Adult Epileptology

Abstract Number: 25

Title: Experience of using the "EpiTapp®" hand-tapping program for focal motor seizures in a patient with neuronal -glial tumor of the frontal lobe

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Purpose: To present a clinical case of using the “EpiTapp” hand tapping program for palliative care in oncogenic epilepsy.

Method: The author's method of hand tapping (RF patent No. 2606489 dated 01/10/2017) was used for a smartphone with Android OS. Wrist - tapping was carried out during the period of aura or focal seizures in patients with OE to prevent FES as an element of urgent palliative therapy of oncogenic epilepsy after training by a doctor and EEG monitoring.

Result: Patient L., 33 y.o., was observed with a neuronal-glial tumor in the convexital parts of the left frontal lobe, complicated by structural-focal epilepsy with frequent focal seizures and BS, pharmacoresistance to antiepileptic drugs. The patient was a candidate for resection neurosurgical treatment. In the preoperative period, she received duotherapy (long-acting valproic acid 1000 mg / s, perampanel 150 mg / s). On an outpatient basis, the patient was advised to use the “EpiTapp” wrist-tapping program as part of emergency self-help. The woman regularly used the program both in the event of an aura, and in case of focal motor hemiclonic seizures. The number of FES decreased by 70% from the initial level, the duration of motor and non-motor focal seizures also decreased.

Conclusions: “EpiTapp” is a promising method of palliative therapy for oncogenic focal epilepsy.

Abstract Number: 82

Title: Efficacy and Safety of Perampanel in Patients with Focal-Onset Seizures (FOS): Post Hoc Analysis of FAME by Dose and First-Line Antiepileptic Drug

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Purpose: In the US/Korea, perampanel is approved for FOS (adjunctive/monotherapy) in patients aged ≥4 years and generalised tonic-clonic seizures (adjunctive) in patients aged ≥12 (≥7, Korea) years. This post hoc analysis of the open-label, single-arm FAME study (NCT02726074) assessed the efficacy and safety of adjunctive perampanel by dose in patients receiving different first-line antiepileptic drugs (AEDs).

Method: Patients in FAME were aged ≥12 years with FOS, with/without focal to bilateral tonic-clonic seizures, and had failed AED monotherapy. First adjunctive perampanel was up-titrated to ≤12 mg/day (12 weeks), followed by a 24-week Maintenance Period. Endpoints included 50% responder/seizure-freedom rates, median

percent change in seizure frequency/28 days and treatment-emergent adverse events (TEAEs). For this analysis, endpoints were stratified by first-line AED and perampanel maintenance dose.

Result: First-line AEDs included levetiracetam, carbamazepine, oxcarbazepine, lamotrigine and valproic acid. Perampanel maintenance doses were 4–12 mg/day. In the Full Analysis Set (n=85), efficacy appeared greatest with perampanel 4 or 6 mg/day: at 4 mg/day, 50% responder rates were 85% with levetiracetam (n=17/20) and 100% with carbamazepine (n=7/7), oxcarbazepine (n=7/7), lamotrigine (n=6/6) and valproic acid (n=2/2), while median percent reductions in seizure frequency were 97–100% with each first-line AED. Seizure-freedom rates were highest with perampanel 4 mg/day plus oxcarbazepine (86%, n=6/7) or valproic acid (100%; n=2/2). Sample sizes were small for perampanel 10–12 mg/day (n=3). In the Safety Analysis set (n=102), the most common TEAE (dizziness) was generally observed most frequently with perampanel 4 mg/day. Eight patients had serious adverse events; one of suicidal ideation with perampanel 4 mg/day and levetiracetam was considered possibly related to treatment, while all others were considered unrelated.

Conclusions: Low-dose perampanel (4–6 mg/day) was effective in achieving seizure control and response with favourable tolerability in patients with FOS, regardless of first-line concomitant AED use.

Funding: Eisai Korea Inc.

Abstract Number: 120

Title: Efficacy/Safety of Adjunctive Perampanel for Myoclonic and Absence Seizures: Post Hoc Analysis of Patients Aged ≥2 Years in Studies 332/311/232

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Purpose: Some anti-seizure medications can exacerbate myoclonic and absence seizures in patients with generalised seizures. As such, this post hoc pooled analysis assessed the efficacy and safety of adjunctive perampanel for myoclonic and absence seizures in adult/adolescent/paediatric patients using data from Phase II/III clinical studies.

Method: During the randomised, double-blind Study 332 (NCT01393743), patients aged ≥12 years with generalised tonic-clonic seizures (GTCS) received placebo or adjunctive perampanel 8 mg/day. In Study 311 (NCT02849626), patients aged 4–<12 years with focal-onset seizures or GTCS received open-label perampanel ≤16 mg/day. In Study 232 (NCT01527006), patients aged 2–<12 years with epilepsy received open-label perampanel ≤0.18 mg/kg/day. Data from patients with myoclonic and/or absence seizures during baseline were pooled. Assessments included median percent change in seizure frequency/28 days, 50% responder rates and treatment-emergent adverse events (TEAEs).

Result: Of 393 patients, 66 had myoclonic seizures (placebo, n=23 [mean (standard deviation) age: 28.1 (8.9) years]; perampanel, n=43 [18.8 (11.9) years]) and 72 had absence seizures (placebo, n=33 [28.8 (13.2) years]; perampanel, n=39 [21.0 (12.2) years]) at baseline; patients with both seizure types are counted in both groups. Reductions in seizure frequency/28 days were observed in both the placebo and perampanel groups: myoclonic, 52.5% and 24.6%; absence, 7.6% and 25.1%, respectively. For placebo and perampanel, 50% responder rates were: myoclonic, 60.9% (n=14/23) and 44.2% (n=19/43); absence, 39.4% (n=13/33) and 38.5% (n=15/39), respectively. TEAEs with placebo and perampanel occurred in 18 (78.3%) and 36 (83.7%) patients

with myoclonic seizures, and 25 (75.8%) and 34 (87.2%) patients with absence seizures, respectively. With perampanel, the most common TEAEs were dizziness and fatigue.

Conclusions: Despite small patient numbers, these data suggest adjunctive perampanel does not worsen myoclonic or absence seizures in adult, adolescent and paediatric patients.

Funding: Eisai Inc.

Abstract Number: 124

Title: PROVE Study 506: Perampanel as Adjunctive Therapy or Monotherapy in Real-World Clinical Care of Patients with Epilepsy

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Purpose: Perampanel is a once-daily oral anti-seizure medication (ASM) for focal-onset seizures and generalised tonic-clonic seizures. We report a subgroup analysis of the retrospective, non-interventional Phase IV PROVE Study 506 (NCT03208660), comparing retention, dosing and safety for patients with epilepsy who received adjunctive perampanel or perampanel monotherapy during routine clinical care.

Method: Data were obtained from records of patients initiating perampanel after 01-Jan-2014. Follow-up completed on 15-Mar-2019. Primary endpoint was retention rate (proportion of patients in Safety Analysis Set [SAS] remaining on perampanel at 3/6/12/18/24 months following initiation). Dosing/safety were secondary objectives. Patients received perampanel as adjunctive therapy (with concomitant ASMs), primary monotherapy (without concomitant ASMs) or secondary monotherapy (conversion to monotherapy by withdrawing concomitant ASMs).

Results: SAS included 1676 (98.4%) patients receiving adjunctive perampanel and 47 (2.8%) receiving perampanel monotherapy (mean [standard deviation (SD)] age, 28.4 [16.4] and 31.5 [18.2] years; female, 52.7% and 53.2%, respectively). Patients receiving adjunctive perampanel and perampanel monotherapy (primary, n=33; secondary, n=14) are included in each relevant group. Most patients on adjunctive perampanel received 1–3 baseline ASMs (n=1321 [77.6%]). Overall, 806 (48.1%) patients discontinued adjunctive perampanel and 23 (48.9%) discontinued monotherapy; most commonly due to adverse events (adjunctive, 22.9%; monotherapy, 14.9%) and inadequate therapeutic effect (adjunctive, 13.1%; monotherapy, 25.5%). Retention rates on perampanel (24 months) were: 47.6% (adjunctive); 31.3% (primary monotherapy); 83.3% (secondary monotherapy). Mean (SD) cumulative durations of perampanel exposure were: adjunctive, 17.3 (15.8) months; monotherapy, 13.5 (11.8) months. Mean (SD) maximum perampanel doses were: adjunctive, 6.6 (3.2) mg; monotherapy, 7.2 (2.7) mg. Treatment-emergent adverse events occurred in 696 (adjunctive; 41.5%) and 17 (monotherapy; 36.2%) patients; dizziness was most common.

Conclusion: This analysis demonstrates favourable retention on perampanel (adjunctive or monotherapy) for ≤2 years in patients with epilepsy during routine clinical care, with similar safety profiles between groups.

Funding: Eisai Inc.

Abstract Number: 125

Title: PROVE Study 506: Analysis of a Retrospective, Phase IV Study of Perampanel in Real-World Clinical Care of Patients Based on Seizure Type

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Purpose: PROVE (NCT03208660) was a retrospective, multicentre, non-interventional Phase IV study of perampanel during real-world clinical care of patients with epilepsy. We report real-world efficacy and safety of perampanel from PROVE, based on baseline seizure type.

Method: Data were obtained from records of patients initiating perampanel after 01-Jan-2014. Follow-up completed on 15-Mar-2019. Primary endpoint was retention rate (proportion of patients remaining on perampanel at 3/6/12/18/24 months following initiation; Safety Analysis Set [SAS]). Dosing, efficacy and safety were secondary objectives. Outcomes were stratified by baseline seizure type: focal-onset seizures (FOS) only, generalised seizures only, generalised tonic-clonic seizures (GTCS) only, myoclonic and absence seizures. There is overlap between the generalised seizure groups; patients with FOS and generalised seizures (n=718) were excluded.

Result: SAS included 1703 patients. Mean (standard deviation) maximum doses (mg/day) were: FOS only (n=545), 6.9 (3.0); generalised only (n=440), 6.0 (3.1); GTCS only (n=110), 6.2 (3.0); myoclonic (n=328), 6.4 (3.2); absence (n=301), 6.5 (3.3). 24-month retention rates were: 48.1% (FOS only, n=164/341); 47.8% (generalised only, n=120/251); 42.9% (GTCS only, n=27/63); 50.3% (myoclonic, n=100/199); 47.7% (absence, n=84/176). Of 51 patients with seizure data at Months 22–24, median reductions in total seizure frequency/28 days were: 75.0% (FOS only, n=20); 91.6% (generalised only, n=10); 40.0% (GTCS only, n=3); 70.0% (myoclonic, n=7); 100.0% (absence, n=4). Corresponding seizure-freedom rates were: 45.0% (FOS only, n=9/20); 30.0% (generalised only, n=3/10); 0.0% (GTCS only, n=0/3); 14.3% (myoclonic, n=1/7); 75.0% (absence, n=3/4); 50% responder rates were 33.3–100.0% across seizure types. Treatment-emergent adverse events occurred in 231/545 (42.4%; FOS only), 185/440 (42.0%; generalised only), 50/110 (45.5%; GTCS only), 117/328 (35.7%; myoclonic) and 154/301 (51.2%; absence) patients; the most common were dizziness and aggression.

Conclusions: Dosing, 24-month retention rates on perampanel and safety were generally similar across seizure types. Seizure frequency reductions were observed across subgroups.

Funding: Eisai Inc.

Abstract Number: 126

Title: Adjunctive Perampanel 4 mg/day for Focal-Onset Seizures (FOS): Time to Seizure Onset in Pivotal Phase III Studies

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Purpose: Although recommended maintenance dosing of perampanel for FOS is 8–12 mg/day, in some patients, efficacy can be seen with doses as low as 4 mg/day. This post hoc analysis evaluated the efficacy of

adjunctive perampanel 4 mg/day for treatment of FOS, with/without focal to bilateral tonic-clonic seizures (FBTCS), by assessing time to first seizure following perampanel administration.

Method: During Phase III Studies 304 (NCT00699972), 305 (NCT00699582) and 306 (NCT00700310), patients (aged ≥12 years) with FOS, with/without FBTCS, despite 1–3 anti-seizure medications were randomised to once-daily placebo or adjunctive perampanel 2–12 mg/day (19-week Double-blind Treatment Period [6-week Titration; 13-week Maintenance]). Time to first seizure from Day 1 of placebo or perampanel administration was assessed in the Intent-to-Treat (ITT) Analysis Set using the Kaplan–Meier method. Placebo data were available from Studies 304, 305 and 306; perampanel 4 mg/day data came from Study 306 (the only study to include the randomised 4-mg/day dose).

Results: The ITT Analysis Set included 437/442 (98.9%) placebo-treated patients (182/185 [98.4%] from Study 306) and 168/172 (97.7%) patients who received perampanel 4 mg/day. Perampanel 4 mg/day was associated with longer time to first seizure vs placebo. Mean (standard deviation) time to first seizure was 9.3 (22.80) days with perampanel 4 mg/day vs 4.9 (7.10) and 4.5 (6.33) days for Study 306 placebo and pooled placebo, respectively; median (range) time to first seizure was 3 (1, 135), 3 (1, 73) and 3 (1, 73) days, respectively.

Conclusion: Adjunctive treatment with once-daily perampanel 4 mg/day delayed the time to first seizure in patients aged ≥12 years with FOS, with/without FBTCS, compared with placebo. These data further support the efficacy of perampanel 4 mg/day.

Funding: Eisai Inc.

Abstract Number: 127

Title: FAME Study: Efficacy and Safety of Perampanel as First Adjunctive Therapy after First or Second Monotherapy in Patients with Focal-Onset Seizures

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Purpose: In the US/Korea, perampanel is approved for focal-onset seizures (FOS) (adjunctive/monotherapy) in patients aged ≥4 years and generalised tonic-clonic seizures (adjunctive) in patients aged ≥12 (≥7, Korea) years. This post hoc analysis of the open-label, single-arm FAME study (NCT02726074) explored whether the efficacy and safety of first adjunctive perampanel is impacted by the number of previous monotherapies (one or two).

Method: Patients in FAME were aged ≥12 years with FOS with/without focal to bilateral tonic-clonic seizures (FBTCS) and had failed antiepileptic drug monotherapy. Perampanel was up-titrated to ≤12 mg/day (12 weeks), followed by a 24-week Maintenance Period. Endpoints included 50% responder/seizure-freedom rates, median percent change in seizure frequency/28 days and treatment-emergent adverse events (TEAEs). For this analysis, endpoints were stratified by whether the prior treatment was a first or second monotherapy.

Results: The Full Analysis Set included 79 patients receiving perampanel 4–10 mg/day with first monotherapies (most commonly: levetiracetam [n=31]; carbamazepine [n=20]; oxcarbazepine [n=14]) and six receiving perampanel 6–12 mg/day with second monotherapies (levetiracetam [n=3]; oxcarbazepine [n=3]). For first vs second monotherapy, 50% responder rates were 83.5% (n=66/79) vs 33.3% (n=2/6; P=0.0134), seizure-freedom rates were 50.6% (n=40/79) vs 0.0% (n=0/6; P=0.0274) and median percent reductions in seizure frequency/28 days were 100.0% vs 21.8% (P=0.0039). In patients with FBTCS (all first monotherapy), the seizure-freedom rate was 75.0% (n=12/16). In the Safety Analysis Set, TEAE profiles were similar with first vs second monotherapy

(TEAE incidence: 75.3% [n=70/93] vs 77.8% [n=7/9]; serious TEAEs: 6.5% [n=6/93] vs 22.2% [n=2/9]; discontinuations due to TEAEs: 14.0% [n=13/93] vs 11.1% [n=1/9]; most common TEAE in both groups: dizziness).

Conclusion: Adjunctive perampanel was associated with improved seizure control following first or second monotherapy. However, the small number of patients on their second monotherapy limits comparisons. These data support early-line perampanel use.

Funding: Eisai Korea Inc.

Abstract Number: 128

Title: Safety of Adjunctive Perampanel by Titration/Maintenance Periods and Dose in Patients With Focal-Onset Seizures: Post hoc Analysis of the FAME Study

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Purpose: In the US/Korea, perampanel is approved for focal-onset seizures (FOS) (adjunctive/monotherapy) in patients aged ≥4 years, and generalised tonic-clonic seizures (adjunctive) in patients aged ≥12 (≥7, Korea) years. This post hoc analysis of the open-label, single-arm FAME study (NCT02726074) assessed the safety of perampanel by study period/dose.

Method: Patients were aged ≥12 years with FOS, with/without focal to bilateral tonic-clonic seizures (FBTCS) and had failed antiepileptic drug monotherapy. First adjunctive perampanel was up-titrated to ≤12 mg/day (12 weeks), followed by a 24-week Maintenance Period. Endpoints included 50% responder/seizure-freedom rates, median percent change in seizure frequency/28 days and treatment-emergent adverse events (TEAEs). For these analyses, safety was assessed during Titration vs Maintenance and safety/efficacy were assessed by perampanel maintenance dose.

Results: Overall, 75.5% (77/102) of patients in the Safety Analysis Set reported 138 TEAEs, most commonly dizziness (50.0% [n=51/102]), somnolence (9.8% [n=10/102]) and headache (8.8% [n=9/102]). TEAEs occurred in 62.7% (n=64/102) of patients during Titration and 24.5% (n=25/102) during Maintenance. Among 88 patients who received maintenance perampanel 4, 6, 8, 10 or 12 mg/day, TEAE incidences across both study periods were 77.8% (n=35/45), 75.0% (n=21/28), 58.3% (n=7/12), 50.0% (n=1/2) and 100% (n=1/1), respectively. In the Full Analysis Set (n=85), 0/3 patients receiving perampanel 10/12 mg/day achieved ≥50% response, but efficacy at lower maintenance doses was demonstrated by 50% responder rates (4 mg/day, 93.0% [n=40/43]; 6 mg/day, 81.5% [n=22/27]; 8 mg/day, 50.0% [n=6/12]), seizure-freedom rates (4 mg/day, 60.5% [n=26/43]; 6 mg/day, 44.4% [n=12/27]; 8 mg/day, 16.7% [n=2/12]) and median percent reductions in seizure frequency/28 days (4 mg/day, 100.0%; 6 mg/day, 91.9%; 8 mg/day, 45.8%).

Conclusion: TEAE rates were lower during Maintenance than Titration, suggesting improved tolerance once maintenance doses were reached. While few patients received high doses, perampanel was otherwise generally well tolerated/efficacious regardless of dose.

Funding: Eisai Korea Inc.

Abstract Number: 132

Title: Disorders of reproduction in young men suffering from epilepsy

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Background: The pathology of the reproductive system in epileptic men can manifest itself both in the form of decreased libido, decreased fertility, erectile dysfunction, orgasm and ejaculation disorders, and lead to infertility. The study involved 30 men aged 18–44 years (31.8 ± 2.12), who were divided into two groups. Group I (14 patients) with congenital central nervous system abnormalities, and group II (16 patients) with post-traumatic epilepsy (the median time is 1.6 years). A control group of 15 practically healthy men of comparable age was formed.

Purpose: to evaluate of the effect of epilepsy on the male reproductive system.

Method: The study included neurological examination, a validated questionnaire "International Index of Erectile Function" (IIEF).

Result: It was found in the course of the study that the average score on the IIEF questionnaire was 13.6 in group I, which corresponds to moderate erectile dysfunction. There was a statistically significant difference with the control group ($p<0.01$). This measure was 22.8 in group II, which actually indicates a normal erection. There was no significant difference with the control group in this indicator ($p>0.05$). The 11 (78.6%) patients from group I noted the absence of pronounced morning erections and weak masturbation erections, which allowed to exclude psychogenic erectile dysfunction. The men from the control group and group II noted the preservation of morning erections. Also, young men from group I were significantly more likely to have asthenozoospermia (71.4 % compared to 20% of the control group; $p<0.05$).

Conclusions: According to the results of the study, it was found out that erectile dysfunction and impaired fertility are more common in people with epilepsy since childhood and adolescence. In contrast, among patients with post-traumatic epilepsy and a short duration of the disease, erectile dysfunction is not more common than in the general population.

Abstract Number: 133

Title: Changes of lipid metabolism in young men with epilepsy

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Background: Epilepsy is one of the most common diseases of the nervous system. It is known that the basis of the disease is increased epileptiform activity, due to the peculiarities of the course of the brain's metabolic processes. A certain role is played by endocrine disorders and metabolic disorders, in particular.

Purpose: to investigate the changes in lipid metabolism in young men with epilepsy in the post-seizure period and against the background of taking antiepileptic drugs (AEDs).

Method: The studies were conducted on the basis of the analysis of clinical symptoms and instrumental studies (biochemical blood analysis - lipid spectrum, determination of the level of AEDs concentration in the blood). EEG, EEG-video monitoring, MRI, Proton MR Spectroscopy (definition of Lip, Lac) were used as the screening methods.

Result: The analysis of the data of 50 young men aged from 18 to 44. After the survey 25 people in the post-seizure period had a Lac peak and 5 people had a Lip peak, which occurs when lipid peroxidation processes are disrupted. Such disorders of lipid metabolism may be one of the factors of neuronal membrane damage. Changes in lipidic metabolism are associated with some AEDs and may cause long-term adverse health effects. These changes were observed in 15 patients. Carbamazepine (CBZ), phenobarbital (PB) and phenytoin (PHT) increase high-density lipoproteins, CBZ has cholesterol-lowering effects, PB and PHT may exert a similar cholesterol-lowering effect.

Conclusions: All patients showed multidirectional changes in lipid metabolism, which require further study. Disorders of lipid metabolism largely depend on the intake and daily dosage of AEDs.

Abstract Number: 138

Title: Sustained Seizure Freedom with Perampanel 4 mg/day Monotherapy in Patients with Newly Diagnosed/Currently Untreated Focal-Onset Seizures: Study 342

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Purpose: FREEDOM (NCT03201900; Japan/South Korea) is a multicentre, open-label Phase III study of perampanel monotherapy in patients (aged 12–74 years) with newly diagnosed/currently untreated recurrent focal-onset seizures (FOS), with/without focal to bilateral tonic-clonic seizures (FBTCS). We assessed if seizure freedom with perampanel 4 mg/day achieved during the Core Study is maintained during 52 weeks' treatment.

Method: During the Core Study, patients received perampanel 4 mg/day (4-week Pretreatment; 32-week Treatment [6-week Titration; 26-week Maintenance]), with titration up to 8 mg/day in case of seizure. Patients completing the Core Study could enter an Extension Phase. Seizure-freedom rates for 52 weeks (Core/Extension Phases) at 4 mg/day for FOS and based on seizure history were assessed in patients who were seizure free during the 4-mg/day Core Study Maintenance Period. Treatment-emergent adverse events (TEAEs) were monitored.

Results: Eighty-nine patients received ≥1 perampanel dose (Safety Analysis Set [SAS]) and 73 entered the Maintenance Period (modified Intent-to-Treat [mITT] population). Seizure freedom for 26 weeks was achieved by 46/73 (63.0%) patients with FOS during Maintenance. Of 32 patients who chose to enter the Extension Phase, 20 (62.5% [27.4% of the mITT population (n=20/73)]) achieved sustained seizure freedom at 4 mg/day for 52 weeks; 4 patients had not completed 52 weeks of treatment at data cutoff. Based on patients in the mITT who entered the Extension Phase, >55% of patients with a history of focal impaired awareness seizures (FIAS), FIAS and/or FBTCS or FBTCS had sustained seizure freedom for 52 weeks on perampanel 4 mg/day. TEAEs occurred in 72 (80.9%) patients in the SAS (Core and Extension Phases); most common was dizziness (36.0%).

Conclusion: Seizure freedom was sustained during long-term (52 weeks) treatment with perampanel monotherapy 4 mg/day in patients with newly diagnosed/currently untreated recurrent FOS with/without FBTCS. Perampanel 4 mg/day was well tolerated.

Funding: Eisai Co., Ltd.

Abstract Number: 142

Title: Clinical Factors Associated with Seizure Freedom in Patients with Focal-Onset Seizures (FOS) Receiving Perampanel 4 mg/day in FREEDOM Study 342

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Purpose: Previous analyses have identified factors that affect treatment responses, e.g. high baseline seizure frequency has been associated with poor prognosis (French JA. Epilepsy Curr 2002;2:69–71). This post hoc analysis identified predictive clinical factors for patients (aged 12–74 years) with FOS, with/without focal to bilateral tonic-clonic seizures (FBTCS), achieving 26 weeks' seizure freedom while receiving perampanel 4 mg/day during FREEDOM Study 342 (NCT03201900).

Method: This analysis was based on the 4-mg/day Treatment Phase (6-week Titration; 26-week Maintenance). Logistic regression was used to determine odds ratios (ORs) and 95% confidence intervals (CIs). Goodness of fit was measured by area under the receiver operating characteristic (ROC) curve. Baseline seizure frequency, seizure history, age at diagnosis, time since diagnosis, etiology and perampanel plasma concentration were assessed individually as continuous and/or categorical variables in univariate analyses. All variables were included in multivariate analyses with forwards/backwards/no selection. Patients who withdrew during Titration were excluded.

Results: Overall, 46/73 (63.0%) patients with ≥1 post-dose efficacy measurement remained seizure free for 26 weeks on perampanel 4 mg/day. In univariate analyses, lower baseline seizure frequency was a predictor of seizure freedom as both a continuous (P=0.0136) or categorical (≤2 vs >2 seizures/12 weeks; P=0.0284) variable. History of focal aware (P=0.7137), focal impaired awareness (P=0.3711) or FBTCS (P=0.7005); age at diagnosis (P=0.9241); time since diagnosis (P=0.1862); idiopathic (P=0.7118) or structural (P=0.9033) etiology; and perampanel plasma concentration (P=0.3940) were not predictors of seizure freedom. In multivariate analyses (no selection), only lower baseline seizure frequency was a predictor of seizure freedom (OR [95% CI], 0.817 [0.696, 0.960]; P=0.0140; area under ROC curve, 0.7483). The same model was selected using forwards/backwards selection.

Conclusion: The best predictor for seizure freedom was baseline seizure frequency; the lower the baseline seizure frequency, the higher the probability of remaining seizure free.

Funding: Eisai Co., Ltd.

Abstract Number: 143

Title: Seizures as the presenting symptom of brain tumors in adults.

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Purpose: Our objective was to describe the incidence of seizures as the presenting symptom of brain tumors in adults.

Method: In a retrospective study, we reviewed all consecutive patients hospitalized with diagnosis of a brain tumor in the Department of Neurosurgery, University Hospital, Kraków, Poland between October 2018 and October 2019. Data collection included: demographics, tumor histology and location, and treatment modalities; for patients with seizures: the timing and frequency of seizures, and antiseizure medication.

Result: We collected data of 402 patients (233, 58% women), aged 58,4 years ±14,2. The most common histological type were: meningiomas (111; 27.6%), followed by glioblastomas (88; 21.9%), astrocytomas (50, 12.4%), metastases (35, 8.7%), and oligodendrogliomas (21, 5.2%). Histopathology results were not available for 34 (8.5%) patients. Seizures were the first symptom of the tumor in 96 (23.9%) cases, in further 5 patients were observed during hospitalization. Seizures were most common in astrocytomas (21, 42%), oligodendrogliomas (8, 38.1%), glioblastomas (26, 29.5%), metastases (10, 28.6%), and meningiomas (15, 13.5%). Antiseizure medication (ASM) was introduced in 82 (81.2 % with seizures) subjects (in 66 before admission). Most patients received valproate and levetiracetam. The majority of cases had isolated seizures or a low seizure frequency at the onset of the disease The majority of patients (332, 82.6%) underwent surgical removal of the tumor, which was either radical (82,8%) or partial (17,2%). Forty two patients underwent only cerebral biopsy. Overall 114 patients received adjuvant therapy: chemo-, radiotherapy or both. In one third (24, 29.3%) of patients seizure were observed during hospitalization, although in almost half of these patients (11, 45.8%) treatment had been introduced before admission.

Conclusions: In a quarter of patients seizures may be the presenting sign of a brain tumor. The prevalence of seizures depends on the tumor type.

Abstract Number: 150

Title: Epileptiform activity index changes for prediction of Oxcarbazepine monotherapy efficacy in adults and adolescents with newly-diagnosed focal epilepsy

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Purpose: Oxcarbazepine (OXC) was synthesized in 1966 and patented in 1969. It has been used in Russia since 2007. Our study is aimed to assess OXC effectiveness, tolerability, and epileptiform activity index (EAI) changes when used as the initial therapy of newly diagnosed focal epilepsy in adults.

Method: 89 patients aged 15–75 with newly diagnosed focal epilepsy were involved in our study. Each of the patients was evaluated at baseline, as well as on 1, 3, 6, and 12 months of treatment. Patients were separated into 3 groups according to the OXC dose they received: less than 1200 mg/day, 1200 mg/day, above 1200 mg/day. OXC tolerability was evaluated using SIDAED scale (Side Effects of Anti-Epileptic Drugs).

Result: Retention rate of OXC monotherapy at 12 months was 71.9% (64 patients), among them: 52.9% took 1200 mg/day, 12.3% - less than 1200 mg/day, 6.7% - above 1200 mg/day. Adverse events were reported in 9.0% of cases (8 patients), in 3.3% of cases hyponatremia developed (n=5). In 12 months total EAI was reduced by 2.5 times showing the effectiveness of the therapy.

Conclusions: OXC showed itself as a highly effective and tolerable medicinal product for focal epilepsy initial monotherapy. Total EAI 2.5-fold reduction allows its usage as an additional objective indicator of OXC therapy effectiveness.

Abstract Number: 157

Title: Elmer Southard and the first decription of limbic encephalitis in 1908

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Purpose: To raise awareness of Elmer E. Southard and his likely first description of limbic encephalitis (LE).

Method: Historic description.

Result: Elmer Ernest Southard (* July 28, 1876; † February 8, 1920), was an U.S.-American neurologist, neuropathologist, and psychiatrist. After studying at Harvard Medical School (HMS) in Boston, Massachusetts, until 1901, he initially trained in neuropathology. Then he travelled to Europe, among other countries to Germany to meet Carl Weigert (1845-1904) in Frankfurt and Emil Kraepelin (1856-1926) as well as Franz Nissl (1860-1919) in Heidelberg. After returning to HMS, he became assistant professor in 1906 and professor in 1909. From 1912 onwards he was the director of a psychiatric clinic (Boston Psychopathic Hospital). He was a founding member of the editorial board of the "Archives of Neurology and Psychiatry" and collaborated for many years with the neuropathologist Myrtelle Canavan (1979-1953). He had a positive attitude toward eugenics and was a member of the U.S. "Eugenics Society " founded by the U.S. biologist and eugenicist Charles Benedict Davenport (1866-1944). He suffered an; early death during a lecture tour due to septic staphylococcal meningitis with cerebral hemorrhage. He also dealt with epilepsy and was probably the first to describe the pathology of limbic encephalitis in 1908 (1): *"Case of acquired epilepsy in a fisherman of sixty-eight years, fatal in nine weeks: Focal acute of right cornu ammonis… The autopsy (four hours after death) showed the following conditions: Intracranial congestion. Focal encephalitis of right cornu ammonis... . The right cornu ammonis shows a grayish-red linear streak running about the convolutions in the nerve-cell layers. This has an anterioposterior extent of perhaps 1 cm" (*Southard EE. On the mechanism of gliosis in acquired epilepsy. Am J Insanity 1908; 64: 607–41).

