31-4.12), six: 4.56 (3.99-5.21), seven: 4.62 (3.88-5.50), eight or more: 6.24 (5.61-6.93).

Conclusion: Hospital contact with infection was associated with an increased risk of developing epilepsy later. The risk of epilepsy was highly associated with the number of admissions with infections. The findings are compatible with an inflammatory hypothesis in subgroups of persons with epilepsy.

p0944

PREMATURE MORTALITY IN PERSONS WITH EPILEPSY AND SCHIZOPHRENIA: A NATIONWIDE COHORT STUDY
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Purpose: Both epilepsy and schizophrenia are associated with premature mortality. However, it is uncertain how comorbidity between the two disorders affects the mortality. We assessed the mortality for persons with epilepsy and schizophrenia in absolute and relative measures.

Method: We included all persons born in Denmark 1960-87, who were alive and residing in Denmark by their 25th birthday. From national health registries we identified persons diagnosed with epilepsy and schizophrenia prior to their 25th birthday. Participants were followed from their 25th birthday to death, emigration, or December 31st 2012. The primary outcome was overall mortality. In sub-analyses estimates were stratified by sex, epilepsy sub-types, and a stricter definition of schizophrenia. Furthermore, in sensitivity analyses we estimated the mortality in participants followed from their 20th and 30th birthday. Data was analysed using Cox regressions.

Results: We followed 1,620,376 persons for 24,167,573 person years of follow up; median 15 years. The mortality rate ratio (MRR) was 4.4 (95% CI: 4.1-4.7) for persons with epilepsy, 6.6 (95% CI: 6.1-7.1) for persons with schizophrenia, and 12.8 (95% CI: 9.1-18.1) for persons with both disorders compared to persons without these disorders. Estimated cumulative mortality at the age of 50 was 3.1 % (95% CI: 3.0-3.1 %) for persons without epilepsy and schizophrenia, 10.7 % (95% CI: 9.7-11.8 %) for persons with epilepsy, 17.4% (95% CI: 16.0-18.8 %) for persons with schizophrenia, and 27.2 % (95% CI: 15.7-40.1 %) for persons with both disorders.

Conclusion: Persons with both epilepsy and schizophrenia have a very high mortality; the absolute risk of dying before the age of 50 was nine times higher compared to persons without epilepsy and schizophrenia, indicating that these patients constitute a vulnerable group that needs special clinical attention.

p0945

THE IMPACT OF GEOGRAPHY ON EPILEPSY MORTALITY: A RETROSPECTIVE CASE SERIES FROM 4 U.S. MEDICAL EXAMINER OFFICES
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Purpose: We examined the impact of correlates of socio-economic status (SES) on decedents with epilepsy presenting for medico-legal investigation (MLI) in four medical examiner (ME) offices in the United States. We hypothesize that there is excess epilepsy mortality in neighborhoods with the lowest median income.

Methods: We queried all decedents for MLI at four ME offices (NYC, Maryland, San Diego Co. and Monmouth Co.) between 1/1/2009-12/31/2010, and identified all decedents where epilepsy or seizure was a cause or contributor to death on the death certificate. We reviewed the available autopsy reports, investigation notes and ME records. We independently adjudicated which deaths were due to SUDEP. We used postal (ZIP) code of residence as a SES surrogate. ZIP code regions were ranked by median household income (American Community Survey, 2009-2013) and divided into quartiles based on total regional population (US Census Bureau, 2010). Region-, age- and income-level adjusted epilepsy prevalence in each ZIP code was estimated using 2010 CDC National Health Interview Survey data. Rates and adjusted rate ratios were calculated using OpenEpi.com.

Results: We identified 317 decedents (168 NYC, 76 Maryland, 62 San Diego, 11 Monmouth) with epilepsy as cause/contributor to death over the 2-year period. The rate of epilepsy-related deaths (per 1000 pt-yrs) undergoing MLI was 0.5 (95% CI: 0.4-0.8) in highest income quartile and 1.3 (95% CI: 1.1-1.6) in the lowest income quartile. ME office-adjusted rate ratio between lowest and highest income quartile was 2.3 (95% CI: 1.6-3.3; p < 0.0001). Considering only SUDEP deaths, the difference between lowest and highest income quartiles remained significant (adjusted RR: 2.6 95% CI: 1.8-3.9).

Conclusion: The rate of all epilepsy-related deaths and SUDEPs undergoing MLI was significantly greater among resident of the poorest ZIP codes compared to the wealthiest ZIP codes. Further studies are needed to understand the causes of these disparities.
**p0947**

**PATERNAL AGE AND RISK OF EPILEPSY IN THE OFFSPRING**

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**Purpose:** Advanced paternal age is associated with a range of adverse neuropsychiatric outcomes possible due to an age-associated increase in de novo mutations in the male germ cells. We examined the relationship between paternal age and risk of epilepsy in the offspring.

**Methods:** The study was designed as a population-based cohort, including all children born in Denmark between 1977 and 2012. The children were followed from birth, and we assessed the risks of epilepsy stratified on paternal age. Cox regressions were used to estimate hazard ratios (HR) and corresponding 95% confidence intervals for epilepsy adjusted for gestational age at birth, birth weight, Apgar scores (5 min), and maternal age.

**Results:** We followed 2,246,886 children for 38,139,744 years of follow-up, of which 31,406 were diagnosed with epilepsy. Compared to offspring of fathers aged 25-29, the risk of epilepsy was increased - both offspring of younger and older fathers (fathers aged: < 20 years (aHR: 1.09 (95% CI: 0.96-1.23)), 20-14 years (aHR: 1.07 (95% CI: 1.02-1.11)); 30-34 years (aHR: 1.00 (95% CI: 0.97-1.03)), 35-39 years (aHR: 1.02 (95% CI: 0.98-1.07)), 40-44 years (aHR: 1.09 (95% CI: 1.02-1.21)), and ≥45 years (aHR: 1.12 (95% CI: 1.03-1.21))

**Conclusions:** For offspring of fathers older than 25-29 years of age, the risk of epilepsy increased with increasing age. However, the results suggest only a modest effect of paternal age on the etiology of epilepsy.

**p0951**

**EXPERIENCES OF ELDERLY EPILEPSY PATIENTS IN EMERGENCY CARE**

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**Purpose:** There is little knowledge about emergency care in elderly epilepsy patients. A multicenter survey was performed to get more information about this relevant topic.

**Method:** In this retrospective survey a structured questionnaire was developed to explore patient experiences during their emergency situations. Epilepsy patients older than 50 years or their family members were included. The multicenter study was accompanied by physicians in different parts of Germany, patients self-help groups and by using an internet platform. The project started in October 2015 and finished in November 2016.

**Results:** Complete information about 83 epilepsy patients was collected via internet platform (n = 36) or a handwritten form (n = 47). The median age was 61 years (range 50-79 years), 94% of the patients knew their epilepsy diagnosis. 45% of the patients lived alone. 59% of all patients reported about seizure-related-injuries in the past. 70% of all patients were treated in a hospital, although they did not want to go in a hospital. 36% of the respondents took epilepsy emergency medications. 52% of the epilepsy patients felt not adequately informed about measures and behavior in case of epilepsy emergency. Only 15% of all participants used an epilepsy emergency card.

**Conclusion:** The emergency care experiences of elderly epilepsy patients were collected using a structured patient questionnaire. The results show a great need for more information and education of elderly epilepsy patients about management of emergency situations. From the patient’s point of view, it is particularly important for elderly patients to avoid unnecessary emergencies.

**p0954**

**ASSOCIATION OF ALPHA SUBUNIT OF GABA<sub>4</sub> RECEPTOR SUBTYPE WITH EPILEPSY SYNDROMES IN INDIAN POPULATION**

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**Aims:** To evaluate GABA<sub>4</sub> (γ-aminobutyric acid) receptor gene as candidates for epilepsy susceptibility, we screened coding single-nucleotide polymorphism of GABRA1 15 A-G in Indian epilepsy syndrome patients.

**Methods:** The genotyping was performed in 100 control subjects and 100 patients with epilepsy syndromes, of whom 50 were Juvenile Myoclonic Epilepsy (JME) patients and 50 were Lennox-Gastaut syndrome (LGS) patients by RFLP-PCR.

**Results:** We determined the genotypic and allelic frequencies in 100 epilepsy syndrome patients (50 JME and 50 LGS) and 100 normal healthy controls by PCR-RFLP assay. In Juvenile Myoclonic Epilepsy, no statistical difference was observed among the patients and control subjects (p = 0.06) and in Lennox-Gastaut syndrome, no statistical difference was observed among the patients and control subjects (p = 1.78). However, a statistical difference was observed among the patients with respect to drug response with a p value of 0.04.

**Conclusion:** GABRA1 15 A-G polymorphism of GABA receptor gene may play a significant role in LGS with respect to drug response.

**p0959**

**EFFICACY AND SAFETY OF INTRAVENOUS LACOSAMIDE IN FOCAL STATUS EPILEPTICUS IN ELDERLY AND CRITICALLY ILL PATIENTS**

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**Introduction:** Non convulsive status epilepticus (NCSE) is a commonly underrecognized condition in clinical practice. In elderly and critically ill patients, NCSE treatment presents pharmacological management challenges and potential serious side effects. Lacosamide (LCM) is an anticonvulsant with a good safety profile.

**Purpose:** To evaluate the efficacy of lacosamide in a prospective observational study enrolling patients with NCSE in focal epilepsy.

**Methods:** Patients were included according to the following inclusion criteria: 1. Diagnosis of NCSE 2. No PLEDS or BPLEDS in EEG monitoring or diagnosis of postanoxic encephalopathy.

**Primary outcome measure was incidence and time to seizure EEG and clinical cessation.** We enrolled 25 consecutive subjects with NCSE in whom LCM at a loading dose of 300 mg over 15 minutes, was added during continuous EEG monitoring for inefficacy of benzodiazepine and levetiracetam (LEV).

**Results:** Twenty five patients (17 men, 8 women) were included, with a median age of 65 (range 19-87) years. The most common etiology of NCSE was intracranial hemorrhage and brain tumor. LCM was introduced as third agent after benzodiazepine and LEV (2000-3000 mg/die). Most (20/25) NCSE was terminated within 8-20 hours after LCM. The time to improvement in the EEG and in clinical observation varied between 6-48 hours. There were no side effects directly attributable to LCM.

**Conclusions:** Both LEV and LCM share some characteristics (rapid acting, little drug-drug interaction) that make them ideal AED in NCSE. Although the lack of randomized clinical trials assessing efficacy, LEV has been shown to be safe and effective in critically ill patients as well in status epilepticus. Our data suggest that LCM is well tolerated and
effective in the treatment of refractory NCSE. Waiting for trials evaluating effectiveness of LCM in comparison to LEV, we suggest to try LCM in NCSE in focal epilepsy before and not after LEV.

p0960
PERAMAPANEL USE IN OLDER PEOPLE WITH EPILEPSY: POOLED DATA FROM EUROPEAN OBSERVATIONAL STUDIES
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Purpose: Phase III clinical trials of antiepileptic drugs include few people aged ≥65 years. To supplement data from randomized controlled studies, real-world evidence with perampanel in older people with epilepsy is therefore essential, when considering treatment choices for this population.

Method: Data from clinical records of patients treated with perampanel at 46 European centres were pooled. One-year retention rate, seizure-freedom (for ≥6 months), and adverse events (AEs) were recorded and are reported here for patients aged ≥65 years. Cumulative logistic regression analysis were performed.

Results: Logistic regression in the full dataset (N = 2332) showed the probability of seizure freedom increased with age (regression coefficient range: 0.032-0.067). There were 135 patients aged ≥65 years (range 65-96 years). Median epilepsy duration in this population of older patients was 45 years, aetiology was mostly cryptogenic (35/128) or symptomatic (92/128), and focal seizures were the most common type. Patients had previously used a median of 5 AEDs, and were taking a median of 2 concomitant AEDs before perampanel. One-year retention rate was 50%; 67 patients discontinued (tolerability in 10, lack of efficacy in 3, not specified in 54). Among the 46 patients for whom full seizure data were available, 13 (28.3%) were seizure free (95% confidence interval 15.2-41.3). AEs were reported in 71% (69 of 97) during 12 months, most commonly dizziness/vertigo (18.0%), somnolence/sleepiness (14.6%), behavioural AEs (11.2%), and mental confusion/slowing (9.0%).

Conclusion: In patients aged ≥65 with predominantly focal epilepsy, seizure freedom with add-on perampanel was seen in 28%, higher than achieved in Phase III trials. Perampanel was well tolerated, with half of the treated patients remaining on perampanel at 1 year, and AEs were in line with previous reports.

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p0961
THE ROLE OF VASCULARIZATION OF THE CORPUS CALLOSUM DURING MICROSURGICAL CALLOSOTOMY IN PATIENTS WITH SEVERE SYMPTOMATIC EPILEPSY
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Purpose: Evaluate of the efficacy and safety of microsurgical callosotomy in the early postoperative period, taking into account the features of the vascularization of the corpus callosum in the surgical treatment of severe symptomatic epilepsy.

Method: In this study were enrolled 13 children with drug-resistant epilepsy aged from 2 to 16 years (mean 7.3 ± 2.8 years) who underwent callosotomy. At the time of the surgery frequency of seizures was 20.3 ± 9.8 per day, 11 from 14 (84.6%) had repeated status epilepticus. Six (46.2%) had one-stage total callosotomy and 7 (53.8%) underwent anterior callosotomy. Postoperative follow-up was from 8 to 30 months (mean - 16.7 ± 3.6 months).

Results: After surgery 4 (30.8%) were seizure-free (Engel scale - 1), 5 (38.5%) had rare short auras (Engel scale - 2), in 3 (23.0%) cases the seizure frequency significantly reduced - over 80%. In 1 (7.7) child who had Rasmussen encephalitis secondary generalised seizures were stopped but partial motor fits persist (Engel scale - 4).

Conclusion: Callosotomy is effective and safe methods of treatment severe epilepsy. Positive outcome is caused less establishing the correct indications for surgery and application of modern microsurgical equipment, taking into account topographic and anatomic features of the blood supply of the corpus callosum.

p0963
OUR EXPERIENCE OF SURGICAL TREATMENT OF MULTIFOCAL EPILEPSY
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Purpose: A characteristic feature of multifocal epilepsy is a high incidence of intractable, severe and traumatic seizures. Patients with multifocal epilepsy are often considered unsuitable for epilepsy surgery. The purpose of the report is to demonstrate our initial experience of surgical treatment of multifocal epilepsy.

Method: 18 patients with multifocal epilepsy were enrolled in study, among them there were 16 (88%) children and 2 (11%) adults. Patient’s age ranged from 4 to 42 years (mean - 12.5 years). Mean duration of epilepsy before surgery was 7.5 years; mean seizure frequency was 21.6 seizures per day. Epileptic encephalopathy observed in 12 cases (67%). Patients underwent the following surgical interventions: topectomy - 4 (22.2%); callosotomy - 7 (38.9%); multilobar resections - 4 (22.2%); callosotomy in combination with resective interventions - 3 (16.7%). Follow-up ranged from 1 to 3.5 years (mean - 2.3 months).

Results: In 10 (55.6%) cases seizure foci were found independently in multiple lobes of the same hemisphere or included a single wide field within several lobes of one hemisphere. In 8 (44.4%) cases seizure foci were found in both hemispheres. After treatment 7 (38.9%) patients became seizure-free (Engel 1), 5 (27.8%) patients had rare short auras (Engel 2), in 4 (22.2%) cases seizure frequency reduced over 75%, in 2 (11.1%) cases seizure frequency reduced less then 75% or did not change. Best results were achieved after multilobar resections and combined resective intervention and callosotomy. There were no postoperative morbidity and mortality.
Conclusion: Our preliminary results may to conclude that multilobar resections and combined resective surgery with callosotomy can be the valuable treatment approach for multifocal epilepsy because of their effectiveness and safeness. Functional disconnecting interventions (callosotomy) aimed to blocking epileptogenic activity and are reserved for patients, suffering from severe epilepsy who are not good candidates for resective surgery.

p0965
ATYPICAL PRESENTATION OF RASMUSSEN’S ENCEPHALITIS: A CASE SERIES
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Purpose: To analyse the unusual clinical, electroclinical, and neuroradiographic features in a group of patients diagnosed with Rasmussen’s encephalitis (RE).

Method: Forty patients with RE seen between 1990 and 2016 meeting the inclusion criteria of the 2014 European Consensus were retrospectively evaluated. Only those with atypical presentations were included in the study.

Results: Of 40 patients, seven presented with atypical forms: Pure motor deficit 3/7 (hemiparesis 2, monoparesis and steppage gait 1); hemichorea and hemidystonia 1/7; isolated focal seizures 3/7. All patients developed epilepsy partialis continua (EPC) 2.8 years after symptom onset (range, 1-6 years). In all patients, EEG recordings at onset showed focal discharges, with unilateral deterioration of the background activity in three. In five patients, the initial MRI did not show signs of atrophy, but in three of them extensive abnormal areas with hyper-intense T2/FLAIR signal in the subcortical white matter compatible with edema and mild mass effect were observed. In another patient, images were suggestive of focal cortical dysplasia and in the remaining one a posterior lesion compatible with tuberous sclerosis (TS) arise from tubers not peri-tuberal cortex (Mohamed, Neurology 2012), and specifically from the dysplastic centre of tubers (Kannan, Brain 2017). We report 6 epilepsy surgeries in 5 children with TS in whom resection was limited to the tuber centre, leaving the tuber rim and surrounding cortex.

Method: The 5 children, aged 0.8-4.2 years at surgery, had epileptogenic tubers in the precentral or postcentral gyri. In 5/6 surgeries, seizures were focal clonic, scalp EEG showed interictal epileptiform discharges (IEDs) and ictal rhythms in the central region, and surgery was performed in 1-stage with intraoperative ECoG. One child had complex seizure patterns and underwent 2-stage surgery with prior intracranial EEG monitoring.

Results: In all 6 surgeries, rhythmic IEDs were recorded from the tuber centre with depth electrodes. To minimize the risk of postoperative motor deficit, surgery was limited to the cortex in the centre of the tubers. Post-resection EEG revealed no rhythmic IEDs in the tuber rim or surrounding cortex. Histopathology revealed a concentration of dysmorphic neurons, compared to tuber rim biopsies. There were no transient or permanent motor deficits following surgery. Focal motor seizures and central IEDs ceased in 5/6 surgeries (follow-up 4 m, 2.1y, 2.2y, 4.7, 4.9y). Seizures continue in the child with complex seizure patterns.

Conclusion: The seizure free outcomes following limited resection of the centre of tubers add to the EEG, MRI and histological evidence of epileptogenicity in TS being localised to dysplastic cortex in the tuber centre.

p0967
MILD MALFORMATION OF CORTICAL DEVELOPMENT WITH OLIGODENDROGLIAL HYPERPLASIA IN FRONTAL LOBE EPILEPSY: CLINICAL AND MANAGEMENT APPROACH OF A NEW ENTITY
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Purpose: Mild Malformation of Cortical Development with Oligodendroglial Hyperplasia in Frontal Lobe Epilepsy (MOGHE) is a recently described clinico-pathological entity associated with a drug-resistant epilepsy. In this communication we report the clinical and prognostic features of patients with MOGHE in our clinic.
p0969
MAPPING HYPEREXCITABLE NEURAL NETWORK CONNECTIONS IN EXTRA-TEMPORAL LOBES IN THE HUMAN BRAIN IN PATIENTS WITH EPILEPSY
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Purpose: Understanding seizure connectivity is of paramount importance if aiming for extensive disconnection of epileptogenic neural networks. The aim of this study is to identify seizure spreading across the extra-temporal lobes of epilepsy patients and to test whether spreading channels are hyperexcitable regions.