Conclusions: Southards paper from 1908 is likely the first description of LE.

Abstract Number: 161

Title: The acceptability of a remote, at home, long-term procedure to monitor EEG and non-EEG biosignals in people with epilepsy (EEG@HOME).

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Purpose: Evaluate the acceptability and feasibility of a procedure (EEG@HOME) that allows patients with epilepsy to independently, remotely, and continuously acquire non-invasive variables at home.

Method: Adults with pharmaco-resistant epilepsy were recruited at King's College Hospital, London. Participants were trained for one week to self-apply a portable EEG recording system (ANT Neuro) to record scalp EEG twice daily, collect non-EEG biosignals using a wrist-worn device (Fitbit Charge 3) and complete a daily questionnaire

about seizure occurrence and triggers through a smartphone app (Seer Medical). Participants were then monitored remotely for 6 months. Standardized questionnaires (Post-Study System Usability Questionnaire, PSSUQ and the System Usability Scale, SUS) were used to assess the acceptability of the procedures after the training and the first month of data collection.

Result: Three participants (mean age 44, range 33-67) were enrolled from November 2020 to March 2021. The mean of their total SUS score after training was 82.2 (high usability), while after one month the SUS was 86.4 and the overall PSSUQ score was 1.31 (high usability). One participant needed a second training and weekly support, and three technical issues were successfully fixed remotely. More than 400 EEG recordings, 4,300 hours of heart rate and 400 daily surveys were collected with an average compliance for the EEG recording sessions of 85.8% (418 out of 497, range 73.8-95.2%), for the questionnaires of 77.2% (402 out of 502, range 47.6-96.2%) and for the wrist-worn device of 99% (215 out of 218 days, range 97.4-100%).

Conclusions: These preliminary results show that the possibility to train, support and monitor participants continuously and remotely from their home is feasible and well accepted by people with epilepsy. The successful implementation of an at-home, long-term monitoring procedure like this could enable an innovative approach for epilepsy management.

Abstract Number: 168

Title: A Phase IV, Prospective, Post-Approval Study of Adjunctive Perampanel in Indian Patients Aged ≥12 Years with Focal-Onset Seizures: Study 508

Anshu Rohatgi[1], Sangeeta Ravat[2], Balaji Patil[3], Amitabh Dash[4], Manoj Malhotra[5]

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Purpose: In the US, EU and India, perampanel is approved for focal-onset seizures (FOS) and generalised tonic-clonic seizures (GTCS) in patients aged ≥12 years (FOS: ≥4 years, US/EU and GTCS: ≥7 years, EU). Study 508 (NCT03836924) evaluated the safety, tolerability and efficacy of real-world adjunctive perampanel in Indian patients aged ≥12 years with FOS.

Method: Study 508 was a prospective, multicentre, post-approval, observational study comprising a Screening/Enrolment Visit, a 6-month Treatment Period (monthly clinical visits) and a 30-day Follow-up Period. Assessments included: incidence of treatment-emergent adverse events (TEAEs; primary endpoint), clinical laboratory parameters/vital signs, median reduction in seizure frequency/28 days and 50%/90% responder and seizure-freedom rates. Patients were aged ≥12 years.

Result: Overall, 200 patients were enrolled and 199 patients were included in the Safety Analysis Set; mean (standard deviation) age was 28.7 (12.4) years. A total of 60 TEAEs of mild-to-moderate severity were reported in 36 (18.1%) patients; 18 events were considered related to perampanel treatment (most common: dizziness and irritability). Three (1.5%) patients discontinued due to TEAEs and no deaths or serious TEAEs occurred. All abnormal clinical laboratory parameters and vital signs were reported as clinically non-significant.

A total of 174 patients completed all study visits; median percent reduction in seizure frequency across the entire Treatment Period was 100.0%. Overall, 145/174 (83.3%) and 113/174 (64.9%) patients reported a ≥50% and ≥90% reduction in seizure frequency, respectively. Seizure freedom was achieved by 76/174 (43.7%), 99/174 (56.9%) and 86/174 (49.4%) patients during the first 3 months, the last 3 months and the entire 6-month Treatment Period, respectively.

Conclusions: Real-world adjunctive perampanel was well-tolerated and efficacious in Indian patients aged ≥12 years with FOS. No unexpected safety signals emerged; seizure freedom was achieved by >56% of patients in the last 3 months of treatment.

Funding: Eisai Pharmaceuticals India Pvt. Ltd.

Abstract Number: 169

Title: Study 508: A Phase IV, Post-Approval Study of Adjunctive Perampanel in Indian Patients Aged ≥12 Years with Epilepsy Based on Seizure Type

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Purpose: In the US/EU/India, perampanel is approved for focal-onset seizures (FOS), with/without focal to bilateral tonic-clonic seizures (FBTCS), and generalised tonic-clonic seizures (GTCS) in patients aged ≥12 years (FOS: ≥4 years, US/EU and GTCS: ≥7 years, EU). This post hoc analysis reports real-world tolerability/efficacy of adjunctive perampanel in Indian patients aged ≥12 years, stratified by seizure type.

Methods: Study 508 (NCT03836924) was a prospective, multicentre, post-approval, observational study comprising a Screening/Enrolment Visit, a 6-month Treatment Period and a 30-day Follow-up Period. Assessments included: incidence of treatment-emergent adverse events (TEAEs; primary endpoint), median reduction in seizure frequency/28 days and 50% responder/seizure-freedom rates. Patients were aged ≥12 years; data were stratified by seizure type.

Results: Overall, 200 patients were enrolled and 199 were included in the Safety Analysis Set. At baseline, 113 (56.5%), 43 (21.5%), 18 (9.0%), 3 (1.5%), 1 (0.5%) and 22 (11.0%) patient(s) had FOS (aware/impaired awareness), FBTCS, GTCS, tonic, myoclonic and 'other' seizures, respectively. TEAEs were experienced by 24 (21.2%), 5 (11.6%), 1 (5.6%) and 5 (22.7%) patient(s) with FOS, FBTCS, GTCS, and 'other' seizures, respectively – only 4

(3.5%) patients discontinued treatment (all FOS). Median reduction in seizure frequency for all seizure types was >92%. Overall, >77.0% (FOS), 100.0% (FBTCS), >66.0% (any generalised seizure; GTCS/tonic/myoclonic) and 85.0% ('other' seizures) of patients reported a ≥50% reduction in seizure frequency; 42.3% (FOS), 72.2% (FBTCS), 0.0–47.1% (any generalised seizure) and 50.0% ('other' seizures) of patients reported seizure freedom across the 6-month Treatment Period. During the last 3 months of treatment, ≥50% of patients in almost all subgroups experienced seizure freedom.

Conclusions: Adjunctive perampanel was safe and efficacious across all seizure types. No unexpected safety signals emerged; ≥50% of patients in almost all seizure type subgroups experienced seizure freedom during the last 3 months of treatment.

Funding: Eisai Pharmaceuticals India Pvt. Ltd.

Abstract Number: 171

Title: Seizure Freedom in Patients with Focal to Bilateral Tonic-Clonic Seizures (FBTCS) during FAME: A Post Hoc Analysis of Low-dose Maintenance Perampanel

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Purpose: In the US/Korea, perampanel is approved for focal-onset seizures (FOS; adjunctive/monotherapy) in patients aged ≥4 years and generalised tonic-clonic seizures (adjunctive) in patients aged ≥12 (≥7, Korea) years. Achieving seizure control is particularly important in patients with convulsive seizures, including FBTCS, as these are often refractory and have been associated with increased mortality rates from sudden unexpected death in epilepsy and other seizure-related complications. This post hoc analysis of the open-label, single-arm FAME study (NCT02726074) assessed seizure-freedom rates in patients with FBTCS by perampanel maintenance dose (4 mg/day and 6 mg/day).

Method: Patients in FAME were aged ≥12 years with FOS, with/without FBTCS, and had failed on antiepileptic drug monotherapy. First adjunctive perampanel was up-titrated to ≤12 mg/day (12 weeks), followed by a 24-week Maintenance Period. Endpoints included 50% and 75% responder rates, seizure-freedom rates and treatment-emergent adverse events (TEAEs). For this analysis, patients with FBTCS were stratified by perampanel maintenance dose.

Results: In the Full Analysis Set, 16/85 (18.8%) patients had FBTCS. Of these, 14/16 (87.5%) patients experienced a ≥50 or ≥75% reduction in seizure frequency, all at perampanel maintenance doses of 4 mg/day (n=7; 50.0%) or 6 mg/day (n=7; 50.0%). Seizure freedom was achieved by 12/16 (75.0%) patients, at perampanel maintenance doses of 4 mg/day (n=7; 58.3%) or 6 mg/day (n=5; 41.7%). Thirteen patients (81.3%) reported TEAEs (4 mg/day [n=8]; 6 mg/day [n=5]); the most common was dizziness (n=8/16; 50.0%). Three patients reported serious TEAEs, one of which led to discontinuation (suicide attempt with perampanel 4 mg/day; considered unrelated to treatment).

Conclusion: Most patients with FBTCS achieved seizure freedom with maintenance perampanel 4–6 mg/day, with favourable tolerability. Despite the small sample size, these results suggest that convulsive seizure freedom can be achieved with low perampanel doses when administered as an early-line treatment.

Funding: Eisai Korea Inc.

Abstract Number: 189

Title: Impairment of cardiac autonomic function during epileptic seizures

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Purpose: Understanding ictal dysautonomia is all the more important that it is thought to be one of the key mechanisms of sudden unexpected deaths in epilepsy (SUDEP). The aim of our study was to explore the links between the ictal cardiac dysautonomia and the seizures localization, lateralization and duration by analysing the heart rate variability (HRV).

Method: We carried out a study based on a French prospective, multicentric cohort of patients with epilepsy who benefited from a video-EEG and ECG recording of their seizures (EPICARD). Different parameters of HRV (Heart Rate, SDNN, RMSSD, HFVI) were calculated before, right at the end and at various times after the end of each seizure (at 1, 2, 4, 8 and 15 minute). We performed a linear regression to analyse the correlation between these different parameters and the patients seizure's characteristics.

Result: Ninety-eight seizures were included, from 59 patients. We have observed a tachycardia, an increase in sympathetic tone and a drop in parasympathetic tone during the seizures, as well as up to 15 minutes after the seizure. This cardiac autonomic alteration was more intense in temporal lobe seizures than in frontal lobe or temporo-perisylvian seizures. Furthermore, the tachycardia and the drop in parasympathetic tone were significantly more important for seizures of prolonged duration (> 2 min). No significant difference was found regarding the epilepsy lateralization.

Conclusions: Impairment of cardiac autonomic function in the ictal and immediate postictal period is greater during temporal lobe seizures, the more so as the duration of the seizure is prolonged

Abstract Number: 199

Title: Analysis of Baseline Characteristics and Common Treatment-Emergent Adverse Events with Perampanel in Patients with Focal-Onset Seizures During FAME

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Purpose: In the US/Korea, perampanel is approved for focal-onset seizures (FOS) (adjunctive/monotherapy) in patients aged ≥4 years and generalised tonic-clonic seizures (adjunctive) in patients aged ≥12 (≥7, Korea) years. This post hoc analysis of the open-label, single-arm FAME study (NCT02726074) assessed potential associations of baseline characteristics with common treatment-emergent adverse events (TEAEs), and the impact of these TEAEs on response.

Method: Patients were aged ≥12 years with FOS, with/without focal to bilateral tonic-clonic seizures, and had failed antiepileptic drug monotherapy. First adjunctive perampanel was up-titrated to ≤12 mg/day (12 weeks), followed by a 24-week Maintenance Period. Endpoints included 50%/75% responder/seizure-freedom rates and TEAEs. Common TEAEs were those reported by ≥2 patients during Titration.

Results: In the Safety Analysis Set, 64/102 (62.7%) patients experienced TEAEs during Titration. The most common were dizziness (n=48 [47.1%]), somnolence (n=9 [8.8%]), headache (n=6 [5.9%]), dysarthria (n=5 [4.9%]), and oedema, fatigue, memory impairment and/or seizure (each n=2/102 [2.0%]). Most patients reporting ≥1 of the most common TEAEs were female (69.7% [n=53/76]); there were no clear associations with baseline comorbidities or age, although mean ages of patients with fatigue, memory impairment and/or dizziness were slightly higher than those of patients with other common TEAEs (40.6–58.0 vs 22.0–39.7 years). The 50% responder, 75% responder and seizure-freedom rates were: 62.5% (n=30/48), 54.2% (n=26/48) and 31.3% (n=15/48) for patients with dizziness; 66.7% (n=6/9), 66.7% (n=6/9) and 44.4% (n=4/9) for somnolence;

and 50.0% (n=3/6), 33.3% (n=2/6) and 33.3% (n=2/6) for headache. Of 13 patients with dysarthria, oedema, fatigue, memory impairment and/or seizure, eight achieved a ≥75% response and four achieved seizure freedom.

Conclusion: There was a possible association between the most common TEAEs during Titration and female sex, but no clear associations with baseline comorbidities or age. Most patients with these TEAEs experienced seizure improvements.

Funding: Eisai Korea Inc.

Abstract Number: 200

Title: Perampanel Monotherapy for the Treatment of Epilepsy: Evidence From a Clinical Trial (Study 342) and Real-World Use (Studies 504 and 506)

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Purpose: In the US and Japan, perampanel is approved for focal-onset seizures (FOS; adjunctive/monotherapy) in patients aged ≥4 years and generalised tonic-clonic seizures (adjunctive) in patients aged ≥12 years. This analysis assessed efficacy/safety of perampanel monotherapy in patients with epilepsy using data from clinical and real-world studies.

Method: Patients with epilepsy were included in Studies 504 (if prescribed perampanel monotherapy) and 506 (if initiating perampanel after 1 January 2014); patients received perampanel as primary/secondary monotherapy. Study 342 recruited untreated patients aged 12–74 years with FOS, with/without focal to bilateral tonic-clonic seizures (FBTCS); patients received perampanel 4 mg/day (maximum: 8 mg/day). Endpoints: retention rate (Studies 504/506, primary); seizure-freedom rate (Study 342, primary; Studies 504/506, secondary); treatment-emergent adverse events (TEAEs).

Result: In Study 504, 60 patients received perampanel monotherapy. Retention rates were 55.6% (n=15/27; 12 months) and 60.0% (n=3/5; 24 months). Mean (standard deviation [SD]) maximum dose: 7.3 (2.8) mg/day. Seizure-freedom rate for ≥3 months was 55.0% (n=22/40).

In Study 506, 47 patients received perampanel monotherapy. Retention rates were 48.7% (n=19/39; 12 months) and 45.5% (n=10/22; 24 months). Mean (SD) maximum dose: 7.2 (2.7) mg/day. Seizure-freedom rate was 100.0% (n=2/2) at Months 22–24. Most patients in Studies 504 and 506 had refractory epilepsy.

In Study 342, 89 patients received ≥1 perampanel dose. Mean (SD) maximum dose: 4.9 (1.7) mg/day. Most patients with ≥1 post-dose efficacy measurement in the 4-mg Maintenance Period (n=73) achieved seizure freedom (4 mg/day: 63.0%; 4 or 8 mg/day: 74.0%).

TEAEs occurred in 22/60 (36.7%; Study 504) and 17/47 (36.2%; Study 506) patients, and 57/89 (64.0%; 4 mg/day) and 67/89 (75.3%; 4 and/or 8 mg/day) patients in Study 342; most common was dizziness.
Conclusions: These data support perampanel monotherapy as treatment for FOS, with/without FBTCS, and refractory epilepsy.

Funding: Eisai Inc., Eisai Co., Ltd., and Eisai Ltd.

Abstract Number: 201

Title: Efficacy/Safety of Low-/High-Dose Perampanel as First Adjunctive Therapy in Patients With Focal-Onset Seizures: Post Hoc Analysis of the FAME Study

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Purpose: In the US/Korea, perampanel is approved for focal-onset seizures (FOS) (adjunctive/monotherapy) in patients aged ≥4 years and generalised tonic-clonic seizures (adjunctive) in patients aged ≥12 (≥7, Korea) years. This post hoc analysis of the open-label, single-arm FAME study (NCT02726074) assessed efficacy and safety of low/high maintenance doses of adjunctive perampanel.

Method: Patients were aged ≥12 years with FOS, with/without focal to bilateral tonic-clonic seizures (FBTCS) and had failed antiepileptic drug monotherapy. First adjunctive perampanel was up-titrated to ≤12 mg/day (12 weeks), followed by a 24-week Maintenance Period. Endpoints included 50% responder rate, seizure-freedom rate, median percent change in seizure frequency/28 days and treatment-emergent adverse events (TEAEs). For this analysis, endpoints were stratified by perampanel dose (low-dose, 4/6 mg/day; high-dose, 8/10/12 mg/day).

Results: In the Full Analysis Set, 70/85 patients (82.4%) received low-dose perampanel (4 mg/day, n=43 [61.4%]; 6 mg/day, n=27 [38.6%]) and 15/85 (17.6%) received high-dose perampanel (8 mg/day, n=12 [80%]; 10 mg/day, n=2 [13.3%]; 12 mg/day, n=1 [6.7%]). With low-dose vs high-dose perampanel, 50% responder rates were 88.6% (n=62/70) vs 40.0% (n=6/15, *P*=0.0002), seizure-freedom rates were 54.3% (n=38/70) vs 13.3% (n=2/15, *P*=0.0039) and median percent reductions in FOS frequency/28 days were 100.0% vs 16.7% (*P*=0.0001). In 16 patients with FBTCS (all low-dose), 50% responder and seizure-freedom rates were 87.5% (n=14/16) and 75.0% (n=12/16), respectively. In the Safety Analysis Set, TEAEs were experienced by 56/73 (76.7%) and 9/15 (60.0%) patients receiving low- or high-dose perampanel, respectively. Six patients experienced serious TEAEs (low-dose, n=5; high-dose, n=1); four discontinued due to TEAEs (all low-dose).

Conclusion: Both low-/high-dose perampanel improved seizure control and were generally well-tolerated. Despite higher patient numbers in the low-dose group, these results suggest some patients may achieve seizure control with low-dose perampanel; however, others may require up-titration to higher doses based on response.
Funding: Eisai Korea Inc.

Abstract Number: 221

Title: Clinical Factors Associated with Response to Perampanel as First Adjunctive Treatment in Patients with Focal-Onset Seizures (FOS) in the FAME study

JiWoong Lee[1], Dong Wook Kim[2], Dae Won Seo[3], Amitabh Dash[4], Manoj Malhotra[5]

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Clinical Factors Associated with Response to Perampanel as First Adjunctive Treatment in Patients with Focal-Onset Seizures (FOS) in the FAME study (147/150 characters, including spaces)

Method: Patients in FAME were aged ≥12 years with FOS, with/without focal to bilateral tonic-clonic seizures (FBTCS), and had failed antiepileptic drug monotherapy. First adjunctive perampanel was up-titrated to ≤12 mg/day (12 weeks), followed by a 24-week Maintenance Period. Post hoc univariate and multivariate analyses using logistic regression were performed to explore if clinical variables predict response to perampanel (≥50%/≥75%/100% reduction in seizure frequency/28 days).

Result: Patients in FAME were aged ≥12 years with FOS, with/without focal to bilateral tonic-clonic seizures (FBTCS), and had failed antiepileptic drug monotherapy. First adjunctive perampanel was up-titrated to ≤12 mg/day (12 weeks), followed by a 24-week Maintenance Period. Post hoc univariate and multivariate analyses using logistic regression were performed to explore if clinical variables predict response to perampanel (≥50%/≥75%/100% reduction in seizure frequency/28 days).

Conclusions: In multivariate analyses, longer administration period, lower dose and presence of a concomitant non-antiepileptic medication were potential predictors of response to perampanel. No epilepsy-specific/demographic variables were associated with response, suggesting that a range of patients may benefit from first adjunctive perampanel.
Funding: Eisai Korea Inc.

Abstract Number: 222

Title: Post Hoc Analysis of Treatment-Emergent Adverse Events (TEAEs) by Treatment Period in Patients Aged ≥12 to <18 and ≥18 Years from Phase III Studies

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Purpose: Adjunctive perampanel has shown efficacy and tolerability across five randomised, double-blind, Phase III studies in patients (aged ≥12 years) with focal-onset seizures (FOS), with/without focal to bilateral tonic-clonic seizures (Studies 304 [NCT00699972], 305 [NCT00699582], 306 [NCT00700310], 335 [NCT01618695]) or generalised tonic-clonic seizures (GTCS) (Study 332 [NCT01393743]). Here, we examined TEAE rates with perampanel by treatment period in patients aged ≥12–<18 and ≥18 years.

Method: Perampanel was up-titrated from 2 mg/day in weekly 2-mg increments to ≤12 mg/day (FOS; 6-week Titration; 13-week Maintenance) or ≤8 mg/day (GTCS; 4-week Titration; 17-week Maintenance). TEAE rates were analysed by treatment period (Titration, Pre-steady-state, Maintenance) in patients who received perampanel and completed the study.

Results: Overall, 1387 patients were included (≥12–<18 years, n=159 [2 mg, n=20; 4 mg, n=35; 8 mg, n=74; 12 mg, n=30]; ≥18 years, n=1235 [2 mg, n=134; 4 mg, n=282; 8 mg, n=509; 12 mg, n=310]). Total perampanel exposure (subject-months [sum of exposures for all patients expressed in months]) for 2, 4, 8 and 12 mg/day in the younger cohort ranged from 5.0–74.5, 17.5–121.3, 74.0–213.5 and 45.0–73.4, respectively, during Titration–Maintenance; and in the older cohort ranged from 33.5–496.1, 141.0–975.1, 509.0–1482.9 and 465.0–759.2, respectively. In both cohorts, overall rates of TEAEs per 100 subject-months were highest during Titration (younger cohort: 35.6–68.6 [range dependent on perampanel dose]; older cohort: 46.1–59.7), lower during Pre-steady-state (younger cohort: 26.7–41.4; older cohort: 26.9–47.7) and at their lowest during Maintenance (younger cohort: 14.0–21.8; older cohort: 13.1–20.8). In general, the most common TEAEs during Titration (dizziness, somnolence and headache) had lower rates during Pre-steady-state and Maintenance in both cohorts.

Conclusion: These data suggest that perampanel tolerability may improve as a patient reaches the Maintenance Period, regardless of age.

Funding: Eisai Inc.

Abstract Number: 227

Title: Clinical characteristics and risk factors of cerebral cavernous malformation related epilepsy

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Purpose: Seizure is the most common clinical symptom of cerebral cavernous malformation (CCM), and about 64% patients progressing to drug-resistant epilepsy. CCM related epilepsy (CRE) has not been completely understood in terms of clinical features and risk factors. Therefore, we aimed to summarize clinical characteristics in patients with CCM and explore factors that increase the risk of CRE.

Method: We retrospectively collected clinical data in patients with CCM from June 2007 to January 2020 in the affiliated hospitals of Chongqing Medical University. Patients were divided into CRE group and non-CRE group according to clinical presentation. Univariate analysis and binary logistic regression analysis were used to analyze the risk factors of CRE.

Result:A total of 199 CCM patients confirmed by postoperative pathological examination were enrolled in this study, 93 (49.7%) of whom were diagnosed with CRE, 17 (18.3%) patients had status epilepticus. The most common seizure type of CRE was secondary general tonic-clonic seizure (SGTCS) (59.0%), followed by complex partial seizure (27.9%) and simple partial seizure (13.1%). In univariate analysis, sex, age, prior hypertension, lesion side, temporal lobe location, deep brain lesion, cortical involvement, supratentorial location and hemosiderin rim showed significant difference between two groups (p = 0.028, 0.012, 0.045, 0.014, 0.001, 0.003, 0.001, 0.001 and 0.001, respectively). Binary logistic regression analysis indicated that young age (≤ 44 years) (OR = 2.67, 95% CI 1.27-5.62, p = 0.010), temporal lobe location (OR = 4.58, 95% CI 2.09-10.05, p < 0.001), cortical involvement (OR = 21.28, 95% CI 2.54-178.19, p = 0.005) and hemosiderin rim (OR = 5.31, 95% CI 2.18-12.94, p < 0.001) significantly increase the risk of CRE.

Conclusions: The most common seizure type of CRE is SGTCS. Young age (≤ 44 years), temporal lobe location, cortical involvement and hemosiderin rim are associated with a higher risk of CRE.

Abstract Number: 230

Title: Long-Term Efficacy and Safety of Adjunctive Perampanel in Elderly Patients with Focal-Onset Seizures by Concomitant Anti-Seizure Medication (ASM) Use

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Purpose: This post hoc analysis evaluated long-term (≤4 years) efficacy/safety of adjunctive perampanel by concomitant baseline ASM use (number/most common) in elderly patients (aged ≥60 years) with focal-onset seizures (FOS) during Studies 307 (NCT00735397) and 335 open-label extension (OLEx; NCT01618695).

Method: Patients completing randomised, double-blind, Phase III studies could enter OLEx Studies 307 (16-week blinded Conversion; 256-week Maintenance) or 335 OLEx (4-week Pre-conversion; 6-week Conversion; ≥46-week Maintenance). Assessments included median percent reduction in seizure frequency/28 days vs pre-perampanel baseline and treatment-emergent adverse events (TEAEs) at Years 1–4.

Results: The Safety Analysis Set included 71 patients (1 ASM, n=8; 2 ASMs, n=33; 3 ASMs, n=30). The most common baseline ASMs were levetiracetam (n=28 [39.4%]), carbamazepine (n=22 [31.0%]) and lamotrigine (n=20 [28.2%]). During Years 1/2, respectively, median percent reductions in seizure frequency were: 1 ASM, 63.7% (n=8) and 59.1% (n=5); 2 ASMs, 49.0% (n=33) and 45.5% (n=15); 3 ASMs, 44.1% (n=30) and 51.8% (n=18); for the most common ASMs, reductions were: levetiracetam, 51.6% (n=28) and 51.2% (n=15); carbamazepine, 45.6% (n=22) and 50.9% (n=12); lamotrigine, 42.8% (n=20) and 53.4% (n=11). Seizure reductions were also observed during Years 3/4 across subgroups, but patient numbers were low. During Years 1/2, respectively, TEAE incidence was: 1 ASM, 100.0% (n=8/8) and 80.0% (n=4/5); 2 ASMs, 81.8% (n=27/33) and 66.7% (n=14/21); 3 ASMs, 90.0% (n=27/30) and 45.8% (n=11/24). For the most common ASMs, incidences were: levetiracetam, 89.3% (n=25/28) and 50.0% (n=11/22); carbamazepine, 77.3% (n=17/22) and 58.8% (n=10/17); lamotrigine, 85.0% (n=17/20) and 66.7% (n=10/15). Overall, dizziness was the most common TEAE during Years 1/2; fall was most common during Years 3/4.

Conclusion: Despite small patient numbers in some subgroups, these data suggest adjunctive perampanel was well tolerated with sustained seizure reduction for ≤4 years in elderly patients with FOS, regardless of concomitant ASM use.

Funding: Eisai Inc.

Abstract Number: 234

Title: Design of the Non-interventional PERPRISE Study (PERampanel in patients with PRImary or SEcondarily generalised seizures) Conducted in Germany

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Purpose: Perampanel is a once-daily oral anti-seizure medication (ASM) approved in the EU for focal-onset seizures (FOS; adjunctive), with/without focal to bilateral tonic-clonic seizures (FBTCS) in patients aged ≥4 years, and generalised tonic-clonic seizures (GTCS; adjunctive) in patients with idiopathic generalised epilepsy (IGE) aged ≥7 years. Data from prospective studies of perampanel in Germany are scarce, reflecting the use of perampanel as a late-line add-on therapy for highly refractory epilepsy, and limited data are available from patients with GTCS. PERPRISE (Study 509; NCT04202159) is a prospective, observational study investigating the efficacy of perampanel as only add-on treatment in adult patients with FBTCS/GTCS during clinical practice in Germany.

Method: Patients are eligible for inclusion if they have a confirmed diagnosis of FBTCS/GTCS based on FOS/IGE with ≥1 FBTCS/GTCS ≤3 months prior to inclusion and are receiving perampanel as only add-on therapy to ASM monotherapy/substitute for one ASM during dual therapy. Exclusion criteria include known psychogenic non-epileptic seizures, previous perampanel treatment or simultaneous treatment with an investigational drug. Data will be collected at baseline and following approximately 6 and 12 months of treatment. The primary endpoint is 12-month retention rate. Secondary endpoints include seizure-freedom and responder rates,

median change in seizure frequency, incidence of treatment-emergent adverse events (TEAEs) and discontinuation due to TEAEs.

Results: Disease characteristics, medical history and perampanel administration will be reported; data will be presented using descriptive statistics. Subgroup analyses are planned to investigate the effect of titration rates/ASM combinations on retention, and the patient-reported efficacy and tolerability of perampanel. PERPRISE aims to enrol 300 patients; 108 have been enrolled by 16/March/2021.

Conclusion: The study design of PERPRISE is comparable to observational studies of other ASMs during clinical practice and will help to inform outcomes of perampanel as only add-on treatment for adult patients with FBTCS/GTCS.

Funding: Eisai GmbH

Abstract Number: 235

Title: Perampanel Monotherapy Beyond Initial Titration to Achieve Seizure Freedom in Patients with Focal-Onset Seizures: Post Hoc Analysis of Study 342

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Purpose: The open-label FREEDOM Study 342 (NCT03201900) evaluated perampanel monotherapy in patients aged 12–74 years with newly diagnosed/currently untreated recurrent focal-onset seizures (FOS), with/without focal to bilateral tonic-clonic seizures (FBTCS), in Japan/South Korea. The Treatment Phase comprised 6-week Titration (2 mg/day [2 weeks], 4 mg/day [4 weeks]) and 26-week Maintenance Periods (4 mg/day; or, in case of seizures, up to 8 mg/day). During Maintenance, seizure freedom was achieved by 46/73 (63.0%) patients receiving 4 mg/day (Yamamoto T et al. Epilepsia Open 2020;5:274–284). This analysis assessed if continued treatment with perampanel monotherapy, beyond initial titration, may be required to achieve seizure freedom with an effective maintenance dose.

Method: Seizure-frequency data from the modified intent-to-treat (mITT) population (patients with ≥1 post-dose efficacy assessment during the 4-mg/day Maintenance Period) were analysed to determine whether patients who achieved seizure freedom over the 26-week 4-mg/day Maintenance Period (4-mg/day responders) experienced an early response during the Titration Period (early-responders; defined as no seizures during Titration).

Result: Of 73 patients in the mITT population, 46 patients achieved seizure freedom over the 26-week Maintenance Period with perampanel 4 mg/day (4-mg/day responders): 37/46 (80.4%) of these had early responses during Titration (early-responders), while 9/46 (19.6%) were not early-responders but went on to achieve seizure freedom during Maintenance. The remaining 27 patients did not achieve seizure freedom over the 26-week 4-mg/day Maintenance Period (4-mg/day non-responders): 18/27 (66.7%) of these had seizures during Titration, while 9/27 (33.3%) had early responses but did not achieve seizure freedom for 26 weeks during Maintenance with perampanel 4 mg/day.

Conclusions: Whilst the majority of patients with an early response during Titration continued to be seizure free during Maintenance, some patients without an early response during Titration could still achieve seizure freedom upon continued maintenance treatment with perampanel 4 mg/day.

Funding: Eisai Co., Ltd.

Abstract Number: 240

Title: Risk and cause of death in individuals with post-traumatic epilepsy

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Purpose: Posttraumatic epilepsy (PTE) constitutes a large proportion of epilepsy cases worldwide and because patients are often young, PTE contributes significantly to the overall burden of epilepsy. Longitudinal data on consequences of PTE are limited, including studies on mortality. We analyzed the risk of death associated with epilepsy after trauma, causes of death, and the contribution of epilepsy as direct or contributing cause of death.

Method: A register-based, retrospective cohort study. All individuals hospitalized in Sweden for traumatic brain injury (TBI) between 2000–2010 (n=111 947) without prior seizures were identified in the National Patient Register. Subsequent epilepsy was identified by ICD10 codes. Time-dependent Cox proportional hazard ratio (HR) was used to assess hazard of death, with epilepsy as a time-updated covariate. Causes of death were analyzed using the Cause of Death Register.

Result: A subsequent epilepsy diagnosis was associated with a twofold-increased HR for death after TBI. The HR for death was even higher in cases of mild TBI, younger individuals and male sex. Epilepsy was listed as a cause of death in one fifth of all individuals with PTE and in half of those dying from a CNS-disorder

Conclusions: PTE is associated with a higher risk of death. Epilepsy seems to contribute to a significant proportion of deaths, especially in younger age groups. Future studies on whether improved epilepsy treatment can reduce mortality are needed.

Abstract Number: 243

Title: Spectral shifts across distributed networks in cortex predict seizure onset

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Purpose: Research has generally focused on the balance between excitation and inhibition at the seizure focus. However, epilepsy is increasingly recognized as a network disorder. With this in mind, we hypothesized that the most predictive pre-seizure changes in activity may be distributed across cortical networks. To test this hypothesis, we sought to understand changes in activity patterns prior to seizure onset using computational analyses.

Method: We studied intracranial electroencephalogram (iEEG) recordings in 5 patients (London Health Sciences Centre) with therapy resistant epilepsy. We seek to understand patterns of narrow- and broad-band spectral

shifts prior to seizure onset in these patients. We quantified changes in carefully normalized δ, α and β frequency bands with respect to the wideband spectrum (1-100 Hz). We then developed a regularized classification model to identify spectral shifts that are predictive of seizure onset.

Result: Patients were 22-63 years old with the onset age of 0.75-24 years when hospitalized and tried 3-9 anti-seizure medications. They were recorded for 154-315 hours with 18-100 seizures detected during recordings. We find predictions of seizure occurrence with high accuracy 15-25 minutes prior to seizure onset, with AUC metrics comparable to or surpassing previous approaches. Moreover, applying the classification model over the stream of iEEG signals reveals the abnormal brain activity, opening the possibility to provide advanced warning. We then estimate network interactions from timeseries to understand the network of brain regions exhibiting predictive spectral shifts prior to seizure onset.

Conclusions: By carefully taking subtle spectral shifts across distributed brain networks into account, we can predict seizure occurrence with high accuracy. In future work, we will investigate how these distributed patterns underlie shifts in the balance of excitation and inhibition at the seizure focus through further computational analyses of cortical dynamics. [L.M. and A.S. contributed equally to this work]

Abstract Number: 246

Title: Long-term memory dysfunction in temporal lobe epilepsy: an observational case-control study

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Long-term memory dysfunction (LTMD) in temporal lobe epilepsy (TLE): an observational case-control study

Purpose: Conventional memory assessment fails to identify LTMD, which is characterised by intact recall at short intervals and rapid forgetting thereafter. We studied patients with TLE for the presence of accelerated long-term forgetting and autobiographical amnesia (AA) using special neuropsychological tests.

Method: This is an observational, single-centre, case-control study done in the Kerala state in South India. Thirty-one patients with TLE were included in the study over a period of 1 year; baseline clinical, electrophysiological, and imaging data were obtained. Comparison of verbal and visual memory in patients (n=31) and healthy (age- and education-matched) controls (n=31) was performed at baseline, 30 minutes, and 5 days, using Rey auditory verbal learning test and Rey complex figure test, respectively. Autobiographical memory was assessed using Autobiographical Memory Interview and was compared with controls.

Results: The age, sex distribution, education and IQ of cases and controls were comparable. AA was significantly higher in the TLE group, in both 'personal semantic' (early adult life[p=0.029], recent life [p< 0.001]) and 'autobiographical incidents' domains (early adult life[p=0.003], recent life [p< 0.001]). Despite normal verbal memory performance at baseline and30-minutes, TLE group has shown a trend for accelerated forgetting at 5-day analysis in comparison to controls (39.92% in cases and 35.92% in controls).

Conclusion: Our study used validated tests to assess the different realms of memory dysfunction; prospective nature and direct follow-up at 5 day of assessment are the strengths of our study. It generated data on LTM functioning and identified the presence of significant AA in patients with TLE. We recommend the incorporation of tests to identify LTMD into the neuropsychological assessment protocol for patients with epilepsy, as early identification and intervention can abate its disabling implications on the quality of life.

Abstract Number: 248

Title: Management of epilepsy secondary to neurocysticercosis during the coronavirus pandemic- a novel approach.

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Purpose: There have been many patients with neurological manifestations reported in medical literature following a Covid-19 infection. We conducted a literature review to identify patients with Coronavirus disease who presented with Neurocysticercosis (NCC) and associated neurological disorders. Currently, there is a new variant of the COVID-19 virus strain invading South Africa and no indication when this pandemic will end and what kind of tardive sequelae may occur going forward.

Method: We searched the medical literature looking for all publications regarding neurocysticercosis (NCC), status epilepticus (SE), epileptic seizures (ES), epilepsy (Ep), and ischemic stroke (IS) in patients infected by COVID-19.

Result: We found a total of six publications referring to COVID-19/ SE. We did not see any published study about NCC/COVID-19/SE/ES/IS in the searched literature from all groups.

Conclusions: During the current pandemic, NCC complications remain to be emergencies. We propose a novel therapeutic approach for the clinical and radiological presentation of NCC and epilepsy associated with COVID-19. The process would classify the clinical profiles into the following categories: NCC with surrounding oedema and recurrent tonic-clonic-generalized seizures (TCGs) and COVID-19, NCC with recurrent partial simple or complex seizures and COVID-19. NCC/SE and COVID-19, Subarachnoid NCC (SNCC), with ischemic stroke (IS), or intraventricular NCC (IVNCC) and COVID-19, and Massive NCC and COVID-19. We recommend assessing all suspected NCC cases with COVID-19 symptoms using a predefined quick checklist for COVID-19 risk and active disease as a high priority and involving an infection control team in the screening and management process. This article is the first publication approaching this comorbidity as far as we know.

Abstract Number: 249

Title: Clinical and neurophysiological peculiarities of structural epilepsy in patients with multiple sclerosis

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In multiple sclerosis (MS) the lesion of the white matter is only part of the burden of the disease. The gray matter is also involved in the pathological process and its damage, in the form of a neuronal lesion, may explain the nature of epileptic seizures in MS patients.
Purpose: to clarify the clinical and neurophysiological peculiarities in patients with comorbid structural epilepsy with MS.
Method: This study included 27 patients with epilepsy and MS (group1), median age was 33year (range 16-60), median EDSS was 2 (range 1-5,5); and 25 patients in the MRI-negative epilepsy comparison group (group2), median age was 31year (range 18-67).
Clinical-anamnestic method, video-EEG monitoring, MRI and PET with 18Fdeoxyglucose were applied.
Result: Epilepsy has clinical differences in patients of mentioned groups. In group1, seizures with a focal non-motor onset (vegetative) predominate (40.7%) compared to group2 (12%) ($p<0.05$); however, bilateral tonic-clonic seizures are less common in group1 (64% versus 100%) ($p<0.05$). Disorganization and suppression of the

main rhythm were observed in 55.5% in group1 versus 12% in group2 ($p<0.05$). Epileptiform patterns were recorded in both study groups more often in fragments of sleep recording than in wakefulness ($p<0.05$). Although there were no differences in the type of epileptiform patterns between study groups, there was a lower amplitude of sleep epileptiform patterns in group1 ($p<0.05$). Interestingly, remission of seizures was observed more often MS group (81.5% versus 68%) and the most of patients in group with MS received antiepileptic drugs monotherapy (68%) in comparison to group2 (32%) ($p<0.05$).
Conclusions: In presented study, the types of seizures, features of the post-ictal period, bioelectric and epileptiform activity of structural epilepsy in MS were determined. It was concluded that video-EEG monitoring is necessary to insert in comprehensive diagnosis of patients with MS and suspected epileptic seizures.

Abstract Number: 253

Title: Perampanel in Patients with a History of Psychiatric Illness: Post Hoc Analysis of Four Randomised Phase III Studies and their Open-Label Extensions

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Purpose: Dose-dependent psychiatric and behavioural treatment-emergent adverse events (TEAEs) have been reported with perampanel, for which dose reduction is advised. This post hoc analysis assesses psychiatric safety data from four randomised controlled trials (RCTs) of perampanel (Studies 304/305/306/335) and their open-label extensions (OLEx; Studies 307/335) in patients with focal epilepsy with/without history of psychiatric events.

Method: TEAEs were analysed for patients with/without history of psychiatric events. RCT patients were pooled by actual perampanel dose or placebo. All OLEx patients received perampanel.

Result: In RCTs, 352 (16.1%) patients had psychiatric history (perampanel n=244; placebo n=108); 1835 (83.9%) had no psychiatric history (perampanel n=1325; placebo n=510). TEAE and psychiatric TEAE frequencies depended on perampanel dose. In patients with psychiatric history, psychiatric TEAEs occurred in 73 (29.9%) and 21 (19.4%) patients with perampanel and placebo, respectively. With perampanel 2 and 4 mg/day, psychiatric TEAEs were less frequent than placebo (11.1%, 15.4% and 19.4%, respectively). Most common psychiatric TEAEs with perampanel with psychiatric history were anxiety (5.3%) and insomnia (4.9%). In patients without psychiatric history, psychiatric TEAEs occurred in 157 (11.8%) and 47 (9.2%) patients with perampanel and placebo, respectively. Psychiatric TEAEs were more frequent in patients with psychiatric history for all combined doses ($P<0.01$) and placebo ($P<0.01$). Most common psychiatric TEAEs with perampanel without psychiatric history were insomnia (2.0%), aggression (2.0%) and anxiety (1.8%).
In OLEx, 283/1895 (14.9%) patients had psychiatric history. Psychiatric TEAEs occurred in 151 (53.4%) and 521 (32.3%) patients with/without psychiatric history, respectively ($P<0.01$). The most common psychiatric TEAE was irritability (16.3%/10.4%, with/without psychiatric history).

Conclusions: Psychiatric TEAEs are reported by more patients with psychiatric history than without, and were dependent on perampanel dose irrespective of previous psychiatric illness. In patients with/without psychiatric history, perampanel 2 and 4 mg/day did not increase psychiatric TEAE incidence vs placebo.

Funding: Eisai Inc.

Abstract Number: 254

Title: ELEVATE Study 410 Initial Results: Phase IV Study of Perampanel as Monotherapy or First Adjunctive Therapy in Patients Aged ≥4 Years with Epilepsy

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Purpose: Data from prospective clinical studies on perampanel as monotherapy/early adjunctive therapy are limited. We report initial results from ELEVATE (NCT03288129), an ongoing 12-month, multicentre, open-label study of perampanel monotherapy/first adjunctive therapy in patients with focal-onset seizures (FOS), with/without focal to bilateral tonic-clonic seizures (FBTCS), or generalised tonic-clonic seizures (GTCS).

Method: Perampanel will be up-titrated to a maximum of 12 mg/day based on clinical response and tolerability (titration: 2-mg/day increments at ≥2-week intervals [patients receiving enzyme-inducing anti-seizure medications: 2-mg/day increments at 1-week intervals]). Primary endpoint: retention rate at 3, 6, 9 and 12 months. Additional endpoints included 50% responder rates, seizure-freedom rates and safety. Baseline seizure counts will be collected retrospectively and prospectively prior to first dose. Seizure diaries will be used to collect seizure counts.

Results: As of 01-10-2020, 30 patients had enrolled: 13 patients completed the study (FOS, n=9 [with FBTCS, n=1]; GTCS, n=3; FOS+GTCS, n=1); 16 patients discontinued. Five patients received perampanel as monotherapy and 24 as first adjunctive therapy; one patient converted to monotherapy. The overall mean (standard deviation) last perampanel dose was 5.7 (2.8) mg. The overall retention rate was 72.4% (n=21/29) at 3 months after treatment initiation, 58.6% (n=17/29) at 6 months, 44.8% (n=13/29) at 9 months and 34.5% (n=10/29) at 12 months. Numbers of patients with non-missing values for calculating seizure endpoints were low (no patients with GTCS); nonetheless, all six patients with seizure-frequency data (FOS/FBTCS) had a ≥50% reduction in seizure frequency during the overall Maintenance Period, with one achieving seizure freedom (FOS). Treatment-emergent adverse events occurred in 89.7% (n=26/29) of patients (FOS, n=15/18; [FBTCS, n=2/3]; GTCS, n=7/7; FOS+GTCS, n=4); most common were dizziness and fatigue.

Conclusion: Despite low patient numbers, initial results from ELEVATE showed that perampanel was generally well tolerated with favourable retention rates and efficacy.

Funding: Eisai Inc.

Abstract Number: 256

Title: Adjunctive Perampanel and Levetiracetam in Patients with Focal-Onset Seizures Co-administered With/Without Enzyme-Inducing Anti-Seizure Medications

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Purpose: We assessed the efficacy and safety of adjunctive perampanel co-administered with levetiracetam across four Phase III Studies (304, 305, 306 and 335) in patients (aged ≥12 years) with focal-onset seizures

(FOS), with or without focal to bilateral tonic-clonic seizures, stratified by concomitant enzyme-inducing anti-seizure medication (EIASM) use.

Method: Patients receiving perampanel 4–12 mg/day were included. Analyses were split by levetiracetam use: patients who were on concurrent use, had prior use or had never used levetiracetam, and by EIASM use (carbamazepine, eslicarbazepine, oxcarbazepine and phenytoin). Endpoints included 50% responder and seizure-freedom rates (Full Analysis Set [FAS]), and treatment-emergent adverse events (TEAEs; Safety Analysis Set [SAS]).

Results: The FAS and SAS included 1386 and 1389 patients, respectively. Fifty-percent responder rates were numerically higher in patients with non-EIASMs compared with those with EIASMs, and were similar in patients with (29.4% vs 44.8% with EIASMs/non-EIASMs, respectively) or without (27.1% vs 43.6% with EIASMs/non-EIASMs, respectively) concurrent levetiracetam use. Seizure-freedom rates were similar across all patient groups with/without EIASM use, and with/without concurrent levetiracetam use (range: 2.0–5.9%). The incidence of TEAEs was slightly lower with EIASMs vs non-EIASMs in patients with/without concurrent levetiracetam use; the most common TEAE was dizziness, regardless of EIASM/levetiracetam use (range: 28.0–40.4%).

Conclusion: These data suggest concurrent use of levetiracetam with perampanel does not affect the efficacy and safety of perampanel treatment, regardless of EIASM use. However, patients receiving concomitant EIASMs may require a higher perampanel dose to achieve similar efficacy to patients receiving non-EIASMs.

Funding: Eisai Inc.

Abstract Number: 263

Title: Management of convulsive seizures on the inpatient video telemetry unit: A quality improvement project.

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Purpose: Patients are admitted to video-telemetry (VT) units to record their habitual seizures. Often drug reduction (DR) is necessary to achieve this goal, increasing the risk of prolonged seizures, clusters of seizures, and status epilepticus (SE).The main objective was to determine frequency and management of bilateral tonic-clonic seizures (BTCS) in the VT unit at the National Hospital for Neurology and Neurosurgery and identify deviations from best practice and hospital protocols.

Method: We retrospectively examined 252 admissions between October 2017 and December 2018 for patients in whom a BTCS was recorded. Following case identification, BTCS were reviewed in detail.

Result: One or more BTCS were recorded in 31 admissions (12%). Mean patient age was 28 years (range 18-47; 17 male). Average total seizure duration was 122 seconds (range 42-380) and one BTCS occurred within a cluster of seizures. 6/31 of the patients had a history of SE but no de novo episodes of SE occurred during VT in this cohort. 28/31 were undergoing DR and rescue medication was given to 25 (in 88% of cases given during the post-ictal phase). Staff attended every seizure (mean 20s to reach the patient [range: 8-45]) and supplementary oxygen and suctioning were administered in all. One fall was recorded, and no significant injuries occurred. 30/31 patients were repositioned to the lateral safety position; of these, 26% during the ictal phase.

Conclusions: A small percentage of patients had a BTCS during the VT admission and the majority happened during DR. There were no cases of status epilepticus and a single fall was observed. Administration of rescue medication was typically post-ictal. These findings highlight that drug reduction in the VT unit is safe overall. The importance of ongoing training for the acute management of seizures should be stressed, as should the relevance of protocols for seizure management.

Abstract Number: 271

Title: Transition of epilepsy patient to Neurology in Showa University, Japan.

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Purpose: To investigate the current status of post-transition epilepsy patients in Neurology and epilepsy patients at 15 years and over in Paediatrics.

Method: From January to June 2019, epilepsy patients in the Department of Neurology and Pediatrics outpatient clinic, Showa University were retrospectively reviewed by medical records.

Result: The number of post-transition epilepsy patients in Neurology was 53 (38 males and 15 females, aged 16-39 years). The seizure type classifications were 17 symptomatological generalized, 16 idiopathic generalized, 8 symptomatological focal, 1 idiopathic focal, and 10 unknown. Epilepsy onset was most often in 0-1 years (14, 26.4 %), and in 7-11 years (13, 24.5 %). The consultation routes were from our hospital in 26 cases, and from other hospitals in 27 cases. The age at transition was 14-31 years old, most often in 18-19 years and 20-25 years old. The reason for transition was patients' age in all cases. 22 cases (41.5%) have intellectual disability and 3 cases have developmental disabilities (2 ADHD, 1 ASD). The number of antiepileptic drugs is one in 26, 2 in 13, 3 in 6, 4 in 3 and drug-free in 2 cases. Disease control was relatively good, 34 having no seizures within the last 6 months, 3 with daily seizures. In Pediatrics, there were 4 patients at 15 years and over (15-22 years old). There were no epilepsy patients. They were cerebral palsy, spinal cord injury, hematological disease, and SLE. Patients other than spinal cord injury were referred to Internal medicine, Hematology, and Rheumatology.

Conclusions: A number of epilepsy patients had undergone transition to Neurology. In Pediatrics, there were no epilepsy patients over 15 years in outpatient clinic during the 6-month observation period.

Abstract Number: 299

Title: Incidence and antiseizure medications of post-stroke epilepsy in Umbria: a population-based retrospective study

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Purpose: up to 30% of patients can develop epilepsy after ischemic or hemorrhagic stroke (post-stroke epilepsy, PSE), qualifying this occurrence as structural epilepsy according to International League Against Epilepsy definition. Data on population-based cohorts, as well as risk factors and types of long-term pharmacological treatments adopted in PSE patients are scanty. Here we estimate incidence, define risk factors and long-term treatment of PSE in Umbria using whole-population administrative healthcare data.

Method: we conducted a population-based, retrospective cohort study, using Umbria health care administrative databases. Population consisted of all patients with a hospitalization due to acute stroke (ischaemic and haemorrhagic) between 2013 and 2018. Patients with strokes were identified using ICD-9-CM codes. PSE was identified with the prescription of at least one EEG and one or more antiseizure medications (ASMs) seven days after stroke, which provides an accuracy of 94.8% in case ascertainment.

Result: during the study period, 11093 incident cases of acute stroke were identified, 75.9% being ischemic. Following these patients until 2019, 275 subjects presented PSE. Patients with PSE were younger (64 vs. 75.7 years), had more frequently haemorrhagic stroke and had longer hospital stay (15.5 vs 11.2 days) compared to patients without PSE ($p<0.001$). The cumulative incidence rate of seizures during the first year after stroke was 2.52%. Multivariable Cox regression showed that onset of PSE was associated with haemorrhagic stroke, younger age and longer duration of hospital stay. Results were confirmed with univariate Cox Survival Analysis. Levetiracetam was the most commonly prescribed ASM (55.3%) for the management of PSE with a retention rate of 63.5%.

Conclusions: This is the first study of incidence of post stroke epilepsy using administrative healthcare data in Italy. PSE was associated with haemorrhagic stroke, younger age, and longer hospital stay. LEV was the ASM most commonly prescribed

Abstract Number: 330

Title: Digital Platform for Epilepsy Management in COVID era: Benefits in Self Management

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Purpose: The objective of this study is to evaluate whether an investigational mobile epilepsy management platform, called Nile, improves self-management in epilepsy populations.

Adherence to medication regimen is critical to ensure the best clinical outcome for patients with epilepsy. However, according to studies, more than 50% of patients do not take their medication as prescribed, prolonging the time to optimal treatment. Keeping a digital diary is one method to encourage compliance. The Epilepsy Self-Management Scale (ESMS) allows a validated assessment of a patient's frequency of self-management behavior including 5 subscales: medication, information, safety, seizure, and lifestyle.
In this pilot study, we evaluate self-management metrics in patients after 4 weeks of interacting with Nile.

Method: The Nile application is a two-way communication platform that connects patients/caregivers to health-care providers. Main features include personalized medication titration instructions and seizure and symptoms tracker. Under an IRB-approved protocol, consented epileptic patients were provided access to Nile. The participants filled out the ESMS survey before and after using the platform. Paired t-tests were performed to evaluate the significance of changes in the ESMS and its subscales.

Result: Twenty patients satisfied the inclusion criteria (age mean(std): 33.4(14.4), 50% female, 85% refractory) and used the platform for 4 weeks. The total ESMS improved from mean(std) of 143.5(14.7) to 148.8(14.6) with change (95%CI) of +5.3(-1.2, 11.7). Although the overall improvement was not statistically significant (p-value=0.1) due to the small sample size, significant improvements (p-value<0.05) were observed in information management with change (95%CI) of +3.2(0.3, 6.1) and safety management (+1.80(0.02, 3.6)).

Conclusions:

Our pilot study revealed that certain aspects of self-management in epileptic patients benefited by tracking medication and seizure diaries on a mobile platform in a relatively short time. Such platforms offer potential advantages in filling the epilepsy treatment gap.
This study is supported by Nile AI, Inc.

Abstract Number: 365

Title: Prevalence and associated factors of drug resistant epilepsy in an adult onset epilepsy population

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Purpose: Primary objective was to determine the burden of drug resistance in adult onset idiopathic epilepsy population and compare the rate of drug resistance among sub groups of different epilepsy types. Subsequently, to identify early predictors of drug resistance in this population.

Method: The study is a cross sectional descriptive study based in Sri Lanka. Selected 445 participants were first categorized according to the seizure type. Then analysed the rate of overall and the individual group's drug resistance, based on ILAE 2010 definition. Afterward, the two main groups, drug resistant (DR) and adequate response (AR) were recognised and compared using t test, to identify possible associations for drug resistance.

Result: The overall rate of drug resistance was 36%. The rate was 48.4% in focal motor onset epilepsy. The lowest, zero resistance seen in generalized non-motor epilepsy. Patients with motor onset seizures (P = 0.003), positive imaging findings (P = 0.001) and history of Status epilepticus (P = 0.02) showed a higher chance for drug resistance. No statistically significant difference with regard to focal/generalized onset seizures, positive family history, history of febrile seizures or presence of EEG abnormalities. Adverse events were more common in DR group (P <0.001). Use of a third drug was significantly lower in AR group (p < 0.00001).

Conclusions: This population of idiopathic adult onset epilepsy had 36% prevalence of drug resistance. Individual percentages of drug resistance according to the seizure type is highly variable. Focal motor seizure has highest possibility of resistance. Motor over non-motor onset seizures, presence of imaging abnormalities and history of status epilepticus are important predictors of drug resistance. Addition of third drug has a limited value on adequate seizure control. Based on the population characteristics, prompt identification of resistance and consideration for next level treatments is recommended.

Abstract Number: 371

Title: Diagnostic benefit of bilateral invasive sEEG evaluation in patients with temporal lobe epilepsy and not clearly lateralizable seizure onset zone

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Purpose: To analyze the additional diagnostic and therapeutic benefit of invasive bitemporal exploration using stereo-electroencephalographic (sEEG) in patients with drug refractory temporal lobe epilepsy (TLE) and potential bilateral seizure onset zone (SOZ) according to non-invasive video-electroencephalographic-monitoring (nVEM).

Method: All patients with TLE and potential bitemporal SOZ according nVEM treated between March 2015 and March 2021 at our epilepsy center were retrospectively identified and analyzed for a possible benefit of invasive VEM (iVEM).

Result: Of a total number of 1,486 patients having received nVEM, 53 (3.6%) received iVEM and 15 patients (1.1%) matched the inclusion criteria mentioned above. During iVEM, unilateral temporal SOZ was revealed in 10 patients (67%) while 5 patients (33%) had a bitemporal SOZs. For all patients with unilateral SOZ curative epilepsy surgery (ES) was recommended, to which 9 patients agreed. In addition, 3 patients with bitemporal SOZ were offered palliative ES intended to reduce seizure frequency, to which one patient agreed. Follow up was available in 6 of 7 already operated patients showing an individual benefit of ES in 5 patients (Engel I-II, ILAE Class 1-3). No improvement of seizure frequency was reported in one patient (Engel IV, ILAE Class 5). Neuropsychological follow-up revealed a stable or improved verbal and non-verbal memory in 5 cases, while 2 patients with left-temporal SOZ showed a slightly worsened verbal memory after ES.

Conclusions: In TLE patients with potential bilateral seizure onset sEEG evaluation provided additional diagnostic information in all and led to therapeutic consequences in 13/15 patients. Seizure and neuropsychological outcomes were favorable in most patents referred to ES. As iVEM using sEEG is a relatively safe diagnostic procedure, patients willing to undergo ES should be provided with this additional diagnostic option.

Abstract Number: 399

Title: Factors influencing the daily evolution of preictal connectivity dynamics in epilepsy

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Purpose: Our understanding of epilepsy mechanisms has shifted its focus towards a more dynamic, whole-brain network perspective in the last decades. Several factors, such as circadian and multi-day cycles, are assumed to influence the likelihood of seizure occurrence. Moreover, this seizure susceptibility is critically dependent on anti-epileptic drug dosage. However, there is a lack of knowledge of how these factors are reflected in inter-regional communication. Uncovering this relationship is important to understand the mechanisms of seizure generation.

Method: We investigated long-term recordings of 9 drug-refractory epileptic patients. In the context of their presurgical evaluation, they were implanted with depth electrodes, and anti-epileptic drugs were continuously decreased until seizures occurred. The first seizures typically occurred between the fourth and sixth day. To analyze brain network changes, we quantified connectivity differences using Directed Transfer Function in the interval between admission and first seizure. Furthermore, each measurement was characterized by various factors, such as time, drug dose, or spike rate. Finally, to track connectivity changes in time, we projected them into low-dimensional space using Principal Component Analysis.

Result: Connectivity changes were consistently linked to slow (Pearson's r range 0.22-0.82) and circadian rhythms (0.21-0.74), drug dosage (0.24-0.79), and the spatio-temporal profile of high-frequency oscillations and spikes (0.25-0.94) as the brain approaches seizure. These correlations were significant in 8/9 subjects ($p<0.05$, FDR corrected). When analyzing connectivity dynamics, we observed time points linked with seizure buildup. The timing of these changes was subject-specific and varied between 1 to 3 days before a seizure.

Conclusions: Seizure susceptibility influences inter-regional communication. The spatio-temporal profile of spikes and high-frequency oscillations are the most prominent factor. Furthermore, connectivity investigations can unveil patient-specific critical time points during a seizure buildup.

Abstract Number: 423

Title: Bone mineral density in adult men with long-term history of antiepileptic therapy: preliminary study results

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Purpose: to evaluate the bone mineral density (BMD) in adult men with epilepsy with long-time antiepileptic drugs (AEDs).

Method: The BMD was examined by Quantitative Computed Tomography (QCT) in 23 men with epilepsy. The first group consisted of 10 patients aged 21-40 years, the second group included 13 patients 41-60 years old. Densitometry was performed at three points (L1, L2 and the femoral neck). All patients received long-term AED therapy for at least 12 months.

Result: BMD values were decrease in 6 (26%) patients. In the 1st group, T-score (BMD) was -1.8 SD (normal T > -1.0 SD, WHO 1994) which corresponds to osteopenia in 2 patients (8.7% of all participants). In the 2nd group T-score (BMD) was -3.62 SD - reaching the degree of osteoporosis in 4 men (17.4% of all participants).

Conclusions: This preliminary study showed a decrease BMD in patients with long-term therapy with AED resulting in both osteopenia and osteoporosis. The long-term AEDs therapy may be a risk factor for bone mass loss, especially in older patients. The evaluation of BMD could be the important diagnostic method in patients with epilepsy with long-term AEDs therapy, especially for patients who receive enzyme-inducing AEDs. Further studies of the long-term effect of different AEDs generations on BMD in patients with epilepsy are of great importance, especially for the treatment of patients in the older age group.

Abstract Number: 430

Title: Cardiac autonomic response to hyperventilation and risk of SUDEP

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Purpose: Sudden unexpected death in epilepsy (SUDEP) is a dramatic complication of epilepsy. A reliable biomarker for the risk of SUDEP is still lacking. We aimed to test whether patients at risk of SUDEP have an abnormal cardiac autonomic response to sympathetic stimulation (such as that as experienced during seizures).

Method: We conducted a retrospective, observational, case-control study of a group of patients who died from SUDEP from January 1, 2010 to March 31, 2019 and controls. We included cases of definite or probable SUDEP with available ECG-EEG data during an episode of hyperventilation. Controls were matched with the patients for sex, age, epilepsy type, drug resistance, age at onset of epilepsy, and duration of epilepsy. We analyzed the heart rate (HR) and heart rate variability (HRV) at rest, during and after hyperventilation performed during the patient's last electroencephalogram recording before SUDEP. In each group, changes over time in HRV indexes were analyzed using linear mixed models. The ability of HR and HRV parameters to discriminate between the SUDEP and control groups was analyzed.