Method: 66 seizures were visually analysed by two independent observers and grouped into 14 different types of unilateral onset seizures from 10 patients with intracranial electrodes implanted at KCH. Patients had the following electrode coverage: Frontal, parietal and temporal (FPT), (FP), (TF) and occipital and temporal (OT). Seizures were classified as: seizure onset (SO), seizure spreading (SS). Single pulse electrical stimulation (SPES) delivered electrical stimuli (1 msec, 4-8mAs every 5 secs) to two adjacent channels at a time to identify hyperexcitable regions (delayed responses).

Results: 10 out of 14 seizures had spreading to different lobes. Patients with FPT and SO in the temporal lobe had SS to frontal and parietal and those with SO in the parietal lobe had SS to frontal and temporal. In patients with FP, 4 had frontal SO with 3 SS to the parietal lobe. In patients with TF, 2 had temporal SO with 1 SS to the frontal lobe. In TP, 1 patient had temporal SO with SS to the parietal. In OT, 1 patient had occipital SO with SS to the temporal.

From 10 spreading seizures analysed, one set of spreading channels were hyperexcitable in the OT patient, who has had resective surgery. This may explain the poor post-surgical outcome (Engel III), after 14 months follow up. The remaining spreading channels were not hyperexcitable and therefore the hyperexcitable regions remained in the SO zone.

Conclusion: SS channels are not usually hyperexcitable. However, in patients with hyperexcitable SS channels, resective surgery should include these channels or consider subacute cortical stimulation of them.

p0970
PROLONGED REVERSIBLE NEUROLOGICAL DYSFUNCTION IN NEUROSURGICAL PATIENTS
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Purpose: In neurosurgical patients, unexplainable neurological deterioration is often observed. We report a new category of transient focal neurological dysfunction with electroencephalography (EEG) suppression of neither ischemic nor epileptic cause. Methods: We describe prolonged but fully reversible focal neurologic dysfunctions without the evidence of ischemia and seizures in 8 patients who received indirect revascularization surgery for moyamoya disease. We performed brain imaging including diffusion weighted MR and perfusion MR or SPECT, and EEG during the episodes and after the resolution of the symptoms.

Results: The symptoms were dysarthria with or without hemiparesis, hemiparesthesia of limbs contralateral to the operation side. A patient had a focal motor seizure in paretic arm for 3 minutes in the middle of the episode. The symptoms developed from 12 hours to 8 days after surgery and lasted for 2 days to 17 days. Brain imaging showed only minimal subdural hemorrhage associated with surgery without interval change. Perfusion imaging showed subtle elevation of cerebral blood flow in the operated hemisphere. EEG revealed low amplitude arrhythmic slowing in corresponding hemisphere. Follow-up imaging and EEG after recovery showed no abnormality.

Conclusion: Sudden neurologic deterioration after surgery embarrasses neurosurgeons but it resolves spontaneously if not accompanied by structural abnormality or ischemia. Hypofunction and EEG suppression characterize this phenomenon whereas hyperactivity and EEG hypersynchrony characterize seizure. We hypothesize that the pathophysiology of this condition is transient cortical depression triggered by surgical procedure, like Leao’s “cortical spreading depression”.

p0972
MODIFIED SUBPIAL “EN BLOC” RESECTION FOR AMYGDALO- HIPPOCAMPECTOMY TO AVOID COMPLICATIONS IN TEMPORAL LOBE SURGERY
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Purpose: Temporal lobe surgery including amygdalo-hippocampectomy (AHE) is the most frequent performed procedure in epilepsy surgery. Due to the anatomical relationship of the mesial temporal structures to the midbrain and choroidal fissure, the risk of severe complications like postoperative stroke is up to 1-2%.

Methods: Thus, we developed a modified subpial en bloc resection technique for removing the mesial structures (hippocampus, parahippocampus, uncus and amygdala,) with early identification of the pes mesencephali and the posterior cerebri arteri through the anterior part of the fronto-mesial temporal horn cleft. Uncus and amygdala were removed as a second step after visualization of the cleavage plane between midbrain and middle cerebral artery.

Results: Altogether, 81 patients had temporal lobe epilepsy surgery including amygdalo-hippocampectomy for various pathologies using this surgical technique (42 hippocampal sclerosis,14 epilepsy associated tumors- gangliogliomas, DNET, 25 other pathologies- cavernomas, scar tissue, mild cortical dysplasia). All patients had anterior temporal resection including amygdalo-hippocampectomy. Seizure outcome was favorable after one year: 64% (35/55) were completely seizure free (Engel1A) and 75% had Engel Class 1 outcome. Surgical complication rate was 3.7% (reoperation for 1 empyema and 2 subdural hematomas), severe neurological complication rate was 1.2% temporarily (1 transient hemiparesis due to postoperative vasospasm) and 0% permanently.

Conclusion: The described subpial modified en bloc resection technique for temporom-dentate structures demonstrated low complication rates in surgery of medically refractory temporal lobe epilepsy. Its attention especially contributes to avoid permanent hemiparesis.
p0974
SEIZURE OUTCOME OF PATIENTS WITH MAGNETIC RESONANCE IMAGING-NEGATIVE EPILEPSIES: STILL AN ONGOING DEBATE
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Purpose: The aim of our study is to present our surgical results and discuss clinical and histopathological parameters related to outcome in patients with MRI-negative epilepsy

Method: 36 MRI-negative epilepsy patients (19 females / 17 males) who had been evaluated for surgery at our institution between 2004 and 2016 were retrospectively analyzed. Histopathological specimens were re-reviewed by two blind neuropathologists and re-classified based on the current classifications. Seizure outcome of the patients were assessed on the basis of Engel’s classification.

Results: The mean age at surgery was 24.5 years (9-51 years) and the mean seizure onset was 9.3 years (1-30 years). Eight patients were younger than 18 years. The mean duration of seizures was 15.3 years (2-41 years). All but two underwent invasive monitoring. A total of 33 patients out of 36 were finally operated on. Eighteen patients had hypometabolism on FDG-PET with temporal lobe involvement in majority (66.7%). Hypometabolism was found in all patients with hippocampal sclerosis (HS), however it was 50 % and 66.7% in Focal Cortical Dysplasia (FCD) type I and II patients, respectively. The frontal lobe resection was the most frequent followed by temporal, parietal and occipital lobes. In 7 patients multilobar resection was necessitated. Histopathological diagnosis was FCD type I, II, III, HS, and gliosis in 14, 12, 2, 3 and 2 patients, respectively. The mean follow-up was 5.8 years (1-12 years). Seventeen patients were seizure free and favorable outcome (Engel I and II) was found in 69.7%. FCD type I tend to have more favorable seizure outcome. Duration of epilepsy and hypometabolism on FDG-PET was significantly related to outcome, whereas involved lobe was not.

Conclusion: Results from our own experience like others, that, it is worth pursuing resective surgery in adults as well as in children with drug-resistant epilepsy with normal MRI.

p0976
ROBOTIC STEREONEUROENCEPHALOGRAPHY WITHOUT HEAD-FRAME AND COMPUTED TOMOGRAPHY – ANALYSIS OF ACCURACY
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Purpose: Recent studies with classical frame-based stereotaxy but also robot-guided stereotaxy use computed tomography (CT) scans for referencing the system to the patients’ head. Thereafter the CT dataset is fused with the preoperative magnetic resonance imaging (MRI), which usually was used for trajectory planning. In order to reduce CT radiation, in particular for children, we have performed robot guided stereotactic procedures using preoperative MRI datasets, only. We will provide evidence that using only preoperative MRI datasets referenced with a laser scan of the patients` face is sufficient for sEEG implantations.

Method: Forty sEEG electrodes for recording of a potential epileptogenic zone due to pharmacoresistant epilepsy in five patients (three male, mean age 31 years) by the robotic surgery assistant (ROSA, Zimmer Biomet Robotics, Monpellier, France) were evaluated. Trajectories were planned on preoperative MRI with a safty margin of 5 mm, where no vessels or sulci were accepted. Postoperative CT identifying electrode positions were fused with the preoperative MRI-based planned and the accuracy was determined by the target point error (TPE) and the entry point error (EPE) applying the Euclidian distance.

Results: In 3 Tesla (T) MRI mean TPE amounted to 2.96 mm (min. 2.04 mm, max. 4.4 mm), mean EPE to 2.53 mm. The TPE was larger in temporal implantations, where it amounted to 3.02 mm, the mean temporal EPE was 2.39 mm. The accuracy was improved 1.5 T MRI, mean TPE amounted to 1.72 mm. The mean time of diagnostic recording amounted to 8.8 days (minimum five days, maximum 11 days), No complications, hemorrhages, infections, etc., were observed.

Conclusion: Robot-guided sEEG based on three Tesla MRI safes radiation for patient and can be still safely performed.

p0977
TESTING QUALITY INDICATORS FOR ADULT EPILEPSY MONITORING UNIT IN THE CENTER FOR TREATMENT OF REFRACTORY EPILEPSY (CETER), A NEW EPILEPSY MONITORING UNIT IN BRAZIL
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Purpose: An evidence-based consensus of quality indicators for epilepsy monitoring units (EMU’s) was developed by Sauro and colleagues, on behalf of the EMU Quality Improvement Team (Epilepsia, https://doi.org/10.1111/epi.13563, 2016). The purpose of our study was to test these indicators in our EMU.

Methods: We implemented and evaluated the 25 evidenced-based indicators selected by Sauro and colleagues in our EMU, The Center for Treatment of Refractory Epilepsy (CETER). CETER is a new two bed EMU that has been used for evaluating patients with epilepsy during the last twelve months in our hospital. CETER is in Hospital de Clínicas de Porto Alegre (HCPA), Brazil.

Results: During one year, 52 patients were admitted in CETER and some of suggested indicators are reported here. Summarizing, three patients (63.5%) were female, with mean age of 41.9 years. Mean time of hospitalization was 10.3 days. Twenty-three patients (44.2%) were referred for diagnostic evaluation, three (5.8%) for optimizing medical treatment and 26 (50.0%) patients were referred for epilepsy surgical work-up. Forty (76.9%) patients had confirmed diagnosis of epilepsy, 8 (15.4%) had only psychogenic non-epileptic seizures and 4 (7.7%) patients had inconclusive video-EEG results. Video-EEG monitoring was considered extremely useful or very useful in 27 (51.9%) and 14 (28.9%) patients respectively, leading to change in treatment in 35 (67.3%) patients. Four (7.7%) patients had adverse events during video-EEG monitoring. Ten temporal and 2 extra-temporal lobe surgeries were done, with 8 patients (66%) showing Engel I outcome.

Conclusion: In our experience, the indicators suggested by Sauro and colleagues were very useful for assessing objectively the quality and safety in our EMU. We approve it and will use these indicators for our practice. We highly recommend implementation of these indicators in any EMU as a simple and effective way to improve medical care in epilepsy. Study funded by CNPq.
P0978 GOOD OUTCOME OF RESECTIVE EPILEPSY SURGERY IN PATIENTS WITH NON-LESIONAL FOCAL EPILEPSY AFTER INVASIVE EVALUATION WITH STEREOTACTICALLY IMPLANTED DEPTH ELECTRODES
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Purpose: To evaluate the outcome of resective surgery after intracranial EEG recording from depth electrodes and identify risk factors for unfavorable outcome.

Method: All patients had noninvasive Video-EEG-monitoring and MRI scans, some had additional SPECT, PET or DTI scans. Implantation of electrodes was planned individually, based on the conclusive interpretation of all available clinical and imaging data. Tailored resections were planned individually and were aided by a MRI-guided navigation system where labelled electrode localizations were available for reference. Clinical characteristics, details of electrode implantation, resection volume and postsurgical outcome were determined. Chi-square / Fisher’s exact test for categorical variables and Student’s t-test / Mann-Whitney U test for continuous variables were used for statistical analysis to identify prognostic factors for postsurgical outcome.

Results: 70 patients were included (median age: 34.9 years). Structural MRI was non-lesional in 29 patients (41%) and showed a structural lesion in 41 (59%). 26 patients (37%) had temporal lobe seizure onset, 44 (63%) were extratemporal. Between 3 and 16 (median 9) depth electrodes were implanted. After a median follow up of 13.1 months 79% of the patients were free of all seizures (Engel IA). Another 17% were free or almost free of disabling seizures (Engel IB, IC and II). There was no significant difference between lesional (81% Engel IA) and non-lesional (77% Engel IA) patients (p = 0.73), between temporal or extratemporal (p = 0.81) and left- or right-sided (p = 0.69) resection, nor between first resection and re-operation (p = 0.78) or an effect of proximity to eloquent cortex (p = 0.59). There was no difference in the average resection volume between lesional (28 cm³) and non-lesional (26 cm³) patients (p = 0.64).

Conclusion: Resective epilepsy surgery after invasive EEG with depth electrodes can achieve as good an outcome in non-lesional as in lesional focal epilepsy with temporal and extra-temporal seizure onset.

P0981 POST-OPERATIVE INFECTIONS SECONDARY TO INVASIVE ELECTRODE MONITORING AND EPILEPSY SURGERY IN PEDIATRIC POPULATION
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Many children with medically refractory epilepsy, who are candidates for epilepsy surgery, require placement of intracranial electrodes to further localize or localize their seizures. The variety of electrodes include subdural grid and strips as well as depth electrodes. These electrodes are left in situ over a week period, after which a decision about resective surgery is made. The factors influencing rate of postoperative infections associated with the procedure is unclear. This retrospective study reports the rate and nature of post operative infection in our pediatric neurosurgery centre in relation to various patient factors. We reviewed 198 consecutive patients who underwent insertion of intracranial electrodes between the 2001 and 2015. The protocol for prophylaxis antibiotics consists of intravenous Vancomycin & Cefotaxime while the electrodes are in situ, intravenous Cloxacillin for 5 days after removal with a final switch to oral Cephalexin for an additional 5-7 days. There were two cases of intracranial infections with six superficial wound infections. We then examined factors that may correlate with infection including number and type of electrode implants, length of operation, number of personnel in the operating room, number of anti-epileptic medication, and preoperative bloodwork. Preliminary analysis did not show a significant correlation between infection and age, length of procedure or number of monitoring days. Quantifying our infection rate and treatment can inform future prospective studies to reduce postoperative infections in children undergoing this procedure.

P0982 DIFFERENT GAIN-OF-FUNCTION EFFECTS IN SCN2A-MUTATIONS
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Purpose: Mutations in the SCN2A gene cause a broad spectrum of epilepsy syndromes of variable severity including neonatal-infantile seizures and epileptic encephalopathies, but also neuropsychiatric disorders such as autism spectrum disorders and schizophrenia. Here, we describe four different mutations in the SCN2A gene causing three distinct phenotypes: benign familial neonatal-infantile seizures (BFNIS), myoclonic atonic epilepsy (MAE) and one patient with intractable neonatal seizures. Although phenotypes were quite diverse, our electrophysiological studies revealed gain-of-function defects for all of them.

Method: We evaluated the clinical and genetic characteristics of the four families, identified four SCN2A mutations - three of them novel - and characterized their functional consequences.

Results: Patient 1 and 2 with BFNIS showed typical clusters of cognitive and bilateral tonic-clonic seizures up to status epilepticus between 3 and 13 months. There were four, respectively two, affected family members. Also in Patient 3 (MAE) the mother was a carrier but without a clinical manifestation. Only Patient 4 carries a de novo mutation. Sequencing of SCN2A revealed 3 novel missense mutations: R28C, T773I, K908E. The V208E mutation was described earlier, but without electrophysiological characterization.

Functional studies using heterologous expression in tsA201 cells and whole cell patch clamping disclosed an increased window current for the K908E, V208E and T773I mutations, as well as an increased persistent current (T773I). By reproducing the physiological dynamic conditions of a firing neuron through the application of action potentials as voltage stimuli, we were able to show that during these stimuli all mutations exhibited an increased sodium inward current, which occurred in the critical subthreshold depolarizing phase. Interestingly, one of the mutations (R28C) disclosed this subthreshold Na⁺ current as sole finding, which we plausibly explain a neuronal hyperexcitability and epileptic seizures.
common specific phenotypical or investigative findings that would prompt SCL6A1 testing.

**Method:** Retrospective chart review.

**Results:** Two of the patients were monozygotic twins and one was an unrelated female.

The monozygotic twins were referred jointly at 23 months and were subsequently diagnosed with atypical myoclonic astatic epilepsy. Both have responded to the initial anti-epileptic drug trialled (sodium valproate). They both had global developmental delay with marked social communication difficulties evident prior to the onset of seizures.

In the third case anti-epileptic therapy is rifampinamide and clonazepam. Previous AEDs include levetiracetam, sodium valproate and topiramate. This patient also has severe learning difficulties and global developmental delay prior to the onset of seizures.

Phenotypically all 3 cases were similar with blonde hair, profound speech delay, global developmental delay preceding the onset of epilepsy and ASD traits. In all cases the diagnosis of Angelman Syndrome was suggested from the EEG reports indicating high amplitude rhythmic 4-6 Hz activity, prominent in the occipital regions, with spikes, which can be facilitated by eye closure on at least one occasion. Subsequent EEGs were more in keeping with MAE.

**Conclusion:** Cognition and development are generally normal at the onset of seizure development (ILAE definition). In these cases, developmental delay was found prior to the onset of seizures. This is not a unique finding and Carville et al. (2015) found that similar across the cohort of patients identified with this mutation. The EEG findings and the common phenotypical blonde hair with profound speech delay may be a common feature that could prompt testing for SLC6A1.

**Epilepsy and Clinical Sleep Disorders Improve in Adolescents and Adults with Angelman Syndrome: A Multicenter Study of 46 Patients**

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**Purpose:** Angelman syndrome (AS) is caused by deficient expression of the maternal copy of the ubiquitin protein ligase E3A gene. Actual knowledge on evolution of AS relies on questionnaire-based cohort studies, phone interviews or small retrospective cohort studies focused on specific clinical-genetic features, providing conflicting results. This study aims to assess long-term outcome of epilepsy, sleep disorders and EEG in a vast series AS subjects.

**Method:** We collected patients with genetically confirmed AS, aged ≤ 14 years, followed in three tertiary epilepsy Centers or attending the meetings of the Italian Organization for AS (OrSA). Retrospective clinical and EEG data were retrieved from hospital archives or family documents. At index evaluation (IE) (last visit at tertiary Centers or single visit during OrSA meetings), caregivers were interviewed about anamnestic data and filled questionnaires on sleep disorders and daily-living skills; patients underwent general and neurologic evaluation, video-EEG recordings. All available EEGs were analyzed to compare evolution of spike-wave index (SWI) over the years.

**Results:** Forty-six subjects aged 14-45 years were included: 24 from tertiary Centers, 22 from OrSA meetings. Forty-two/46 (91.3%) had seizures during childhood, which improved over the years in all subjects. Among epileptic patients, 27/39 (69%) over the years. At IE, daily-living skills corresponded to age ≥ 1.6 years in 29/46 (63%). EEG showed typical AS patterns in 35/46 (76.1%). SWI was not significantly different between infancy/childhood and adolescence/adulthood in EEGs recorded from 10 patients.

**Conclusion:** Improvement of epilepsy or sleep disorders should not disregard clinical suspicion of AS in adolescent or adult patients with suggestive features. Drug withdrawal might be considered in the management of epilepsy during adolescence or adulthood, despite the persistence of epileptiform abnormalities.

**DISCOVERY AND PATHOGENICITY ASSESSMENT OF NEUROPATHOLOGY-ASSOCIATED GENE VARIANTS**

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Germline and brain-specific somatic variants have been reported as an underlying cause in patients with epilepsy-associated neuropathologies, including focal cortical dysplasias (FCDs) and long-term epilepsy associated tumors (LEAT). However, evaluation of identified neuropathology-associated variants in genetic screens is complex since not all observed variants contribute to the etiology of neuropathologies not even in genuinely disease-associated genes. Here, we critically reevaluated the pathogenicity of 12 previously published disease-related genes and of 79 neuropathology-associated missense variants listed in the PubMed and ClinVar databases. We

1. assessed the evolutionary gene constraint using the pLI and the missense z score,
2. used the latest American College of Medical Genetics and Genomics (ACMG) guidelines, and
3. performed bioinformatic variant pathogenicity prediction analyses using PolyPhen-2, CADD and GERP.