Result: Twenty patients were included in each group (10 males, 10 females; median age: 34y). We did not find any significant intergroup differences in the resting parameters. In the SUDEP group, the HR did not change significantly during or after hyperventilation. In the control group, however, the HR increased during the hyperventilation and then returned to the baseline value. A difference in HR between the end of the hyperventilation and 4 min after its end discriminated well between SUDEP patients and control patients (AUC: 0.870; sensitivity: 85%; specificity: 75%).

Conclusions: Most of patients with subsequent SUDEP have an abnormal cardiac autonomic response to sympathetic stimulation through hyperventilation. Analysis of change in HR upon hyperventilation (dHRh) could be of interest to select patients at risk of SUDEP.

Abstract Number: 435

Title: Causes of decompensation in epilepsy

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Purpose: The aim of this study was to determine the main factors of provocation leading to an increase in the frequency of seizures with epilepsy.

Method: We conducted a retrospective analysis of 43 medical records of patients with various types of epileptic seizures with their frequency. During the conversation with the patients, the provoking factors that determine the likelihood of increased frequency of seizures were evaluated. The average age of patients was 43 years: men - 27 (62.8%), women - 16 (37.2%). The largest number of patients is under the age of 45 years – 28 (65.1%), the average duration of the disease was 11.3 years. The onset of epilepsy in most patients occurs before the age of 18-21 (48.8%).

Result: According to the ILAE classification (2017), generalized tonic-clonic seizures (67.4%) and the genetic etiology of epilepsy (51.1%) are more common in this sample. The frequency of seizures that worsen the quality of life, the patients consider from 0.5-1 to 3-6 per month (41.9% and 32.5%). Against the background of the use of antiepileptic drugs (PEP), epileptiform activity persists in 46% of patients. At the beginning of anticonvulsant therapy, with the right choice of PEP, remission of seizures was achieved in the first year of treatment in 30

patients (69.0%); in cases of increased frequency of epileptic seizures later in the overwhelming majority of patients (81.5%), the provocation factor is non-compliance with the monotherapy regime.

Conclusions: The lack of awareness of patients about the goals of therapy, especially the pharmacokinetics of PEP, and the low motivation of patients and their doctors to achieve the goals of treatment contribute to the decrease in the effectiveness of treatment of patients with epilepsy. Treatment adherence can be increased by emphasizing adherence to the treatment regimen and taking into account the patient's lifestyle.

Abstract Number: 436

Title: Epileptic seizures in adult patients with elevated Pyridoxine phosphate levels: a common disease manifestation or incidental finding?

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Purpose: Pyridoxal phosphate (PLP), the active form of vitamin B6 is an essential factor in the process of decarboxylation of glutamine into GABA and its deficiency have been related to seizures. Reported cases of vitamin B6 deficiency related seizures, in adults were much less than that in neonates, including dietary deficiency and pregnancy. Commonly used drugs are associated with vitamin B6 insufficiency, including isoniazid, penicillamine, levodopa, phenytoin, carbamazepine. Elevated PLP levels could provoke seizures, like in cases of Hypophosphatasia, a rare inherited disease. The aim of this study was to explore the association of PLP insufficiency and seizure.

Method: We measured the PLP serum level of consecutive adult patients admitted to a neurological ward in a general community hospital with a diagnosis of epileptic seizures from May to August 2020. As a control group, 20 patients with acute ischemic stroke, matched to age and gender, were examined. A level of 8.7 – 27.2 ng/mL was reported as normal.

Result: In 27 consecutive seizure patients (14 males) with age 18 – 81 years (mean 46.9) the average PLP serum level was 50.2 ng/mL (range 30.5 to 85.7). Mean range for males was 55.7 and for females 43.2 ng/mL. None of the patients had low levels and an increased level of PLP was revealed in 9 patients (33.3%). Regarding seizure etiology, 21 patients were classified as structural/metabolic including 7 with elevated PLP level, 4 patients as genetic (2 PLP elevated) and 2 as unknown cause without any patient with elevated PLP. Only one patient with a stroke had an increased PLP.

Conclusions: Unexpected results revealed no case of PLP insufficiency in this series, indeed there were a trend for increased PLP levels, more pronounced in mails. It can be inferred that there was association between PLP elevated level and seizures in those adult patients.

Abstract Number: 438

Title: Digital epilepsy assistant facilitates patient engagement through patient-physician connection and data sharing

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Purpose: Digital healthcare solutions aim to improve patients' quality of care and empowerment, with an extra challenge addressing app retention due to app fatigue. Six-month retention rates ranging from 30 to 40% characterize best-in-class mHealth solutions. The Helpilepsy® solution (Neuroventis, Belgium) allows interactive data sharing between patients and physicians through use of a dashboard, video consultations and seizure video uploads. We compared app use between physician-connected patients and unconnected, standalone patients.

Method: We analysed anonymized data from Belgian patients having signed up to the epilepsy app between 01-Jan-2019 and 31-Aug-2020. The number of reported seizures per patient and per active day in the app, number of datapoints entered, type of data shared and retention rates after the first 3 and 6 months of usage were compared for connected and unconnected patients.

Result: A total of 560 patients with epilepsy were enrolled. Retention rates at 3 and 6 months were 36% and 26% for unconnected versus 76% and 64% for connected patients. Standalone users reported a mean of 12 seizures per 100 active app days compared to 21 for users sharing data with their physician. Over 80% and 30% of connected patients reported at least one event or side effect respectively. Connected users also uploaded a seizure video recording 9.9 times more often than unconnected ones.

Conclusions: Comparing connected to unconnected patients, we observed higher retention rates in patients who share data interactively in Helpilepsy®. Retention rates of connected patients topped observed numbers of other mHealth apps. Higher number of datapoints, increased app engagement and more varied type of data were recorded by connected patients. Future research should address the impact of this data sharing on the management of epilepsy for physicians and quality of life for patients living with epilepsy.

Abstract Number: 450

Title: epilepsy in neuromylitis optica spectrum disorders

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Purpose: Neuromyelitis optica (NMO) is a severe idiopathic immune-mediated demyelinating and necrotizing disease that predominantly involves optic nerves and spinal cord. Epileptic seizure and encephalopathy are infrequent presentation of NMO and it can explained by brain involvement of NMO (hemispheric demyelinating plaques affecting whit matter).

Method: We reviewed the clinical, radiological and electrophysiological features of four adult patients 3 female and 1 male who presented with acute memory deficits, psychiatric symptoms and focal seizures with demyelinating lesion involving mesial temporal and midbrain and extreme delta brush on EEG and found to have high titer of NMO-IgG autoantibody. We also follow up them for one year after treatment.

Result: All four patients developed acute onset of cognitive impairment , psychomotor changes and seizure consistent with encephalitis which are resolved completely after immunomodulating therapy , one case found to have seropositive SLE. Brain MRI studies revealed T2 weighted hyperintense signal abnormalities, primarily in Temporal, Midbrain and frontal lobe, EEG consist mainly of extensive delta brushing and slow wave abnormalities corresponded to the clinical severity of underling encephalopathy. Follow-up EEGs of 4 patients showed slowing in 1 and a back to normal in 3 . focal onset epilepsy with impaired consciousness was the most common seizure type, However the TLE and GTC also were detected among all of them in some occasion.

Conclusions: since the discovery of AQ-4 antibodies, there has been an increase in the number of clinical and radiological manifestations of NMO beyond involvement of optic nerve and the spinal cord including encephalitis and seizure with unique EEG pattern including Delta brush. Patients made an excellent recovery with immunotherapy which emphasize the importance of early diagnosis and intervention of NMO to achieve good out come and prevent further attack.

Abstract Number: 468

Title: Juvenile myoclonic epilepsy: Outcome beyond three decades from onset- A hospital based cohort study

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Purpose: We aimed to elucidate the long-term outcome of Juvenile myoclonic epilepsy (JME) beyond 30 years from onset

Method: We identified 220 persons (105 males, 115 females) with JME by screening the outpatient and EEG registers in a tertiary epilepsy care center between 1991 and 1999. The initial clinical details of patients were extracted from the medical records. Their clinical status was updated in 2020 by telephone/postal contact (n=41) or clinic reviews (n=31). No updates could be done for remaining persons. Remission was defined as seizure freedom for two or more years.

Result: The cohort consisted of 72 persons (39 females). Median age at epilepsy onset was 13 years (IQR=12-17). Median duration of epilepsy was 32 years (IQR=27 – 36). Seizure type at onset was myoclonus alone in 12 (17%), generalized tonic clonic seizure (GTCS) alone in 35 (49%) and both myoclonus and GTCS in 24 (34%). 14 persons (19%) had absence seizures. Family history was positive for 21.16%.13.8% had history of febrile seizures. The common antiseizure medications (ASM) used were Valproate (69.4%), Carbamazepine (37.1%), Phenytoin (27.7%). Newer ASMs like Levetiracetam (6.9%) and Lamotrigine (4.1%) were sparingly used. On final follow up (in 2020), 2 persons (2.8%) had died, 58 (80.5%) were in remission (4 of them continued to have myoclonus); 12 (16.6%) had relapsing remitting course with 3 (5%) of them requiring polytherapy. Median period of remission was 12 years (IQR= 6.5-18). Off those in remission, 12 (22.2%) were off ASM, while 9(21%) were on two or more ASMs. Valproate (83%) was the most common ASM in patients on medications at the time of remission.

Conclusions: After 30 years from onset of epilepsy, over 80% of persons with JME achieved seizure remission and 16.7% could remain off ASMs. However, around 5% had a relapsing remitting course continuing to require polytherapy.

Abstract Number: 483

Title: idiopathic photosensitive occipital lobe epilepsy: an exceedingly rare reflex epilepsy syndrome

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Purpose: Idiopathic photosensitive occipital lobe epilepsy (IPOE) is a rare epilepsy syndrome that should be suspected in patients with normal MRI who have occipital lobe epilepsy (OLE) triggered by light stimulation.

Definitive diagnostic criteria have not been determined, and it is important to recognize this syndrome, which has a good prognosis with appropriate antiepileptic selection. It is aimed to examine the clinical and EEG features of IPOE patients.

Method: By retrospectively examining 5430 files in our epilepsy clinic, 32 patients OLE were identified: nine patients with normal brain MRI and photosensitivity in both clinical and EEG data were diagnosed with IPOE.

Result: The age at seizure onset of the IPOE (F/M: 4/5) patients was 11±2.5 years (7-14). TV and computer screen were the main triggers. Three patients also had spontaneous generalized seizures which were fewer than their reflex seizures. Two patients had self-induction in the form of compulsive attraction to the TV. Seven patients had positive (colored bright lights), while two had negative (blindness) ictal visual symptoms. Three patients had focal motor seizures; eight patients had focal to bilateral generalized seizures. Four patients were suffering from postictal migraine headaches. While seizure remission was achieved in only one patient by avoiding triggers, it was achieved with dual- in one and monotherapy in 7 patients. Migraine attacks started in two patients after remission.

Conclusions: The age at onset of IPOE was late childhood/adolescence. Self-induction feature may accompany and although most of the seizures are reflex in character, spontaneous seizures may occur rarely. Visual symptoms had predominantly positive character. A relationship with postictal migraine pain was noted and prevention of triggers would not be sufficient for seizure control in most patients. Increasing the recognition of this syndrome will distinguish it from other syndromes with different treatment approaches and prognoses like OLE in childhood.

Abstract Number: 549

Title: Prospective Identification of Ictal Electroencephalogram

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Purpose: This paper aims to implement a prospective study on epileptic seizure detection for immediate clinical utility that reduces the time commitment required by expect staff by at least ten folds.

Method: This work implements a convolutional long short-term memory (ConvLSTM) network that is pre-trained and tested on Temple University Hospital (TUH) EEG corpus. It is then deployed prospectively at the Comprehensive Epilepsy Service at the Royal Prince Alfred Hospital (RPAH) in Sydney, Australia, testing nearly 14,590 hours of EEG data across nine years. Our system prospectively labelled RPAH epilepsy ward data and subsequently reviewed by two neurologists and three certified EEG specialists.

Result: Our clinical result shows the proposed method achieves a 92.19% detection rate for an average time of 7.62 mins per 24 hrs of recorded 18-channel EEG. A human expert usually requires about 2 hrs of reviewing and labelling per any 24 hrs of recorded EEG and is often assisted by a wide range of auxiliary data such as patient, carer, or nurse inputs. In this prospective analysis, we consider humans' role as an expert arbiter who confirms to reject each alarm raised by our system. We achieved an average of 56 false alarms per 24 hrs.

Conclusions: A vast majority of epileptic seizure (ictal) detection on electroencephalogram (EEG) data has been retrospective. Therefore, even though some may include many patients and extensive evaluation benchmarking, they all share a heavy reliance on labelled data. This is perhaps the most significant obstacle against the utility of seizure detection systems in clinical settings. In this paper, we present a prospective

automatic ictal detection and labelling performed at the level of a human expert (arbiter) and reduces labelling time by more than an order of magnitude.

Abstract Number: 561

Title: Five-day observation program in adult epileptology for undergraduate medical students

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Purposes: The competency-based educational curriculum, launched by the International League Against Epilepsy (ILAE), mainly targets post-graduate specialists. We have been developing an observation program for "undergraduate medical students" to learn about adult epileptology since the launch of the first Department of Epileptology in Japan at our medical school in 2010. Here we describe the basic content of our program and analyze student feedback for further improvement.

Methods: Our 5-day observation program consists of i) a primer lecture to learn about basic seizure semiology, such as lateralizing sign, and interpretation of ictal/interictal electroencephalography by focusing on laterality; ii) observation at clinics for new patients to learn about the importance of history taking by focusing on the early focal seizure symptoms rather than generalized seizures; iii) observation of psychologist interviews to learn about the importance of psychosocial evaluation in comprehensive epilepsy care; and iv) attendance at multidisciplinary comprehensive epilepsy conferences to integrate all medical and psychological information for each patient. We have also combined the teleconference system into most of these program components for both students and medical professionals outside our institute. We obtained written feedback at the end of the program from all 41 students participating in 2016.

Results: Positive feedback can be summarized as "achieving increased knowledge (7 of 41 students)" due to the "efficient program structure (5)" of the above-mentioned i) to iv) components (34) with "highly educational mood (12)" conducted by the "multidisciplinary team (4)".

Conclusions: Despite the short period of the 5-day program, undergraduate medical students could obtain positive experience in education about adult epileptology. Our motivational model for learning will be helpful to modify the ILAE competency-based educational curriculum for undergraduate students.

Abstract Number: 564

Title: Intensity of Diagnostic Testing and Subsequent Seizure-related Events

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Purpose: The level of diagnostic testing around initial diagnosis of epilepsy is highly variable. In this study, we perform a population-level analysis to determine whether early utilization of diagnostic modalities is associated with differences in subsequent seizure-related events.

Method: We conducted a retrospective cohort study using 2007-2019 Optum® Clinformatics® Data Mart, a database derived from administrative health claims for members of large commercial and Medicare Advantage health plans in the U.S. Patients were included if they were aged ≥18 years with newly diagnosed epilepsy using

published claims-based algorithms for identification of epilepsy cases. Primary exposure was utilization of outpatient diagnostic services including EEG and neuroimaging studies (CT, MRI, and PET scan) performed in the 18-month time period spanning from 1 year before to 6 months after the diagnosis of epilepsy. We assessed seizure events defined as seizure-related ED visit or hospitalization following this time period by the level of diagnostic testing, and hazard ratios (HRs) were estimated.

Result: Among 76,790 adults with newly diagnosed epilepsy, 57% were female, median age was 67 [IQR 50-77]), and median follow-up time was 2.9 [1.8-4.8] years. The probability of seizure event within one year of the follow-up was lower among patients with both EEG and neuroimaging evaluations (7.5% (95% CI, 7.1-8.0%)) compared those with only one (11.1% (95% CI, 10.7-11.6%)) or none (12.3% (95% CI, 12.0-12.6%). In Cox survival analysis, patients with both EEG and neuroimaging evaluation had significantly lower risk of subsequent seizure events compared to those with either EEG or imaging (HR 0.70, 95% CI 0.66-0.74) or those without either (HR 0.61, 95% CI 0.58-0.64).

Conclusions: In patients with newly diagnosed epilepsy, initial intensive evaluations were associated with decreased risk for subsequent seizure-related events. Such evaluations may identify etiologies that drive appropriate treatments and interventions that prevent seizure recurrences and intractability.

Abstract Number: 575

Title: A focus on hidden grime - A cross sectional study on dental illness in people living with epilepsy

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Purpose: With major attention paid on the most evidently manifested illness like a seizure, few of the silent and deep boring illness like dental issues are often neglected. This study aims to analyse the dental issues in people living with epilepsy.

Method: This study was conducted in our centre among inpatients and outpatients with epilepsy from October 2020 to December 2020. A survey on dental hygiene practices, symptoms of dental illness and detailed dental examination was performed in a total of 69 patients. About 33 controls without epilepsy were selected from the family members of the selected patients after informed consent and dental health survey was done similarly to compare the dental illness among patients with epilepsy and people without epilepsy.

Result: Among 69 patients, 38 were males and 31 were females with a mean age of 32.5 $\pm$ 2.4 years. As per BG Prasad Scale, about 46 individuals belonged to higher middle and higher socioeconomic status, while 23 belonged to lower socio economic status. Among 69, 45 (63%) patients had symptomatic dental illness, 22 (33%) had asymptomatic dental issues. The mean percentage of soft tissue, hard tissue and periodontal abnormalities was seen in 25%, 59%, 13% among asymptomatic and 28%, 63%, 45% among symptomatic respectively. Patients from higher socioeconomic status were found to have better dental hygiene practices and had higher prevalence of bone wasting. Interestingly, individuals in seizure remission had lower dental problems (26%) as compared to others. Of the 33 controls studied, only 5 individuals were symptomatic and 19 individuals (57%) had good dental health as compared to only 2 (3%) with good health in patients with epilepsy, which is statistically significant.

Conclusions: The hidden yet significant burden of dental illness must be addressed in people living with epilepsy to avoid impairment of good quality life.

Abstract Number: 605

Title: Seizures with high-risk paraneoplastic antibodies

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Purpose: The objective of this study was to describe seizure presentations, course, and outcome in patients with paraneoplastic neurological syndrome and seropositivity for high risk antibodies (>70% cancer association).

Method: Patients with seizures in the setting of neurological disorders associated with high-risk antibodies were identified; including ANNA1 (anti-Hu), CRMP5/CV2, AGNA1 (SOX-1), PCA2, amphiphysin, ANNA2 (anti-Ri), PCA-1 (anti-Yo), PCA-Tr (DNER), Neurofilament light (NF-L), Ma2, KLHL11 and LUZP4. Patients with a prior history of epilepsy were excluded. Charts were reviewed to describe seizure types, imaging and electrographic findings, and outcomes. Patients with enough data available were analyzed to determine factors associated with risk of ongoing seizures.

Result: There were 54 (30 men, 56%) who had at least one seizure (19 ANNA1, 14 Ma2, 11 CRMP5, 3 KLHL11, 4 AGNA1, 1 ANNA2, 1 PCA2, 1 NF-L). Median age of onset of neurologic symptoms was 51 (range 10-80). Twenty-one (39%) initially presented with seizures, and 34 (63%) had an underlying malignancy. Early MRI evidence of limbic encephalitis was present in 33 (61%). Of the 45 patients with enough information available, 28 (62%) had ongoing seizures, with 6/28 (21%) having ≥50% seizure reduction with immunotherapy. Ongoing seizures were associated with Ma2 and ANNA1 antibodies (22/28, 79% vs. 6/17, 35%, p-value 0.004), memory impairment (26/28, 93% vs. 11/17, 65%, p-value 0.02) and evidence of limbic encephalitis on initial MRI (20/28, 71% vs. 7/17, 41%; p-value 0.04). Long-term immunotherapy was not associated with seizure freedom. Throughout the course of a median follow-up of 36 months (range 1-230 months) from disease onset, 26 patients (42%) died.

Conclusions: Nearly half of patients with seizures associated with paraneoplastic antibodies develop chronic refractory epilepsy, likely secondary to cortical injury from the initial neuroinflammatory event. Ma2 or ANNA1 seropositivity, cognitive dysfunction and limbic encephalitis are associated with increased risk of chronic epilepsy.

Abstract Number: 619

Title: Ictal positive facial expression of emotion

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Purpose: Ictal positive facial expressions of emotion (PFEE) – smiling and laughing- have long been considered a hallmark of epilepsy related to hypothalamic hamartomas, but recent data shows they can also be seen in other types of epilepsy. Our objective was to see if PFEE can offer reliable information regarding the localization of the seizure onset zone (SOZ).

Method: We retrospectively reviewed the records of 976 patients admitted in our Epilepsy Monitoring Unit, over a 5-year period (2012-2017) to find patients whose seizures had a gelastic component. Nine patients were included in our study. All of them underwent long-term video-EEG monitoring and had at least one 1.5 T MRI performed.

Result: Our study included 2 adults and 7 children, with a mean age of 12,5 years (range 2-28 years). We analysed a total of 23 seizures. Smiling was observed in 4 patients and laughing in 5. Five of the patients had a left sided SOZ and 5 had a right sided one. The localization was frontal in 4 of the cases, parietal in another 4 and temporal in one. We had no cases where the ictal activity began in the posterior cortex. We did not find any correlation between the side or site of the SOZ and the presence of either smiling or laughing. However, we did notice that all of the cases with a frontal SOZ were lateralized to the right hemisphere.Visual analysis of the ictal EEG during PFEE revealed that the discharge was lateralised to the right side in all of the cases with a frontal onset (p=0.04) and it was lateralised to the left in the cases with either a parietal or temporal onset.

Conclusions: We have found that ictal smiling and laughing are both infrequent automatisms, that do not have a reliable lateralizing or localizing value.

Abstract Number: 647

Title: Practice-induced reflex seizures mainly precipitated by haste

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Purpose: Reflex seizures are defined as epileptic seizures reproducibly precipitated by external stimuli or cognitive behaviours. In addition to the choice of appropriate antiepileptic drugs, avoidance of triggers is important in its treatment. Complex cognitive tasks (praxis) can induce reflex seizures, however, usually a specific kind of task is associated with each patient. We investigated clinical and EEG features of a case of praxis-induced reflex seizures precipitated by haste, whose seizures are triggered by various activities.

Method:A 24-year-old female, who was diagnosed as idiopathic generalize epilepsy (IGE) and started antiepileptic drug treatment at the previous hospital, but remained with intractable seizures for more than a decade, was examined. Thorough medical history of seizure semiology and precipitating factors and data on long-term video EEG monitoring were analyzed.

Result: Her seizures were triggered by various tasks such as taking notes, calculation on paper, drawing, playing the electric piano, and playing puzzle games, regardless of the side of the hands, more frequently when she was in haste due to a time limit. Ictal EEG showed electrographic seizure patterns arising from the left posterior parietal area. Interictal EEG showed no photoparoxysmal responses. Head MRI was unremarkable. Clobazam add-on therapy was effective, and she did not show any seizures for follow-up period of more than 1 year.

Conclusions: The characteristics of seizures and EEG findings of our case suggest that the epileptic focus can reside in the posterior parietal cortex which is known to integrate somatic and visual input and coordinate motor output, as well as participate in time interval management. Since the triggers of reflex epilepsy reflect the function of the epileptic focus and related areas, the information is also useful to search for brain functional localization and brain functional networks associated with haste.

Abstract Number: 655

Title: remission and recurrence rates of seizures after anti-epileptic drugs withdrawal

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Purpose: The objective of this study was to evaluate remission-recurrence rates of seizures in patients whose antiepileptic drug (AED) treatments were discontinued after long-term seizure-free period in clinical follow-up.

Method: The files of 1985 patients who were followed up from the epilepsy outpatient clinic between 1998-2021 were evaluated retrospectively. Patients who gave up medication voluntarily were not included in the study. 67 patients were followed up without medication. 11 patients were excluded from the study due to, insufficient data. The study continued on the data of 56 patients. Recurrence was defined as the development of at least one seizure after drug withdrawal.

Result: Mean age of onset of seizures was 13.9 ± 10.04 years. The age of starting treatment was 15.87 ± 9.69 years, and the termination of treatment was 24.58 ± 11.54 years. 66.1% of the patients had generalized epilepsy and only 4 patients (7.1%) had a history of status epilepticus.The most frequently used AEDs were valproic acid (39.3%) and carbamazepine (30.4%). 67.9% of the patients who had AED witdrawal had a total of 1-5 seizures during clinical follow-up. Patients had seizure-free periods of 64.46 ± 32.27 months before termination of treatment and 43.73 ± 38.87 months after termination of treatment. Recurrence was observed in 23.2% of the patients after termination of treatment. It was observed that 64% of the recurrences seen in within the first two months. The age of onset of seizures and the age of starting and discontinuation of treatment were earlier in recurrence group compared to the group in remission (p>0.005).

Conclusions: Early relapses can be observed in patients who are given antiepileptic drug discontinuation. For this reason, close follow-up of the patients is important, especially in the first two years.

Abstract Number: 658

Title: International case control study of Sudden Unexpected Death in Epilepsy (SUDEP)

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Purpose: To identify factors associated with an increased or decreased risk of SUDEP.

Method: The EpiNet study group is undertaking a prospective case-control study, aiming to recruit 200 participants from approximately 40 international centres over four years. Patients with epilepsy from a pre-defined cohort who die of definite or probable SUDEP will be included. Cases must be alive when the cohort is defined. For each case, three true controls and one proxy control will be recruited from the same cohort.

A structured telephone interview with the next-of-kin of SUDEP cases will be conducted. Controls will be asked about their epilepsy and lifestyle. Proxy controls will be asked about the control patient they know. Information regarding seizure type and medication, sleeping arrangements, nocturnal supervision, use of seizure-detection devices, socio-economic factors and other health issues will be entered into the EpiNet database. Pathologists' and coroners' data regarding circumstances and cause of death will also be recorded if available.

The data will be analysed to identify risk factors for SUDEP. Odds ratios will be calculated using the Mantel-Haenszel method and logistic regression to control for covariates. 200 cases and 800 controls will detect an odds ratio of 1.7 over a control exposure range of 22-65%, with 80% power and 95% confidence level (2-sided).

Result: The study is now underway in 8 countries through Asia-Oceania, Europe and North America. COVID-19 has adversely affected case enrolment, and new centres are being sought.

Conclusions:SUDEP is second only to stroke as the leading neurological cause of years of potential life lost. The causes remain uncertain. A large prospective case-control study is the best way to determine the extent of the association between specific variables and SUDEP, in particular, those that could be modified to prevent this tragedy. Anyone interested in participating is welcome to contact: epinetadmin@adhb.govt.nz.

Abstract Number: 710

Title: Neurocognitive performance in short-term and long-term temporal lobe epilepsy patients

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Purpose: to explore the relationship between duration of epilepsy and cognitive changes in patients with refractive temporal lobe epilepsy (TLE).

Method: retrospective data from adult patients with short-term (ST, < 10 years, N=43) and long-term (LT, >25 years, N=57) refractory TLE were evaluated in the Presurgical Epilepsy Evaluation Unit at the Geneva University Hospital. Results of memory (list learning, Rey visual design, verbal and visual SPAN), language (phonemic and semantic fluency) and executive functions tests (trail making, figural fluency, Stroop) were compared between groups.

Result: median epilepsy duration in the ST-TLE group was 5 years and 32 years in the LT-TLE group. Age at epilepsy onset (ST-TLE: median 30 years vs. LT-TLE 6 years), age at evaluation (29 vs 37 years), number of AEDs

(3.5 vs. 6.0), etiology (hippocampal sclerosis: 23.3% vs 70%) were different between both groups (p< 0.05). There was no difference in laterality of epileptogenic lesion: 15 (40%) left and 22 (60%) right in ST-TLE vs. 25 (52%) left, 23 (48%) right in LT-TLE (p=0.29). There was no difference in gender, education, seizure type or frequency. Cognitive evaluation revealed differences in visual memory (ST-TLE median 49.0 IQR 44.5 – 55.0 vs. LT-TLE 41.3, IQR 32.0 – 50.3, p=0.005) and figural fluency (ST-TLE 28, IQR 21-33 vs. LT-TLE 24, IQR 14-33, p=0.012), but no difference in other tests results between the groups. 67.4% of ST-TLE patients had at least one cognitive domain deficit compared to 87.7% of LT-TLE (p=0.024).

Conclusions: epilepsy duration of > 25 years impaired in particular visual memory and figural fluency test results. With longer duration, more cognitive domains were affected. Differences could be due to different underlying etiology, but also longer and more intensive exposure to seizures as well as to antiseizure medication.

Abstract Number: 757

Title: Emergency Department Prioritization of Transient Loss of Consciousness due to Epileptic Seizures

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Purpose: To evaluate the performance of the Manchester Triage System (MTS) in prioritizing patients presenting to the Emergency Department (ED) with non-traumatic transient loss of consciousness (TLOC) secondary to epileptic seizures (ES). To evaluate the concordance in the diagnosis of ES between medical and nursing staff in the ED.

Method: Single-center observational retrospective study. We dichotomized MTS codes into low (codes blue, green and yellow) and high priority (codes orange and red). We compared the association of MTS priority classification codes with a final diagnosis of a TLOC due to ES, calculating the sensitivity (proportion of TLOC due to ES categorized with high priority), specificity (proportion of TLOC unrelated to ES categorized with low priority), and accuracy. We also evaluated the inter-rater agreement of ED nurses and physicians in the evaluation of clinical features suspicious of ES and in the final diagnosis of ES.

Result: Over 30 months, 2291 triage evaluations on TLOC were included, of which 201 (8.8%) due to ES. In the overall population: sensitivity 43.2%, specificity 85.5%, accuracy 81.8%; excluding cardiogenic syncope: sensitivity 43.2%, specificity 87.9%, accuracy, 83.7%; excluding pre-syncope: sensitivity 43.1%, specificity 84.2%, accuracy 79.1%; including only alert and responsive patients: sensitivity 74.1%, specificity 86.6%, accuracy 82.8%. Agreement in the evaluation of clinical features suspicious of ES between nurses and physicians: 99.4% (Kappa Cohen 0.96; p <0.001); agreement in the final diagnosis of ES: 99.5% (Kappa Cohen 0.97; p <0.001).

Conclusions: MTS adequately categorizes TLOC unrelated to ES, but is not equally effective in prioritizing TLOC due to ES. There is high agreement between ED nurses and physicians in the evaluation of clinical features suspicious of ES and in the final diagnosis of TLOC due to ES.

Abstract Number: 767

Title: Impaired Facial Emotion Perception in Temporal Lobe Epilepsy Demonstrated by Event-related Ossilations

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Purpose: Temporale lobe and occipito-temporal cortical areas play an important role in facial emotion perception (FEP). In patients with temporal lobe epilepsy (TLE) impairment of FEP was shown with behavioral and functional neuroimaging (FMRI, PET, MEG) but not event-related ossilations which is a well known method for cognitive research studies. Therefore, we aimed to explore FEP by analyzing EEG event-related theta oscillations in patients with TLE.
Method: Twenty-one patients with TLE and 19 healty volunteers of similar age and gender distribution were included. During EEG recording, 15 photographs from Ekman and Friesen's photo series showing 5 different facial expressions (angry, happy, neutral, fear, sad) were used. Event-related theta (3-8 Hz) power spectrum and phase locking were analyzed by wavelet transform method using Brain Vision Analyzer program. ANOVA was used for statistical analysis.
Result: In our study, the difference between TLE patients and healty volunteers was found to be significant for theta power (P=,017), but there was no significant difference between right and left TLE patients (P=,052). In the patient group, lower theta power was observed against all faces, especially in temporo-parietal and parietal areas compared to healty volunteers (P=,005). Patients with left TLE were significantly impaired in happy, patients with right TLE were significantly impaired in fearful facial expressions. Phase locking analysis revealed higher theta phase locking in occipital area compared with other regions (P=,001).
Conclusions: Impaired FEP in patients with TLE is characterized by decreased event-related theta responses, particularly in temporo-parietal and parietal areas. Moreover, perception of happy face was more impaired in left, and fearful in right TLE. Also, both hemispheres are found to be contributing jointly to face recognition. Finally, this study could be a guide for future research related to neural networks in cognitive tasks and epilepsy.

Abstract Number: 781

Title: Sudden Unexpected Death in Epilepsy, What Saudi Epileptic Patients would like to know? Cross Sectional Study.

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Purpose: Sudden unexpected death in epilepsy (SUDEP) is a significant mortality cause in people with epilepsy (PWE) with incidence of 1 per 1000. There is no data from Saudi Arabia that inform local clinical practitioners about the attitude of PWE toward the entity of SUDEP. This study aims to investigate the perspective of Saudi PWE toward SUDEP and to assess their knowledge about sudden unexpected death in epilepsy.

Method: The study is a cross-sectional questionnaire based study which was conducted at neurology clinics in King Abdulaziz medical City-Riyadh (KAMC-R) and Prince Sultan Military Medical City-Riyadh (PSMMC-R). We included all mentally competent patients who are older than 16 years of age. The sampling technique was non-probability convenient sampling by including those who meet the criteria. The questionnaire was administered by the research team.

Result: For 201 patients who met the criteria for answering the questionnaire, the mean age was 33.4 with a standard deviation of 13.4. Half (50.5%) of the study subjects were female. Only 11 participants (5.5%) had heard about SUDEP. The vast majority of the participants (97%) wanted to know about SUDEP and 193 (96%)

participants wanted to receive this information by a neurologist. The majority 131 (65.2%) thought that the appropriate time to be told about SUDEP is after the second visit while only nine (4.5%) wanted to know during the first visit with their neurologist. However, 29 (14.4%) participants thought that the appropriate time to be told about SUDEP is when the seizure control get worse. The majority of participants 140 (69.9%) did not know if SUDEP can be prevented or not.

Conclusions: The majority of Saudi PWE do not know about SUDEP although they want to be counseled about this risk by their physicians. There is a need to improve education of Saudi PWE about SUDEP.

Abstract Number: 798

Title: Change in side of faciobrachial dystonic seizures and EEG features of anti-LGI1 antibody encephalitis during the disease course

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Purpose: To investigate the correlation between clinical and EEG features of faciobrachial dystonic seizures (FBDSs), that changed the side during the disease course.

Method: A 72-year-old male with three months history of right-sided FBDSs due to anti-LGI1 antibody encephalitis was investigated. His symptoms were once improved by infusion of midazolam and corticosteroid, but recurred with left-sided FBDSs in 5 months. His serum sodium was normal. His cerebrospinal fluid showed positivity of anti-LGI1 antibody. Clinical and EEG features were serially analyzed. EEG record of FBDSs was further analyzed to investigate the relationship among direct current (DC) shifts, rhythmic slow activities (RSA), and movement onset.

Result: Initially, his MRI showed contrast-enhanced T1 hyperintensity of the right basal ganglia and T2 hyperintensity of the left basal ganglia. The first EEG showed DC shifts and RSA in 80% and 100% of FBDSs. The latency from DC shifts and RSA to movement onset of the right orbicularis oris was 53.2 ± 29.9 seconds (mean ± SD) and 25.9 ± 6.9 seconds. The amplitude of DC shifts was maximum in the right frontal area (69.7 ± 19.4 μV, averaged reference montage, time constant 2.0), whereas RSA was regional in the right frontotemporal area. Two months later, a new T1 hyperintensity lesion appeared in the left basal ganglia, and he started having the left FBDSs. DC shifts and RSA were in the right frontal region at five months. Onset of DC shifts was significantly earlier than that of RSA (25.3 ±8.3 vs 12.1 ±6.3, $p<0.01$, paired t test)

Conclusions: The present study showed that the side of FBDSs can change during the disease course, and that MRI and EEG abnormalities can distribute ipsilateral to FBDSs. Autoimmune epilepsy should be considered when serial clinical semiology and side of examination findings are inconsistent.

Abstract Number: 810

Title: The influence of the transferred new coronavirus infection (COVID-19) on the course of epilepsy and bioelectric activity of the brain

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Purpose: to study patients with epilepsy who have suffered a coronavirus infection (COVID-19).

Method: the study included 13 patients with epilepsy who had suffered a coronavirus infection (COVID-19) in 2020, confirmed by laboratory tests. All the patients underwent neurological examination, continuous video-EEG monitoring with the inclusion of sleep, MRI of the brain. The study included 5 men and 8 women aged 19 to 60 years (average age 42.8+14.8). Of these, 9 patients were diagnosed with structural focal epilepsy, 2 patients with idiopathic (genetic) generalized epilepsy, 2 patients with focal epilepsy of unknown etiology. According to medical records, 4 patients had an asymptomatic COVID-19, and 9 patients had a mild severity of the disease. In 4 patients, COVID-19 was transferred against the background of the remission of epilepsy, in 9 patients against the background of continuing seizures.

Result: the results of video-EEG monitoring showed that in the remission group, epileptiform discharges were absent in 2 patients (50%), and in the group of patients with continuing attacks, epileptiform discharges were present in 5 patients (55%). In no case there was a failure of remission or an increase in the frequency of seizures.

Conclusions: our study showed that in patients who had an asymptomatic coronavirus infection, as well as a mild severity of the disease, there was no significant change in the course of epilepsy.

Abstract Number: 874

Title: A retrospective, real world experienced of perampanel monotherapy in patient with first new onset focal seizure: A Thailand experience

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Purpose:
Real-world data on efficacy and tolerability of perampanel (PER) monotherapy in treatment naïve patients with focal onset seizures (FOS) and/or focal-to-bilateral tonic-clonic seizures (FBTCS) to assess efficacy effectiveness and tolerability.

Method:
This is a retrospective review of study patients with new FOS with or without FBTCS, aged ≥15 years, who had been prescribed PER as monotherapy. Treatment outcome included retention rate, responder, and seizure-free rate at observational point 3, 6, and 12 months (OP3, OP6 and OP12). Treatment-emergent adverse events (TEAEs) and adverse drug reactions were recorded.

Result:
A total of 41 patients who enrolled in the study (M : F; 17:22, mean age = 46.1 ± 21.8 years), with new FOS and/or FBTCS. The proportions of individuals remaining on PER monotherapy at 3, 6, and 12 months were evaluated. The median Perampanel dosage was 4 mg (range 2-8 mg). The retention rates at 3, 6, and 12 months were 88%, 73%, and 61%, respectively. The seizure freedom rates at 3, 6, and 12 months were 78%, 80%, and 76%, respectively, whereas seizure freedom rates in elderly (>60 years old) was 85%, 91% and 80%,

respectively. About 14% had discontinued the PER monotherapy because of lack of efficacy. Sixteen individuals (41%) had TEAEs, common AEs were dizziness, somnolence, ataxia, and only one case had depression. The AEs with somnolence and ataxia were found higher in elderly (15% and 30%) than adult patients (7% and 3%), respectively.

Conclusions:
Real-world data of PER monotherapy in naïve patients with focal onset seizures demonstrated good effectiveness and a good safety profile at relatively low doses. By starting with low dosage and slow titration of PER help to minimize the impact of AEs, maximize adherence, and increase patient retention. PER has a once-daily dosing schedule that supports patient adherence contributes to achieving seizure freedom.

Abstract Number: 924

Title: Clinical features and longterm outcome of recurrent Status Epilepticus

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Clinical features and longterm outcome of recurrent Status Epilepticus

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Purpose: to evaluate the clinical features and the longterm outcome of patients with recurrent SE and assessed the risk of recurrence after an incident event.

Method: we reviewed our prospective register of SE episodes of adult patients admitted to the OCB hospital (Modena, Italy), from September 1st 2013 to September 1st 2020. We performed a comparison between recurrent (rSE) and incident SE (iSE) and evaluated the risk of recurrence through a survival analysis. Post-anoxic events were excluded.

Result: 478 patients were observed. 44 patients (mean age: 67 y/o, 69% female) experienced SE recurrence, whereas 434 patients (mean age: 71 y/o, 61% female) presented an incident event. Among demographic and clinical variables, an acute symptomatic etiology was less frequently observed in relapsing patients ($p<0.01$), without differences in terms of previously known epilepsy ($p=0.53$). The highest risk of recurrence was observed in the first 6 months following the incident SE (7.6%), whereas the cumulative recurrence rate in our population was 9.1%, 12.8%, and 15.8% at 6 months, 1 year, and 3-years respectively. Among rSE, a trend for a late recurrence was associated with a remote symptomatic etiology ($p=0.09$). Comparing iSE and rSE, we did not find any differences in terms of longterm survival ($p=0.62$).
Conclusions: SE recurrence was less frequently observed after an acute symptomatic incident event, it was often experienced during the first 6 months of follow-up and apparently did not influence longterm survival in our cohort.

Abstract Number: 937

Title: Structural changes in foci of epileptogenesis in patients with pharmacoresistant focal temporal lobe epilepsy

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Purpose: To clarify the features of morphological changes in the foci of epileptogenesis and identify a possible relationship between the severity of epilepsy and glial structures of the brain**.**

Method: Biopsy samples from 76 operated patients aged 19 to 52 years with focal pharmacoresistant temporal lobe epilepsy were studied. In all cases, histological examination of tissues removed during surgery was performed using standard techniques. In some cases, immunohistochemistry techniques were used, as well as electron microscopy.

Result: 76 patients aged from 19 to 52 years with structural pharmacoresistant temporal lobe epilepsy were examined and operated on. Focal cortical dysplasia was detected in 14 patients. In 5 cases, mesial temporal lobe sclerosis developed.Glia changes in epileptogenesis foci deserve special attention. Clinical and morphological comparisons showed that in the mechanisms of the course of epilepsy in the white matter of the temporal lobe, glial reactions turned out to be extremely pronounced - we ascertained gliosis, which is characteristic precisely for those cases of epilepsy that proceeded relatively easily, although they were drug-resistant. On the other hand, with a particularly severe course of epilepsy, including a history of status epilepticus, there was a mild astrocytic reaction with the presence of foci of demyelination in the white matter of the temporal lobe.

Conclusions: When studying glial structures in foci of epileptogenesis, we came to the conclusion that astrocytic gliosis in foci of epileptic activity with structural pharmacoresistant focal temporal lobe epilepsy is not a pathological, but an adaptive (protective) response.

Abstract Number: 986

Title: The efficacy equivalence of generic levetiracetam in West China: a perspective study

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Purpose: During the COVID-19 pandemic, the supply chain of the anti-seizure medication has been challenged. On the other side, the “4+7“ drug procurement reform launching in China also force the promotion of generics. This study is aimed to investigate the attitude and efficacy of the antiseizure drug levetiracetam and its genric production in Chinese people with epilepsy.

Method: The study is conducting in the clinic in 10 epilepsy centers in Westchina.The inclusion criteria are 1) diagnosed with epilepsy for more than 3 months; 2) has started standard levetiracetam treatment for more than 3 months during the course; 3) informed consent was obtained. Participates were consecutively recruited. The data is collected through fact-to-face interview and self-report surveys.

Result: This ongoing study has currently enrolled 40 people with epilepsy. The average age is 24.3 yrs, the median age is 25.0 yrs. 72.5% of them was female. Twenty-eight of them were diagnosed with focal onset seizure, four has generalized onset seizure. Of 39 patients who are currently using levetiracetam, 29 (74.3%)

were using the brand drug. 30% of patients had switch the brand without discussion with doctors. Mainly because of the unstabled supply and expenses. In 3 cases, participates complains the difference in efficacy of the treatment. Only 40% of the participates agree that the efficacy and safety of generic drugs are equal to the brand product.

Conclusions: From the preliminary results, there are a large proportion of people with epilepsy has switched the brand of their levetiracetam drug. While a limited number of cases showed differences in efficacy and safety, most of the patients doubt the equivalence.

Abstract Number: 988

Title: The Severity of Autonomic Dysfunction is Associated with the Long Duration of Focal Epilepsy

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Purpose: Interictal autonomic dysfunction might contribute to sudden unexpected death in epilepsy patients (SUDEP). The risk of SUDEP is particularly high in patients who had epilepsy for more than 15 years (Devinsky et al. Lancet Neurol 2016;15:1075-1088). We aimed to compare autonomic cardiovascular regulation between patients with 'short duration' (SD-patients, ≤15 years) and 'long duration' (LD-patients, >15 years) of focal epilepsy.

Method: In 26 SD-patients (mean age 32.4±6.8 years, 11 males), 17 LD-patients (mean age 34.2±5.9 years, 7 males) and 30 healthy controls (mean age 31.3±6.3 years, 13 males), we recorded RR-intervals (RRI), beat-to-beat systolic blood pressure (BPsys), and respiratory frequency during 5 minutes at supine rest, during 75 seconds of metronomic breathing, and upon active standing. We calculated RRI-standard-deviation (RRI-SD), RRI-coefficient-of-variation (RRI-CV), total-RRI-powers (TP-RRI) reflecting total cardiac autonomic modulation, low-frequency-powers of RRI-modulation (LF-RRI) and of BPsys-modulation (LF-BPsys) reflecting sympathetic modulation, root-mean-square-of-successive-RRI-differences (RMSSD), high-frequency-powers of RRI-modulation (HF-RRI) and RRI-expiration:inspiration-ratio reflecting parasympathetic modulation, supine and standing baroreflex sensitivity (BRS), and RRI-30:15-ratio reflecting baroreflex response to active standing. We compared autonomic parameters between SD-patients, LD-patients, and controls (Kruskal-Wallis test and post-hoc Mann-Whitney-U-tests; significance: $p<0.05$).

Result: Kruskal-Wallis test revealed significant differences in all the above parameters between the three groups. Compared to controls, SD-patients had lower RRI-SD, RRI-CV, TP-RRI, HF-RRI, LF-RRI, LF-BPsys. Compared to controls and SD-patients, LD-patients had higher respiratory frequency and heart rate, and lower all calculated autonomic parameters, except for LF-BPsys when compared to SD-patients.

Conclusions: Patients with duration of focal epilepsy of >15 years had more prominent decrease in autonomic cardiovascular modulation compared to patients with a shorter disease duration. Our findings are in line with the evidence of the higher risk of SUDEP in persons with the long disease duration. Acknowledgement: We are grateful to Professor Max Hilz (Erlangen, Germany) for the invaluable support regarding this work.

Abstract Number: 997

Title: Limitations of the UMRS for the evaluation of progression of myoclonus in progressive myoclonus epilepsy type 1 (EPM1) in the prospective follow-up

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Purpose: Progressive myoclonus epilepsy type 1 (EPM1) is an autosomal recessive form of progressive myoclonus epilepsy caused by cystatin B gene mutations. Our aim was to evaluate progression of myoclonus symptoms in Finnish EPM1 patients using unified myoclonus rating scale (UMRS) during short- and long-term follow-ups.

Method: Twenty-five genetically confirmed EPM1 patients (21 with homozygous repeat expansions, 4 compound heterozygotes) were included in this prospective study. Two or three study visits included clinical evaluation, medication history and video-recorded UMRS. The interval between the first and the second assessments was 5-12 years for twenty-two patients and 1 year for nineteen patients.

Result: Myoclonus assessed with UMRS action myoclonus (AM) scores progressed significantly during the long-term follow up period (paired T-test, P<0,001, mean change 30, SEM 5,6). The UMRS AM score correlated significantly with physical disability assessed with Singer scoring model (r^2 = -0,836, P<0,001). During the short-term follow-up the changes in AM scores varied substantially (mean change 0,6±13, min-max -27–33). For the one-year follow-up, there was no significant correlation between the changes in AM score and changes in functional disability assessed with Singer scoring model. The type of genetic mutation or changes in antiseizure medication regimes did not explain the changes in UMRS AM scores during this one-year follow-up.

Conclusions: We show that in a long run myoclonus symptoms progressed in Finnish EPM1 patients. However, in the short-term follow-up action myoclonus showed great variability. The changes seen in UMRS AM score did not correlate with changes in patients' functional disability. Therefore, UMRS test is not the optimal evaluation method of action myoclonus in short-term follow-ups such as eg. drug trials. There is a need for the development of extensive continuous myoclonus evaluation in patient's home.

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Abstract Number: 1022

Title: Non-Ketotic Hyperglicemia–Related seizures: "sweet jerks" are made of this. Description of two cases and review analysis.

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Purpose: Non-Ketotic Hyperglycemia (NKH) is an acute complication of Diabetes Mellitus (DM)[1], manifesting with neurological symptoms, including epileptic seizures[2]. We aim to describe two cases of NKH-related seizures and their electroclinical features, and to provide an overview of the published literature.

Method: A systematic search of case reports and case series was conducted on MEDLINE and Embase from inception to June 10, 2020. Two reviewers independently selected the retrieved references to identify studies including patients older than 16 years presenting with NKH and newly-onset seizures.

Results: Two male patients (60 and 54 years old) presented for repetitive focal motor seizures, respectively, associated to auditory-hallucination and speech arrest. Ictal-EEG showed 3 seizures in the right posterior temporal regions and 1 seizure in the left parietal region, respectively. In both patients, brain MRI showed subcortical hypointensity on FLAIR images associated with cortical hyperintensity, while laboratory tests were consistent with NKH. The seizures resolved after insulin and anticonvulsive therapy.

The literature search returned 395 results, 106 of which were eligible, including 292 patients, 163 males, mean age 60.1 years (range±11.13), mean glycemia 548.69 mg/dL (range±303,86). DM was newly diagnosed in 120 patients (41%). Focal aware seizures, motor manifestations and sensory visual symptoms were the most common semiology, occurring in 80%, 59% and 14% of patients, respectively, while 70% of patients showed seizure-clusters and 33% post-ictal deficits. MRI, when available, disclosed the characteristic findings above mentioned in 41% of the cases. Anti-Seizures-Medication were administered in 122 patients (42%) without satisfactory response in most cases (68%). Insulin-therapy controlled seizure in 74% of the cases.

Conclusion: NKH-related seizures are a monophasic condition characterized by clusters of focal seizures secondary to elevated glycemic values. Their timely recognition allows treatment with insulin and glycemic normalization, providing the patient with appropriate care and avoiding waste of healthcare resources.

Abstract Number: 1032

Title: Lexical abilities in naming and discourse in temporal lobe epilepsy

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Purpose: Several studies, that used verb and noun production tests, showed that individuals with temporal lobe epilepsy (TLE) have difficulties with single word production, whereas spontaneous speech typically remained unattended. Our goal was to investigate the lexical characteristics of fluent discourse (lexical diversity) in individuals with left and right TLE as compared to healthy controls.

Method: 26 individuals with left TLE, 26 individuals with right TLE, and 26 healthy Russian speakers participated in the study. During the discourse production task, they were asked to create a story based on a complex picture presenting a situation. Noun and verb production was assessed based on naming of pictures of objects and actions. We analyzed the data using linear regression modeling with group, education, and clinical parameters as independent factors. Dependent measures were percent of correct answers for the naming tests and the length and Measure of Lexical Diversity in Text (MLTD) for the discourse.

Result: As compared to the healthy controls, individuals with left and right TLE showed lower performance in both object (87.5% vs. 97.6%, 91.6% vs. 97.6%, correspondingly; adjusted r-squared = 0.27, $p < 0.001$) and action (90.4% vs. 97.8%, 92.7% vs. 97.8%; adjusted r-squared = 0.18, $p < 0.001$) naming tasks. MLTD also differed across groups (49.7 vs. 65.6, 56.3 vs. 65.6; adjusted r-squared = 0.09, $p = 0.012$), whereas the length of the discourse did not. No differences were observed between the individuals with left and right TLE in any of the tasks.

Conclusions: Our results are in line with previous research showing impaired single word production in individuals with left and right TLE. In addition, the decreased lexical diversity indicates that difficulties with

lexical retrieval or reduced vocabulary size can be reflected in spontaneous discourse, irrespective of the lateralization of the epileptogenic focus.

Abstract Number: 1073

Title: Effect of seizure viewing on quality of life among persons with epilepsy

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Purpose: Psychiatric disease is the most common comorbidity seen in persons with epilepsy (PWE) and is often secondary to psychosocial disturbance due to poor adaptation to the disease. This study aims to assess anxiety and depression among PWE and its impact on Quality of life (QOL) using validated questionnaires We also assessed the effect of seizure viewing on these psychological scores by the same scales

Method: A prospective interventional study was conducted enrolling 52 PWE. Their baseline psychological status was assessed using Hospital Anxiety Depression Scale (HADS) and its impact on QOL using Quality of Life in Epilepsy (QOLIE 31). The scores were reassessed 3 months post seizure viewing and compared with the baseline scores.

Result: Among 52 patients analyzed, 20 (38.4 %) had anxiety and 8(15.3%) had depression.The mean HADS A scorewas 9.56±4.12 ie; borderline range. Gender, income status, risk factors antedating index seizure, type of seizure, temporal semiology, seizure frequency, MRI or EEG characteristics did not have any significant association with baseline psychological scores. There was strong negative correlation between HADS scores and QOLIE 31 scores(r=-0.548(<0.001)and 0.343 (0.013) for HADS-A and HADS-D respectively). QOLIE subscores also showed significant negative correlation with HADS-A except for overall QOLand with HADS-D except for seizure worry, medication effects and social function. There was statistically significant reduction in the HADS-A scores from 9.56±4.12 to 8.35±3.85 after seizure viewing (p=0.049).We identified patient characteristics that benefit seizure viewing with respect to each of the psychological scores.

Conclusions: The study emphasises association of anxiety and depression and its impact on QOL of PWE and highlights the role of seizure-viewing in improving their psychological milieu and hence QOL.

Abstract Number: 1091

Title: NATURAL HISTORY OF LAFORA DISEASE A Prognostic Systematic Review and Individual Participant Data Meta-Analysis.

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Purpose: To describe the clinical course of Lafora Disease (LD) and identify predictors of outcome by means of a prognostic systematic review with individual participant data meta-analysis.

Method: A search was conducted on MEDLINE and Embase with no restrictions on publication date. Only studies reporting genetically confirmed LD cases were included. Kaplan-Meier estimate was used to assess probability of death and of loss of autonomy. Univariable and multivariable Cox regression models with mixed effects (clustered survival data) were performed to evaluate prognostic factors.

Result: Seventy-one papers describing 284 genetically confirmed LD cases were selected. Mean age at disease onset was 13.4 years (SD 3.7), with 9.2% aged≥ 18 years. Overall survival rates in 258 cases were 93% [95% CI 89-96] at 5 years, 60% [95% CI 51-68] at 10 years and 55% [95% CI 46-63] at 15 years. Median survival time was 11 years. The probability of loss of autonomy in 110 cases was 46% [95% CI 37-57] at 5 years, 77% [95% CI 67-85] at 10 years, and 85% [95% CI 75-92] at 15 years. Median loss of autonomy time was 6 years. Asian origin, age at onset <18 years and cognitive symptoms at onset emerged as negative prognostic factors, while type of mutated gene was not related to survival or disability.

Conclusions: This study documented that half of patients survived at least 11 years, suggesting that disease course may be longer than previously reported. The notion of actual survival rate and prognostic factors is crucial to design studies on the effectiveness of upcoming new disease-modifying therapies.

Abstract Number: 1109

Title: An early analysis of an ongoing project examining the impact of driving restrictions on patients with epilepsy

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Purpose: Driving restrictions have a significant impact on patients with epilepsy and their families. This is documented in international studies but has not been reported in an Irish context. The goal of this study is to examine this impact on an Irish based tertiary hospital cohort.

Method: Patients are recruited through the Beaumont hospital neurology service following communication of driving restriction due to a seizure. Phone interviews are then conducted using a standardized proforma.

Result: Our analysis to date includes the first 10 patients interviewed (female 90%, mean age: 40.5 years). Ninety per cent (n=9) reported a car as their primary mode of transport prior to driving restriction. During restriction, 60% (n=6) continued to primarily use a car driven by a family member. Eighty per cent (n=8) reported access to public transport with 60% (n=60) indicating potential benefit from a free travel pass. Fifty per cent (n=5) reported that their transportation was limited by cost, and 20% (n=2) were forced to give up their job and primary income. Ninety per cent (n=9) of patients denied a negative impact on the doctor-patient relationship, 10% (n=1) had sought a second opinion and 10% (n=1) of patients admitted to driving during the restriction.

Conclusions: Personal car is the primary mode of transport in this cohort both before and after driving restriction. Access and cost of public transport, reliance on family and financial loss are significant factors affecting patients. This study is ongoing and aims to conduct 100 patient interviews across institution

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Abstract Number: 1125

Title: Post-stroke seizures in a university hospital Stroke Registry

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Purpose: Seizures after age 60 years are often ascribed to cerebrovascular disease, and may be associated with increased morbidity. Few studies have examined the relation of post stroke seizures (PSS) with stroke characteristics or outcome. This study examines the association of PSS with type and location of ischemic stroke(IS), clinical and laboratory characteristics, and outcome.

Method: Patients with IS entered prospectively into a University-hospital based stroke registry were studied. Patients recognized to have PSS were compared with those without seizures for: type of IS, stroke location, sensorium, major risk factors, biochemical profile and outcome (modified Rankin Score). Univariate and multivariate regression analyses were used.

Result: Among 1220 patients with IS (age: 64±13 years; M:F::63%:37%), large artery stroke(LAA) was present in 45%, cardioembolism(CE) in 10% and small vessel disease(SVD) in 25%. 93(7.75%) IS patients were recognized to have PSS. 62% of PSS occurred among patients with large-artery stroke (p=0.001). PSS was associated with lower GCS (p=0.007), higher WBC (p<0.001), and poor outcome at discharge as well as follow up (mean 13 months)(p<0.001). PSS showed no association with stroke location or side of stroke. Multivariate regression analysis revealed age, sensorium, IV thrombolysis and heart disease to be independently predictive of outcome but not PSS.

Conclusions: Post-stroke seizures are a relatively common complication of ischemic stroke. They are associated with large artery stroke and poor outcome. Future studies may examine possible predictors of PSS among patients with large-artery stroke and possible preventive measures.

Abstract Number: 1134

Title: Evidences from Multimodal Smartwatch: A Link to Pathogenesis of SUDEP

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Purpose: To assess 1) differences of extracerebral biosignal changes during awake-related seizures (AWS) versus sleep-related seizures (SS); 2) correlations between baseline heart rate variability (HRV) and heart rate (HR) change during AWS vs SS; and 3) predictors for HRV in drug-resistant epilepsy.

Method: We prospectively recruited the patients with drug-resistant epilepsy who were admitted in our epilepsy monitoring unit for presurgical evaluation. All were recorded simultaneously a scalp video-EEG monitoring and wrist-worn Empatica E4®. Electrodermal activity (EDA) and HR changes during AWS vs SS were compared using Mann-Whitney test and Student t-test, respectively. Correlations between baseline HRV and HR change during AWS vs SS was also assessed. Linear regression model was employed to assess predictors for HRV.

Result: Ninety seizures were captured, 63 and 27 were AWS and SS, respectively. Thirteen seizures were focal seizures with bilateral tonic-clonic seizures (BTCs) and 77 were focal aware or impaired awareness seizures (non-BTCs). Differences of EDA and HR changes during AWS vs SS were pronounced for BTCs (EDA 1.317 vs 0.244 µS, p = 0.010; HR 98.5 vs 82.2 beats/min, p = 0.055), but not significantly different for non-BTCs (EDA 0.183 vs 0.253 µS, p = 0.546; HR 82.8 vs 80.5 beats/min, p = 0.404). Baseline HRV was positively correlated with HR change only during AWS (r = 0.240, p = 0.031). Upon multivariate analysis, duration of epilepsy and concurrent use of carbamazepine were inversely associated with HRV.

Conclusions: Multimodal smartwatch demonstrated the effects of sleep on autonomic changes (EDA and HR) during seizures, where biosignal elevations during sleep-related BTCs were not as high as awake-related BTCs. Individual HRV may reflect ability of their HR response only during AWS, but not SS. In the context of high-demanding autonomic response during BTCs, inadequate response during sleep may shed light on SUDEP pathogenesis.

Abstract Number: 1138

Title: Design of a double-blind, randomized, phase II trial in the prevention of epilepsy in stroke: anti-epileptogenic effects of eslicarbazepine acetate

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Purpose:

Epilepsy is a prevalent neurological disorder with significant morbidity and mortality, but available drug therapies target its symptoms rather than the underlying cause[1]. There is yet no approved therapy for individuals at risk of epileptogenesis[2], however in experimental animal models, ESL demonstrated a possible antiepileptogenic effect.[3,4] Stroke is the most common cause of epilepsy in the elderly[5], and 5-15% of all stroke patients experience a seizure within 2 years of the event. [6] This phase-II, multicentre, randomized, double-blind, placebo-controlled study aims to assess if the treatment with ESL for 1 month, started within 120 hours after stroke occurrence, changes the incidence of unprovoked seizures (USs) within the first 18 months after randomisation.

Method:
Patients ≥ 18 years at high risk of developing USs, after acute stroke (intracerebral haemorrhage or ischaemic), will be randomized (1:1) to ESL 800 mg or placebo. Treatment will start within 120 hours after primary stroke occurrence and continue until 1 month after randomization and then is tapered off. Patients will be followed up until 18 months. Exclusion criteria include, amongst others, history of previous clinical cerebral cortical stroke, history of USs prior to stroke or impaired pre-stroke level of function. Primary and key secondary efficacy endpoints include proportion of patients who experience the first US within 6, 12 and 18 months after randomization (failure rate). Sample size is planned to have at least 80% power to demonstrate a significantly lower failure rate under ESL *vs*. placebo.