Constraint analysis classified only seven out of 12 genes to be likely disease-associated. Furthermore, 78 (89%) of 88 neuropathology-associated missense variants were classified as being of unknown significance (VUS) and only 10 (11%) as being likely pathogenic (LPII). Pathogenicity prediction yielded a discrimination between LPII variants and a discrimination for VUS compared with rare variant scores from individuals present in the Genome Aggregation Database (gnomAD). In summary, our results demonstrate that interpretation of variants associated with neuropathologies is complex while the application of current ACMG guidelines including bioinformatic pathogenicity prediction can help improving variant evaluation. Furthermore, we will augment this set of literature-identified variants at the conference by results from our variant screen using self-generated deep sequencing data in >150 candidate genes in >50 patients not yet analyzed.
p0986
NOVEL MUTATIONS IN SLC2A1 GENE: PHENOTYPE VARIABILITY OF GLUT1 DEFICIENCY SYNDROME IN A SMALL CASE SERIES

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Purpose: Glucose transporter type 1 (GLUT1) deficiency due to SLC2A1 gene mutation has been recognised to cause a widespread range of neurologic disorders ranging from severe encephalopathy with developmental delay, epilepsy, ataxia and acquired microcephaly of the “classical” phenotype, to atypical variants with less severe manifestations. Early diagnosis is crucial because it allows the start of the ketogenic diet. However, recognizing GLUT1 deficiency syndrome (GLUT1DS) may represent a challenge for the clinician, leading to a late diagnosis. Hereby we present the clinical and genetic features of a small case series of both sporadic and familial cases confirming the wide spectrum of clinical phenotype of GLUT1DS.

Method: Patients with a clinical history suggestive for GLUT1DS have been screened for SLC2A1 mutations. Blood samples were collected from proband and first degree relatives. All patients underwent a full clinical, neuroradiologic (MRI), neurophysiologic examination (EEG recording) and neuropsychological assessment. A lumbar puncture was performed in 2 patients in fasting state and both cerebrospinal fluid and blood glucose measurement were undertaken at the same time.

Results: Since 2010, 19 patients with a clinical history suggestive for GLUT1DS have been screened for SLC2A1 mutations. We identified 4 different SLC2A1 pathogenic variants in 3 sporadic cases and one pedigree. In 2 patients the GLUT1DS was related to novel SLC2A1 mutations. Two patients presented mutations already reported in literature but associated with different phenotypes.

Conclusion: Here we describe a small case series of patients with sporadic (3 cases) and familial (1 pedigree) GLUT1DS presenting with a wide phenotypic heterogeneity, leading us to a considerable delay in the diagnosis. In 2 of our patients the GLUT1DS was related to novel SLC2A1 mutations.

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p0988
AUDIOGENIC SEIZURES INDUCE CHANGES IN THE GENE EXPRESSION IN THE INFERIOR COLICULUS OF TWO ANIMAL MODELS OF EPILEPSY, THE WAR AND GASH: SAL STRAINS


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Purpose: Genetic animal models of epilepsy are important tools for understanding the cellular mechanisms underlying epileptogenesis and for developing novel antiepileptic drugs. We conducted a comparative study of gene expression in the inferior colliculus (IC), a nucleus that triggers audiogenic seizures, using two animal models of reflex epilepsy, the Wistar audiogenic rat (WAR) and the genetic audiogenic seizure hamster (GASH:Sal).

Method: WAR and GASH:Sal animals were exposed to high intensity auditory stimulation, collecting the IC 60 min later. RNA was isolated, and microarray analysis was performed using the rat (Gene 1.0 ST Array) or mouse (GeneChip® Mouse Gene ST Array) microarrays. We also carried out RT-qPCR analyses to validate some genes in the microarrays of the IC. In the case of the hamster study, we employed Chinese hamster probes (Cricetulus griseus) via transcriptomic analysis for results verification. For comparison, controls animals were subjected to the same stimulus, tissue preparations, protocols and gene expression analysis than those carried out in the epileptic models.

Results: Among the common genes differentially expressed in both models, we identified the zinc finger imidazole-endothelial growth response gene (Egr3), the ATP-transport protein gene (Abch1), the gene encoding neuropeptide Y (Npy), the Regulator of G protein signaling (Rgs2) and the gene encoding the carrier protein Translhyretin (Tir). These genes are associated with stress responses (Egr3 and Npy), with epilepsy encoded protein is expressed in the central nervous system and contains a 7-transmembrane receptor domain that binds calcium. Diseases associated with this gene include Usher syndrome 2 and familial febrile seizures. We study the expression of this gene in the Mesocricetus auratus strain GASH:Sal, a genetic audiogenic seizure hamster, inbred at the University of Salamanca.

Method: Ictal events in strains susceptible to audiogenic seizures cause gene deregulation in the inferior colliculus, an auditory nucleus involved in epileptogenesis. Thus, we study the expression of ADGRV1 gene with real-time RT-PCR, comparing controls and GASH:Sal under stimulated and basal conditions. Since ADGRV1 gene is required for proper stereocilia maturation of cochlear hair cells, we also study the cochlear receptor of the control and GASH:Sal using scanning electron microscopy.

Results: Compared to controls, ADGRV1 expression was found to be very reduced in the inferior colliculus of the GASH:Sal under stimulated and basal conditions. At electron microscopy level, the GASH:Sal showed cochlear damage characterized by marked distortions in the organization and number of the stereocilia.

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phenotypes (Npy and Achebila) and one of them (Rgs2) is the target of the antiepileptic drug Levetiracetam®.

**Conclusion:** Ictal events in strains susceptible to audiogenic seizures cause gene deregulation in the IC. These data may contribute to the knowledge of new targets on which antiepileptic drugs act.

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**Abstract**

**Purpose:** To identify the genetic cause underlying SHE (also known as Nocturnal Frontal Lobe Epilepsy) in a large cohort of patients.

**Methods:** We performed genetic analysis using different approaches (screening, NGS epilepsy gene panel, MPS targeted sequencing and WES), in patients with clinical/confirmed SHE, according to predefined diagnostic criteria. Both familial and sporadic cases were enrolled.

**Results:** From a pool of 191 SHE probands, 128 underwent at least one genetic test.

**Findings:**

(i) three variants were found 126 patients where CHRNA4 was sequenced (2.4%). A novel missense change with incomplete penetrance (p.G307V) in the proband of an ADSHE pedigree; two mutations (de novo p.S284L; p.S284W) in two sporadic patients with refractory SHE;

(ii) two mutations in KCNQ1 were found in 2/112 pts (1.8%): a de novo p. Ab397 in a sporadic case with intellectual disability (ID) and an inherited p.Tyr796His in a proband with ID and psychiatric disorders of an ADSHE pedigree;

(iii) six mutations in DEPDC5 were found in 6/107 pts (5.6%). Five loss-of-function mutations (p.T295Lfs*7; p.R165Yfs*13; c.279 +1G>A; p.R389Ps*2; p.R422*) in the probands of three families and in two sporadic cases, and one pathogenic missense variant (p.Y281F) in a sporadic case:

(iv) a missense mutation (p.L1105P) of NPR1 (1/87) was found in the proband of a FFEVF pedigree with prevalent SHE phenotype;

(v) no mutations were identified in the other genes coding for neuronal acetylcholine receptor subunits (nAChRs) CHRNA2 (0/123), nor in PRIMA1 (0/64), nor in NPRL3 (0/87).

**Conclusions:** Mutations in GATOR1 genes account for 6.5% of our cases, with DEPDC5 showing the highest frequency. KCNQ1 accounts for a low proportion of our cohort and is confirmed to be involved in SHE associated with ID. nAChRs genes and PRIMA1 appear to have a minor role in this disorder.

**DNA METHYLATION OF THE BRD2 PROMOTER IS ASSOCIATED WITH JUVENILE MYOCLONIC EPILEPSY ETIOLOGY**

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Juvenile Myoclonic Epilepsy (JME) is one of the most common of the adolescent onset generalized epilepsy syndromes. BRD2 has consistently been found to be involved in the expression of JME and the BRD2-JME link in humans is further corroborated by our murine model (Brd2+/−), which demonstrated that Brd2 insufficiency leads, in mice, to clinical hallmark signs of JME. Yet no JME-related exonic mutations were ever found in human BRD2, so we have focused on testing putative non-coding regions for influence on JME susceptibility. The BRD2 promoter harbors a JME associated SNP (rs3918149) and a CpG island (CpG75) making it a potential “hotspot” for JME-associated epigenetic variants. Methylation of the promoter CpG sites in BRD2 has been shown to lead to gene silencing. We tested whether DNA methylation of the BRD2 promoter (and therefore lead to a deficit of BRD2 transcription) is tied to the JME phenotype. We did bisulfite sequencing, pyrosequencing, and glo-
**Abstracts**


**Purpose:** Epilepsy is one of the most common neurological disorders, and is known to have a very heterogeneous background with a strong genetic contribution. However, making a genetic diagnosis can be challenging as there is both genetic heterogeneity and phenotypic heterogeneity for a specific gene. The most severe epilepsy phenotypes are often caused by de novo variants, however, some of these might be inherited from mosaic parents, which will influence genetic counselling. The aim of this study was to develop a diagnostic screening method to analyze the genetic basis of childhood epilepsies, and to investigate the ratio of variants inherited from mosaic parents. 

**Method:** A cohort of 644 patients were analyzed on evolving NGS gene panels targeting from 31 to 97 known epilepsy genes. Epileptic encephalopathy or childhood epilepsy were the predominant phenotypes amongst the cohort. Potentially causative variants were evaluated by literature and database searches and submitted to bioinformatic prediction algorithms. All variants were confirmed by conventional Sanger sequencing and, when possible, validated by parental testing and segregation analysis. Parents of 42 patients carrying an apparent de novo variant were screened by NGS deep sequencing to analyze for parental mosaicism.

**Results:** We identified a presumed disease-causing variant in 131 of 644 patients (20%). The aberrations encompassed known and unknown variants in 39 different genes. In 3/42 cases (7%), parental DNA showed mosaicism of the causative variant.

**Conclusion:** We have developed a rapid and cost-efficient screening panel for the analysis of the genetic basis of childhood epilepsies. With this panel we were able to find a disease-causing genetic variant in 20% of the analyzed patients. Seven % of the patients tested negative by Sanger sequencing could be showed to be mosaic.

**S177**

**p0998 RECESSIVE VARIANTS IN VARS CAUSE A CLINICAL SYNDROME WITH SEVERE DEVELOPMENTAL DELAY, EPILEPSY AND MICROCEPHALY**


**Purpose:** Recessive variants in tRNA synthetases, like QARS, AARS and KAARS, have been previously linked to epilepsy and developmental delay. In this study, we focus on recessive variants in VARS, encoding a valyl tRNA synthetase, which might play an important role in development and epilepsy.

**Method:** All variants were identified with whole exome or whole genome sequencing and validated with conventional Sanger sequencing. A zebrafish knockout (KO) model was developed using CRISPR-Cas9 to study the zebrafish phenotype.

**Results:** Through international collaborations we identified three families with compound heterozygous or homozygous missense variants (p.Arg173Leu) in VARS. The three patients with compound heterozygous variants had severe developmental delay (DD), early onset epilepsy and microcephaly, whereas the homozygous variant was identified in a consanguineous family, in which five out of six pregnancies ended prematurely due to intra-uterine fetal death. Yeast complementation assays showed a loss of function effect for the Gly822Ser variant. Results from a KO zebrafish model showed that vares HO larvae died prematurely, had smaller head and eyes and their locomotor activity was decreased in comparison to heterozygote and wild type larvae. Moreover, investigation of abnormal brain activity demonstrated that recurrent spontaneous epileptiform events occurred in ~55% of all HO larvae.

**Conclusion:** We identified three families with novel recessive variants in VARS. All patients had a complex developmental disorder including severe DD, early onset epilepsy and microcephaly except for one family where intra-uterine lethality repeatedly occurred. The results from a zebrafish KO model provided a functional proof that vares KO in a vertebrate in vivo system caused abnormal seizure-like behaviour.
p1000
GENETIC CAUSES OF PEDIATRIC EPILEPTIC ENCEPHALOPATHY: A RETROSPECTIVE CHART REVIEW
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Purpose: Advances in genetic diagnostics has led to the identification of etiology in upto 30% previously labeled ‘idiopathic’ epilepsies. The Genetic counseling should be available to all epilepsy patients. The candidate genes span the entire neuronal structure with widespread functional implications. A retrospective review of genetic causes of pediatric epileptic encephalopathy (EE) is being presented from a tertiary care center in north India.

Method: Between January 2015 to December 2016, 218 children presented with EE, of which, in 72, an etiology was not identified. The detailed etiological evaluation included MRI brain EEG/metabolic testing (arterial lactate/pH, blood sugar, urine ketones, blood tandem mass spectrometry and urine gas chromatography mass spectrometry) and cerebrospinal fluid (CSF) analysis (CSF: serum glycine, CSF: blood glucose and lactate) and enzyme analysis for neuronal ceroid lipofuscinoses 1 and 2. Results: Of these 72 children, 29 underwent gene panel testing by next generation sequencing (NGS). Eight neonates presented with EE, of which five had additional extrapyramidal features. The neonates with isolated EE demonstrated KCNT-1 mutations (N = 3), while the five with additional extrapyramidal features demonstrated mutations in PNPO, KCNQ2, GRIN2B, APTP7A, and GPR98 genes. Three patients presenting with early infantile EE showed SCN2A, SCN8A, and NUBPL mutations. Seven patients (aged 6 to 24 months) presented with Genetic Epilepsy Febrile Seizures Plus phenotype and were detected to have SCN1A (N = 5), SCN2A (N = 1) and PRODH (N = 1) mutations. Five children presenting as west syndrome were noted to have PRRT2, ALG13, SCN8A, CHRNA2 and DEPDC5 mutations. One child presenting at four years with myoclonic-astatic phenotype demonstrated CLCN5 mutation, while another presenting at 8 years with focal seizures, neuroregression and dystonias showed POLG mutation. Two children with myoclonia-astasia did not reveal any mutation.

Conclusion: It is advisable to obtain a genetic diagnosis wherever feasible in children with EE as it has important diagnostic, therapeutic and prognostic implications.

p1002
DISTRIBUTION OF GENETIC EPILEPSIES AND ACCORDINGLY ADJUSTED MEDICAL TREATMENT AT THE DANISH EPILEPSY CENTRE: A SYSTEMATIC ANALYSIS OF CHILDREN BORN BETWEEN 2006 AND 2011
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Purpose: We aimed to assess the distribution of genetic epilepsies and accordingly adjusted Medical treatment at a tertiary epilepsy centre.

Method: The records of all children born between 2006 and 2011 and followed at the Danish Epilepsy Centre in 2015 were systematically analyzed regarding: diagnosis, epilepsy syndrome, age of seizure onset, cognitive skills, MRI findings, co-morbidities, genetic diagnosis, and medical treatment adjustments due to the genetic diagnosis.

Results: A total of 357 patients were included, however 27 (7.5%) of them turned out not to have epilepsy, and 40 children (11%) had epilepsy due to an acquired damage. These two groups of patients were excluded from further analysis. The remaining 290 children were mainly diagnosed with epileptic encephalopathies or intractable focal or multifocal epilepsies. Only 177/290 cases (61%) underwent genetic testing and a genetic cause for their epilepsy was found in 87 of them (49%). The most common genetic syndromes were Dravet syndrome and tuberous sclerosis followed by the PCDH19 and SCN2A related disorders. The medical treatment was subsequently adjusted as a result of the genetic diagnosis in 29/87 of the cases (33%), meaning that the genetic diagnosis ensured the best possible medical treatment of these children. The adjustments included more specific treatment for patients with Dravet syndrome, SCN2A, SCN8A, SLC2A1, and KCNQ2 related disorders.

Conclusion: In the present study, we found that 49% of the genetically tested children at the Danish Epilepsy Centre had a proved genetic cause of their epilepsy and that 33% of the children with a genetic diagnosis were ensured the best possible medical treatment due to their genetic diagnosis. This study supports that a genetic diagnosis leads the way toward more personalized medical treatment.

p1003
WIDESPREAD WHITE MATTER ALTERATIONS PREDICT REFRACTORINESS IN MILD TEMPORAL LOBE EPILEPTIC PATIENTS
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Purpose: Mild mesial temporal lobe epilepsy (mMTLE) is characterized by adult-onset, long-term seizure freedom (> 24 months) and drug-responsiveness. About a quarter of patients with mMTLE develop refractoriness after a decade. We aim to identify potential early imaging biomarkers of refractoriness already at baseline.

Method: Fifty-five participants were drawn from a larger cohort of previously described mMTLE patients. At baseline, all 55 patients had mMTLE and underwent structural MRI at 1.5T, including a 3D T1-weighted spoiled gradient echo sequence. Based on the long-term outcome after a mean follow-up of 12 ± 3 years, we divided the baseline group into two cohorts: 19 patients with refractoriness and 36 patients with continued drug-responsive epilepsy. We then performed an Advanced Structural Imaging Analysis using the Freesurfer software package.
cohort into two groups for statistical analyses: true mMTLE patients (N = 39) and "shifted" (sMTLE) patients (N = 16). All T1 images were processed using FSL and FreeSurfer. We performed voxel-based morphometry, cortical thickness and local gyrification index analyses, in order to compare grey and white matter density (GM, WM), cortical GM thickness and cortical folding abnormalities, respectively. Statistical analyses were carried out accounting for age, age at onset, gender, presence of HS, left and right hippocampal volumes, correcting for multiple comparisons across space using Threshold-Free Cluster Enhancement (in FSL) or False Discovery Rate (in FreeSurfer) methods.

**Results:** All analyses concerning GM structure revealed no significant difference at baseline between mMTLE and sMTLE. On the contrary, VBM highlighted a widespread bilateral region in which temporal, frontal and parietal WM density was significantly reduced in sMTLE vs mMTLE already at baseline, i.e., when all patients were drug-responsive.

**Conclusion:** Due to its clinical and radiological features, mMTLE represents a superb resource to better delineate the biological substrates underlying the epileptic syndrome itself. In this work, we found further evidence that WM alterations may play a crucial role in the processes that lead to the development of refractoriness in MTLE later on.

**p1005 MRI T2-HYPERINTENSIVE LESIONS IN TSC CHILDREN TREATED WITH VIGABATRIN**


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**Purpose:** To assess T2- and DWI- MRI changes in the basal ganglia observed in pediatric patients with epilepsy associated with tuberous sclerosis treated with vigabatrin. It has been uncertain whether these lesions should be regarded as pathological and are ADC values of any clinical importance.

**Method:** MRI brain examinations of 54 TSC patients were analyzed. 32 were male (59 %) and 22 female (41 %). Their age varied from 7 weeks to 11 years, median 15 months. All children were treated with vigabatrin. The control group consisted of 10 age-matched children with no known history of neurological disorder or brain MRI pathology. The ADC was measured with a manual placement of regions of interest (ROIs) in the thalamus. The signal intensities of the thalamus, basal ganglia, midbrain, dorsal brainstem, and dentate nuclei were analyzed visually. ADC values of the thalamus were measured and compared with control.

**Results:** 9 patients (17 %) demonstrated at least one focus of abnormal MRI signal, 4 were female and 5 male. In 88 % of patients the lesions were observed in thalamus, in 66 % in midbrain in 88 % in tegmentum, in 66 % in globi pallidi and 22 % had abnormal signal in dentate nuclei. 2 patients out of 9 (22 %) had lesions in all analyzed regions. We detected no correlation between these lesions and sex, TSC type, VGB dosage, treatment duration or clinical state of patients. ADC values were notably lower in children with DWI/T2WI signal abnormalities therefore seem unlikely to be a variant of physiological development.