Result:
Study is planned to include approximately 200 subjects. Clinical phase is ongoing, and recruitment is open in Austria, Germany, Italy, Israel, Portugal, Spain, Sweden and UK.

Conclusions:
Following promising experimental results and the need of further research in patients, the antiepileptogenic effect of prophylactic ESL will be investigated in stroke patients at high risk for USs.

Abstract Number: 1151

Title: Can poor sleep quality be associated with insufficient seizure control?

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Purpose: Sleep-related problems are common among patients with epilepsy as epilepsy and epileptic seizures are very sensitive to sleep habits and sleep related problems. Sleep quality is a sleep feature that can be an essential factor in patients with epilepsy (PWE). Thus, it can have negative effects on epilepsy and on epileptic seizures as well. Our aim was to study the possible impact of poor sleep quality on epilepsy control.

Method: We used Pittsburgh Sleep Quality Index (PSQI) to assess quality of sleep in PWE. Based on clinical interview they were also classified as controlled epilepsy (CE, no seizures during previous year) and uncontrolled epilepsy (UE). PSQI has a specific scoring system with final score cut-off point >5 dividing patients with good and poor quality of sleep. As for yearly controlled-uncontrolled means that patients had at least one seizure in the last year but not in the last month. Chi-Square test was used to analyse the association of sleep quality in relation to the level of control upon epileptic seizures

Result: Overall 166 PWE, with mean age 35.2 years (18-71), 47% females (78) - were interviewed and assessed at a tertiary sleep center. All patients were at the age of 18 and above. From 166 patients 10.24% were CE whereas 89.76% were UE. For CE and UE poor sleep quality was seen in 37.95% (63) and 62.05% (103) respectively, with $p<0.02$ (Chi-Square Value 5.75).

Conclusions: Our data suggest that poor sleep quality is associated with significantly more cases of uncontrolled epilepsy. Better control over sleep schedule and sleep disorders in PWE would lead to improved control over the course of epilepsy.

Abstract Number: 1152

Title: Restless legs syndrome in epilepsy: a new contributor to affective comorbidity

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Purpose: Sleep disorders represent a variety of conditions affecting overall sleep quality. Epilepsy is sensitive towards changes in sleep parameters. Restless legs syndrome (RLS) is a clinical entity representing unpleasant sensations in limbs, particularly in legs, causing the individual to move and perform other activities in order to relieve those sensations, which worsen at rest. RLS impacts overall sleep quality by delaying sleep onset and leading to sleep fragmentation. RLS is more frequently observed in PWE compared to healthy population. Affective symptoms (AS) also play a significant role in epilepsy. Mood disorders such as depression and anxiety are reported to be prevalent among patients with epilepsy (PWE).

The aim of our study was to reveal potential connections between epilepsy, RLS, and AS.

Method: In our study we enrolled PWE admitted to a tertiary sleep centre. The international criteria for diagnosing RLS were applied (IRLSSG). Affective disorders were assessed by using Hamilton Depression and Anxiety Rating Scales (HAMD, HAMA). Mann Whitney U test was applied for statistical analysis.

Result: Our study involved 175 participants – PWE with or without RLS (mean age – 35.4 years (18-71); Female – 47.4%). The patients with definite RLS were 20.6% (mean age – 42.6, females – 50%). Body mass index (BMI) was significantly higher in PWE with definite RLS – 25.7 vs 23.4, $p<0.05$.

Anxiety rates were significantly higher among PWE with definite RLS, compared to others - 18.9 vs 13.5, $p<0.01$, respectively. Depressive symptoms were observed with significantly higher scores among PWE with definite RLS: 15.6 vs 11.7, $p<0.01$.

Conclusions: Our data suggest that restless legs syndrome is a contributing factor in worsening of affective symptoms in patients with epilepsy.

Abstract Number: 1189

Title: Stimulus induced repetitive periodic or ictal discharges (SIRPIDs) are associated with high prevalence of non-convulsive status epilepticus

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Purpose: Stimulus induced repetitive periodic or ictal discharges (SIRPIDs) are a rare EEG pattern in critically ill patients and associated with poor prognosis. However, its clinical significance regarding epileptic risk and anticonvulsive treatment is yet unclear.

Method: In a retrospective analysis, we reviewed 55 patients with SIRPIDs according to the American Clinical Neurophysiological Society (ACNS) criteria. SIRPIDs occurred after standardized painful stimulus in the hand during a standard 20-minute EEG. These cases were investigated regarding non-convulsive status epilepticus (NCSE) according to Salzburg consensus criteria and mortality.

Result: In 36/55 patients (65.5 %), SIRPIDs were associated with either non-convulsive status epilepticus. In 26/36 cases (72.2 %) of the patients with concurrent status epilepticus, SIRPIDs occurred after status epilepticus (on average 4.8 days later), but in 4/36 patients 11.1 %) they were observed before a later to come status epilepticus. Three patients suffered from non-convulsive status epilepticus before and after the appearance of SIRPIDs and in three other cases SIRPIDs and NCSE coexisted in the same EEG. In half of the cases status epilepticus was refractory, super-refractory or the patient died before its resolution. The overall mortality in the cohort was 50.9 %. Mortality after occurrence of SIRPIDs was lower in patients who also had a status epilepticus.

Conclusions: These findings corroborate the hypothesis that SIRPIDs are epileptiform interictal phenomena, commonly co-occurring with non-convulsive status epilepticus. Furthermore, SIRPIDs are associated with therapy-refractory course of status epilepticus. These findings suggest that initiation of prophylactic anticonvulsive treatment for SIRPIDs might be beneficial.

Abstract Number: 1211

Title: Innovating Epilepsy Care during the COVID-19 Pandemic: The Virtual Rapid Access Epilepsy Clinic

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Purpose: Wait-times for a neurologist in Ontario, Canada can range from 2-6 months. The COVID-19 pandemic has exacerbated wait-times, making it more difficult for patients living with epilepsy to access timely medical care. The Virtual Rapid Access Epilepsy Clinic (VEC) was developed in response to these concerns. The clinic combines novel infrastructural approaches to virtual care: a multidisciplinary consultative model and an online referral pathway that permits patients to be evaluated by an epilepsy specialist within 1 week from referral.

Method: The VEC is an online, "walk-in" style clinic where appointments are conducted by video conference. Patients across Ontario obtain a referral and register online the day of the clinic to receive a same-day appointment. The Virtual Care Team consists of an epilepsy specialist, a preliminary assessor (physician assistant or nurse) and a social worker from Epilepsy Toronto - a local patient advocacy and services organization. Following every appointment, patients complete a survey based on their experience.

Result: Responder rate was 51% (44/86). Majority of the patients reported that the team listened to their needs and explained treatment options "extremely well" (28/44, 64%) or "very well" (15/44, 34%). Patients' concerns significantly decreased after being seen (reduction from 74/100 to 50/100). Majority of patients were "very likely" or "likely" (34/44, 77%) to use the virtual clinic over a traditional in-person appointment assuming absence of COVID-19 limitations.

Conclusions: High satisfaction from the surveyed patients supports the patient-centred care model. Results indicate that patients are interested in adopting this model of virtual care for specialized areas within medicine, such as epilepsy. It is our goal that these virtual clinics catalyse the improvement of access to specialist care and reduce wait-times in Ontario and Canada.

Abstract Number: 1269

Title: Pilot study on tympanic temperature asymmetry and the lateralization of the epileptogenic zone

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Purpose: Lateralization of the epileptogenic zone remains challenging in some refractory epilepsy patients, and additional sources of information would be useful. There is evidence linking different states of autonomic activation with varying degrees of asymmetry in tympanic membrane temperature (ATMT), and epileptic seizures with hemodynamic changes in the internal carotid artery ipsilateral to the seizure onset in the peri-ictal period. We hypothesized that epileptic seizures could influence ATMT though these processes and that this asymmetry could correlate to the hemisphere of seizure onset.

Methods: We recruited patients consecutively admitted to an epilepsy monitoring unit, where they were under video-EEG monitoring and measured their bilateral tympanic temperatures periodically. These measurements were compared to temperatures measured after any epileptic seizures (as soon as feasible, 5 minutes and one hour afterwards). Lateralization of seizures was determined by analysis of semiology and EEG records.

Results: Patients who had seizures while admitted tended to have higher basal temperatures in their left ears, and five minutes after a seizure, tympanic temperatures tended to be higher in the left ear, regardless of onset.

Comparison of post-ictal temperature records from right and left-sided seizures suggested symmetrically opposite patterns of variation.

Conclusions: Our results suggest that patients' basal ATMT might correlate with susceptibility to seizures, and that the pattern of variation of this asymmetry between the immediate post-ictal and one hour post-ictal could help distinguish right from left hemisphere-onset seizures. A larger study sample will be necessary to draw more definitive conclusions.

Abstract Number: 1270

Title: Safety and tolerability of COVID-19 vaccine among Patients with Epilepsy (PWE) in a tertiary hospital in kuwait: A patient Survey.

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Purpose: With the introduction of COVID-19 vaccines there was a concern among PWE about its safety. This Patient-survey aimed to evaluate the side effects experienced after vaccination.

Method: We administered a survey to PWE who visited the epilepsy clinic at Ibn Sina hospital in Kuwait during the first two weeks of April. It included socio-demographic, epilepsy-related, and vaccine data. Those who were not vaccinated yet were asked about the reasons and their plan.

Result: 111 PWE were surveyed. 80.5% out of 82 vaccinated patients reported at least one side effect. The side effects reported for BNT162b2 (first,second dose); and first dose of ChAdOx1 nCoV-19 were as follows: Injection site pain (40% ,67.6%); 43.8%, fatigue (47%, 32.4%) ;46.9%, Headache (33.3%,35.3%); 34.4% and Myalgia (40%,35%); 50% respectively. Fever (56.3%, p <0.0001), chills (37.5%, p=<0.0001), fatigue (46.9%, p = 0.012), and myalgia (50%, p=<0.0001) were higher after the first dose of ChAdOx1 nCoV-19. Of patients who reported side effects, 66.7% were females, 90.9% were younger than 55 years and 63.6% were on polytherapy. The severity of symptoms was mild in 68% and moderate in 29.3%. The majority (93.9%) did not report seizure worsening. The relative risk of seizure worsening after the first, second BNT162b2, and first ChAdOx1 nCoV-19 vaccines was 1.027 (95% CI 0.891-1.183), 1.019(95% CI 0.928-1.119) and 1.026 (95% CI 0.929-1.134) respectively. Only one patient reported status epilepticus after the first dose of BNT162b2. Out of 29 patients who did not receive the vaccine, 37.9% were still undecided while 34.9% refused. The main reason for opting out was the fear of side effects (42.9%) and epilepsy worsening (23.8%).

Conclusions: This survey demonstrates that the available vaccines have a good safety profile with minimal risk of seizure worsening.

Abstract Number: 1278

Title: Valproic acid-induced hyperammonaemia: clinical significance, standards of management

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Purpose: Hyperammonaemia can be caused by anti-epileptic drug therapy.
The aim of the study was to draw attention to the need for routine determination of serum ammonia levels in this patients.

Method: The analysis included 14 patients (6F, 8M), aged 24-77 years (mean ± SD – 52,36 ± 13,71) with diagnosed epilepsy, implementing VPA monotherapy or polytherapy within the range of 900-2000 mg (mean ± SD – 1292,86 ± 412,24) and L-carnitine, in which the main clinical complaints, apart from poor control of epileptic seizures, were concentration disorders and memory impairment.

Result: VPA levels ranged from 16,9 to 104 µg/mL (mean ± SD – 61,13 ± 23,14). Ammonia concentration ranged from 31 to 100 µmol/L (mean ± SD – 53,42 ± 16,80), in 6 patients (42,85%: 4K – 28,57%, 2M – 14,28%), its value was found to be elevated and also in 1 case, it was also correlated with the increased concentration of VPA in the serum. The neuropsychological examination revealed DCD (discreet cognitive decline) in 4 patients (28,57%) and mild dementia in 1 patient (7,14%). The group of patients with DCD included 4 patients (3F, 1M), aged 49-77 years (mean ± SD – 59,25±12,23)with daily dose 1000 – 1800 mg (mean ± SD –1450±331,66), VPA levels ranged from 68 – 104 µg/mL (mean ± SD –87,54±16,82) and ammonia concentration ranged from 45,6 – 100µmol/L (mean ± SD – 65,40±23,92). In a patient with toxic serum levels of VPA, a decision was made to gradually discontinue treatment, most likely as a consequence of a control neuropsychological examination in terms of cognitive functions. In 1 patient diagnosed with mild dementia, after discontinuation of VPA and conversion to LEV, no improvement was achieved in the control neuropsychological examination.

Conclusions: Determination of ammonia concentration in patients diagnosed with epilepsy using VPA should become routine procedures.

Abstract Number: 1317

Title: Epileptic discharges occur during vulnerable time windows opened by slow oscillations

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Purpose: In patients with epilepsy, high amplitude-short duration events, called interictal epileptic discharges (IEDs) switch abruptly, unpredictably and presumably randomly the spontaneous brain activity to a pathological state during less than a second. The underlying neural syntax that allows such an abrupt transition remains vastly unknown, despite the broad clinical relevance of IEDs. Here, we studied the pre-IED time window to identify potential reproducible neural activity patterns that anticipate IEDs.

Method: We included ten patients who benefitted from intracranial evaluation of refractory, focal epilepsy. We analysed slow oscillations (SO, 0.5-4 Hz and 4-7 Hz) amplitude and spatial synchronization in the second preceding IEDs. Then, we analysed whether IEDs are phase-locked to SO. Finally, we computed the coupling between the amplitude of high-gamma activity, a proxy of neuronal activity, and the phase of SO during the same time window before IEDs.

Result: We show that in the second preceding IEDs, the amplitude and spatial synchronization of SO increase before IEDs, with a spatial selectivity for the irritative zone (IZ). We then show that IEDs are phase-locked to SO, including those recorded remote from the IZ. Finally, we show that the coupling between the amplitude of high-gamma activity and the phase of SO increases only within the IZ in the second before IEDs.

Conclusions: IEDs occur on vulnerable time windows defined by a specific phase, amplitude and spatial synchronization of SO. The locking of IEDs to widespread SO raises the possibility that a large-scale network might participate in the generation of focal epileptic activities. Our interpretation is that during these susceptible windows, the increase in high-gamma modulation might eventually triggers the IEDs. Our findings add to the growing body of evidence that epilepsy should be seen as a distributed oscillopathy.

Abstract Number: 1332

Title: Effect of pharmacotherapy on multidien cycles and seizures in focal epilepsy

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Purpose: In refractory focal epilepsy, cycles of epileptic brain activity organize seizures over multi-day (multidien) timescales, but the effect of treatment on these cycles and their link to seizure rates is unknown. We hypothesized that cycles of epileptic brain activity may vanish with successful treatments.
Method: Epileptiform activity (EA) was recorded over years in 163 participants in the RNS-System clinical trials, who were implanted with an intracranial brain stimulator for detecting and treating seizures. Participants kept a seizure diary, and changes in medications were logged. Using a wavelet transform, we extracted underlying multidien cycles from recordings of EA. We identified timepoints where a new anti-seizure medication (ASM) was started and compared seizure rates among epochs with present or absent multidien cycles of EA after beginning ASM. This measure was evaluated for predictive power by the area under the curve (AUC) of the receiver operating characteristic.
Result: We identified 334 new ASM-trials, of which 91 (27%) led to a >=50% decrease in seizure rate (responders). Relative seizure rate was significantly lower ($p<0.05$ Wilcoxon test) when multidien rhythms of EA vanished after introduction of a new ASM. When measuring the sensitivity-specificity trade-off of using decreases in multidien rhythms of EA as predictor for reduction in seizures at a 3-month horizon, we found an AUC of 0.77-0.79 and 0.80 when predicting 50-90% reduction of seizure rate and seizure freedom, respectively. The same method yielded an AUC of 0.82 when predicting seizure freedom at six and 12 months.
Conclusions: In this cohort, vanishing of multidien cycles of EA following beginning of new ASM was consistently associated with reduced clinical seizure rates and seizure freedom for up to 12 months. Although causality cannot be established, this suggests that multidien EA cycles may play an important role in seizure recurrence over long periods (months to years).

Abstract Number: 1339

Title: 18F-F-FDG-PET characteristics and SPM scoring in patients with anti-GABAb receptor encephalitis

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Purpose: To analyze the brain (FDG)-PET/CT metabolic characteristics of anti-GABAb receptor encephalitis and compare with other defined autoimmune encephalitis.

Method: We retrospectively reviewed clinical data and FDG-PET/CT characters of patients with with anti-GABAb receptor encephalitis. We assessed FDG metabolism of brain regions. The model of metabolism melting with MRI T1 images was established by SPM. Z-score was tested and brain region mean Z scores with magnitudes ≥2.00 were interpreted as significant. SPM-z-score was compared between anti-GABAB receptor encephalitis and other definited AE. The relationship of FDG-PET/CT finding with clinical features also was assessed.

Result: Nine patients with GABAb receptor encephalitis and 33 patients with other definite AE were included in the study. Seven (78.%) patients demonstrated hyper-metabolic regions mainly involving mesial temporal lobe than patients with other AE (P=0.05).%). Notably, the patients with anti-GABAB receptor encephalitis more likely presented seizures than the patients with other definite AE (p=0.02). High metabolism in mesial temporal lobe is also associated with short disease course and poor neurological outcome: Three patients with disease course in 4 weeks showed higher mechanism than the others with disease course more than 4 weeks. (p=0.001). Three patients with high mRS score (mRS 4–5) at discharge also showed higher metabolism in mesial temporal region compared with those who without high mRS score (mRS 0–3) (p=0.001).

Conclusions: (FDG)-PET of patients with GAGAB receptor encephalitis showed hypermetabolism on mesial temporal regions may be the significant pattern. High metabolism is also associated with seizure occurrence, short disease course and high mRS score.

Basic Sciences

Abstract Number: 64

Title: Collaborative Cross mice reveal extreme epilepsy phenotypes and genetic loci for seizure outcomes

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Purpose: Epilepsy is a neurological disorder with complex etiologies and genetic architecture. Animal models play a fundamental role in understanding the pathophysiology of epilepsy and identifying therapeutic interventions. However, existing animal models of epilepsy do not reflect the high level of genetic diversity found in the human population. The Collaborative Cross (CC) population is an innovative recombinant inbred panel of mice. The CC offers large genotypic and phenotypic diversity, as well as powerful genomic tools including whole genome sequence to facilitate identification of candidate genes and candidate variants.

Method: Here we measured multiple epilepsy related traits in 35 CC strains using flurothyl kindling model. We created an F2 population with extreme seizure susceptibility and performed quantitative trait loci (QTL) mapping to identify genomic regions associated with seizure sensitivity. We used quantitative RNA sequencing from CC hippocampal tissue to identify candidate genes and whole genome sequence to identify genetic variants likely affecting gene expression.

Result: Among 35 CC strains, we identified novel animal models that exhibit extreme outcomes in seizure susceptibility, seizure propagation, epileptogenesis, and sudden unexpected death in epilepsy. To identify the genetic loci that control the seizure sensitivity, we characterized a F2 mapping population by crossing the seizure susceptible and seizure resistant strains. We then performed QTL mapping and identified one known and seven novel loci associated with seizure sensitivity. We found *Gabra2* is differentially expressed in hippocampi between the parental strains and identified an intronic indel (rs225241970) that most likely causes gene expression variation in *Gabra2*.

Conclusions: The CC provides a powerful toolbox for studying complex features of seizures and for identifying genes associated with seizure outcomes, and hence will facilitate the development of new therapeutic targets for epilepsy

Abstract Number: 85

Title: Temporal evaluation of type 2 and 4 muscarinic receptors transcripts in rats with status epileticus treated with sparteine

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Purpose: Evaluate the effect of sparteine (Sp) on type 2 and 4 muscarinic-receptors transcripts (m2 y m4, respectively) in rats after 24 and 72h of *status epilepticus* induced by kainic acid (KA).

Method: Wistar rats (200-350 g) were separated in two groups according with time of transcripts evaluation: 24 and 72h (n=18, per time); each group included three control subgroups (n=4, per subgroup): saline solution (SS; 0.09%, i.p.), Sp (30 mg/kg, i.p.) and KA (10 mg/kg, i.p.); also one experimental subgroup (n=6): Sp administrated 30 min before KA (Sp+KA). Animals were sacrifice; hippocampi were extracted and preserved with TRIZOL reagent at -80°C until total RNA extraction and cDNA synthesis for qPCR assays. Relative expressions were calculated by the 1/ΔCt method, and two-way ANOVA with Tukey post-hoc were performed.

Result: Relative expression of m2-receptor did not show significant differences between subgroups or time. While the expression of m4, after 24h of drugs administrations was significantly reduced in Sp+KA compared with SS (0.095±0.0048 vs 0.1275±0.0030; $p<0.0004$) and with Sp (0.1276±0.0026; $p=0.0107$); likewise, it was reduced in KA (0.099±0.0048) versus SS ($p=0.0013$) and Sp ($p=0.0324$), but no significant changes were observed in Sp+KA versus KA. After 72h, m4 expression in Sp+KA was increased compared with KA (0.140±0.0115 vs 10.65±0.0044; $p=0.0085$) and with Sp (0.079±0.0078; $p<0.0001$); as well as in KA group compared with Sp ($p=0.0421$). In addition, the expression of m4 at 24h compared with 72h was significantly increased in Sp+KA but reduced in Sp subgroups.

Conclusions: Increased expression of m4 after 72h of treatment in KA and Sp+KA subgroups could be due to a compensatory response to reduce hyper-excitability. Moreover, the significantly enhanced expression of m4 by Sp pre-treatment, agrees with its proposed anti-convulsive mechanism of action. However, more assays are needed to elucidate the subjacent anticonvulsive mechanism of Sp.

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Abstract Number: 152

Title: Spike component of EEG seizures has identical frequency properties across different rat models of epilepsy

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Purpose: Frequency properties of the EEG characteristics of different seizure types including spike-wave discharges (SWD) have been described for various rodent models of epilepsy. However, little attention has been paid to the frequency properties of individual spike-wave complexes (SWC) constituting these electrographic seizures. Meanwhile, knowledge of these properties is important for understanding the mechanisms underlying seizure generation. Besides, these properties may be used for identification of

epileptiform activity and seizure detection. Here we compared the frequency properties of SWCs in different models of epilepsy.

Method:A software package was designed and used for extraction and frequency analysis of SWCs from long-term EEG of four spontaneously seizing, chronic epilepsy models: post-status epilepticus model of temporal lobe epilepsy; fluid percussion injury model of post-traumatic epilepsy; and two genetic models of absence epilepsy – GAERS and rats of the WAG/Rij strain. The SWCs were separated into fast (three-phasic spike) and slow (mostly containing the wave) components. Eight different animals from each model were used (24 recordings, 108362 SWCs in total). In addition, we compared the amplitude spectra (AS) of experimental SWCs with AS of SWCs generated by a computer model of a cortical neuronal population.

Result: We found that the three-phasic spike component was similar in all animal models both in time and frequency domains, their AS showed a single expressed peak at 18-20Hz. The AS of the SWC generated by computer model resembled the shape and peak frequency of experimental ASs. The slow component showed larger variability across rat models.

Conclusions: Despite differences in seizure morphology between different rat models, the frequency composition of spike component of single SWCs is identical and probably does not depend on the particular epilepsy model or type. This fact may be used for development of universal algorithms for seizure detection applicable to different rat models of epilepsy.

Abstract Number: 176

Title: Differential Characteristics of Regional Brain Activation in Three Different Epilepsy Models---An EEG study

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Purpose: To investigate the electrophysiological characteristics of different epilepsy models, especially the EEG activities of different brain subareas, clarify the temporal-spatial effects of specific biomarkers expression in different epileptic models and summarize the characteristics of different epilepsy models.

Method: Seizure response by a convulsive dose of PTZ, Lithium-pilocarpine and kainic acid, which establish three different epilepsy models. Local activity was recorded in different brain regions by EEG recording and c-Fos staining at different time points after seizure induction in each model. Spontaneous recurrent seizures were observed in different models and mossy fiber sprouting were studied by Znt-3 staining.

Result: PTZ, Li-Pilo and KA epilepsy models all showed significant seizure activities in behavioral and electrophysiological aspects in the acute phase of seizure induction. Their behavioral and electroencephalographic process from low-stage seizures to synchronized high-stage seizures were similar, but the latency and duration of seizures at different stages and their EEG pattern were different. EEG and c-Fos expression studies showed that a group of activated brain structures including mPFC, hippocampal structure, amygdala and striatum could be found in all three models, and the activation degree of hippocampal DG was the strongest, followed by CA3, suggesting that these brain structures were involved in the occurrence, development and regulation of epilepsy. EEG activities of spontaneous recurrent epilepsy were observed in Li-Pilo and KA model from 7-14 days after initial seizure induction. Mossy fiber sprouting was positive in animals with spontaneous recurrent epilepsy, which might validate mossy fiber sprouting as pathological basis of spontaneous recurrent epilepsy.
Conclusions: These findings validated general behavioral and electrophysiological features of three different epilepsy models. In these models, instinct spatial-temporal profiles of regional brain activation were observed, which might implicate different underlying mechanisms. It provides a theoretical basis for future study on epilepsy to select appropriate epilepsy models.

Abstract Number: 241

Title: Mechanistic approach behind neuroprotective effect of Brivaracetam against seizures induced cognitive impairment in rats: A one bullet two hit model

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Purpose: Epilepsy is a chronic neurological disorder mostly associated with cognitive impairment in many patients. Multiple factors were found to be involved in causing cognitive decline in patients with epilepsy. The present study aim to evaluate the mechanisms for protective effect of brivaracetam against cognitive impairment induced by kindling model of seizures in rats.

Methods: Male Wistar rats were kindled with pentylenetetrazole (30 mg/kg, i.p.) for 28 days. Brivaracetam (10 and 20 mg/kg, i.p.) was administered to kindled rats for 15 days. The seizure scoring was done by Racine scale for 30 mins daily. The cognitive functions were determined by Morris water maze, elevated plus maze and passive avoidance tests. Inflammatory markers (IL-1β, IL-6 & TNF-α), apoptotic markers (caspase-1 and 9), metalloproteinases (MMP-2 and 9), BDNF, GSK-3β, MAPK/JNK/ERK pathway, Protein Kinase C and PP2A, amyloid beta and phosphorylated tau were studied.

Results: Kindling model of epilepsy produced significant cognitive impairment ($p<0.01$) in rats and brivaracetam showed dose dependent protection against it. BRV at 10 ($p<0.05$) and 20 mg/kg ($p<0.01$) significantly improved cognitive impairment [Morris water maze, elevated plus maze and passive avoidance tests ($p<0.01$)] in the PTZ kindled rats. It also showed significant anti-inflammatory [IL-1β, IL-6 & TNF-α ($p<0.01$)], anti-oxidant [GSH, MDA, SOD ($p<0.001$)] and anti-apoptotic [caspase 1 and 9 ($p<0.001$)] potential. It markedly reversed the levels of MMP-2, MMP-9, GSK-3β, BDNF at the dose of 20 mg/kg as compared to PTZ kindled rats. Treatment with BRV normalized the expression of p38, JNK, ERK1/2, PKC and PP2A in kindled rats.

Conclusion: Multiple pathways have been found to be involved in cognitive impairment induced by seizures. The present study provided the evidence for different mechanisms of protective action of BRV against seizures induced cognitive impairment so as to establish a model of one bullet with two hits.

Abstract Number: 260

Title: Non-cell autonomous hyperexcitability underlies focal epileptogenesis mediated by low-level brain somatic mutations in MTOR

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Purpose: Low-level somatic mutation in neurons in the brain causes intractable focal epilepsy, including focal cortical dysplasia type 2 (FCD II) (Lim *et al. Nat Med* 2015;21:395-400.) and ganglioglioma (Koh *et al. Nat Med* 2018;24:1662-1668.). However, a specific mechanism, how these few mutation-carrying neurons induce epileptogenesis at the "local network level", remains poorly understood.

Method: We generated FCD II model mice having a somatic mutation in *MTOR* L2427P presenting seizures by *in utero* electroporation and ascertained the number of mutated neurons ($MTOR^{L2427P}$) throughout the whole brain along with patients-derived tissue. To probe the origin of epileptogenesis, we measured the neuronal excitability in $MTOR^{L2427P}$ and nearby non-mutated neurons ($L2427P^{nearby}$) by current injection and multi-

electrode recording comparing the topographic distribution of mutation. Computational connectivity using the leaky-integrate-and-fire model recapitulates network changes based on measured properties. To examine the underlying mechanism, we measured excitatory and inhibitory (E-I) synaptic inputs in $MTOR^{L2427P}$ and $L2427P^{nearby}$ by electrophysiological and immunofluorescence studies. To explain non-cell autonomous hyperexcitability, an inhibitor of adenosine kinase (ADK), which translation is increased by $MTOR^{L2427P}$ in ribosome-sequencing, was injected into mice *in vivo*.

Result: 1.85±0.80% of neurons carried the *MTOR* somatic mutation in the whole brain. Interestingly, the seizure-triggering hyperexcitability was originated from $L2427P^{nearby}$, but $MTOR^{L2427P}$ was less excitable than $L2427P^{nearby}$(P<0.0001). Consistent with estimation by the network simulation, functional and molecular study showed that the net balance between E-I synaptic inputs onto $MTOR^{L2427P}$ remained unchanged in mice and FCD II patients' tissues, implying that intrinsic synaptic changes driven by *MTOR* mutation are less likely to be explanatory. Instead, we found that ADK inhibition reduced the hyperexcitability of $L2427P^{nearby}$(P<0.0001), affecting adenosine metabolism in the local network.

Conclusions: Taken together, neurons carrying somatic mutations in *MTOR* lead to focal epileptogenesis via non-cell autonomous hyperexcitability of nearby non-mutated neurons.

Abstract Number: 269

Title: Correlation Between Weight and Apomorphine Induced Rotation in Genetic Absence Epilepsy Rats from Strasbourg

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Purpose: Although there are clinical data on the coexistence of epilepsy and Parkinson's disease (PD) in literature, this interaction has not been studied experimentally. The administration of 6-hydroxydopamine (6-OHDA) to nigrostriatal pathway is one of the common experimental animal models of PD. In this model apomorphine-induced rotation test can be used to evaluate the degree of motor deficit. Present study evaluated relation between body weight change (BWC) and the degree of neurodegeneration in Genetic Absence Epilepsy Rats from Strasbourg (GAERS).

Method: According to injection site, 30-days old GAERS (15 male) were divided into 2 groups: Striatum (n=6) and medial forebrain bundle (MFB) (n=9). GAERS were stereotaxically injected unilaterally with 8 µg/4 µL 6-OHDA per location. Injections were performed at two locations for striatum lesion (AP:-0.5, ML:3.0, DV:6; AP:-1, ML:3.0, DV:6) and one for MFB (AP:-1.4, ML:1.6, V:7.1). Three weeks later, rotation test was performed with 0.05 mg/kg subcutaneous apomorphine. Rotation was counted for 30 minutes. Rats were weighed before 6-OHDA injection (first measurement) and rotation test (second measurement). BWC was calculated as [(second measurement-first measurement)/first measurement]x100. Data were expressed as mean±standard error of mean and analyzed with Pearson Correlation test by using GraphPad Prism. Statistical significance was set at p<0.05.