**Conclusion:** MRI abnormalities in infants with TSC treated with VGB are relatively common, benign findings. Lesions are most frequently found in the thalamus. ADC has proven to be a useful and objective parameter in evaluating these lesions when they are not clearly visible on DWI/T2WI.

**p1006 RELIABILITY OF PRESURGICAL BRAIN MRI PROTOCOLS IN EPILEPTOGENIC LESION DETECTION: THE TERTIARY EPILEPSY CENTER EXPERIENCE**

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**Purpose:** To assess the reliability of presurgical brain MRI examination in detection of epileptogenic lesions in patients with focal farmacoressistant epilepsies.

**Method:** We conducted two year prospective study in 222 consecutive patients (110 men and 111 women) with focal farmacoressistant epilepsies. We compared the standard prehospital brain MRI findings with the findings of MRI reinvestigation performed according to the protocol based on electroclinical diagnosis of an epileptic syndrome. The patients with temporal lobe epilepsy (91/222; 41%) were undergone brain MRI protocol with axial planes aligned with the longitudinal axis of hippocampus. In patients with extratemporal epilepsies MRI axial planes were aligned with anterior-posterior commissure line. The starting point for coronal planes was frontal pole in frontal and periradicl epidemies (37/222; 16%) or occipital pole in posterior epidemies (26/222; 12%). All other patients (68/222; 31%) diagnosed as nonlocalised epilepsies were excluded from the analysis. MRI structural images were acquired using 1.5T MRI Scanner with all preferred sequences in sagital, axial and coronal orientation. MRI findings were analyzed by the experienced neuroradiologists.

**Results:** Epileptogenic lesion was detected in 59.9% of all prehospital MRI scans and 72.4% of all presurgical MRI scans (p = 0.0064). Presurgical MRI scans comparing to presurgical MRI scans were much more valuable in discovering epileptogenic lesion among temporal (84.4% vs. 70.1%; p = 0.032) then extratemporal epilepsy patients (50.1% vs. 65.1%; p = 0.1452). Regarding the type of epileptogenic lesion, presurgical MRI was the most reliable in detecting hippocampal sclerosis (29.4% vs. 19.35%; p = 0.0148) and malformations of cortical development (10.41% vs. 4.15%; p = 0.0159).

**Conclusion:** Comparing prehospital and presurgical MRI findings in the same cohort of patients with focal farmacoressistant epilepsies, we found the latter much more valuable in revealing epileptogenic lesions especially among the patients with temporal lobe epilepsy and hippocampal sclerosis.

**p1008 EPILEPTIC NETWORK IN ACTION: SYNCHRONY OF INTRACRANIAL SPIKING ACTIVITY IN DISTANT INTERICTAL DISCHARGE-RELATED HEMODYNAMIC RESPONSES REVEALED BY EEG/FMRI**

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**Purpose:** Structural and functional imaging studies in focal epilepsy often reveal distributed regions of abnormality. These are interpreted as representing the existence of epileptic networks but the presence of actual neuronal interactions between these regions has not been demonstrated. We sought to determine if the distributed hemodynamic responses often seen in functional MRI (fMRI) studies of scalp interictal epileptic discharges (IEDs) actually correspond to synchronized neuronal activities...
p1010 INTERICTAL GRANGER’S CAUSALITY SYNCHRONIZATION IN EEG, MAPS CONGRUENT BOLD CHANGES IN POSTERIOR QUADRANT EPILEPSY: A SIMULTANEOUS EEG-FMRI STUDY
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Purpose: Lesional parietal (PLE) and occipital lobe epilepsy (OLE) present with prominent interictal discharges (IEDs). We propose a method of a spatial mapping of temporally locked neuro-vascular coupling synchrony between IED related neuronal activity and the hemodynamic changes in patients with Posterior Quadrant Epilepsy (PQE).

Method: Twenty one EEG-fMRI sessions were available from PLE: [6 (Right-R. 3, Left-L:3)] and OLE: [Bilateral-BL:15] of 9 patients (M: F = 6:3, Age = 18.25 ± 7.2 years) with BrainAmpMR and 3T Siemens MAGNETOM Skyra (Erlangen, Germany) were analyzed. IED timed EEG synchronization was tested using GC estimated between 1 - 20 Hz [sampling rate:500 Hz, window length:200 ms, overlap:50%, surrogate: 50]. Synchronization peaking at 300 - 500 ms window at a network threshold value of 0.8, FDR corrected p < 0.05 was compared with spike timed fMRI activation network determined using time and dispersion derivatives of the hemodynamic response function.

Results: GC networks in EEG had good spatial concordance with fMRI. In PLE, GC showed mainly a paramedian parieto-occipital networking. fMRI mainly showed involvement of the DMN areas mainly the precuneus and posterior cingulate cortex. In LPLE, GC showed increased connectivity in BL parieto-temporo-occipital leads. GC was spatially more concordant with the fMRI map which showed mainly regions of precuneus and inferior parietal lobule. In BL OLE, GC showed BL parieto-occipital connectivity pattern concordant with the fMRI activation pattern involving the left cerebellum, BL occipital, and parietal cortices. Network abnormality tended to be more widespread in PLE compared to OLE groups particularly involving posterior DMN.

Conclusion: Granger’s Causality can spatially map the IED related EEG networks that spatially mapped to the fMRI IED related BOLD activations. This method demonstrates that short term neural behaviours such as IEDs and large-scale cortical activations involved in spontaneous epileptic brain activity can be mapped with good spatial congruence.

Abstracts

p1099 SPATIAL CONGRUENCE OF INTEGRATED EEG/FMRI NETWORKS IN TEMPORAL LOBE EPILEPSY
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Purpose: Integrating EEG-fMRI (fusion/time-series regression) helps understand neurovascular coupling. We studied interictal discharge (IED) network synchronization in EEG with Granger’s Causality (GC) and Phase Lag Index (PLI) and compared it with the fMRI spatial extent in temporal lobe epilepsy (TLE).

Method: Thirty two EEG-fMRI (R:20, L:12) sessions from 17 patients with TLE (M:F = 10:7, Age = 25.9 ± 9.2 years) with BrainAmpMR and 3T Siemens MAGNETOM Skyra (Germany) were analyzed. EEG synchronization was tested using GC and PLI across central brand frequencies at 6 (theta), 10 (alpha), 14 (beta1), 18 (beta2) and 25 (beta3) Hz (sampling rate:500 Hz, window length:200 ms, overlap:50%). Synchronization peaking at 300 - 500 ms window at a network threshold value of 0.8, FDR corrected p < 0.05 was compared with spike timed fMRI activation network.

Results: Beta1 synchronization networks in EEG had good spatial concordance with fMRI. Synchronization pattern of smEEG during the IED phase in left temporal lobe epilepsy (LTEL) using GC showed sparsely networking but widely distributed connections in left (L)-right (R)temporal and frontal leads along with involvement of parieto-occipital leads ipsilaterally. PLI didn’t show a concordant network. GC network was concordant with the fMRI activation pattern involving widespread areas of the frontotemporal cortices and left parietal regions. In right temporal lobe epilepsy (R-TLE) GC showed R temporal frontal mapping along with involvement of parieto-occipital leads ipsilaterally. PLI did not show any above threshold connections. fMRI showed above threshold epileptic network pattern in right fronto-temporal and bilateral posterior temporal, and dorsolateral cortex, anterior cingulate and inferior parietal regions.

Conclusion: Network analysis of EEG in beta frequency band width and fMRI provide good spatial concordance of the IED derived networks and the fMRI BOLD changes in TLE.

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Method: Two Sprague-Dawley rats were scanned at two different times: baseline, and 24 h after three systemic injections of 5 mg/kg KA. The scanning process consisted of a first scan with microPET (Focus 120), during 1 hour, using [18F]UCB-H (41 ± 5 MBq IV tail vein). This is followed by MRI (9.4T Agilent, anatomical T2). A coregistration was performed with PMOD 3.6 software. Data were expressed as SUV and AUC and were calculated for the different brain regions.

Results: [18F]UCB-H microPET images exhibited a small reduction (around 10%) in SV2A brain levels after KA injections are in accordance with previous histological studies, revealing inflammatory edema, tissue necrosis and increased ventricle volume (Sperk et al., 1983). These preliminary results obtained in KA treated rats show that [18F]UCB-H is able to detect alterations in SV2A levels after KA injections are in accordance with previous histological studies, revealing inflammatory edema, tissue necrosis and increased ventricle volume (Sperk et al., 1983).

Conclusion: These preliminary results obtained in KA treated rats show that [18F]UCB-H is able to detect alterations in SV2A levels after KA injections are in accordance with previous histological studies, revealing inflammatory edema, tissue necrosis and increased ventricle volume (Sperk et al., 1983).

p1012

NEUROPSYCHOLOGIC AND METABOLIC CHANGES IN PATIENTS WITH LEFT MESIAL TEMPORAL LOBE EPILEPSY WITH HIPPOCAMPAL SCLEROSIS AFTER EPILEPSY SURGERY


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Purpose: Epilepsy surgery may cause changes in cognition and cerebral glucose metabolism. Our aim was to explore relationships between pre- and postoperative cerebral FDG-PET metabolism and neuropsychologic performance in patients with left mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS), who were rendered seizure free after epilepsy surgery.

Method: Thirteen patients were included. All had neuropsychologic testing and an interictal FDG-PET scan of the brain pre- and postoperatively. Correlations between changes in neuropsychologic test scores and metabolism were examined using Statistical Parametric Mapping (SPM 12).

Results: Postoperative neuropsychologic test scores were not significantly different from preoperative scores at the group level. Metabolism decreased postoperatively in ipsilateral mesial temporal regions and increased in frontal and occipital lobes, as well as cerebellum. In these regions, we did not find a correlation between changes in metabolism and in neuropsychologic test scores. A significant positive correlation, however, was found between metabolic changes in the precuneus and in Boston Naming Test (BNT) scores.

Conclusion: There are significant metabolic decreases in ipsilateral mesial temporal regions, and increases in frontal and occipital lobes, and cerebellum post-compared to preoperatively in patients with MTLE-HS who were rendered seizure free after epilepsy surgery. We could not confirm that these changes translate into significant cognitive changes. A negative correlation between metabolic changes in the precuneus and changes in BNT scores was unsuspected. We speculate that the precuneus may play a compensatory role in patients with postoperative naming difficulties after left TLE surgery. Understanding of these neural mechanisms may aid in designing cognitive rehabilitation strategies.

p1015

AUTOMATED EPILEPSY DIAGNOSIS AND SEIZURE FOCUS LATERALIZATION BASED ON DEEP LEARNING

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Purpose: Randomized controlled trials indicate that resective surgery may be the currently most effective treatment to control the seizures in patients with drug-resistant temporal lobe epilepsy (TLE). The lateralization of the seizure focus is one of the core determinants for surgical target identification and, thus, successful surgery. Deep learning techniques have recently made a tremendous impact on a variety of automated visual recognition tasks but the translation of these tools to epilepsy diagnostics has remained absent. Here, we present a novel analytical framework to harness the power of deep learning algorithms for the analysis of MRI-derived shape information of the hippocampus in patients with drug-resistant temporal lobe epilepsy (TLE).

Method: Our approach parameterizes shape information in individual subjects using spherical harmonics with a point-distribution model (SPHARM-PDM). This model represents thousands of surface points on a triangular mesh along the outer hippocampal boundary using a grid of spherical coordinates and offers shape-inherent point-correspondence to assess local deformations. Correspondence across individuals allows interpolating shape-derived volume change measures to 2D images, on which deep convolutional networks can be readily applied. We evaluated our framework in a consecutive cohort of 40 patients with drug-resistant temporal lobe epilepsy and pathologically validated hippocampal sclerosis, and 46 healthy controls. Manually segmented hippocampi were converted into SPHARM-PDM representations for every participant. Deformation fields describing inward/outward displacements in a given subject relative to a template were then interpolated onto a 2D grid.

Results: Our deep convolutional network algorithm achieved excellent (>95%) performance for both patient vs. control discrimination and seizure focus lateralization in patients using 5-fold cross-validation. Our approach outperformed seizure focus lateralization and patient-vs-control classification algorithms operating on global volumetry alone.

Conclusion: The proposed analytical framework enables efficient deployment of deep learning techniques for hippocampal shape metrics, with suggested benefits for individualized diagnostics in disease.
functional dynamics. Multivariate analysis evaluated the modulation of network markers by degrees of hippocampal subfield pathology.

**Results:** We observed a gradual pattern of topological changes in TLE cohorts compared to controls, with marked increases in path length and decreases in clustering and controllability in TLE-HS and trends for these changes in TLE-G. Notably, controllability reductions in TLE-HS were largely confined to posterior default mode regions known to be densely integrated with the mesiotemporal lobe. Last, multivariate correlation analysis indicated a significant relationship between hippocampal and network-level anomalies in patients.

**Conclusion:** Combining hippocampal subfield phenotyping with whole-brain network analysis indicates that the histological make-up and severity of the hippocampal pathology ultimately relates to the extent of large-scale connectome anomalies. Hippocampal cell loss may exert a cascading impact on large-scale networks, likely via processes related to secondary degeneration.

### p1017

**DIRECTED FUNCTIONAL CONNECTIVITY IN PATIENTS WITH FOCAL EPILEPSY USING LOW-DENSITY EEG**


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**Purpose:** Several high-density EEG studies have shown that directed functional connectivity can be useful for depicting the main drivers of epileptic activity, which could ultimately help in the diagnosis and prognosis of patients with focal epilepsy. However, the utility of these measures in the clinical environment is limited by the availability of high-density EEG in clinical settings worldwide. Therefore, we investigated the reliability of directed functional connectivity and Electrical Source Imaging (ESI) using low-density EEG (19-32 channels) to estimate the epileptogenic zone (EZ).

**Method:** We searched in the databases of the Cantonal Hospital of Aarau and the University Hospital of Geneva for patients with focal epilepsy who had a focal lesion and a presumably well-localized EZ. We report here the results for the first 14 (10 temporal and 4 extra-temporal epilepsy) patients of our study. Interictal spikes were visually marked and ESI was performed for source activity estimation in 82 regions of interest (ROIs) using a distributed inverse solution and the Finite Difference Method (FDM) for the head model. A time-varying and frequency-resolved Granger-causality measure was applied to all ROIs source signals in order to investigate whole-brain dynamic and directed functional connectivity for the frequency of maximal spectral power. The summed outflow from each ROI and the connectivity in between the regions with the highest summed outflow were coincident with the presumed EZ.

**Results:** In all patients analysed, the ROIs with the strongest source activity and also summed outflow were coincident with the presumed EZ and the strongest connections originated from ROIs inside the presumed EZ, as confirmed by EEG experts.

**Conclusion:** Our preliminary results suggest that directed functional connectivity could be applied to low-density EEG to help clinicians in the diagnosis and management of patients with focal epilepsy.

### p1018

**MAPPING THE VERBAL SEMANTIC MEMORY NETWORK BEFORE ANTERIOR TEMPORAL LOBECTOMY USING A COMBINATION OF RTMS AND fMRI**

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**Purpose:** The left lateral anterior temporal lobe is posited as a hub within a distributed left lateralised verbal semantic memory network. We used fMRI to image a verbal task-related network and resting state functional connectivity before and after and offline inhibitory rTMS induced ‘virtual lesion’ of the left lateral anterior temporal lobe. Data from an initial subject forming a part of an ongoing larger cohort is presented.

**Method:** Ethical permission was obtained from the Austin Health Human Research Ethics Committee. 1 T1 weighted images from a pre-surgical right-handed patient with left temporal lobe epilepsy were obtained. Fiducial landmarks were co-registered to structural images using a frameless stereotactic neuro-navigation system (Brainsight, Rogue Research Inc, Canada). Resting motor threshold (rMT) was obtained from the ipsilateral hemispheres using standard protocols. 11 min (660 stimuli, 120% of rMT) of 1 Hz rTMS was applied to the left anterior temporal lobe 2 cm posterior to the pole along the middle temporal gyrus. A figure-of-eight coil and Magstim Rapid2 stimulator (Magstim Whitley, UK) were used. fMRI (semantic task and rest) was before and after rTMS.

**Results:** Time between rTMS and fMRI was 3.5 minutes. There was increased task related activation in the contralateral anterior temporal and frontal regions post rTMS without a significant change in task performance (reaction time and number of correct responses). Resting state connectivity was altered among multiple brain regions post rTMS.

**Conclusion:** The results suggest the presence of a bilaterally distributed, partially redundant, verbal semantic memory network that in this subject reorganises post rTMS to maintain task performance in this subject. Future studies will determine if characterising networks using rTMS-fMRI predicts network reorganisation and memory outcomes after anterior temporal lobectomy.

### p1021

**BRAIN SURFACE MAPPING OF OBJECTIVELY DEFINED GLUCOSE METABOLIC ABNORMALITIES BEFORE TWO-STAGE EPILEPSY SURGERY IN CHILDREN ABOVE 1 YEAR OF AGE**


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**Purpose:** Interictal 2-deoxy-2-[18F]-fluoro-D-glucose (FDG)-PET abnormalities can assist presurgical localization of epileptic foci, particularly when MRI is non-focal or discordant with electro-clinical findings. However, objective, accurate delineation of hypo- and hypermetabolic cortical regions is difficult in young children. In this study we used a quantitative 3D brain surface mapping approach with statistical parametric mapping (SPM) to evaluate the accuracy of FDG-PET in lobar and
sublobar localization of epileptic cortex defined by intracranial EEG in children 1-18 years of age.

**Method:** Preoperative FDG-PET scans of 37 children with intractable epilepsy (mean age: 9.7 years) were compared to age-matched pseudo-normal pediatric control PET data (N = 64; mean age: 9.3 years). SPM-defined hypo- and hypermetabolic maps were transformed to native 3D-MRI brain surface where subdural grid electrodes were also mapped. Accuracy of intracranial seizure onset zone (SOZ)-detection by these metabolic abnormalities was determined both on the lobar level as well by comparing the surface locations of metabolic changes with brain-surface electrode coordinates.

**Results:** MRI showed focal cortical abnormality in 6 children (16%). At least one cluster of metabolic abnormality was found in 34 (92%) patients for hypometabolism and in 25 (67%) for hypermetabolism. Hypometabolic clusters had a sensitivity of 75% and specificity of 64% to detect the lobe(s) of SOZ. Hypermetabolic clusters had a slightly higher lobar specificity (69%) but lower sensitivity (34%). Detailed surface-based distance analysis showed that the SOZ often extended ≥ 3 cm beyond metabolic abnormalities.

**Conclusion:** Objective PET analysis utilizing age-matched pseudocounters can reliably detect hypo- and hypermetabolic cortex on the lobar level even in young children (above 1 year of age), providing a lobar accuracy similar to accuracy reported in previous studies in older groups for SOZ detection. However, seizure onset electrodes are often found at least 3 cm away from cortical metabolic abnormalities.

### p1022
**THE USE OF FMRI FOR PREDICTING POST-OPERATIVE MEMORY DECLINE IN TEMPORAL LOBE EPILEPSY**

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**Purpose:** Postoperative amnesia is a serious consequence of temporal lobe epilepsy surgery. The gold standard procedure to anticipate the risk of amnesia is WADA test. However due to practical difficulties, WADA test is not frequently used. An alternative method is functional magnetic resonance imaging (fmri), which can allow calculation of a lateralization index for memory functions.

**Method:** Seven patients with left temporal lobe epilepsy were scanned preoperatively using a memory paradigm. The paradigm consisted of blocks that include verbal (words) and non-verbal (houses) memory items. Lateralization indices were calculated separately for verbal and non-verbal memory activations. Patients were also examined with verbal and non-verbal memory tests both preoperatively and post-operatively.