Result: BWC was %81.5±6.95 and rotation count was 153±51 in the striatum group while BWC was %91.6±4.28 and rotation count was 252±40 in the MFB group. There was statistically significant negative correlation between BWC and rotation counts in striatum group (r=-0.89; p=0.017) while there was low negative correlation in MFB group (r=-0.48; p=0.191). The correlation in MFB group was not statistically significant, but had moderate effect size (0.3<r<0.5)

Conclusions: This study shows that as the BWC decreases, the rotation counts increases, suggesting that BWC can be used as a predictor of neurodegeneration.

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Abstract Number: 309

Title: Chemogenetic Activation of Corticothalamocortical Feedforward Inhibitory Parvalbumin Expressing Interneurons During Absence Seizures: An EEG Study

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Purpose: Feedforward inhibition (FFI) within the brain controls the firing of principal excitatory neurons and prevents runaway excitation. In the corticothalamocortical (CTC) network, dysfunctional FFI has been implicated in absence seizure generation in some rodent models of absence epilepsy. FFI is primarily mediated by parvalbumin-expressing (PV+) inhibitory interneurons. The hallmark of absence seizures is spike-wave discharges (SWDs) measuring 3-4 Hz on electroencephalogram with concomitant behavioural arrest. We previously demonstrated that functionally silencing PV+ interneurons in the CTC network is sufficient to generate absence-like SWDs. In this study, we aimed to investigate the consequences of activating PV+ interneurons during absence seizures.

Method: We used Designer Receptors Exclusively Activated by Designer Drug (DREADD) technology to excite CTC PV+ interneurons during chemically-induced absence seizures. Selective expression of DREADDs in PV+ interneurons was achieved by breeding excitatory Gq-DREADD (hM3Dq-flox) mice with PV-Cre mice; and confirmed using confocal microscopy. Gq-DREADD receptors in PV+ interneurons were activated by the 'designer drug' clozapine-N-oxide (CNO) during pentylenetetrazole (PTZ) induced seizures.

Result: CNO activation of PV+ interneurons in PV^{Cre}/Gq-DREADD mice, treated with PTZ to chemically induce absence seizures, either prevented (in 36% animals) or significantly reduced the severity of seizures. Overall, the time spent in absence seizures was reduced by more than 80% (day 1: 24.5±8.1 sec; day 2: 3.68±1.97 sec); the total number of discharges was also reduced (day 1: 5.92±1.67 sec; day 2: 1.64±0.82 sec); and seizure onset was delayed (day 1 with PTZ: 3.84±0.43 min; day 2 with PTZ and CNO: 9.16±2.11 min; p=0.02). In contrast, CNO injection was ineffective against PTZ-induced seizures in non-DREADD wildtype control animals.
Conclusions: These data suggest that activation of FFI within the CTC network could be a strategy for anti-seizure therapy. PV+ interneurons could be a potential therapeutic target to control absence seizures in some cases of human absence epilepsy.

Abstract Number: 325

Title: Dravet Syndrome Advanced Therapies European Working Group: An innovative Patient Advocacy Organization-driven approach to accelerate research

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Purpose: Dravet syndrome (DS) is a rare and severe type of epilepsy with a high risk of sudden unexpected death. There is no current cure for it, and traditional pharmacology has not been able to tackle this condition. Given that 80-90% of cases originate due to mutations in *SCN1A*, gene replacement and regulation approaches arise now as potential treatments for DS. A number of research groups are currently working on novel advanced therapy strategies to cure DS. Collaboration usually speeds up drug development timelines, but this is often impaired by scientific academic competition.

Method: Here, we present a first-in-class approach to foster collaboration and speed up project timelines, put in place in 2020 by Dravet Syndrome Foundation Spain, a patient advocacy organization strongly involved in research. This consortium, named DS Advanced Therapies European Working Group (DS ATEWG), gathers the main European experts investigating innovative therapies for DS, and it functions on the basis of networking, mutual learning and collaboration.

Result: Group members interact during confidential bimonthly online meetings where results are discussed and troubleshooting is applied. Resources to increase engagement and education, such as industry and clinical webinars and face-to-face networking events and workshops, are also provided.

Conclusions: By presenting the DS ATEWG and the strategy followed for its implementation, we expect to encourage other organizations and laboratories to replicate our system to maximize resources and the impact of their research, eventually accelerating the development of novel therapies for the benefit of patients.

Abstract Number: 328

Title: Predicting excitation and inhibition changes underlying epileptic state transitions in hippocampal rodent slices with and without stimulation

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Purpose: Computational modeling is a powerful tool for exploring brain mechanisms underlying neurophysiological observations. Nowadays, it is increasingly used to design and evaluate the effect of therapeutic interventions, such as brain stimulation. In this contribution, the computational approach is used to predict the dynamics of excitation, slow dendritic and fast somatic inhibition associated with seizure-like events in a high potassium model of epilepsy with and without single pulse stimulation.

Method: Building on the modeling work of Wendling et al. (J Clin Neurophysiol 2005;22(5):343–356.), we replicate hippocampal rat slice data recorded in our group. We fit simulated and real data segments and identify different types of epileptic activity (interictal, pre-onset, onset, ictal). The procedure provides us with estimates of the time-evolving levels of excitatory and inhibitory synaptic gains. We investigate the likelihood of immediate, pairwise transitions between the types of activity, long-term transitions (cycles from interictal to ictal and back), and associated excitation and inhibition changes.

Result: Spontaneous transitions (n=1266) show a high stability of the interictal state (90.9±6.1% remaining interictal) that is significantly decreased for stimulation-induced transitions (n=95, 24.5±23.4%, $p<0.001$). This seizure facilitation effect is accompanied by a modulation of fast inhibition. Long-term results evidence a shortened cycle length, measured in number of segments per cycle, for stimulation (n=25, 9.6±3.8) compared to no stimulation (n=65, 12.2±4.7, $p=0.014$). We find a steady increase of slow inhibition accompanying the long-term transition to seizure.

Conclusions: Seizure facilitation effects of single pulse stimulation might be associated with changes in somatic inhibition. Long-term increases in dendritic inhibition might be linked to ictogenesis and could serve as a target for designing anti-seizure stimulation.

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Abstract Number: 344

Title: Electrophysiological and behavioral evaluation of anticonvulsant effect of the antioxidants allopurinol and ellagic acid on the status epilepticus

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Purpose: Determine the anticonvulsant effect of the antioxidants allopurinol and ellagic acid during status epilepticus (SE) induced by pilocarpine.

Method: Male Wistar rats (200-250 g) were implanted with a guide cannula in the lateral ventricle for pilocarpine (PILO) administration as well as electrodes for recording the electrical activity of the hippocampus during SE. Study groups: NaCl (0.9%, control group, n = 6), PILO (2.4 mg / 2µl, n = 6), PILO + allopurinol (ALL, 50 mg / kg ip, administered 60 min post-SE, n = 6), ALL + PILO (administered 30 min before PILO, n = 6), PILO + ellagic acid (EA, 50 mg / kg ip, administered 60 min post-SE, n = 6), EA+ PILO (n = 6, administered 30 min before PILO). Amplitude and frequency were analyzed 5, 15 and 30 min post-PILO, during SE and 60, 75 and 90 min post-SE. Convulsive behavior was evaluated with Racine's scale at the same time to obtain a better correlation.
Result: Administration of ALL or EA decreased the convulsive behavior and epileptiform activity during SE compared to PILO group. However, a greater effect was observed when ALL or EA was administered as pretreatment 30 min before PILO, decreasing epileptiform activity (amplitude of discharges) 57.6% and 79.1%, respectively. In addition, the severity of SE was decreased, showing a lower presence of seizures type 4 and 5. Even the antioxidants increased the latency period for the SE from 27.2 ± 2.6 to 45.8 ± 3.31 min.

Conclusions: The antioxidants ALL or EA significantly decreased the convulsive behavior and epileptiform activity, having a potential effect on the reduction of SE severity, being able to be a promising candidate against seizures in this model to mitigate or decrease oxidative damage as well as a therapeutic strategy against seizures. Financed by PROMEP 511-6/18-9169/UDG-PTC-1467 and PROSNI-2020-KPP.

Abstract Number: 353

Title: Effects of selective septo-hippocampal lesions in experimental epilepsy

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Purpose: Temporal lobe epilepsy (TLE) is the most common type of partial epilepsy in adults, characterized by recurrent spontaneous seizures, and associated with tissue abnormalities of gray and white matter structures. Although the septo-hippocampal pathway has shown structural alterations in TLE patients, the specific role of the medial septum (MS)-hippocampus GABAergic and cholinergic circuit has not been fully elucidated. This

study aimed to longitudinally evaluate tissue changes after lesioning the MS and how depletion of specific neuronal populations modulate the establishment of status epilepticus (SE) in an animal model of chronic TLE.

Method: Young adult male Sprague-Dawley rats received either sham (PBS), or GABAergic or cholinergic MS lesion using GAT1-saporin or 192IgG-saporin, respectively. Twelve days later, the animals were submitted to a systemic pilocarpine-induced SE. Animals were scanned using diffusion tensor imaging (DTI) at four time-points: prior and after lesion, and 24 and 64 days post-induction. Fractional anisotropy was evaluated in fimbria and dorsal hippocampus for all time-points. Immunoreactivity for parvalbumin and choline acetyltransferase was used to visualize GABAergic and cholinergic MS neurons, respectively.

Result: Both intraseptal treatments significantly reduced the number of parvalbumin and choline acetyltransferase-ir neurons. However, no progressive changes of DTI parameters in fimbria and dorsal hippocampus were observed. Those animals submitted to the septal lesion and the SE induction showed: the expected time-dependent diffusion changes in fimbria due to the SE and an increased mortality rate in the case of the GABAergic lesion. Contrastingly, injection of the cholinergic saporin did not increase mortality rate.

Conclusions: Selective septo-hippocampal modulation impacts the animals' susceptibility during the pilocarpine model. Current DTI evaluations were not sensitive to down-stream axonal alterations induced by septal lesions, yet showed substantial abnormalities after SE induction.

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Abstract Number: 357

Title: Identifying the Top 10 Epilepsy Research Priorities in Canada

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Purpose: A common gap in health research agendas is that they may not reflect the needs of people who live and work with the condition or disease. The James Lind Alliance (JLA) provides a process for increasing public engagement in research by consulting patients, caregivers and health care providers regarding their most pressing unanswered questions or evidence uncertainties. The JLA epilepsy priority-setting partnership was undertaken to identify and prioritize unanswered questions relating to the cause, diagnosis, treatment and management of epilepsy and its comorbidities.

Method: In a survey conducted from October 2019–Feb 2020, stakeholders across Canada were asked to submit their questions about epilepsy and seizures. Basic demographic information was also collected. Under the guidance of a national steering committee composed of patients, caregivers and clinicians, and led by a team of information specialists, submissions were formed into research questions and checked against existing evidence. A list of 43 unanswered questions was sent out in an interim survey between January and March 2021. This survey asked respondents to select up to 10 questions they thought were most important. In April 2021, a workshop will be held with representatives from all stakeholder groups where a final top 10 list will be reached by consensus.

Result: A total of 516 Canadians submitted over 1000 questions for review. Submissions were refined, summarized and categorized into 198 unique research questions. Results from the interim survey were used to generate a short list of 16 questions which will help inform the top 10 list to be compiled at the final workshop.

Conclusions: The top 10 list will be shared with researchers and research funding organizations to help them identify what is most important to people with epilepsy and/or seizures as well as their care providers and incorporate their priorities when planning future research projects.

Abstract Number: 370

Title: Selection of the interictal segment for localization of the seizure focus: Timing matters

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Purpose: Localization of the epileptogenic zone (EZ) is crucial for successful surgical treatment of drug-resistant focal epilepsy. Interictal markers are usually assessed in random 5-10-minute stereo-electroencephalographic (SEEG) segments. However, state of vigilance, circadian and multidien rhythms are known modulators of epileptic activity. To study differences in EZ localization between various interictal segments, we analyzed segments with minimum and maximum spiking, reflecting the two extremes of variability in epileptic activity.

Method: Ten patients with drug-resistant focal epilepsy undergoing SEEG and subsequent surgery with Engel 1 outcome were selected. Spikes were detected in 48-72-hour recordings. Sleep was scored visually. Ten-minute segments (>10-minutes away from seizures) with minimum (SEG1) and maximum (SEG2) spike rates were selected in each patient. Spike and high-frequency oscillation rates, power, spectral entropy, correlation, relative entropy, phase-synchrony, phase-consistency, and phase-lag index were calculated in 1-4Hz, 4-8Hz, 8-12Hz, 12-20Hz, 20-45Hz, 65-80Hz, 80-250Hz, and 250-600Hz, and used to train a support vector machine model. The model labeled each SEEG contact as EZ or non-EZ. The labels were tested against resected-SOZ contacts, and evaluated by the area under the receiver operating curves (AUCs) for SEG1 and SEG2.

Results: A mean AUC of 0.79 was achieved in SEG1 and 0.85 in SEG2 ($p=0.028$). Distribution of vigilance states associated with SEG1 (6 Wake, 2 N2, 2 N3) and SEG2 (9 Wake, 1 N2) did not differ ($p=0.13$). The average distance between SEG1-SEG2 was 19.7±12.8 hours. The average distance from seizure was 7.7±6.3 hours in SEG1 and 4.9±4.6 in SEG2 ($p=0.26$).

Conclusion: Preselection of interictal SEEG segment influences the performance of EZ localization algorithms. We propose a data driven approach by selecting the 10 minutes with maximum spiking. The state of vigilance seems to be less important than multidien modulation.

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Abstract Number: 388

Title: Modulation of kynurenine pathway in the hippocampus of patients with hippocampal sclerosis: A possible cause of hyperexcitability

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Purpose: Hippocampal sclerosis (HS) is the most common form of drug-resistant epilepsy where temporal lobe structures are responsible for unprovoked seizures. The hallmark of HS is enhanced glutamatergic excitatory neurotransmission. Kynurenic acid (KYNA), a tryptophan-kynurenine pathway metabolite, is the only natural inhibitor of glutamate receptors. It is synthesized from kynurenine (KYN) in presence of kynurenine aminotransferase II (KAT II) and Pyridoxal 5-phosphate (PLP; co-factor for KAT II) within cortical astrocytes. PLP, in turn, is synthesized from pyridoxine in presence of Pyridoxamine 5'-Phosphate Oxidase (PNPO). The present study was designed to test the hypothesis that in HS, altered endogenous kynurenic acid synthesis results in hyperexcitable synaptic transmission.

Method: The total KYN, KYNA and PLP concentration in tissue were determined using HPLC. Spontaneous excitatory post synaptic currents (EPSCs) were recorded from pyramidal neurons in presence of endogenously synthesized KYNA using whole cell patch clamp. mRNA and protein expression of KAT II and PNPO enzyme were investigated by qPCR and western blot respectively.

Result: KYN concentration was unchanged but KYNA concentration was significantly reduced in HS hippocampus (0.028 ± 0.003 ng/µg protein; n=43) compared to non-seizure controls (0.16 ± 0.03 ng/µg protein; n=24). De novo synthesis of KYNA from kynurenine was also significantly reduced in HS hippocampus. Spontaneous EPSCs were not suppressed in presence of endogenously synthesized KYNA in HS hippocampus. KAT II mRNA expression was unaltered but protein expression was downregulated. PLP concentration also significantly reduced in HS hippocampus (9.31 ± 2.49 ng/mg of wet tissue in non-seizure control vs 2.04 ± 0.75 ng/mg of wet tissue in HS). PNPO mRNA as well as protein level expressions were downregulated.

Conclusions: Dysfunctional KYNA synthesizing machinery results from reduced PLP concentration and KAT II expression which consequence in reduced endogenous KYNA synthesis from KYN. This contributes to hyperexcitabilty associated with HS.

Abstract Number: 419

Title: Electrographic Features of Spontaneous Recurrent Seizures in A Mouse Model of Extended Hippocampal Kindling

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Purpose: Kindling through repetitive brief stimulation of a limbic structure is a commonly used model of temporal lobe epilepsy. Particularly, extended kindling over a period up to a few months can induce SRS, which may simulate slowly evolving epileptogenesis of temporal lobe epilepsy. Currently, electroencephalographic (EEG) features of SRS in rodent models of extended kindling remain to be detailedWe ainm to establish a mouse model for future examinations of kindling induced spontaneous recurrent seizures (SRS) in genetically/molecularly manipulated mice.

Method: We recorded intracranial EEG from the kindled hippocampus and an unstimulated forebrain structure in individual mice. The unstimulated structure was alternated in five groups of mice and targeted the hippocampus, parietal cortex, piriform cortex, entorhinal cortex, or dorsomedial thalamus. We also prepared brain slices from kindled and control mice to examine local circuitry excitability and susceptibility to induce epileptiform activity.

Result: Spontaneous EEG discharges with concurrent low voltage fast onsets were observed from the two corresponding areas in nearly all SRS detected, irrespective of associated motor seizures. Examined in brain slices, epileptiform discharges were induced by alkaline artificial cerebrospinal fluid in the hippocampal CA3, piriform and entorhinal cortical areas of extended kindled mice but not control mice.

Conclusions: Together these in vivo and in vitro observations suggest that the epileptic activity involving a macroscopic network may generate concurrent discharges in forebrain areas and initiate SRS in hippocampally kindled mice.

Abstract Number: 455

Title: Robust chronic convulsive seizures, high-frequency oscillations, and human seizure onset patterns in an intrahippocampal kainic acid model in mice

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Purpose: Although the intrahippocampal kainic acid (IHKA) model has been widely used to simulate temporal lobe epilepsy (TLE) in mice, there is variation in outcomes, with many studies showing few robust seizures long-term, especially convulsive seizures. We present an implementation of the IHKA model with frequent chronic convulsive seizures that are robust in frequency, duration and both sexes can be used.

Method: Our methods varied slightly from prior studies. We employed continuous wideband video-EEG from 2 cortical and 2 hippocampal sites to characterize chronic epilepsy outcomes in both sexes and 2 timepoints (2-4 and 10-12wks post-IHKA).

Result: Analysis of convulsive seizures at 2-4 and 10-12wks post-IHKA showed a robust frequency (2-4/day on average) and duration (typically 20-30 sec) at each time. Comparison of the 2 timepoints showed that seizure burden became more severe in approximately 50% of the animals. We show that almost all convulsive seizures could be characterized as either low-voltage fast or hypersynchronous onset seizures, which has not been reported in a mouse model of epilepsy and is important because these seizure types are found in humans. In addition, we report that high-frequency oscillations (HFOs, >250Hz) occur, resembling findings from IHKA in rats and TLE patients. Pathology in the hippocampus at the site of IHKA injection was similar to mesial temporal lobe sclerosis and reduced contralaterally.

Conclusions: In summary, our methods produce a model of TLE in mice with robust convulsive seizures, show variable progression, that HFOs are robust also, and that the model has seizures with onset patterns and pathology like human TLE. We believe our results will advance the ability to use the IHKA model of TLE in mice. The results also have important implications for our understanding of HFOs, progression and other topics of broad interest to the epilepsy research community including preclinical drug screening.

Abstract Number: 460

Title: Identifying different seizure onset and termination patterns and detecting the driver region preceding different onset patterns

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Purpose: The study of seizure onset and termination patterns has the potential to enhance our understanding of the underlying mechanisms of seizure generation and cessation. Seizure onset patterns have received considerable attention; however, it is largely unclear whether seizures with distinct onset patterns terminate

through different mechanisms. On the other hand, at the network scale, it remains to be elucidated if the network interactions leading to the emergence of different onset patterns is different.

Method: We investigated the morphology of 103 ictal intracranial EEG recordings from 20 patients with drug-resistant focal epilepsy, classified onset and termination patterns and performed spatial network analysis.
Result: We identified nine seizure onset and seven seizure termination patterns. However, we detected an association between some onset and termination patterns, our results indicated that seizures with almost any onset pattern could terminate through common termination patterns. By investigating the directionality of the net flow between seizure onset zone and the surroundings using a measure of directed functional connectivity during the preictal period, we found higher inflow to seizure onset zone from other regions in gamma and high gamma frequency ranges prior to the generation of seizures with fast activity onset compared to seizures with hypersynchronous onset.

Conclusions: Considering the suggested association of high-frequency oscillations with the inhibitory activity, our findings indicate the involvement of inhibitory inflow to seizure onset zone from the surrounding regions in the generation of seizures with Fast onset activity as opposed to the Hypersynchronous onset pattern. This suggests the existence of different mechanisms underlying the generation of seizures with different onset patterns.

Abstract Number: 506

Title: Genetic susceptibility to acquired epilepsy determines the acute response to traumatic brain injury in rats

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Purpose: Traumatic brain injury (TBI) is a common cause of seizures and epilepsy. While poorly understood, genetic differences may contribute to why seizures develop after TBI in some individuals but not others. In this study, we investigated whether strain-specific differences in inherent susceptibility to seizures influence the acute response to an experimental TBI, using selectively-bred rats that are seizure-prone (FAST) or seizure-resistant (SLOW).

Method: 11-week old male rats (FAST, SLOW, or two control strains) received a moderate fluid percussion injury or sham-surgery (n=6-16/group). Rats then underwent acute injury measures, serial blood collection and neuromotor assessments. Brains were collected at 7 days for immunofluorescent staining of activated inflammatory cells, to explore the hypothesis that inflammation may be associated with seizure susceptibility after TBI.

Result: FAST rats showed an exacerbated physiological response acutely post-injury, with a 100% seizure rate and mortality within 24 hours. Conversely, SLOW rats showed a reduced response, with no acute seizures and a more rapid neuromotor recovery, returning to baseline by 7 days post-TBI. Differences were also apparent between the control strains, with TBI Long Evans rats showing a neuromotor deficit persisting to day 7 ($p<0.001$), when the performance of TBI Wistar rats had returned to baseline. Long Evans TBI rats showed the most pronounced inflammatory response to TBI, in several regions including the fimbria, internal and external capsules, lateral cortex, hippocampus and thalamus. Region-specific brain atrophy after TBI was also strain-dependent, with Wistar rats being the only strain to show a reduction in fimbria and corpus callosum volumes compared to their sham controls.

Conclusions: Results together indicate strain differences in the acute response to TBI, as well as acute seizure susceptibility. Findings support further investigation into whether strain differences determine the chronic development of post-traumatic epilepsy, to provide novel insight into the genetic basis of epilepsy risk.

Abstract Number: 508

Title: GABAA Receptor subunit configuration alteration & its correlation with age of epilepsy onset

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Purpose: Focal cortical dysplasia (FCD) is known as a group of malformations of cortical development, which are supposedly related to early developmental defects in the brain. The aim of our study was to determine any differences in FCD based on age of onset.

Methods: Clinical and experimental studies were conducted in patients with early age of onset (EO) FCD--refractory seizures between 0-9 years of age (n=29) vs late age of onset (LO) FCD had drug refractory seizures after 10 years of age (n=10) as compared to non-epileptic controls. Differential expression of $GABA_A$ receptor subunits α1, α4, α5, β3, γ2, δ and Chloride Co transporter expression of NKCC1 and KCC2 were evaluated using qPCR, western blot and immunohistochemistry. The qualitative analysis of GABA and glutamate neurotransmitters were done using HPLC.

Results: More drug resistant cases with FCD type II in patient with EO FCD with a predilection to the frontal lobe. A stark contrast from patients with LO FCD which had fewer drug resistant cases and dominance of FCD type I with changes present in the temporal lobe. The experimental data revealed a significantly lower concentration of GABA neurotransmitter in patients with EO FCD as compared to patients with LO FCD. The ratio of α4/α1 $GABA_A$ receptor subunits was significantly higher for patients with EO FCD as compared to patients with LO FCD. Further the Chloride Co transporter ratio expression NKCC1/KCC2 was also increased in patients with EO FCD.

Conclusion: These results suggest a more critical disruption of inhibitory network causing aberrant depolarizing $GABA_A$ receptor currents resembling immature brain in patients with EO FCD. Such effects were not as prominent in patients with LO FCD. Therefore, age of onset emerged as a strong predictor of severity of the dysregulation of inhibitory neurotransmission in patients with FCD.

Abstract Number: 511

Title: Early administration of brivaracetam prevents evoked and spontaneous epileptiform activity in the controlled cortical impact model of neurotrauma

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Purpose: There is no effective therapy to prevent the development of posttraumatic epilepsy (PTE). Recently we reported that levetiracetam (LEV) administered within one hour after trauma prevented the development of epileptiform activity in two experimental models of neurotrauma (Yang et al., Exp. Neurol.2021;337:113571). The current study tested whether early administration of brivaracetam (BRV), a SV2A ligand with 20 times the affinity of LEV, could match or improve upon the antiepileptiform action observed with LEV. Tests were conducted in *ex-vivo* neocortical slices from rats subjected to controlled cortical impact (CCI) injury.

Method: Rats (P24-32) subjected to CCI injury were given a single dose of BRV (21 or 100mg/kg, i.p.) at one of three timepoints post-injury: immediately (0-2 min), 30, or 60 min. Control animals received only the saline (0.9%) vehicle. Posttraumatic epileptiform activity was assayed *ex-vivo* via electrophysiological recordings from coronal neocortical slices collected proximal to the injury (4 per rat) 3 – 4 weeks after injury. In this model, epileptiform burst discharges that include prolonged ictal-like discharges occur spontaneously or can be evoked in an "all or none" manner with externally applied electrical cathodal stimuli (Yang et al., J Neurotrauma 2010;27:1541-1548).

Result: A single dose of BRV administered to rats up to 60 min after TBI significantly reduced the development of posttraumatic epileptiform activity by 1) inhibiting the development of both evoked and spontaneous epileptiform activity, 2) raising the threshold stimulus needed to evoke epileptiform discharges, and 3) reducing the intensity of epileptiform bursts that arise after cortical neurotrauma.

Conclusions: Clinically there has been little success preventing the development of posttraumatic epilepsy. The results of this study support the hypothesis that early intervention with BRV has the potential to prevent or reduce posttraumatic epileptogenesis and that there may be a narrow window for successful prophylactic intervention.
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Abstract Number: 538

Title: Clptm1 involves in epileptogenesis via regulating GABAAR-mediated inhibitory synaptic transmission

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Purpose: Gamma-aminobutyric acid type A receptor (GABAAR) can regulate the vast majority of GABAergic inhibitory synaptic transmission. More than 80% of GABAAR contain GABAARγ2 subunits. Reduction of GABAAR-mediated inhibitory synaptic transmission plays an important role in epileptic seizures and epileptogenesis. Dysfunction of GABAARγ2 is involved in simple febrile convulsion and multiple hereditary epilepsy syndrome. Cleft lip and palate associated transmembrane protein 1 (Clptm1), as a negative regulatory factor of synaptic transmission, can inhibit post-synaptic and extra-synaptic GABAAR accumulation. Downregulation of Clptm1 can increase GABA-induced current or miniature inhibitory post-synaptic current (mIPSC). Therefore, we hypothesized that Clptm1 may be involved in epileptogenesis by regulating GABAAR-mediated inhibitory synaptic transmission.

Method: Double-labeling immunofluorescence was performed to observe the colocalization between Clptm1 and MAP2 or GFAP. Western blot was used to detect the protein expression of Clptm1 and GABAARγ2 in patients with temporal lobe epilepsy (TLE) and in pentylenetetrazole (PTZ)-kindling epileptic rats. Then, Clptm1-shRNA was used to downregulate the protein expression of Clptm1, and behavioral and electrophysiological

experiments were conducted in PTZ-kindling rat model. Finally, coimmunoprecipitation was used to explore the protein interaction between Clptm1 and GABAARγ2.

Result: Immunofluorescence showed that Clptm1 was colocalization with MAP2 but not with GFAP. Compared with non-epileptic patients and normal control rats, the protein expression of Clptm1 was up-regulated and the protein expression of GABAARγ2 was down-regulated in temporal neocortex of TLE patients, and in the hippocampus and adjacent temporal cortex of PTZ-kindling rat model. Downregulation of Clptm1 shorten the latency of first epileptic seizure, decrease seizure severity and the frequency of epileptic discharge in the hippocampus, and increase the amplitude of mIPSCs and protein expression of GABAARγ2. Coimmunoprecipitation indicated protein interaction between Clptm1 and GABAARγ2 in the hippocampus of PTZ-kindling model.

Conclusions: These findings indicate that Clptm1 is involved in epileptogenesis by inhibiting GABAAR-mediated inhibitory synaptic transmission.

Abstract Number: 558

Title: Levetiracetam attenuates acute and chronic seizures in mice through adenosinergic pathway: a possible involvement of adenosine A1 receptor

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Purpose: : The present study aimed to explore the possible levetiracetam mechanisms of action in the adenosine signalling systems using the PTZ-induced acute seizure and the pentylenetetrazole-induced kindling model of epileptogenesis.

Method: In acute model, male mice received caffeine (non-specific adenosine receptor antagonist), or dipropylcyclopentylxanthine (DPCPX) (specific A1 receptor antagonist) prior to levetiracetam. After 30 minutes, a convulsant dose of PTZ (100 mg/kg) was administered to determine whether caffeine or DPCPX have any antagonistic effects on antiseizure activity of levetiracetam by analysing the onset of first myoclonic jerk (FMJ), generalized clonic seizures (GCS) and percent mortality.
The chronic PTZ-induced kindling model was set to assess the gene expression changes in adenosine A1 receptor, inwardly-rectifying potassium channel (Kir3.2) and equilibrative nucleoside transporter-1 (ENT-1) through RT-qPCR. Data were analysed using Origin statistical software version 8.5 and represented as Mean ± SEM.

Result: The results showed in the acute model, caffeine (100 mg/kg) and DPCPX (25 mg/kg) shortened the delay in onset of FMJ, GCS and enhanced the percent mortality significantly ($P<0.05$) as compared to levetiracetam treated group. In the 2nd Phase of the experiment, RT-qPCR results showed that levetiracetam increased the mRNA expression the A1R (fold change: 1.76121±0.14464) and Kir3.2 (2.08942±0.21463 fold change) significantly ($P < 0.05$) in hippocampus as compared to the PTZ-treated group. Moreover, ENT1 is one of the regulators of adenosine in the CNS. In PTZ-kindling group gene expression of ENT-1 increased by 1.7 fold. Levetiracetam decreased significantly the mRNA expression of ENT1 by 0.5 fold change in hippocampus that supposed to prevent the influx of extracellular adenosine into the cells.

Conclusions: The results suggest that the neuroprotective effect of levetiracetam observed during the investigation could have a straight connection to its action on A_1 adenosine receptors.