**Results:** Preoperative lateralization index for verbal and non-verbal memory predicted significantly postoperative decline in both verbal and non-verbal memory. The patients with verbal memory lateralized to left medial temporal lobe suffered from more post-operative verbal memory loss. Likewise patients with non-verbal memory lateralized to right side had lower post-operative decline.

**Conclusion:** The results indicate that fmri may be an effective and non-invasive alternative to WADA test in predicting post-operative memory decline after temporal lobe surgery.

### p1023
**POOPLY CONTROLLED SEIZURES DISRUP RESTING STATE NETWORKS IN PATIENTS WITH GENERALIZED EPILEPSIES**

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**Purpose:** Although generalized epilepsies are considered “easy to control”, some individuals present persistent seizures despite optimized polytherapy. The impact of refractory seizures on large-scale resting state networks (RSNs) in generalized epilepsies (GE) has not been entirely explored; therefore here, we compared interactions among RSNs between refractory and seizure-free subjects to evaluate disruptions in normal pattern of brain connectivity.

**Materials and methods:** Resting-state fMRI was acquired on 3T-PHILIPS from two groups of patients [23 SEIZURE-FREE (free of seizures for at least one year before MRI acquisition; SZ-free, 15 women, 36.6 ± 12 years) and 37 REFRACTORY (persistent seizures, 22 women, 34.2 ± 12 years)] and 60 CONTROLS matched by age (p = 0.7) and gender (p = 0.9). To compare interactions of 12 RSNs (from resting-state functional-MRIs, parcellated in 70 regions of interest (ROIs)), images were processed with UF2C-toolbox (running on MATLAB2014/SPM12), for ROI parcellation, matrix construction and statistical analysis (with intranetwork and internetwork connectivity). Each group of patients was compared with matched controls. Reported results have a 0.001 alpha.

**Results:** Compared to controls, there were intranetwork and internetwork dysfunction. Both groups presented abnormal correlations in the posterior salience network, default mode network (dorsal and ventral portions) and auditory network. Despite some similarities between groups, Refractory group displayed a more widespread array of abnormalities, including reduced correlations mainly involving the visuospatial network and an intriguing opposite correlation between basal ganglia and sensorimotor networks. Although more restricted alterations occurred in the SZ-free group, we identified specific alterations involving left executive control and visual networks.

**Conclusion:** These results suggest that both SZ-free and refractory patients present abnormal interactions of large-scale brain network; however, Refractory patients displayed a more extensive network dysfunction, mainly in the left hemisphere. Further investigation is necessary to evaluate the impact of such dysfunctional networks on both cognition, behavior and mood alterations.

### p1024
**AUTOMATED HIPPOCAMPAL VOLUMETRY PROFILES ALONG THE ANTERIOR-POSTERIOR AXIS FOR HIPPOCAMPAL SCLEROSIS DETECTION**

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**Purpose:** Hippocampal sclerosis (HS) is the most common cause of refractory temporal lobe epilepsy (TLE). It is radiologically recognized by hippocampal atrophy and increased T2-weighted signal, with quantitative imaging such as hippocampal volumetry improving sensitivity. Following our automation of hippocampal volumetry (HippoSeg, https://hipposeg.cs.ucl.ac.uk) we present an automated method to evaluate volumetric profiles along the anterior-posterior (AP) axis, to improve our sensitivity to detect localised atrophy.

**Methods:** 50 TLE-patients with radiologically-confirmed HS (mean age 42.9 years, 23 male) and 50 age- and gender-matched healthy controls underwent imaging on a 3T GE MR750 scanner with a 1 mm isotropic 3D T1-weighted MPRAGE. Hippocampi were automatically segmented using HippoSeg†. Subject scans were reoriented to have their hippocampi along the AP axis (found using principal component analysis) and cross-sectional area was obtained at each slice. MNI-152 template and Harvard-Oxford hippocampal delineations were similarly reoriented (template named MNI-HC). To compare across subjects, all scans were then registered to the MNI-HC atlas with an initial affine alignment followed by a b-spline registration, with the matching between template and subject scan excluding the hippocampi, to ensure no influence of pathology on outcome. Cross-
sectional areas were transformed according to this registration and sampled along the centre of the Harvard-Oxford hippocampal segmentations, using the 50 control subjects to generate a normative range (median-2*IQR to median+2*IQR).

**Results:** Global volumetric values from HippoSeg showed significant atrophy in 83.6% of radiologically-confirmed sclerotic, and 2% of control subjects, hippocampi. Including hippocampal volume profiling along the AP axis, while keeping the control rate detection at 2%, increased automated detection of atrophy to 87.7%.

**Conclusion:** Manual hippocampal volume profiling has previously shown potential to improve the distinction between healthy and sclerotic hippocampi but is very labour-intensive. Our work demonstrates the feasibility of automating this process to increase atrophy detection rates in a time- and cost-effective way.

**p1025**

**ABERRANT FUNCTIONAL CONNECTIVITY PATTERNS OF THE DEFAULT MODE NETWORK IN TLE-HS PATIENTS WITH ANTI-NMDAR ANTIBODIES**

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**Purpose:** Previous studies have found specific neurologic antibodies in a small proportion of people with epilepsy, mostly of unknown cause. Studies also suggested a potential role of autoimmunity in the precipitation of adult-onset temporal lobe epilepsy with hippocampal sclerosis (TLE-HS). Structural MRI reveals abnormalities in up to 50% of patients with anti-NMDAR encephalitis, without relationship with severity of symptoms. Functional MRI (fMRI) connectivity patterns of the default mode network (DMN) using resting state fMRI (RS-fMRI) may correlate better with clinical presentation. We aim to describe connectivity patterns of DMN in anti-NMDAR positive TLE-HS patients.

**Method:** We acquired RS-fMRI in 3 anti-NMDAR positive TLE-HS patients: two were tested for autoantibodies because of severe exacerbation of psychiatric symptoms; and one patient was randomly tested. Images were acquired in a 3T scanner. We performed images preprocessing and analysis with FSL toolbox: realignment, normalization, smoothing, and tissue segmentation. We regressed the fMRIs for head motion, white-matter and CSF global signals and band-pass filtered (0.008-0.1 Hz). We used 18 ROIs (regions-of-interest) of the DMN for individual cross-correlations. Sequentially the individual’s adjacency matrices were taken to the second level analysis: results from each patient were compared separately to 20 subjects with TLE-HS who tested negative for anti-NMDAR, using Z-test (p < 0.001 FDR corrected for multiple ROI-wise comparisons).

**Results:** The two patients with exacerbation of psychiatric symptoms had widespread abnormalities in DMN connectivity, including frontal, parietal, medial and lateral temporal lobes, and insula. The patient who tested positive for anti-NMDAR Abs and presented mild psychiatry symptoms had less alterations in DMN connectivity involving insula and medial parietal lobe.

**Conclusion:** These preliminary findings suggest that aberrant patterns of connectivity in RS-fMRI occur in anti-NMDAR positive TLE-HS patients, and its abnormalities may correlate to clinical presentation. Further longitudinal studies with more patients are necessary to confirm these findings.

**p1027**

**SPATIO-TEMPORAL CHARACTERIZATION OF NEURONAL ACTIVITY IN A ZEBRAFISH MODEL OF EPILEPTIC SEIZURES**


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**Purpose:** Epilepsy is a chronic brain disorder of unprovoked and recurrent seizures. Cellular and molecular mechanisms of seizures and epilepsy have been proposed, such as genetic mutations that affect neuronal activity. However, epilepsy is ultimately a disease of functionally and/or structurally aberrant neuronal networks and the mechanisms that link cellular/molecular alterations into dysfunctional neuronal circuits are poorly understood. Recent advances in neuroimaging and electrophysiology opened the possibility to characterize local neuronal networks of in vitro and in vivo models. However, brain volume limits a detailed analysis of larger neuronal circuits using the available recent techniques. The zebrafish larvae model offers the possibility of a whole network-level functional imaging due to their small size and optically transparent brain. Therefore, this project aims to investigate the spatio-temporal profile of neuronal activity in the epileptic zebrafish brain using both electroencephalography and calcium imaging.

**Method:** Seizure-like behavioural activity of zebrafish larvae exposed to picrotoxin, a pro-convulsant and GABAA receptor antagonist, was characterized by visual observation and quantification of locomotor activity. Afterwards, zebrafish larvae expressing a genetically encoded calcium indicator were incubated with picrotoxin, the brain imaged with a confocal microscope, and calcium levels analysed with imaging softwares.

**Results:** Picrotoxin induces increased hyperactivity, followed by jerky movements, body stiffening and loss of posture. This behaviour is concentration-dependent, shown by an increased locomotor activity. Picrotoxin induces a time-dependent increase in the amplitude and duration of low-frequency calcium peaks in a focal plane of the optic tectum and hindbrain.

**Conclusion:** The calcium dynamics in the zebrafish brain after exposure to picrotoxin suggests an increased neuronal hyperactivity and/or synchronization. Ongoing work will address a correlation between calcium peaks and electrical brain activity, and in response to anti-epileptic drugs. Additionally, the whole brain activity will be analysed using microscopy techniques that offer high spatial and temporal resolution.

**p1028**

**DIFFUSION-WEIGHTED IMAGING IN THE BABOON MODEL OF GENETIC GENERALIZED EPILEPSY**

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**Purpose:** The baboon provides a natural model of genetic generalized epilepsy (GGE) that closely resembles juvenile myoclonic epilepsy. This study uses diffusion-weighted imaging (DWI) to determine any microstructural brain abnormalities between a cohort of epileptic (EPI) and healthy control (CTL) baboons.

**Method:** Twenty-seven baboons, matched for age and weight, were classified into two groups (13 EPI, 14 CTL) on the basis of scalp EEG findings. All 3T MRI images were pre-processed using FSL’s FDT pipeline and DWI maps were created for each animal’s fractional anisotropy (FA)
and mean diffusivity (MD) values. Voxel-wise analysis of group-wise differences were compared using FSL’s TBSS program after correcting for gender and age distributions within each group. Region-specific differences in each group’s DWI indices were also assessed using FSL’s probabilistic tractography program (Protrackk) in the primary motor (M1), posterior limb of the internal capsule (PLIC), parietal and the anteromedial thalamus - all of which have been implicated in previous human GGE MRI studies.

**Results:** Similar to human studies of GGE, the epileptic baboons demonstrated significant (p < 0.05, family-wise error (FWE) corrected) decreases in the FA of the left M1, right M1, and left anteromedial thalamus. We also found increases (p < 0.10, FWE corrected) in the MD of each of these regions. The parietal and PLIC regions did not have any significant differences between groups.

**Conclusion:** This is the first study (using DWI) to demonstrate microstructural differences between EPI and CTL baboons that resemble the network differences observed in human GGE patients. Additionally, these regions have also been implicated in the functional connectivity differences found in our previous resting-state fMRI studies of the baboon model of GGE. With DWI of the baboon model of GGE, we also have more investigative options available when assessing the effects of neuromodulatory and/or anti-epileptic medications on a naive patient population.

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**p1029**

**TEMPORAL LOBE EPILEPSY: QUALITATIVE READING OF 1H MR SPECTROSCOPIC IMAGES FOR PRESURGICAL EVALUATION IN UZBEKISTAN**

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**Purpose:** To study the feasibility and clinical potential of visual inspection of hydrogen 1 magnetic resonance (MR) spectroscopic metabolite images for the lateralization of unilateral nonlesional temporal lobe epilepsy (TLE).

**Method:** MR imaging and 1H MR spectroscopic imaging were performed of the temporal lobes in 50 patients with TLE and 23 age-matched healthy volunteers. N-acetylaspartate (NAA) and creatine plus choline metabolite images were read by two neuroradiologists who determined lateralization according to the side of lower NAA signal intensity. Quantitative estimates of NAA were calculated by using an automated fitting program.

**Results:** Agreement in lateralization between readers was significant with a kappa score of 0.53 for all patients with TLE and 0.63 for patients displaying mild or marked NAA asymmetry. Among the 50 patients with TLE, lateralization was determined correctly by reader 1 in 38 (77%) of 39 and 16 (80%) of 20 patients, respectively. Combined qualitative reading and quantitative spectral fitting enabled lateralization in 34 (85%) of 40 patients with TLE for reader 1 and 30 (77%) of 39 for reader 2, including nine of 14 patients with TLE with negative MR images.

**Conclusion:** Reading of metabolite images is a feasible and fast means for noninvasive evaluation of patients with TLE who are candidates for surgery and enables lateralization in some patients with negative MR images.

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**p1030**

**RELIABILITY OF THE DIAGNOSIS OF HETEROPOI IN PATIENTS WITH PHARMACORESISTANT EPILEPSIES**

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**Purpose:** Perventricular nodular, subcortical focal and band heterotopias, are rare causes of neuronal migration disorders in which a group of neurons fail to migrate from the inner lining of ventricles to cortical plate, leaving tracks or nodules of normal neurons in abnormal locations, usually adjacent to the ependymal lining. Interaction of the nodular tissue and the overlying cortex in the generation of seizures can be variable, so the surgical resection of heterotopias may not be sufficient for rendering patients seizure free. Visibility of heterotopias depends on size, location and MRI quality. Based on the high number of MRI scans performed before the final diagnosis is reached, we hypothesize that heterotopias are more frequent than usually perceived.

**Method:** We conducted retrospective study of the frequency of heterotopias among patients with pharmacoresistant epilepsy subjected to noninvasive presurgical evaluation comprising 5-15 days of noninvasive video-EEG telemetry, 1.5T MRI, extensive neuropsychologic testing, and FDG PET-CT scan (in one third of patients). MRI was performed on Philips Achieva 1.5T DS MR system with paracoronal or coronal angulation according to hypothesis reached after video-EEG telemetry.

**Results:** Between 01.07.2010 and 30.06.2016 we performed presurgical evaluation in 872 patients with uncontrolled seizures. Heterotopia was diagnosed in 25 patients (2.8%). In 7 patients (28%) the diagnosis was established after the first MRI. The median number of previous nondiagnostic MRI scans was 4 (range 2-7) in 16 patients (64%) although subsequent MRI reevaluation showed signs of heterotopia in 7 of them. In 2 patients MRI showed unilateral hippocampal sclerosis (HS) and temporal lobectomy on appropriate side was performed. Histology showed nodular heterotopia adjacent to HS in both of them and only one patient remained seizure free.

**Conclusion:** We conclude that heterotopias are probably underdiagnosed and that proper analysis of high quality MRI scans could improve the diagnostic yield.

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**p1034**

**RISK FACTORS FOR NEUROPSYCHOLOGICAL IMPAIRMENT IN BENIGN EPILEPSY WITH CENTROTEMPORAL SPIKES**


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**Purpose:** This study evaluates risk factors for neuropsychological impairment in benign epilepsy with centrotemporal spikes (BECTS).

**Method:** In a retrospective cohort of 36 children with BECTs, we compared the electroclinical features of 25 who were neuropsychologically normal (Group1) and 11 who developed impairments (Group2) consisting of hyperactivity and attention deficit disorder in all 11 with additional language disturbances in 6.

**Results:** Median onset age was younger in Group2 than Group1 (4 vs. 8 years), and median epilepsy duration was longer (6.5 vs. 2 years) (p < 0.001). Most patients with onset age < 5 years and especially those with >5-year duration were in Group2, while most patients with onset age >5 years and < 5-year duration fell into Group1 (p < 0.001). A greater proportion of Group2 took >1 anticonvulsant (36% vs. 4%,

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p 0.05). Classical or atypical benign epileptiform discharges of childhood (BEDC) were frequent in both groups, but were the only EEG abnormality in half of Group 1 vs. none of Group 2 (p < 0.01). A greater proportion of Group 2 had multiregional epileptiform abnormalities (73% vs. 8%), regional intermittent slow activity (91% vs. 16%), or both (73% vs. none) (p < 0.001).

Conclusion: Possible risk factors for neuropsychological impairments in BECTS include onset age < 5 years, >5-year epilepsy duration, taking ≥1 anticonvulsant, multiregional epileptiform abnormalities, and regional intermittent slow activity. Features against these complications may include onset age > 5 years and EEG disclosing only BEDC. Risk factor identification might guide potentially beneficial cognitive and educational intervention.

p1035 DEVELOPMENT AND VALIDATION OF ICTAL COGNITIVE TESTING AND LOCALIZATION (ICTAL): AN INDIVIDUALISED HYPOTHESIS-TESTING TABLET BASED NEUROPSYCHOLOGICAL TEST PROGRAM TO EVALUATE COGNITIVE DEFICITS DURING ICTAL EEG ABNORMALITIES, WADA-TESTING, INTRACRANIAL EEG RECORDINGS AND AWAKE SURGERY

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Purpose: Evaluation of cognitive deficits during epileptic seizures, Wada-testing, or intracranial stimulation depth-EEG and awake surgery is critical for decision making in epilepsy surgery. In clinical practice these diagnostic procedures are considered as independent. We developed ICTAL: a cognitive testing procedure that can be used for all four diagnostic applications. ICTAL is an individualised hypothesis-testing neuropsychological test program that runs on a tablet-based computer. The program presents cognitive stimuli to assess multiple cognitive domains depending on the clinical hypotheses formulated by the neuropsychologist and neurophysiologist. In this study we validated the clinical applicability of ICTAL for the use at the video-EEG monitoring unit.

Method: 41 Epilepsy patients undergoing prolonged video-EEG-monitoring, and 41 healthy controls took part in the study. All participants received a testbattery during 30 seconds 4 times. Patients were randomly assigned to a hypothesized right temporal lobe battery or a left temporal lobe battery.

Results: A chi-square test of independence indicate that epilepsy patients made significantly more errors (p < 0.001). Crosstabs displayed 15 patients made one error compared to 4 controls, and 5 patients making 1 error compared to 0 controls. Errors were rare except for one item, that was excluded from the test battery.

Conclusion: We concluded that ICTAL is a feasible neurocognitive assessment battery that is presented on a tablet pc to be used during ictal anomalies at the video-EEG-monitoring. Stimuli from all different cognitive domains are generated at random depending on patient based hypotheses. All patients and controls show 100 percent correct responses on all stimuli. ICTAL is also applicable for Wada-testing, intracranial EEG and awake surgery.

p1037 BILATERAL TEMPORAL LOBE EPILEPSY VERSUS UNILATERAL TEMPORAL LOBE EPILEPSY: DO THEY HAVE DISTINCT NEUROPSYCHOLOGICAL PROFILES?

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Purpose: Anatomo-electro-clinical characteristics in temporal lobe epilepsy (TLE) with bilateral ictal involvement (bitemporal epilepsy BTLE), are different from the pattern found in unilateral temporal lobe epilepsy (UTLE). As only in UTLE is surgery good clinical practise, the type of epilepsy needs to be early identified. Electro-clinical and neuromaging information should be integrated with a wider cognitive assessment. The purpose of this work was to define specific neuropsychological differences between TLE and BTLE, in order to understand the type of epilepsy and the patients suitable for surgical intervention.

Method: Neuropsychological data from eighteen BTLE patients (6 males, mean age 39,89 years) and Seventeen UTLE patients (6 males, mean age 33,80 years) were retrospectively compared. The assessment included the WAIS-R scale with measures of the Verbal Intelligence Quotient (VIQ), the Performance Intelligence Quotient (PIQ) and the Full Scale Intelligence Quotient (FSIQ). Moreover, other cognitive functions like verbal and visuospatial short-term memory, verbal and visuospatial long-term memory, and attention were assessed.

Results: BTLE showed a wider impairment of neuropsychological functions, and a lower IQ. Significant differences were found in two verbal and one performance subtest of WAIS-R, as well as in VIQ (mean BTLE-VIQ 75,94 (21,27); mean UTLE-VIQ 85,47 (19,34)), PIQ (mean BTLE-PIQ 81,72 (20,25); mean UTLE-PIQ 89,12 (22,71)), and FSIQ (mean BTLE-FSIQ 80,31 (18,69); mean UTLE-FSIQ 85,60 (18,14)). Considering the clinical cut-off, verbal long-term memory was found compromised in more BTLE (45,5%) than UTLE (10%) patients. Moreover, in visuospatial long-term memory, the average performance of UTLE reached the 10th percentile, whereas in BTLE it was below the clinical cut-off.

Conclusion: BTLE shows a wider impairment of neuropsychological functions, and a lower IQ. BTLE patients probably have distinct neuropsychological profiles, thus neuropsychological assessment could be used like a marker of bilateral temporal lobe epilepsy.

p1039 COGNITIVE OUTCOMES FOLLOWING RADIOFREQUENCY-THERMOCOAGULATION IN TEMPORAL LOBE EPILEPSY (TLE): PRELIMINARY DATA


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Purpose: Radiofrequency-thermocoagulation (RF-TC) is a treatment option for pharmacoresistant focal epilepsy when resective surgery is not feasible. However, RF-TC can be performed in the SEEG-evaluation frame. Despite the increasing use of neuro-ablative procedures in epilepsy surgery, there is a lack of evidence whether this treatment can cause alterations in the cognitive sphere. This work aims to the characterization of the neuropsychological profile before and after RF-TC in a group of patients with non-lesional TLE.
Method: 10 non-lesional TLE patients (70% males; age range 21-44 years, IQ 102.6 ± 18.5) under SEEG monitoring were selected. The main thamic/LG nuclei were basal temporal (2.5 ± 2.9 contacts pairs), amygdala (2.4 ± 1.7), temporal pole (2.0 ± 1.9) hippocampus (1.9 ± 2.0) and entorhinal cortex (1.0 ± 1.5). All underwent a neuropsychological protocol, before unilateral RF-TC (70% left and 30% right) and a follow-up 5 months later. Epileptic seizure frequency and cognitive status were used to evaluate the outcome.

Results: After RF-TC, 20% of the patients were seizure free and the remaining had a significant reduction of seizure frequency, decreasing from 10.6 ± 10.0 before, RF-TC to 3.8 ± 8.5 after. Significant improvements were found in some cognitive fields between pre- and post-RF-TC assessments, mainly those in which processing speed and executive function were involved (Tower of London p = 0.018 and Trail Making Test scores p = 0.027). In non-case cognitive tests performance was worse after RF-TC. Interestingly, there was an improvement of depressive symptoms only when RF-TC was applied to the amygdala (p = 0.029).

Conclusion: Our study shows an improvement after RF-TC in cognitive fields such as processing speed and executive function and no-significant differences in other cognitive/affective outcomes. These preliminary results indicate that RF-TC generated lesions can lead to a significant seizure frequency reduction without concerns an impairment in neuropsychological function.

p1044

DIURNAL VARIATION OF POTENTIAL Ictal ONSETs DETECTED BY A RESPONSIVE NEUROSTIMULATION DEVICE

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Purpose: To describe the diurnal variation of brief ictal rhythmic discharges (BIRDs) with intracranial electrodes that are programmed to detect potential intracranial onset of subclinical or clinical seizures.

Method: 9 Patients had intracranial electrodes implanted with a responsive neurostimulation system (RNS) (NeuroPace) at our center. All had up to 8 electrodes recorded. These cases had seizure detection programming to identify potential ictal onsets or BIRDs, based on comparisons to actual clinical seizures recorded. Ictal onsets could include repetitive spike wave epochs, or high or low voltage fast activity most commonly. Due to responsive neurostimulation, the BIRDs may have been terminated and this may have prevented conversion to a clinical seizure. Inter- ictal spikes were ignored. The data was downloaded for 3–6 days of EEG where the detection was functional and where the detected EEG segments were logged for date and time.

Results: 4 cases had bitemporal depths from a posterior approach; 4 cases had unilateral temporal strips, depths or both, and 1 case had extratemporal neocortical strips. 6/9 had increased sleep detections only; 2/9 had increased awake detections and 1/9 had awake or sleep detections varying from day to day. Naps generally showed the same increase in BIRDs seen during night time sleep in cases with naps. Interesting, one case with 11 seizures had 9/11 when awake, while the BIRDs were predominant in sleep.

Conclusion: BIRDs showed a nocturnal or daytime predominance in all 9 of our RNS cases with most showing a nighttime (sleep) pattern. While these findings are similar to reports of interictal spiking, this study is looking at BIRDs, possibly for the first time. Studies are ongoing to determine if the BIRDs are predictive of seizures occurring with the same diurnal pattern.

p1042

INTRATHALAMIC HIGH-FREQUENCY EEG CAN PREDICT DEEP BRAIN STIMULATION EFFICACY IN EPILEPSY

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Purpose: Deep brain stimulation (DBS) is a promising therapeutic approach in pharmacoresistant epilepsy.

Method: We analyzed intracranial EEG recordings from depth electrodes placed bilaterally in ncl. thalami anterior, sampled at 5 kHz (15 minutes resting condition, recorded before DBS therapy, medication on), in 7 epileptic patients with > 1-year follow-up (4 patients with positive response - at least 50% reduction of seizures, 3 without response). We analyzed relative power (normalized to power in Ripple Band, 80-200 Hz) in the Fast Ripples (FR, 200-500 Hz), Very Fast Ripples (VFR, 500-1000 Hz) and Ultra Fast Ripples (UFR, 1000-2000 Hz) bands.

Results: Our results show significantly increased relative power (p < 0.01) in patients with a positive response to DBS (relative power in FR: 2.37 ± 0.52, 1.73 ± 0.39, VFR: 2.89 ± 1.53, 0.87 ± 0.33, and UFR: 1.92 ± 1.45, 0.06 ± 0.03 for positive and negative response, respectively).

Conclusion: We hypothesize that high-frequency EEG recordings can predict the DBS outcome in epilepsy treatment. Our preliminary results must be verified on a larger group of DBS-epilepsy patients.

p1045

CLINICAL OUTCOMES OF VNS-ASPIRRES IN PATIENTS WITH REFRACTORY EPILEPSY IN SHEBA MEDICAL CENTER, ISRAEL

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Objectives: The Vagus Nerve Stimulation (VNS) Therapy System has been shown to be effective in reducing the number of seizures in people with partial and secondarily generalized seizures. The Automatic Stimulation Mode (AutoStim) feature of the Aspire SR Therapy System stimulates the left vagus nerve on detecting tachycardia which may precede seizures in addition to normal and magnet mode. This “upgraded” device was approved for use in epilepsy by the Israeli ministry of health in January 2015. This study evaluates long-term clinical outcomes in patients using the device in the epilepsy clinics in Sheba Medical Centre.

Methods: A retrospective follow up of the effect of AspireSR in patients with drug-resistant epilepsy treated in both pediatric and adult epilepsy clinics in Sheba Medical Centres. Outpatient visits tracked seizure frequency, severity, quality of life, and adverse events from the device insertion to now.

Results: 61 patients (ages 4-66) were implanted with the Aspire device between March 2015 to November 2016. 12(20%) of them were reimplanted replacing the 103 model VNS and for the rest of them it was the first VNS implantation.
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p1046
VENTRAL ANTERIOR CINGULATE GYRUS: INTEGRATION OF BODY POSITION AND COMPLEX MOTOR RESPONSES
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Purpose: Although the voluntariness of an action and its complexity often go hand-in-hand, rapid, highly automatic movements must sometimes be remarkably complex. Falling, for example, requires an instant response to the potential consequences of unopposed gravity that necessarily integrates a multiplicity of facts about the state of the body and its environment. The anterior cingulum (AC) is a potential node where motor control, emotional, and vegetative responses may integrate. It has been involved in the production of stereotypical complex motor responses limited to small body areas (Talairach 1972). AC is also involved in the generation of the sensation of body movement being part of the so-called part of “the human vestibular cortex” (Kahane 2003).

Here we report two cases of complex, rapid, stereotyped motor actions associated with sensations of body position change triggered by stimulation of the ventral aspect of AC.

Method: Patients were implanted with depth EEG electrodes for epilepsy presurgical investigations. Bipolar stimulation to 50 Hz with intensities of 1-7 mA was performed in each patient. Their motor, sensory, emotional, and vegetative responses were recorded, including, in one patient, head and eye position sampled at 1 kHz.

Results: Stimulation induced a stereotypical complex motor response involving the trunk and all four limbs (contralateral > ipsilateral) in both patients. This complex action was adapted to the environment, naturally interacting with surrounding elements. Patients reported a contemporaneous sensation of falling/sliding down. Motor response could not be voluntarily suppressed and was experienced as externally induced.

Conclusion: This case study reveals complex, yet highly automatic, motor patterns activated in response situations such as a falling where a rapid but stereotyped response is required. That they are reliably elicited from ventral AC suggests it is key in integrating body position information and retrieving rapid, adaptive motor patterns in response.

p1047
CEREBELLAR TRANSCRANIAL DIRECT CURRENT STIMULATION (tDCS) IN DRUG-RESISTANT EPILEPSY: PRELIMINARY RESULTS FROM 10 PATIENTS
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Purpose: Transcranial direct current stimulation (tDCS) is an emerging non-invasive neuromodulation therapy, preliminary studies support its safety and efficacy on seizures and EEG modulation in epilepsy but target and stimulation parameters have not been yet established. Cerebellum has been proposed as a safe and efficient target for neuromodulation techniques and could be a good target for patients with multifocal or generalized epilepsy.

Method: Ten patients (4 males - 6 females, aged 22-55) with drug resistant multifocal or generalized epilepsy of unknown origin or associated with diffuse MRI abnormalities, with seizure frequency >4 per month, underwent to 5 consecutive daily session of cerebellar anodic tDCS (2 mA, 20 min). Five patients presented intellectual disability. Seizure frequency was recorded during the 30 days before and after stimulation’s week, adverse events were assessed before, during and at the end of every session. Standard EEG was recorded before stimulation on day 1, on day 5 at the end of the last session and after 30 days. Interictal epileptic activities was manually detected and quantified.

Results: All patients completed the study period, no major adverse events were recorded. Frequent complaints were itching and redness on the stimulation site vanishing within few minutes after stimulation. Four patients referred increased sleepiness during the treatment week. At 7 and 30 days from last stimulation session no statistically differences were observed in seizure frequency and interictal EEG abnormalities. Despite this, 5/10 patients reported subjective benefit on seizure control (particularly on seizure intensity).

Conclusion: We confirmed safety and good tolerability of cerebellar tDCS in epilepsy patients, also in presence of intellectual disability. No major effects on seizure frequency and EEG abnormalities were detected, but half of our patients reported subjective benefit on seizure control.

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p1056 DIETARY TREATMENT OF CHILDREN WITH EPILEPSY: SIMPLE INTERVENTIONS LEAD TO A NEAR THREEFOLD INCREASE IN RETENTION RATE
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Purpose: Recent reports suggest that the modified Atkins diet (MAD) may be as efficient as the established classical ketogenic diet (KD), at least in children >2 years of age. Even if MAD is considered less strict and requires less stringent weighing and planning of meals, poor retention rates remain a major challenge for both the KD and the MAD treatments. The goal of our study was to test whether simple interventions could increase the retention rate in children with epilepsy treated with MAD.

Method: We studied two cohorts of children with refractory epilepsy where MAD was initiated as treatment. In the first cohort, treatment with MAD was initiated using our regular follow-up protocol. The second cohort was followed applying a protocol where several measures had been added, including pre-treatment and motivational consultations and education of patients and parents/guardians.

Results: A total of 40 patients were included, 21 adhering to the regular protocol (62% female, age 5-18 years, median 12 years) and 19 in the intervention group (74% female, age 5-15 years, median 11 years). The two groups were similar; no significant difference in age, gender nor number of previous antiepileptic drugs (median 7). After 1 month, there was a trend towards higher retention rate in the intervention group (71% vs. 95%, p = 0.09), and after 3 and 6 months, this was significant (52% vs. 95%, p = 0.004 and 35% vs. 90%, p < 0.001, respectively).

Conclusion: Ensuring the patients try the diet properly is important for the success rate. Our results show that retention rate of dietary treatment can be significantly increased with simple measures added to the follow-up protocol. Motivational consultations, education of the patients and their parents/guardians, and tight follow-up during the initiation of dietary treatment seem to be key features.

p1061 RELIABILITY AND VALIDITY ‘IMPACT OF PEDIATRIC EPILEPSY SCALE’ OF TURKISH VERSION IN CHILDREN WITH EPILEPSY
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Purpose: ‘Impact Of Pediatric Epilepsy Scale (IPES)’ was developed by Carol Camfield, containing 11 items. The assessment scored with the overall health, family, social environment, activity number of schools and the academic status of self-care situation, the question of family activities. At the end of assessment there is a visual scale for measure the quality of life that ask the verbal score between 1-6. Our aim in this study, IPES scale by translate the Turkish ensure the validity and reliability of our language, is used to make clinical trial in patients with epilepsy.

Method: The scale was translated into Turkish by following the appropriate translation step. The demographic data of patients were recorded. Internal structure consistency and test-retest reliability for reliability analysis were measured. Cronbach’s alpha coefficients for all subscales for each item separately and the scale and item-total correlations were calculated. Test-retest reliability, including baseline and 2 week after the scale was applied twice by physiotherapist. Test-retest reliability was assessed statistically using Pearson correlation test for validity ‘with validity’ was investigated.

Results: 28 female (35%), 52 male (65%) 80 patients were included. Mean age was 6.94 ± 1.453 year, the mothers education level was found 58 (72.5%) primary school, 5 (6.3%) secondary school, 11 (13.8%) high school, 6 (7.5%) college level. In the 95% confidence interval assessors from 0.851- 0.922 found that Cronbach’s alpha; Intraclass Correlation Coefficient (p <0.0890 (p = 0.091), 0.001, respectively).

Conclusion: The IPES is a valid and reliable measurement for assessing functions in children with epilepsy in Turkey.

p1064 ELECTROCLINICAL FEATURES OF EPILEPSY IN THREE FEMALE PATIENTS WITH KIAA2022 MUTATION
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Purpose: KIAA2022 is located on Xq13.3 and known to be an X-linked intellectual disability gene in males. Recently, female patients who carry de novo KIAA2022 mutations have been reported. These female individuals share the same phenotypes of intellectual disability, facial dysmorphism and epilepsy as males, with similar severity. Although there are some reports of seizures, detailed characterization of seizure manifestation and EEG abnormality based on video-EEG recording are still limited. We evaluated three patients with KIAA2022 mutation in our hospital to elucidate the electro-clinical features of epilepsy in those patients.

Results: Patient 1 was a 19 year-old female with a de novo nonsense mutation (p.(K560*)) in KIAA2022. Since the age of 2 years, she had generalized epilepsy with eyelid myoclonia or myoclonic seizures induced by closing eyes, with concomitant generalized spike and waves (GWS) on EEG. Her interictal EEG showed GSW at 2.5-3.5 Hz. The seizures persisted despite treatment with several drugs. Patient 2 was a 9 year-old female with a de novo frameshift mutation (p.(D660I)) in KIAA2022. She had epilepsy with myoclonic absence at the age of three years. Her interictal and ictal EEG showed GSW burst at 2-3 Hz. Epilepsy was controlled by valproic acid (VPA) and ethosuximide. Patient 3 was a 42 year-old female with a de novo nonsense mutation (p.(R481*)) in KIAA2022. She has had epilepsy with tonic seizures and nonconvulsive status epilepticus since the age of four years. Her interictal and ictal EEG showed bilateral diffuse sharp waves in the alpha range. Her seizures responded partially to VPA, clobazam, topiramate, lamotrigine and clonazepam, but seizures remained refractory.

Conclusion: Three patients with KIAA2022 mutation in our hospital manifest various types of epilepsy, and tend to have generalized seizures including myoclonic seizure and absence.

p1065 CHARACTERISTICS OF POLYMICROGYRIA-RELATED EPILEPSY
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Purpose: This study aims to investigate characteristics of polymicrogyria (PMG)-related epilepsy in pediatric population.

Method: A retrospective study was conducted for all patients whose who visited Department of Pediatric Neurology in Severance Children’s Hospital between 2006 and 2016 and whose brain MRI revealed polymicrogyria of any extent, by review of clinical data.

Results: Sixty one patients were reviewed. The median age of the diagnosis of PMG - the age of initial brain MRI taken for any reasons - was 8 (2-32) months, and 37 (60.7%) were boys. Of 61, 9 patients (14.8%)
showed unilateral unilateral involvements of PMG, 14 (23.0%) showed unilateral multifocal involvements, and 38 (62.3%) showed involvements of bilateral hemispheres, 14 (23.0%) patients showed other cortical malformations: 8 (13.1%) showed gray matter heterotopia, 3 (4.9%) partial or complete agenesis of corpus callosum, 2 (3.3%) schizencephaly, and 2 (3.3%) focal cortical dysplasia of other natures (1 patient had both heterotopia and partial agenesis of corpus callosum). 52 patients (85.2%) showed seizures. 56 patients (91.8%) showed developmental delay, and among them, 38 patients (67.9%) showed developmental delay before onset of seizures. The median age of onset of seizures was 10.5 (2-48) months. Among 52 patients who had seizures, 26 (50.0%) showed focal seizures, 19 (36.5%) showed spasms, 3 (5.8%) showed myoclonic seizures, 3 (5.8%) showed tonic seizures, and 1 (1.9%) showed head nodding. By syndromic classification, 19 (36.5%) patients were diagnosed with infantile spasms, and 7 (13.5%) with Lennox-Gastaut syndrome. 29 (55.8%) patients were intractable to more than 2 antiepileptic drugs.

Conclusion: The incidence of epilepsy in patients with PMG is as high as 85.2%, and among them, 55.8% are intractable to medical therapy.

**p1068 EFFICACY, ACCEPTABILITY AND TOLERABILITY OF LOW GLYCEMIC INDEX DIET IN SOUTH INDIAN CHILDREN WITH REFRACTORY EPILEPSY**

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**Purpose:** This study was conducted to determine the efficacy, acceptability and tolerability of Low Glycemic Index Treatment (LGIT) in South Indian children with pharmacoresistant epilepsy.

**Method:** We identified children with refractory epilepsy from the diet clinic of a tertiary care university hospital for LGIT initiation over a period of 2 yrs. Demographic and clinical informations were collected. Initiation of the LGIT was done in an outpatient setting as per the institutional protocol. LGIT was classified as Step 1- only sugar restriction and Step 2 - restriction of sugar, rice, roots and tubers. Change in seizure frequency was assessed at 1st, 3rd, 6th, 9th, 12th, and 24th month follow-up intervals.

**Results:** 60 children were enrolled for LGIT during the study period. Male:female ratio 34:26. Age ranged from 1 year to 19 years with mean age 5.54 ± 4.41 years. 80% of children were on 3 or more AED. 63% of patients were categorized as having more than one seizure per day at the study entry, with the remaining children as experiencing over one seizure per week. 33 patients were started on Step 1 LGIT and 44 patients were on Step 2 LGIT. 33.3% of patients were seizure free at the end of the first month. At the last follow up 42.80% of children had >80% seizure reduction and 14.2% had 50-80% reduction in seizures. Complete withdrawal of current medications was possible in 2 patients at the end of 3 months. Diet was discontinued in 14 patients due to poor compliance and no response in seizure control, In 3 patients due to seizure freedom diet was changed to normal. Otherwise no significant complications were observed during the administration of the diet.

**Conclusion:** LGIT is a safe and effective adjuvant antiepileptic therapy and may be used as an alternative to the ketogenic diet.
two AEDs. 2 patients achieved seizure remission after discontinuation of all AEDs. 4 patients with FE were treated with everolimus - 1 for SEGA, 2 for AML, 1 for epilepsy. Two reported improvement of epilepsy.

Conclusion: 83% patients in our cohort had epilepsy. 44% had IS, VGB was the first AED used in 75%, with 50% success in controlling the spasms. 72% of patients had FE, in 46% epilepsy was pharmacoresistant.

p1070
A NEW COMPUTER BASED ALGORITHM FOR CALCULATING KETONIC PARENTERAL NUTRITION IN CHILDHOOD EPILEPTIC ENCEPHALOPATHIES

F. Benninger, Vienna, Austria, according to guidelines and to both age and individual nutritional needs. The computer based algorithm helped to tailor the kPN intake not exceeding a fat intake of 3.5-4.0 g/kg/d is effective and safe. The computer based algorithm for calculating the ketogenic ratio and daily energy requirements was established based on the ESPGHAN guidelines, fat-intake not exceeding 4 g/kg/d, age-adequate supply of protein, electrolytes, vitamins and trace elements and reduced of carbohydrate.

Primary outcome was the success to achieve/maintain relevant ketosis defined as beta-hydroxybutyrate plasma evel of ≥ 2 mmol/l. Efficacy was defined as the reduction of seizures ≥ 50% in de novo kPN and as maintenance of seizure reduction in children already on KD. Safety was assessed by adverse effects, laboratory findings and the appropriateness of nutritional intake.

Results: 17 children (median age of 1.84 years) were studied. Indications for kPN were surgery, Status epilepticus, vomiting, food refusal, and introduction of enteral feeding in neonatal age. The parenteral fat/non-fat ratio was mean 0.9 (± 0.3; range 0.6 - 1.5). Relevant ketosis was achieved/maintained in ten children (median 2.9 mmol/l), target levels were not reached in 7 (median -1.4 mmol/l). In de novo kPN significant response was observed in 50% (2/4), in the remaining patients previously on KD 77% (10/13) maintained response and 23% (3/13) were still within the evaluation period. The correlation between the degree of ketosis and seizure reduction was significant (correlation coefficient = 0.691; p = 0.002). No adverse events were observed.

Conclusion: KPN not exceeding a fat intake of 3.5-4.0 g/kg/d is effective and safe. The computer based algorithm helped to tailor the kPN according to guidelines and to both age and individual nutritional needs.

p1074
AUTOIMMUNE EPILEPSY IN CHILDREN: IDENTIFICATION AND MANAGEMENT STRATEGIES

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Purpose: Ketogenic parenteral nutrition (KPN) is indicated when enteral intake is temporarily limited or not possible. Evidence-based prescriptions are lacking.

Objective was to evaluate the efficacy and safety of a KPN in children with epileptic encephalopathies using a new computer based algorithm for accurate component calculating.

Method: Children with epilepsy receiving a KPN were included. A new computer based algorithm for calculating the ketogenic ratio and daily energy requirements was established based on the ESPGHAN guidelines, fat-intake not exceeding 4 g/kg/d, age-adequate supply of protein, electrolytes, vitamins and trace elements and reduced of carbohydrate.

Primary outcome was the success to achieve/maintain relevant ketosis defined as beta-hydroxybutyrate plasma evel of ≥ 2 mmol/l. Efficacy was defined as the reduction of seizures ≥ 50% in de novo kPN and as maintenance of seizure reduction in children already on KD. Safety was assessed by adverse effects, laboratory findings and the appropriateness of nutritional intake.

Results: 17 children (median age of 1.84 years) were studied. Indications for kPN were surgery, Status epilepticus, vomiting, food refusal, and introduction of enteral feeding in neonatal age. The parenteral fat/non-fat ratio was mean 0.9 (± 0.3; range 0.6 - 1.5). Relevant ketosis was achieved/maintained in ten children (median 2.9 mmol/l), target levels were not reached in 7 (median -1.4 mmol/l). In de novo kPN significant response was observed in 50% (2/4), in the remaining patients previously on KD 77% (10/13) maintained response and 23% (3/13) were still within the evaluation period. The correlation between the degree of ketosis and seizure reduction was significant (correlation coefficient = 0.691; p = 0.002). No adverse events were observed.

Conclusion: KPN not exceeding a fat intake of 3.5-4.0 g/kg/d is effective and safe. The computer based algorithm helped to tailor the KPN according to guidelines and to both age and individual nutritional needs.

p1072
LONG-TERM SEIZURE AND DEVELOPMENTAL OUTCOME IN SURGICAL CASES OF INFANTILE EPILEPTIC ENCEPHALOPATHIES


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Purpose: Infantile epileptic encephalopathies (IEE) are severe disorders.

Long-term seizure and developmental outcome of surgical cases of IEE were evaluated.

Method: Surgical cases of IEE followed up for one to 15 years after surgery were studied.

Results: The subjects included Ohtahara syndrome (OS), 26 cases [hemigigantencephaly (HME) 21, multilobar dysplasia (MCD) 3, no cortical dysplasia (CD) 2, West syndrome (WS), 30 [HME 5, MCD 7, focal cortical dysplasia (FCD) 6, no CD 11], early myoclonic encephalopathy (EME), 1 [MCD 1], and Aicardi syndrome (AS), 1 [MCD 1]. All the cases underwent surgery after non-invasive evaluations. Surgical procedures included hemispherotomy (Hemi) in 28, multilobar resection/disconnection (M/D) in10, focal resection (FR) in 6, and callosotomy (Cal) in 14 cases. Surgery was done at 58 days and under 12 months in 41 cases, and 1 and 3 years in 17 cases. At the last evaluation aged 1-year-1-month and 15-year-9-month, seizure outcome of Engel Class I was 36, Class II 1, Class III 13, and Class IV 8 cases. IQ/DQ > 80 was in 7 (OS 1, WS 6/Engel Class I 7/Hemi 1, M/D 2, FR 4), 79-70 in 1 (OS/Class I/Hemi), 69-50 in 9 (OS 3, WS 6/Class I 8, Class II1/Hemi 4, M/D 2, FR 1, Cal 2), 49-35 in 8 (OS 4, WS 4/Class I4, Class III 4/Hemi 4, FR 1, Cal 3), 34-20 in 11 (OS 9, WS 2/Class I 10, Class III 1/Hemi 8, M/D 3), and < 20 in 22 cases (OS 8, WS 12, EME 1, AS 1/Class I 13, Class II 1, Class III 11, Class IV 7/Hemi 9, M/D 2, FR 2, Cal 9).

Conclusion: In view of the severity and pathology of the present IEE cases, early surgery for IEE is encouraging for long-term seizure and developmental outcome.
Abstracts

p1076
KETONIC DIET SERVICE –SPECTRUM OF REFERRED CASES ACCORDING TO AGE
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Background: The ketogenic diet (KD) is an established treatment for drug resistant epilepsy. Recent published data and guidelines suggest that the KD is also safe and effective in infants under 2 years with drug resistant epilepsy.

Purpose: We aimed to review referral practice for KD to a single epilepsy specialist centre and compare tolerability, retention and response in different age groups.

Method: Patients referred over a 2 year period (July 2012 - June 2014) to the KD service of a single specialist epilepsy centre were identified from an electronic data base and case notes reviewed retrospectively.

Results: Eighty six patients were identified, of which 5/86(6%) were under 2 years of age.

Results in mental health in those with higher LAEP scores. Predictors of different age groups.

Conclusion: Although the KD can be effective and safe, with good retention in infants, this age group forms a low proportion of those referred. More data from prospective research are required to establish this intervention also in the very young and vulnerable age group.

p1077
ADVERSE EFFECTS OF ANTI-EPILEPTIC DRUGS REPORTED BY CAREGIVERS AS A SURROGATE MARKER OF QUALITY OF LIFE AND MENTAL HEALTH IN CHILDREN WITH EPILEPSY
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Purpose: Adverse effects caused by antiepileptic drugs (AEDs) often lead to treatment failure in childhood epilepsy. Instruments for measuring AED adverse effects are already used in adults but with more difficulties in children. This study aims to evaluate:

(1) Liverpool Adverse Effects Profile (LAEP) use by proxy in children and adolescents with epilepsy;
(2) relation of LAEP with instruments measuring caregiver burden, child's quality of life (QOL) and mental health;
(3) comparison of LAEP reports between adolescents and caregivers.

Method: Cross-sectional sample survey at tertiary university outpatient childhood epilepsy center in Brazil with 84 patients aged 2-19 yrs. and caregivers who completed four screening instruments: LAEP, QOL, QVCE by Soura Maia Filho et al. (2007), Strengths and Difficulties Questionnaire (SDQ) and Burden Interview (BI).

Results: There were positive correlations of LAEP scores reported by caregivers with seizure frequency (r = 0.257, p = 0.018), BI (r = 0.464, p = 0.010) and negative with QOL (r = -0.669, p = 0.010). There were differences between LAEP in SDQ subgroups (p = 0.031) with worst results in mental health in those with higher LAEP scores. Predictors of LAEP were polytherapy, QOL, SDQ and BI scores. There was strong correlation between caregiver and adolescent reports on LAEP (r = 0.751, p = 0.010).

Conclusion: High scores on caregiver reported LAEP are strongly correlated with seizure frequency, caregiver burden and QOL measurements in children with epilepsy as well are associated to mental health reported problems. LAEP may be used in children as objective screening tool for psychical and health assessment.

p1078
OCCIPITAL INTERMITTENT RHYTHMIC DELTA ACTIVITY (OIRDA) IN CHILDREN
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Purpose: Occipital intermittent rhythmic delta activity (OIRDA) is an electroencephalographic (EEG) pattern observed mainly in children with epilepsy, particularly in childhood absence epilepsy (CAE), in encephalopathy, and sometimes is not associated with epilepsy. Many studies suggest that OIRDA occurs exclusively in the case of epilepsy. We reviewed EEG that had been conducted on children and we found OIRDA activity in non-epileptic patients (NEP) too.

Method: The awake 770 EEG were analyzed. In that group 39 OIRDA were detected. Mean age on the group was 8.4 years.

Results: In the group of 39 patients with OIRDA there were 21 patients with CAE (54%), 3 patients with focal epilepsy (8%) and 15 NEP (38%). NEP had different diagnoses: one had mental retardation, one cerebral palsy (CP), two had migraine, two conversion disorders, two separation anxiety disorder, three of them had tics and four attention-deficit hyperactivity disorder. The mean age of CAE was lower than in the rest of the group and it was 7 years, of the focal epilepsy group was 9 years. and of the NEP was 9 years. In the CAE group boys were 52%, in the focal epilepsy group were 33% and in NEP were 40%. Analysis of neurological and neuroimaging examinations were normal except one patient with CP. All patients had normal intellectual development. The background of EEG was normal in all the cases. In the groups of CAE and focal epilepsy epileptiform discharges different from OIRDA were observed.

Conclusion: The importance of OIRDA in EEG is unclear. OIRDA is significantly more often observed among children, children with epilepsy, in particular in CAE. Sometimes OIRDA can be present in NEP. It is not known how to interpret the fact that OIRDA occurs in the cases of NEP. It appears that presence of OIRDA is not pathognomonic for epilepsy.

p1082
LYSINE RESTRICTION IN PYRIDOXINE DEPENDENT EPILEPSY; RESULTS AFTER 2 YEARS OF FOLLOW-UP
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Purpose: To evaluate the efficacy of lysine restricted diet in pyridoxine dependent epilepsy, a neonatal epilepsy syndrome.

Method: Data were collected from children that had a proven PDE, and were receiving a lysine restricted diet from an international PDE network database. Data were reviewed trough literature afterwards.

Results: 14 patients were enrolled. All of them had a genetically proven PDE. All of them had clinical seizures in the first week of life. Age at start of lysine restriction ranged from 4 months to 4.5 years. Duration of lysine restriction was between 6 months and 8 years. Most of them had lysine intake between 32 and 60 mg/kg/day. Half of the patients used concomitant anticonvulsant medications at any point, while all received...
p1083

STARTING ANTIEPILEPTIC MEDICATIONS BY NON SPECIALISTS: WHAT ARE THE HAZARDS?

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Aim: To study the prescription of (AEDs) in children before they were referred to specialist (pediatric neurologists).

Methods: This was a prospective study. Six hundred children referred for the first time to the epilepsy clinic in a tertiary university hospital were recruited. Detailed (AEDs) history was retrieved from the parents in their first visit regarding the number of seizure after which they start treatment, AEDs prescribed at the beginning of diagnosis and in the following 12 months, if the drug has changed and the reasons. Patients were classified as truly epileptic and non epileptic after being reviewed by 2 neurologists.

Results: Truly epileptic patients represented 65% of the newly referred patients. Of those, forty five percent have started one or more of AEDs before referral. Thirty nine percent started after their first seizure. Monotherapy was initiated in 65% of epileptic patients. Sodium Valproate (65.1%) was the most frequently prescribed AED followed by Levetiracetam (41.0%) and topiramate (38.0%). The combination of Sodium valproate and Levetiracetam as a starting therapy was the most common. Twenty five percent of patients have changed the initial (AEDs) in the first 3 months of starting treatment. Worsening of seizures and non availability of the medication were the most common causes of changing (AEDs).

The non epileptic patients included diagnosis of: Febrile seizures, breath holding attacks, pallid attacks and self stimulating. When offered to withdraw treatment after explanation of the condition by two neurologists, twenty eight percent refused to stop AEDs.

Conclusion: Starting AEDs by non specialist pediatrician has the hazards of wrong diagnosis, inappropriate starting and changing of AEDs.

p1088

THE PREVALENCE OF AUTISTIC SPECTRUM DISORDER IN CHILDREN WITH EPILEPSY

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Purpose: Determine the prevalence of ASD in children with epilepsy:

Method: Children with epilepsy seen in a tertiary care paediatrics department were evaluated using validated autism screening questionnaires (ASQ). In addition, questions about sleep-related disorders, behavior, seizure characteristics, and antiepileptic agents. An attempt was then made to determine if there was a correlation between the factors identified and ASD.

Results: Approximately 12% of children fit the ASQ criteria for having ASD. The majority had onset of seizures before the age of 1 year. Most children had not been previously diagnosed. Worst behavior and daytime sleepiness was seen in those at greater risk (p < 0.01). Seizures also occurred earlier (before the age of 1 year) in children at risk of having ASD.

Conclusion: This study suggest that children with epilepsy are at greater risk of having ASD, and illustrates the need for more clinical vigilance.

Behavioral difficulties and daytime sleepiness identified in these children could potentially affect their ability to learn.

p1089

PATHOGENIC VARIANTS IN KCTD7 PERTURB NEURONAL K+ FLUXES AND GLUTAMINE TRANSPORT

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Purpose: To reveal the molecular mechanisms involved in the pathophysiology of KCTD7-related progressive myoclonus epilepsy.

Method: We present two affected brothers with progressive myoclonic epilepsy. At 9 months of age the elder brother developed ataxia and myoclonic jerks. In his second year he lost the ability to walk and talk, and he developed drug-resistant progressive myoclonus epilepsy. The cerebrospinal fluid level of glutamate was decreased while glutamine was increased. His younger brother manifested similar symptoms from 6 months of age. Exome sequencing of the proband done.

Results: We identified a novel homozygous frameshift variant in the potassium channel tetramerization domain 7 (KCTD7) gene (NM_153033.1:c.696delT: p.F232 fs), which results in a truncated protein. The identified F232 fs variant is inherited in an autosomal recessive manner, and the healthy consanguineous parents carry the variant in a heterozygous state. Bioinformatic analyses and structure modelling showed that KCTD7 is a highly conserved protein, structurally similar to KCTD5 and several voltage-gated potassium channels, and that it may form homo- or heteromultimers. By heterologous expression in Xenopus laevis oocytes, we demonstrate that wild-type KCTD7 hyperpolarizes cells in a K+ dependent manner and regulates activity of the neuronal glutamate transporter SAT2 (Slc38a2), while the F232 fs variant impairs K+ fluxes and obliterates SAT2-dependent glutamate transport. Characterization of four additional disease-causing variants (R94W, R184C, N273I, Y276C) bolster these results and reveal the molecular mechanisms involved in the pathophysiology of KCTD7-related progressive myoclonus epilepsy.

Conclusion: Our data demonstrate that KCTD7 has an impact on K+ fluxes, neurotransmitter synthesis and neuronal function, and that malfunction of the encoded protein may lead to progressive myoclonus epilepsy.

p1090

JUVENILE MYOCLONUC EPILEPSY IN MOROCCO: EXPERIENCE OF MARRAKESH THIRD LEVEL HOSPITAL

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Introduction: Juvenile myoclonic epilepsy (JME) is an adolescent benign epilepsy representing 5 to 11% of all forms of epilepsy. It is quite common in our Moroccan context. The aim of this study is to describe the epidemiological, clinical, electroencephalographic (EEG) and therapeutic features and the outcomes of our patients followed for JME.

Patients and methods: This is a retrospective study of 12 years (2004-2015) including all patients followed for JME, collected at the neurology
department of the University Hospital Mohammed VI, Marrakech. The diagnosis of JME was based on clinical and electric criteria from the (ILAE) We noted epidemiological data, patient’s history, clinical signs, type and frequency of seizures and their triggers, data from the neurologi- cal examination, electromyography (EMG), treatment received and outcome of patients.

**Results:** We collected 120 cases (56 girls and 64 boys). The mean age of onset was 21 years. The family history of epilepsy was noted in 42 patients and consanguinity in 32. The diagnostic delay was estimated at four years (+/- 2 years). Myoclonic jerks were often associated with tonic-clonic seizures (81%) but, rarely with absences (14%). The electroencephalogram was pathological in 77%; polyspike waves were found in 28.4%, spike waves in 33% and focal abnormalities in 12%. The neuro-genetic study of 4 inbred families showed significant peaks on chromosome 1 (logarithm of odds (LOD) score > 3.0) and on chromosome 6 (LOD score of 3.0) in one family. Monotherapy was used in 86.6% of cases (104) and the sodium valproate was the most widely used treatment. Patient follow-up showed good control of seizures in 93.3% of cases.

**Conclusion:** Juvenile myoclonic epilepsy is a common and benign epilepsy syndrome with a good clinical response to monotherapy. The frequency of JME in our study could be explained by the amount of inbreeding in our context.

**p1094**

**TREATMENT AND OUTCOME OF WEST SYNDROME: ABOUT 22 CASES**


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**Purpose:** Evaluate and correlate the outcome of West syndrome (WS) with the underlying causes.

**Method:** We conducted a retrospective study of all cases of WS in pediatrics department of Hedi Chaker University Hospital in Sfax, during a period of 12 years (2005 to 2016). The studied variables were the epidemiological, clinical, imaging, therapeutic and evolutionary data.

**Results:** Our study included 22 cases. The mean age at spasm onset was 6 months, and mean age at diagnosis and treatment 7.2 months. According to the etiology, 3 (20%) were idiopathic, and 2 (13%) were cryptogenic. In 10 (67%) symptomatic cases, malformation of cortical development (33%) was the most common etiologic factor followed by hypoxic-ischemic encephalopathy (13%). Vigabatrin was used for the first line treatment in 13 patients (one cryptogenic and 10 symptomatic), and was added after failure of corticosteroids in 9 patients. The mean follow-up was 6.6 (0.5 to 10 years). Three patients have normal psychomotor development (1children with cryptogenic and two with idiopathic WS), two had psychomotor retardation, without epileptic fits and still receiving AED. Ten children (67%) had severe psychomotor retardation. Lennox-Gastaut syndrome developed in 27%.

**Conclusion:** The poor prognosis concerning intractable nature of the seizures and serious neurologic deficit is recorded in children with malformation of cortical development and hypoxic-ischemic encephalopathy. The outcome of these children is determined by the brain damage other than by epilepsy itself.
Clinical data elements were based off the diagnostic criteria of LD and include measures of epilepsy, cognition, ataxia and quality of life/function modified from Franceschetti et al. Common data elements (CDEs) that were likely to be recorded as part of routine care were identified and included (e.g. demographic data, MMSE, MOCA, neurologic examination). Data elements which could be extracted from the chart and applied to standardized instruments for scoring were also included (e.g. scoring of performance on tandem gait with selected standardized ataxia scales).

Conclusion: A data collection tool has been developed for a retrospective longitudinal natural history study of LD. The data collection tool will inform future prospective studies and ultimately contribute to the development of an LD Progression Scale.

p1099
MATHEMATICAL MODELING OF MELATONIN DIURNAL SECRETION IN CHILDREN WITH EPILEPSY
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Purpose: The main objective of the study was to create a mathematical model that describes the melatonin circadian secretion and, then the functionality of the model was tested by a comparison of the melatonin secretions in children with and without epilepsy.

Method: The patients were divided into the epilepsy group (EG = 54) and the comparison group (CG = 32). The melatonin level was assessed by a radioimmunoassay method. The diurnal melatonin secretion was described using a nonlinear least squares method. Spearman’s rank correlation coefficient was chosen to estimate the parameters of the model curve. This model reproduces blood concentration profiles and its parameters were statistically analyzed using the Mann-Whitney-Wilcoxon test and logistic regression

Results: The correlation analysis performed for the EG and CG groups showed moderate correlations between age and the melatonin secretion model parameters. Patients with epilepsy are characterized by an increased phase shift of melatonin release.

Conclusion: Mathematical modeling of circadian melatonin cycle facilitates statistical analysis of the patients’ hormone levels offering a set of parameters that enable objectification of the secretion description.

p1102
DIFFUSION TENSOR IMAGE IN INTERICTAL PSYCHOSIS AND TEMPORAL LOBE EPILEPSY: WIDESPREAD WHITE MATTER ALTERATIONS AND DISRUPTIONS IN INSULA AND CINGULUM CONNECTIVITY
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Purpose: Psychosis has greater prevalence in epilepsy than in general population, specially in refractory epilepsy, yet few studies investigate this condition. White matter and connectivity abnormalities are well described in temporal lobe epilepsy (TLE) an are considered a hallmark of schizophrenia. The objective of this study was to investigate white matter integrity and brain connectivity in TLE subjects with IP comorbidity.

Method: Diffusion weighted images scans were obtained from nine subjects with TLE associated with hippocampal sclerosis (TLE-HS) and interictal psychosis (IP), (mean age: 46.33, ±7.78), nine subjects with TLE-HS and no psychiatric comorbidity (mean age 46.22, ± 9.82) and nine healthy matched controls (mean age 43.89, ± 9.62). The images were analyzed by tract-based spatial statistic (TBSS) and by a quantitative analysis of connectivity based in graph theory. The quantitative analysis was centered on limbic system’s structures.

Results: White matter abnormalities, presented as reduction in fractional anisotropy (FA), were found in both epilepsy groups, compared to control group. IP subjects displayed more extensive reduction in FA than the epilepsy group without comorbidity, although the difference was not statistically significant. The graph analysis showed significantly bilateral reduction of connectivity between cingulum-hippocampus and cingulum-parahippocampal gyri, and increased connectivity between insula and amygdala in psychosis, compared with the other two groups.

Conclusion: While both groups presented abnormalities in white matter, some characteristics seem to be related only to psychosis. IP group has more extensive reduction in FA, including brain regions not altered in TLE. The disconnection in cingulum is a important finding, since it has been described previously in persons schizophrenia, suggesting that IP and schizophrenia share some physiopathological characteristics. The aberrant insula connectivity is also noteworthy, due to its importance in executive functions and processing of sensory information, whose disruptions are related to psychotic symptoms.

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Abstracts

p1104

PSYCHOGENIC NON-EPILEPTIC SEIZURES IN ADULTS WITH INTELLECTUAL DISABILITY


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Purpose: Psychogenic non-epileptic seizures (PNES) are episodes of movement, behavior or sensations that resemble epileptic seizures but are not accompanied by epileptiform brain activity on an electroencephalogram. Although PNES might be common in people with epilepsy and intellectual disability (ID), little is known about the exact presentation and (co-morbid) problems in this population. Our study aims to describe the features of a group of adult patients with epilepsy, ID and PNES and to analyze the differences between this group and a control group of patients with epilepsy and ID, without PNES. We hope to contribute to a better understanding of this complex group of patients in order to optimize treatment.

Method: This observational case-control study was conducted at Kempenhaeghe Epilepsy Center, The Netherlands. Adult patients, living at Kempenhaeghe, with epilepsy, ID and a registration of non-epileptic events in their medical records were selected and evaluated on how certain the PNES diagnosis was in terms of the classification of LaFrance (2013). Clinical characteristics of PNES were provided by the subject’s mentor, using a standardized questionnaire. As a control group, patients with epilepsy and ID, without PNES, (N = 100) were included. Clinical information was retrieved from patient charts retrospectively and data on neuropsychiatric symptoms were collected by standardized questionnaires.

Results: This study is ongoing and results will be presented at the congress. Clinical characteristics of PNES in adults with ID (N = 20; mean age: 46.2) will be described qualitatively. The PNES group comprised 50% females and 60% had mild-moderate ID, versus 40% with severe ID. Differences between the PNES group and the non-PNES group are analyzed with respect to epilepsy characteristics, level of ID and neuropsychiatric symptoms.

Conclusion: In the population of patients with epilepsy and ID there are diagnostic questions whether the seizures manifest as PNES or represent a reinforced behavior pattern.

p1107

PREDICTIVE VALUES OF PSYCHOSOMATIC TOOLS FOR SEIZURE RECURRENT THE FOLLOWING MONTH IN PATIENTS WITH WELL-CONTROLLED EPILEPSY

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Purpose: Stress, fatigue, sleep problems, and emotional distress such as depression or anxiety have been reported as psychosomatic factors for triggering seizure in patients with epilepsy. Those factors always draw their attention, but can be ignored by patients with well-controlled epilepsy (WCE). Although unexpected seizures can elicit embarrassing situation in patients with WCE, there are no studies to evaluate predictive values of psychosomatic factors for future recurrence of seizure in those patients.

Method: We enrolled patients who had a year of seizure freedom. Subjects were asked to complete screening tools including the Perceived Stress Scale-4 (PSS-4), the Korean version of the Neurological Disorders Depression Inventory for Epilepsy (K-NDDE-I), the Generalized Anxiety Disorder-7 (GAD-7), Fatigue Severity Scale (FSS), and the short forms of the Patient-Reported Outcomes Measurement Information System Sleep-Related Impairment (PROMIS-SRI) and Sleep Disturbance (PROMIS-SD) scales. We observed seizure recurrence the following month. We examined predictive values of screening tools for seizure recurrence using receiver operating characteristic (ROC) analyses.

Results: One hundred forty-three patients were initially invited. Nine patients with irregular antiepileptic drug intake during the study period were excluded. Seven patients (5.2%) experienced seizure recurrence the following month. They usually had complex partial seizures with symptomatic etiology. Five screening tools except the PROMIS-SRI had significant predictive values for seizure recurrence (AUC ranging from 0.729 to 0.907). The most valuable screening tool was the PSS-4, followed by the GAD-7, the PROMIS-SD, the K-NDDE-I, and the FSS. Cronbach’s α coefficients for the PSS-4 was 0.746. At a cutoff score of 9, the PSS-4 had a sensitivity of 85.7% and a specificity of 92.4%.

Conclusion: Clinicians can alert patients with WCE to occur seizure in the following month by using the PSS-4.

p1116

EDUCATION AND JOB INDEPENDENCE OF PATIENTS WITH REFRACTORY EPILEPSY WHO WERE ASSESSED AS POTENTIAL CANDIDATES FOR EPILEPSY SURGERY IN AN EPILEPSY REFERENCE CENTER IN GUATEMALA

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Purpose: Highlight the burden of epilepsy on education and job independence of patients with refractory epilepsy who were assessed as potential candidates for epilepsy surgery.

Method: It is a descriptive and retrospective study. All the clinical records of patients with refractory epilepsy, who were assessed as potential candidates for epilepsy surgery from March 2014 to December 2016, were reviewed to document the information about education, causes of school dropout and job status.

Results: 92 clinical records of patients with refractory epilepsy were reviewed. 43 female, 49 male. 73 patients were older than 17 years old. 9.8% completed university, 21.7% finished high school, 3.2% completed middle school, 32.6% completed only primary education, 11.9% did not complete primary school, 9.7% never attended school, 10.8% are currently studying. From all the patients who are older than 17 year old: 64.3% do not work, 27.3% are currently working. From those patients who are currently working: 45% work in informal jobs. Causes of school dropout of all the patients who did not complete high school or never went to school (53 patients); 25 (55.5%) due to epilepsy issues; 6 (13.3%) learning disabilities; 6 (13.3%) lack of financial support; 3 (6.6%) psychomotor impairment; 3 (6.6%) behavior issues; 2 (4.4%) because they did not want to study; 8 patients did not answer the reason of school drop out.

Conclusion: Epilepsy causes a negative effect on education and job independence of patients with refractory epilepsy. In this study more than half of the patients (57.4%) were not able to complete high school, and only 27.3% are currently working. Stabilizing the impact of the condition and the causes of school dropout, school non-attendance and unemployment is important to develop campaigns of education for teachers, employers and caregivers, in order to reduce the burden of epilepsy.
Background: While the social burden of epilepsy has been extensively studied, an evaluation of social media related to epilepsy may provide novel insights into disease perceptions, patient needs and access to treatments that cannot otherwise be gleaned. The objective of this study is to assess patterns in the social media and online communications usage related to epilepsy and associated topics.

Methods: We performed a search of two major social media platforms (Facebook and Twitter) for public accounts dedicated to epilepsy. Results were analyzed using qualitative and quantitative methodology. The former involved thematic and word count analysis for online posts and tweets on these platforms, while the employed non-parametric tests for statistical significance.

Results: Facebook had a higher number of pages (840 accounts) and users (3 million) compared to Twitter (137 accounts and 274,663 users). Foundation and support groups comprised most of the accounts and users on both Facebook and Twitter. The number of accounts increased by 100% from 2012 to 2016. Among the 403 posts and tweets analyzed, “providing information” on medications or correcting common misconceptions in epilepsy, was the most common theme (48%). Surgical interventions for epilepsy were only mentioned in 1% of all comments and tweets.

Conclusions: The current study provides a comprehensive reference on the usage of social media in epilepsy. The number of online users interested in epilepsy is likely the highest amongst all neurological conditions. Surgery as method of treating refractory epilepsy is however, underrepresented on social media.
attempts to taper phenobarbital. 2/7 had regression: One had regression after each of 3 status episodes: gross motor; swallowing, feeding, fine motor and sign language. Another had poor coordination and lost babbling after an episode. The first regained prior function after periods of few weeks after each episode and the second after second episode after few days.

Conclusion: Long term outcome after status epilepticus in AHC patients ranges from no regression to severe motor and linguistic regression. Regression is not a must, but clinicians should be aware to treat early.

p1130
EPIDEMIOLOGY-BASED MORTALITY SCORE VS. STATUS EPILEPTICUS SEVERITY SCORE FOR PREDICTION OF LONG TIME SURVIVAL IN STATUS EPILEPTICUS IN A DANISH COHORT
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Purpose: Status Epilepticus (SE) is an life threatening condition. Prognostic factors predicting long-term mortality after SE are lacking. The Status Epilepticus Severity Score (STESS) was developed to predict short-term survival and only poorly correlates with long-term survival. A recent study suggested that Epidemiology-Based Mortality Score in Status Epilepticus (EMSE) is more precise to predict in-house mortality and the consideration of etiology may also improve the predictive value for long-term survival. The aim of the study was to compare if EMSE was superior to STESS to predict long-term mortality.

Method: We retrospectively assess EMSE and STESS in a Danish cohort of 96 SE patients admitted to Odense University Hospital from 01/2008 to 01/2015. We used cut-off value of 64 points in EMSE and STESS to predict mortality (EMSE: >64 point bad outcome, STESS: >4 point bad outcome). The primary endpoint of the study was to compare the ability of EMSE or STESS to predict overall outcome. Further, we compared sensitivity and specificity between EMSE and STESS to predict mortality at 3 months and at the end of follow up.

Results: The mean time of survival were 865 days (1-2863 days). EMSE was slightly superior to STESS to predict long-term mortality in a Kaplan Meier analysis (average survival: STESS 328 vs. 1247 days, EMSE 420 vs. 1595 days). There was no difference in predicting short-term mortality after 3 month (AUC: 0.656 vs. 0.660). At end of follow up EMSE was slightly better than STESS (AUC: 0.780 vs. 0.703).

Conclusion: Although EMSE predicted long-term mortality slightly better than STESS, we did not find a clinically meaningful difference. Given that assessment of STESS is solely based on clinical data already available in the emergency room, our data does not indicate that EMSE is superior to STESS to predict long-term mortality in clinical practice.

p1136
RE-EVALUATION OF THE CRITICALLY ILL PATIENTS WITH NON-CONVULSIVE STATUS EPILEPTICUS BY USING SALZBURG CONSENSUS CRITERIA
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Purpose: Systematic studies on the incidence of nonconvulsive status epilepticus(NCSE) in critically ill patients related to etiologic groups, electrophysiological features of “true” ictal patterns associated with NCSE and the factors shown to be correlated with clinical and EEG improvement are still scarce.

Method: We retrospectively reviewed all EEG data of the consecutive patients with critical illness, followed up in the Intensive Care Unit(ICU) with clinical suspicion of NCSE during 2 years. Two experienced, certified clinical neurophysiologists reviewed all EEG data independently and determined NCSE according to Salzburg Consensus Criteria. The incidence and predominant features of clearly defined ictal EEG patterns and their relationship to clinical, laboratory, neuroradiological, and prognostic findings were assessed.

Results: A total of 107 consecutive patients with the mean age of 68.2 ± 15.3 years(57 females) were enrolled in the study. In 62 patients, continuous EEG monitoring was applied with a mean duration of 45.3 ± 24.5 hours. Primary neuronal injury was detected in 57 patients (62.6%) including post-anoxic coma in 10 patients, whereas the remaining patients had various metabolic, systemic problems. Twenty-four patients(22.4%) were diagnosed as NCSE fulfilling the suggested criteria. While authors decided to treat in 33 patients (30.8%), 32 patients (29.9%) had been treated in real-life evaluation. The presence of clinical seizures and a high mortality rate along with a long duration of stay in the ICU were more common in the group with definite NCSE. Among the investigated EEG features, fluctuation and triphasic waves were not predictive to diagnose NCSE. Clinical and EEG improvement was detected in 12 patients(11.3%) in real-life treatment group showing correlation with absence of mechanical ventilation, infection, and sepsis.

Conclusion: The diagnosis of NCSE in critically ill patients is a matter of debate. Our findings suggest that Salzburg Criteria is compatible with clinical practice in the decision for treatment of patients with NCSE.

p1138
THE PRACTICE OF REVISED CLASSIFICATION OF FOCAL CORTICAL DYSPLASIA ON DRUG-RESISTANT EPILEPSY IN WEST CHINA: AN URGENT DIAGNOSTIC GAP FOR FILLING
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Purpose: To clinically and histopathologically re-examine refractory epilepsy cases using the revised 2011 ILAE classification of focal cortical dysplasia (FCD).

Method: Consecutive patients with drug-resistant epilepsy submitted to surgery from July 2012 to Jun 2014 were included. Pathological diagnosis, clinical histories and surgery outcome were reviewed. A questionnaire was developed to explore changes in histopathology practice. A short-term training program on FCD was carried out to improve pathological diagnosis accuracy.

Results: 260 cases (177 male and 83 female) were included with mean age at surgery of 25.1 years. Pathological diagnosis was changed in 70 cases (26.9%) after re-examination. The five most common pathologies were hippocampal sclerosis (HS) (92.0%), 50/260), brain tumors (17.7%, 46/260), vascular malformations (16.2%, 42/260), glial scars (11.2%, 29/260) and FCD (10.0%, 26/260). The most common subtype of isolated FCD was FCD IIb (53.8%, 42/260), followed by FCD Ib (3.8%, 1/26). Forty-five cases were diagnosed with associated FCD type III (17.3%, 45/260). Half of patients with FCD achieved Engel class I at two-year follow-up. The diagnosis of HS with FCD IIIa was poorer in HS without associated FCD IIIa. Questionnaire investigation suggested most participant pathologists lack sufficient knowledge and training courses on the new classification. The diagnostic sensitivity for different FCD subtypes was significantly improved by two to six folds after short-term training.

Conclusion: FCD is an important etiological factor in drug-resistant epilepsy in southwest China. It is essential to provide continuing training to improve pathological practice and diagnosis in developing countries.
EARLY IDENTIFICATION OF PATIENTS WITH DRUG-RESISTANT EPILEPSY
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Purpose: Whilst 60 to 70% of people with epilepsy have a good prognosis and enter a remission from seizures, 30 to 40% do not. Currently patients wait years before clinicians are confident that their epilepsy is drug-resistant. Early identification of drug-resistance could alter management strategies and speed up access to epilepsy surgery. We aimed to use data from the SANAD study to identify patients with drug resistant epilepsy as early as possible.

Method: The SANAD study is the largest prospective study in patients with epilepsy to date. Here we apply multivariate longitudinal discriminant analysis to the SANAD dataset in order to dynamically predict the risk of a patient having drug resistant epilepsy. External validation was performed with the MESS and NGPSE datasets.

Results: We have developed a model that is able to identify patients with drug resistant epilepsy with a high degree of accuracy. 95% of patients with drug resistant epilepsy were correctly classified (sensitivity) and the majority of these patients were identified at least 2 years earlier than currently possible. 97% of patients who achieved remission were correctly classified (specificity). For patients who the model predicted as being drug resistant, 76% were truly drug resistant (Positive Predictive Value).

Changes in patient’s seizure and treatment history were the most informative longitudinal variables. Several baseline variables informed the evolution of the longitudinal variables over time: Number of seizures before randomisation, history of neurological insult, type of epilepsy, Age at randomisation, sex, and having a first degree relative with epilepsy.

Conclusion: This externally validated model could be of use in the early identification of patients with drug resistant epilepsy in order to consider possible further interventions and offer patients more appropriate counselling regarding their condition.

DELAYED RESPONSES EVOKED BY SINGLE PULSE ELECTRICAL STIMULATION LOCALISE THE EPILEPTOGENIC ZONE FOR TEMPORAL LOBE RESECTIVE SURGERY: A LONG-TERM STUDY
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Purpose: The epileptogenic zone is the region of cortex that needs to be resected to achieve seizure freedom. Single pulse electrical stimulation (SPES) is a technique used to help identify the epileptogenic zone in patients with epilepsy. Delayed responses (DRs) elicited by SPES are a reliable indicator of epileptogenic cortex. Short-term studies show that surgical outcome is favourable when DRs are present within the resected region. Here we have studied the long-term outcome of patients who underwent temporal lobe resections for the treatment of epilepsy.

Method: A total of 308 patients who underwent invasive presurgical assessment at King’s College Hospital from 1999 - 2015 were analysed. Only 46 patients fulfilling the following criteria were included:

(a) SPES recordings and clinical notes were available,
(b) patients had unilateral DRs or no DRs,
(c) there was a post-surgical follow-up of at least 12 months,
(d) the patient underwent a temporal lobe resection.

If the area where DRs were recorded was completely removed by resection, surgery was said to be congruent with DRs. The relationship between surgery that was congruent with DRs and surgical outcome was explored. Engel classification grades I-II were considered favourable, and III-IV were considered poor.

Results: In 27 out of the 46 patients (58.7%), surgery was congruent with DRs. Of these patients, 81.5% had a favourable outcome, whereas 18.5% had a poor outcome. In 5 of the 46 patients (10.9%), surgery was incongruent or partially congruent with DRs. Of these patients, 40% had a favourable outcome, whereas 60% had a poor outcome. In 14 patients out of 46 (30.4%), no DRs were found. Of these patients, 57.1% had a favourable surgical outcome, and 42.9% had a poor outcome. The average follow up was 51.8 months.

Conclusion: Resection that is guided by DRs is associated with favourable long-term surgical outcome.