Abstract Number: 559

Title: Proteomic Analysis of a Rat Model of Genetic Generalised Epilepsy with Absence Seizures

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Purpose: Absence epilepsy is the most common form of genetic generalised epilepsy (GGE). Its seizures are characterized by behavioural arrests, automatisms, and a 3 Hz spike-wave discharge on the EEG (Danober L et al. Prog Neurobiol 1998;55(1):27-57. Scheffer I et al. Epilepsia 2017;58(4):512-21.). While the symptoms of absence epilepsy are well-known, associated molecular changes are less understood. Proteomic analysis is increasingly utilised to elucidate molecular changes involved in epilepsy development. This has improved our understanding of disease progression and allows for the identification of potential therapeutic targets and biomarkers. The Genetic Absence Epilepsy Rats from Strasbourg (GAERS) are a well-validated GGE model. Like in humans, the proteomic changes resulting in GGE in GAERS are unclear. Here, we assess proteomic differences between the GAERS and Non-Epileptic Control (NEC) strains to explore the molecular mechanisms and to identify novel potential biomarkers and treatment targets in GGE.

Method: Liquid chromatography high-resolution tandem mass-spectrometry (LC-MS/MS) was performed using the somatosensory cortex (SCx) and thalamus of the GAERS (n = 6) and NEC rats (n = 6). Differentially expressed proteins between the groups were determined using the limma package in R. Enriched pathways were identified using g:Profiler.

Result: A total of 123 and 102 proteins were found to be significantly differentially expressed between GAERS and NEC in the thalamus and the SCx respectively. Among these proteins, aspartoacylase, glial fibrillary acidic protein, and glutamate metabotropic receptor 2 have been previously associated with absence epilepsy, and an additional 11 proteins were found to be previously associated with epilepsy in general. Pathway analysis identified terms that were mostly related to metabolism.

Conclusions: This study has identified both novel and previously identified absence epilepsy-associated proteins and candidate biological pathways. These results could be utilised to inform future biomarker and therapeutic target research.

Abstract Number: 567

Title: Identification of microRNAs as biomarker candidates for epilepsy-associated psychiatric comorbidities in animal models of epilepsy

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Purpose: Psychiatric comorbidities like anxiety and depression have been identified as prevalent and serious comorbidities, which have a major impact on quality of life in patients suffering from epilepsy. Therefore, there is a need to detect and manage these comorbidities.
We aimed to identify microRNAs as potential circulatory biomarkers for identification of patients with epilepsy-associated psychiatric comorbidities.

Method: The microRNA expression profile (750 microRNAs) was analyzed in blood samples of rats from the electrical post-status-epilepticus (SE) model (naïve n=5, sham n=5, epileptic n=6). Based on missing values, p value ($p<0.05$), fold change (<-1 and >1), correlation with seizure frequency and duration (coefficient <0.5) to exclude microRNAs directly related to epilepsy, and CT value (<30) microRNAs were preselected (n=11). MicroRNA levels were correlated with selected behavioral and biochemical parameters (e.g. nest building, brain-derived neurotrophic growth factor (BDNF); Spearman). The regulation of preselected microRNAs was further assessed by quantitative real-time PCR in three well-described animal models of epilepsy (amygdala kindling with focal/generalized seizures, chemical induced SE).

Result: Assessment of the correlation identified six microRNA candidates (miR-376a, miR-429, mmu-miR-763, miR-494, mmu-miR-697, mmu-miR-1903) showing a strong positive correlation with weight gain (correlation coefficients: 0.63 – 0.83) and food intake (0.65 – 0.75) in the early post-insult phase and a strong negative correlation with social interaction (-0.82 – -0.65), saccharin preference (-0.82 – -0.53) and plasma BDNF (-0.62 – -0.34).
Real-time PCR validation in additional epilepsy models identified mmu-miR-429, mmu-miR-203 and mmu-miR-712 as differentially expressed with mmu-miR-429 being upregulated across epilepsy models ($p<0.05$; animals with seizure activity n=40, sham controls n=41).

Conclusions: The findings suggest mmu-miR-429 as a potential circulatory blood biomarker candidate for epilepsy-associated psychiatric comorbidities. Studies e.g. in blood samples of patients suffering from epilepsy are necessary to further explore the informative value of this potential biomarker.

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Abstract Number: 572

Title: Effectiveness of cold atmospheric plasma jet is dependent on the thickness of tumor samples obtained from patients with glioma

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Purpose: Non-invasive treatment with cold atmospheric plasma (CAP) through generation of reactive oxygen and nitrogen species (RONS), is a promising adjunctive therapy for the treatment of gliomas. A significant number of patients with glioma experience seizures even after surgery, primarily due to incomplete resection of the tumor. Treatment of tumor bed with CAP post resection provides an opportunity to reduce recurrence in patients with glioma. The effectiveness of CAP in deeper layers of human tissue remains a challenge and very few studies have investigated CAP tissue penetration. This study was designed to study the efficacy of CAP to penetrate resected tissues obtained from glioma patients by measuring the levels of RONS in tumor tissues of various thickness.

Method: Helium CAP jet with 4 kV voltage and 3 LPM flowrate was used in this study. Surgically resected tumor tissue specimens of ten glioma patients were obtained. Tumor tissue (~10 mm thickness) or 600 µm-thick slices were treated for 5 mins with plasma jet and intracellular RONS were measured.

Result: Increase in intracellular RONS was observed in both glioma tissues (0.1064 ± 0.0436 nmoles/mg) and slices (0.175 ± 0.075 nmoles/mg) on plasma jet treatment as compared to untreated tissues (0.0584±0.0127 nmoles/mg) and slices (0.072 ± 0.015 nmoles/mg) respectively. However, glioma slices with lesser thickness showed higher percentage increase in RONS (133.31 ± 54.85 %) compared to glioma tissues with higher thickness (81.35 ± 53.57 %).

Conclusions: The magnitude of effect of plasma jet is higher in thinner tumor samples as compared to the thicker samples. Thus, penetration depth of CAP is a critical factor that needs to be considered for the treatment of tumor bed in patients with glioma. CAP could be used as a potential adjunct therapy post-resection for a seizure-free surgical outcome in patients with glioma.

Abstract Number: 573

Title: Effect of Degeneration of Nigro-Striatal Pathway on Calretinin Immunoreactivity in Genetic Absence Epilepsy and Non-Epileptic Rats

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Purpose: Calcium binding proteins have essential roles on neurogenesis and neuronal functions. One of the calcium binding proteins, calretinin (CR), is expressed in aspiny and GABAergic interneurons and forms synaptic connections between dopaminergic and glutamatergic cortico-striatal inputs. The number of striatal CR positive neurons has been shown to change following the degeneration of neurons in nigro-striatal dopaminergic pathway. Moreover there are clinical and experimental results showing the sensitivity of CR expressing interneurons to epilepsy. This study focused on the effect of nigrostriatal dopaminergic neuronal loss on calretinin positive neurons during the epileptogenesis in genetic rat model of absence epilepsy.

Method: Stereotaxic surgery was used for injection of 6-hydroxydopamine (6-OHDA, 4mg/µl) to the medial forebrain bundle (AP:-1.4,ML:1,6 V:7,1 mm) of 30-day old Wistar (n=5) or genetic absence epilepsy rats from Strasbourg (GAERS) (n=5) in order to degenerate nigrostriatal dopaminergic pathway whereas naive rats were used as control groups. The rat brain sections (40 µm) were immunohistochemically stained for CR. The number of the CR positive neurons in the striatum and substantia nigra (SN) were counted on the fluorescence staining sections. GraphPad Prism V6 was used for the analysis of the results.

Result: There was no difference in the number of calretinin positive neurons in striatum between 6-OHDA injected groups and their control groups. The number of calretinin positive neurons significantly decreased in SN pars compacta ($p<0.05$) and SN pars reticulata ($p<0.05$) in 6-OHDA-injected Wistar rats and GAERS compared to their control groups.

Conclusions: Our results show that CR may have a protective role for the dopaminergic neurons against to degeneration of the nigro-striatal pathway. This study supported by the Scientific and Technological Research Council of Turkey, Project number:TUBITAK-SBAG-218S653

Abstract Number: 578

Title: Dynamics of microRNA expression in neonatal acute seizure model

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Purpose: Approximately, 0.3% of infants are suffering from neonatal seizures. Even though these episodes of abnormal brain firing usually dissipate with age, they often lead to the development of neuropsychiatric impairments, and in some cases initiate epilepsy. This study aims to address the miRNA profile in the neonatal flurothyl-seizure model as an indicator of the long-term outcome of neonatal acute seizures without epilepsy development.

Method: Rats (n=30) were subjected to flurothyl-induced repeated generalized tonic-clonic seizures (n=5) for 5 consecutive days starting at postnatal day (P) 7. Animals of the same age were used as controls (n=30). Hippocampal tissues were harvested 24 hours, 7days, and 3months after the last seizure and snap-frozen. Total RNA was isolated from the frozen tissues. To address miRNA expression, we employed massive parallel sequencing (Illumina) followed by DESeq2 and Limma differential expression analyzes.

Result: Sequencing analysis showed a distinct miRNA dysregulation at 24hours (13 miRNAs), 7 days (17 miRNAs), and 3 months (13 miRNAs) after the last flurothyl-induced seizure. miR-206-3p was commonly dysregulated for the first two time points, while miR-205 was common for the latter two; and let-7a-1-3p, -7c-2-3p were altered at 24hours and 3months. 67% of these differentially expressed miRNAs are associated with epilepsy in animal models or patients – including miR-129-5p, -135a-5p, and -155-5p.

Conclusions: We identified miRNA expression profile in rat brains across the period following acute neonatal seizures until adulthood. Our results indicate that despite the early seizure cessation this brief period of abnormal firing in the neonatal brain commences long-term disruption in gene expression regulation.

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Abstract Number: 588

Title: Cellular localization of epilepsy-related microRNAs in P12 and P60 rat hippocampi

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Purpose: In recent years, microRNA (miRNA) involvement in temporal lobe epilepsy is investigated, as miRNAs serve as general regulators of gene expression. Previously, we have profiled a hippocampal miRNome from 120 animals with epilepsy onset in infancy (P12, P-postnatal day) and adulthood at three stages of epileptogenesis. 11 candidate miRNAs with altered expression (miR-129-2-3p, -132-3p, -132-5p, -142-3p, -142-5p, -146a-5p, -155-5p, -221-3p, -330-3p, -361-3p, -451-5p) were chosen for subsequent cellular localization in naïve animals, to track their localization in healthy niche.

Method: Male naïve intact Wistar albino rats P12 and P60 were used for cellular localization of miRNAs by LNA-based (Qiagen) in situ hybridization and immunohistochemistry (IHC). Astrocytic glial fibrillary acidic protein (GFAP) and neuronal calbindin antibodies were used to determine cell type in IHC. Imagining was done with Leica DM5500 Q confocal microscope and Olympus IX83 fluorescent microscope, colocalization was analysed with Pearson correlation coefficient in CellProfiler 4.1.3.

Result: Predominantly present in neurons were miR-129-2-3p and miR-132-5p in both ages and miR-142-3p, miR-155-5p, miR-221-3p, miR-330-3p, miR-361-3p, and miR-451-5p in P60 (mean 0,509±0,182). miR-146a-5p and miR-132-3p in both ages and miR-142-3p, miR-221-3p, miR-330-3p, miR-361-3p, and miR-451-5p in P12 demonstrated only partial colocalization with calbindin (mean 0,252±0,079). miR-155-5p (P12) and miR-142-5p (P12, P60) localized predominantly in other cell types, but for miR-142-5p some degree of calbindin colocalization was noticeable in the dentate gyrus of P60. None of the miRNAs showed marked colocalization with GFAP (mean -0,078±0,120).

Conclusions: Cellular localization of miRNAs could provide insights into the role of different cell types during epileptogenesis. We have visualized specific cellular localization of chosen miRNAs in calbindine positive hippocampal neurons of P12, P60 naïve animals.
Acknowledgement: This work was supported by GACR (19-11931S), the Ministry of Education, Youth and Sports of the Czech Republic under the project CEITEC 2020 (LQ1601), research organization RVO: 67985823.

Abstract Number: 622

Title: Comparison of rotational behaviour in Wistar and genetic absence epilepsy rats injected with 6-Hydroxydopamine

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Purpose: 6-Hydroxydopamine (6-OHDA) which shows a neurotoxic effect on the nigro-striatal dopaminergic pathway, is commonly used as a model of Parkinson's disease in rats (1). This study aimed to compare the apomorphine-induced rotational behavior between Wistar rats and genetic absence epilepsy rats from Strasbourg (GAERS) following 6-OHDA injection to the medial forebrain bundle (MFB) of the animals.

Method: In this study, 30 day-old Wistar rats and GAERS were included. Stereotaxic surgery was used for unilateral injections of 6-OHDA (8 µg/4 µL/4 minutes) into the MFB (AP:-1.4; ML:1.6; V:7.1 mm) of GAERS-MFB group (n=12) and Wistar-MFB group (n=10). All animals were injected with apomorphine (0.05 mg/kg, subcutaneously) after 21 days of surgery and total turns (360^0) of the animals to the unoperated side were recorded for 30 minutes. Data were expressed as mean±standart error. Unpaired t test was used ($p < 0.05$ was considered significant).

Result: The mean of the total turns in GAERS-MFB group was 7.39±1.19 per minute while it was 5.90±1.19 per minute for Wistar-MFB group. However, there was no statistically significant difference between the groups.

Conclusions: Although the findings showed no difference between the groups, we aim to continue the study by increasing the number of rats in order to understand whether the effects of 6-OHDA on rotational behavior differs in the epileptic rats compared to the non-epileptic animals.

This study is supported by the scientific and Technological Research Council of Turkey (TUBITAK) (218S653).

Abstract Number: 657

Title: Evaluation of biomarkers for glial cells and connexins in the epileptic predisposition of rats treated with pilocarpine

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Purpose: To evaluate the protein expression of biomarkers for glial cells and connexins as facilitators of neuroinflammation in the epileptic predisposition of rats treated with pilocarpine.

Method: Male Wistar rats (210-250 g, n=9) were injected with pilocarpine (2.4 mg/2 µl in saline solution, i.c.v.) to induce *Status epilepticus* (SE) and were video-monitored 24 h/day until spontaneous and recurrent seizures (SRS) were observed (2/9 rats showed SRS). In all animals left and right neocortices were removed to carry out the new technique called nanodotblot for biomarkers of activate microglia (Iba-1, CD 40 and mannose), astrocytes (glial fibrillary acidic protein, GFAP) and connexins 32, 36 and 45. The results of relative expression (RE) were showed as mean ± MSE, the ANOVA of Sidak´s multiple comparisons test was performed in order to determine significant differences (p<0.05).

Result: In epileptic animals compared with no epileptic animals with acute SE, we found increases in the RE of: a) Iba-1, right and left cortices (0.76±0.02 vs. 0.34±0.05, p=0.002; 0.62± 0.02 vs. 0.28±0.0 , p=0.01, respectively); b) CD-40, left cortex (0.96± 0.13 vs. 0.54±0.05,p=0.01, respectively); c) mannose, right cortex (0.68± 0.006 vs. 0.34± 0.04, p=0.002, respectively); d) GFAP, right and left cortices (9.8 ±2.3 vs. 4.0 ± 0.52, p=0.002; 9.7±2.1 vs. 3.9±0.55, p=0.002, respectively); e) Cx32, right cortex (0.957±0.20 vs. 0.562±0.07, p=0.04, respectively); f) Cx-43, left cortex (1.7± 0.80 vs. 0.8± 0.09, p=0.029), and g) not significant differences in the RE of Cx36.

Conclusions: Epileptic predisposition of animals with acute SE could be related with relevant biomarkers that favor this pathologic condition such as GFAP, CD40, mannose, CX32 and 45 compared with animals that despite having acute SE did not show SRS. This study was support by U. de G. program (Fortalecimiento a la Investigación 2020) to LMC and internal founding of MexBio to AMV.

Abstract Number: 660

Title: Analysis of the expression of the neuroinflammasome 3 and interleukins in the epileptic predisposition of rats with previous status epilepticus

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Purpose: To determine differences in the protein expression of biomarkers for the neuroinflammasome 3 and interleukines, in rats with *status epilepticus* (SE) induced by pilocarpine in which spontaneous and recurrent seizures were or were not observed, to relate with epileptic predisposition.

Method: We used the model of temporal lobe epilepsy by pilocarpine administration (2.4 mg/2 µl in saline solution, i.c.v.) in male Wistar rats (210-250 g, n=10) to induce SE (acute phase). All rats were video-monitored 24 h/day until spontaneous and recurrent seizures (SRS) were observed (33.3%, chronic phase), and left and

right neocortices were removed to perform a new technique called nanodotblot for biomarkers of the neuroinflammasome 3 (NLRP3, IL-1β, IL-18, Caspase-1) and IL-6 and IL-10. Relative expression (RE) of biomarkers were showed as mean ± MES and the ANOVA of Sidak´s multiple comparisons test was performed to determine significant differences (p<0.05).

Result: Results showed an increase in the RE of IL-1β and IL-10 in the right and left cortices of epileptic animals compared with animals that despite having SE did not show SRS (IL-1 β: right cortex, 0.68± 0.11 vs. 0.33±0.02, p=0.008; left cortex, 0.73±0.09 vs. 0.43±0.07, p=0.02; IL-10: right cortex 0.87±0.014 vs. 0.30±0.03; p<0.0001; left cortex 0.86±0.03 vs. 0.36±0.04; p<0.0001). No significant differences in the NLRP3, IL-18 and caspase-1 were observed as well as in the RE of the IL-6.

Conclusions: The results suggest an important involvement of the pro-inflammatory IL-1 β in the epileptic predisposition of animals with SRS compared with animals with SE but without SRS. In addition, the increase in the anti-inflammatory IL-10 could act as a compensatory mechanism to stop the chronic process of neuroinflammation. This study was support by internal founding of MexBio to AMV and U. de G. program (Fortalecimiento a la Investigación 2020) to LMC.

Abstract Number: 666

Title: Sensorial and motor deficits in injured animals produced with a new Traumatic Brain Injury hydro-pneumatic device

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Purpose: To evaluate animals with a brain lesion produced with a new device for inducing Traumatic Brain Injury (TBI) through sensorial and motor testing.

Method: Male Wistar rats (245-300 g, n=14) were trepanned and implanted with a small plastic ring in right parietal cortex (AP 4 mm, ML -4 mm from bregma) in which a small tube was inserted to produce a lesion through a new TBI hydro-pneumatic device in the experimental group, while the sham group was trepanned only. Before (5 consecutive days) and after surgeries (5 and 24 hours, 7, 14 and 21 days) all animals were evaluated according the Revised Neurobehavioral Severity Scale (NSS-R) for Rodents (Yarnell et al., 2016) and score deficit was evaluated from 0 (no deficit) to 2 (being 2 the high score with a significant deficit). The mean and standard deviation of data were calculated and t student test were performed to determine significant differences (p<0.05).

Results: Results showed an important sensorial and motor deficit in injured animals compared with the same animals before lesion produced with the new TBI hydro-pneumatic device (0.65 vs. 0.02, p=0.000036). In addition, a significant deficit were observed in these animals compared with sham group after trepanation and surgery (0.65 vs. 0.08, p=0.011). There were not differences between animals of sham group before and after trepanation and surgery.

Conclusion: This new TBI device produces a controlled hydraulic pressure to induce a fine lesion that is associated with a sensorial and motor deficit in animals. It will be a useful tool to study pathologic process associated with TBI such as neuroinflammation and epilepsy.

Abstract Number: 668

Title: Level change of TNF, BDNF in the blood serum temporal lobe epilepsy patients

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Purpose: to study the concentration of brain neurotrophic factor (BDNF), tumor necrosis factor (TNF) in patients with TLE and in healthy people.

Method: We studied the concentration of BDNF, TNF in blood plasma in 69 patients with TLE and in 27 healthy people using enzyme immunoassay (ELISA). Patients group (32,5% - women and 37,5% - men, median age 34 [28; 44] years), control group (62,5% -women and 37,5% - men, median age 25 [23; 29] years).

Result: In the group of patients with TLE, the concentration of BDNF was 25,87 [20,81; 32,17] ng/mL; in the control group was 74,85 [45,11; 128,85] ng/mL, p<0,001. In the group of patients with TLE, the TNF concentration was 12,30 [10,27; 20,95] pg/mL, in the control group - 73,40 [56,42; 92,88] pg/mL, p<0,001. In the group of patients with TLE with hippocampal sclerosis, the concentration of BDNF was 26,28 [22,73; 31,27] ng/ mL; TNF - 11,27 [8,41; 18,68] pg/mL compared to healthy people, p<0,001. In the group of radiology negative TLE, the concentration of BDNF was 24,44 [19,56; 32,62] ng/ mL; TNF - 10,85 [10,29; 18,35] pg/mL compared to healthy people, p<0,001. Also, we found a statistically significant decrease in TNF levels (p<0,05) in patients with TLE the duration of the disease is more than 10 years, TNF concentration was 10,58 [8,70; 16,30] pg/mL compared to patients with TLE the duration of the disease is less than 10 years, TNF concentration was 14,30 [11,22; 26,85] pg/mL. A ROC analysis was performed and the AUC for BDNF was 0,975, p<0,001; for TNF was 0,895, p<0,001, which is at the level of "good" values.

Conclusions: We found a statistically significant decrease in BDNF levels (p<0,001), as well as TNF (p<0,001) in peripheral blood in patients with TLE compared to healthy people.

Abstract Number: 696

Title: Addressed delivery of valproic acid to target cells in treatment of epilepsy using aptamers

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Purpose: To develop a drug based on aptamers that cross the blood-brain barrier, targeting the delivery of valproic acid to the brain.

Method: We used the Brain 1 and Co 451 aptamers passing through the blood-brain barrier, obtained using the in vivo-SELEX technology, the affinity of which was determined using flow cytometry fluorescence microscopy. The drug for targeted delivery of valproic acid was obtained using the conjugation of Konvulex, biotinylated aptamers, and streptavidin protein. The antiepileptic efficacy of the drug was evaluated in ICR mice with a lithium-pilocarpine model of the development of epilepsy. After the injection of pilocarpine, the animals were monitored using round-the-clock video recording. For the treatment of epilepsy, a valproic acid dose of 130 µg / g of animal weight was used. During treatment with a drug for targeted delivery, the dose of valproic acid was reduced to 5 µg / g. Evaluation of status epilepticus in mice was performed using the Racine Scale.

Results. In animals, using the lithium-pilocarpine model, status epilepticus was formed at different stages - from the 1st to the 5th. In all groups of animals, complete overcoming of status epilepticus did not occur in 120 min. In the group of mice treated with valroic acid, no change in their status occurred within 80 minutes. When

mice were treated with conjugates based on the Brain 1 and Co 451 aptamers, the blockade of status epilepticus in mice, despite the lower (26 times) doses of the administered antiepileptic drug, occurred faster.

Conclusion. A scientific platform has been developed for the development of drugs for targeted delivery of antiepileptic drugs with high efficiency and low toxicity.

Abstract Number: 733

Title: Expression of Glutamate receptor subunits in the hippocampus, anterior temporal lobe and neocortex of pilocarpine model of temporal lobe epilepsy

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Purpose: Temporal lobe epilepsy (TLE), most common form of drug-resistant epilepsy, is a distributed network disorder. Hyperexcitability mediated by glutamate receptors may be generated not only in the hippocampus but in extra-hippocampal regions as well. Region-specific alteration of NMDA/AMPA receptors at molecular level will help understand the complex network hubs distributed among different regions. This study is designed to investigate the region-specific alterations of glutamate receptors in TLE.
Method: We measured the spontaneous glutamatergic synaptic transmission using whole-cell patch clamp technique in the anterior temporal lobe (ATL), hippocampal and neocortical samples of pilocarpine rat model of TLE. Further, mRNA levels of AMPA/NMDA receptor subunits were evaluated by quantitative PCR and immunohistochemistry was performed to evaluate the expression of these proteins

Result: We observed increased glutamatergic activity in the hippocampus and ATL samples on TLE rats, but the magnitude of increase in glutamatergic activity was higher in the hippocampal samples compared to ATL. The glutamatergic activity was not altered in neocortical samples of TLE rats. mRNA level of NR1 was upregulated in both the hippocampus as well as ATL in TLE. mRNA level of NR2B was up regulated in the hippocampal region, however, no change was observed inthe ATL and neocortex. NR2A expression was found to be upregulated only in the hippocampal samples of TLE. AMPA receptor subunit GLUR4 expression was significantly upregulated in the hippocampal and ATL samples, but the expression ofGLUR1, GLUR2 and GLUR3 remained unchanged inTLE rats. Similar expression level changes were reflected in the immunohistochemical studies.

Conclusions: This study indicates differential reorganization of glutamatergic network between the hippocampus and extra-hippocampal regions in TLE. Region-specific alteration in glutamate receptor expression and function suggests that not only the hippocampus but, other temporal lobe structures may be involved in generation of independent epileptogenic networks in TLE.

Abstract Number: 771

Title: Comparative assessment of network-level defects in rodent models of subcortical band heterotopia and periventricular heterotopia

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Purpose: Subcortical band heterotopia (SBH) and periventricular nodular heterotopia (PVNH) are two types of malformations of cortical development associated with epilepsy. SBH describes a heterotopic band separated from the cortex and lateral ventricles by zones of white matter, whereas PVNH describes heterotopic nodular masses located along the ventricles. Although it is clear that these cortical malformations contribute to creating an abnormal circuitry prone to generate epileptic discharges, the precise location of these epileptogenic neuronal networks remain unclear. Here, we sought to identify them in two genetic mouse models of SBH and PVNH.

Method: Wide-field two-photon calcium imaging was used to simultaneously monitor the activity of hundreds of neurons in acute slices comprising both the heterotopia and the overlying normotopic cortex. Epileptiform activity was induced by gabazine, and the activity of individual neurons and that of neuronal assemblies sharing similar single-cell dynamics was quantified. Positions of individual neurons in the heterotopia and overlying cortex were registered so that the relative contribution of either of the two area to epileptiform activity is evaluated.

Result: We show that slices with both SBH and PVNH are more excitable than control slices with no malformations, and display a higher numbers of calcium transients. Area-specific analysis indicates that both the heterotopic and normotopic cortices are active during epileptiform activity. Last, neuronal assemblies sharing similar single-cell dynamics comprise neurons located within both area, with inter-individual differences in the proportion of neurons belonging to either of the two structures.

Conclusions: Our results suggest that network-level defects in grey matter heterotopia extend beyond macroscopically identifiable lesions, and comprise neurons located within both the heterotopic masses and the overlying cortex.

Abstract Number: 779

Title: Effects of a vagus nerve stimulator for experimental epilepsy

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Purpose: The interest in vagus nerve stimulation (VNS) is rapidly growing due to its broad potential in treating numerous diseases. Considering this and due to the impossibility of finding a commercial device, we created an electrical stimuli generator. This device allows us to conduct cost-effective, reproducible and safe VNS research in an experimental model of epilepsy - the Genetic Audiogenic Seizures Hamster of Salamanca (GASH/Sal).

Method: We tested the prototype by implanting it in GASH/Sal for 14 days. The electrical parameters set were similar to those used for the clinical treatment of refractory epilepsy, and the Ethomatic software was used to evaluate the characteristics of the seizures. In addition, we analysed the effect of VNS on inflammation indicators and used the open field test to assess its outcome on behavioural parameters.

Result: The GASH/Sal that receive VNS showed that the seizures were significantly reduced or entirely suppressed when compared with sham animals. Furthermore, VNS modulated the levels of inflammatory cytokines. Open field test showed that motor and exploratory activity was significantly different between animals that received VNS and those that did not. In this regard, behavioural values of GASH/Sal that received VNS are closer to those shown by wild type animals than exhibited by the sham group.

Conclusions: By employing a homemade device with parameters used in clinical practice, we demonstrated the VNS in the GASH/Sal model of epilepsy, almost or entirely eliminates seizures. It also reduces markers of inflammation and restores behavioural parameters altered in the strain mentioned above.

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Abstract Number: 801

Title: Adenovirus-mediated expression of NaV1.1 ameliorates Dravet syndrome epilepsy in mice

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Purpose: Dravet syndrome (DS) is a severe childhood-onset encephalopathy, characterized by febrile and spontaneous intractable seizures, global developmental delay, motor deficits and high incidence of sudden unexpected death in epilepsy (SUDEP). Over 80% of DS cases are caused by *de novo* loss of function mutations in the *SCN1A* gene, encoding for the voltage-gated sodium channel, $Na_V1.1$. Restoring $Na_V1.1$ activity, via vector-mediated gene transfer, offers unique chances for global, long-term, improvement in DS-associated comorbidities. Adenovirus vectors have the capacity to transfer large expression cassettes containing complex transcriptional regulatory elements.

Method: We explored the use of adenovirus-mediated expression of *SCN1A* to modify DS-associated comorbidities at the onset (postnatal day 21) of severe epileptic comorbidities and the presentation of multiple behavioral alterations.

Results: We found that our therapeutic vector was protective in DS mice ($Scn1a^{A1783V/WT}$). Specifically, it reduced the frequency of spontaneous seizures and interictal spikes observed on EEG, and increased the threshold temperature for thermally induced seizures, consistent with the amelioration of epileptic phenotypes. Moreover, our approach led to a reduction in the occurrence of premature mortality.

Conclusions: Adenovirus-mediated deliver of *SCN1A* in the brain of DS mice improves DS-associated comorbidities, providing proof of concept for the effectiveness of increased $Na_V1.1$ activity.

Abstract Number: 813

Title: Mimicking white matter pathology in a 3D-nanofiber cell culture system derived from children with drug-resistant epilepsies

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Purpose: In children with epilepsy, malformations of cortical development (MCD) are often associated with early-onset pharmaco-resistant epileptic encephalopathies. Therefore, focal cortical dysplasia type 2B (FCD2B) and the histologically indistinguishable cortical tuber of tuberous sclerosis complex patients (TSC) are quite common in pediatric surgical series. One outstanding characteristic found in surgically resected specimens from these patients is aberrant myelination of the white matter. We recently reported impaired oligodendroglial turnover with depleted myelin and oligodendroglia in FCD2B and TSC patients. However, data of the dynamics of oligodendrocyte biology and myelin formation are scarce. In this study we further characterized the pathophysiology of abnormal myelin formation in a cell culture model of pediatric epilepsy surgery patients.
Method: We analyzed primary mixed glial cell cultures derived from epilepsy surgery specimens of one TSC and seven FCD2B patients grown on polycaprolactone fiber matrices. Samples of unaffected white matter of three age-matched patients with mild malformations of cortical development (mMCD) served as controls. Different methodological approaches (i.e. immunofluorescence, western blot, fibre metrics and electron microscopy) were used to characterize oligodendrocyte and myelination dynamics.

Result: Our preliminary results suggest that cells derived from TSC and FCD2B surgery specimens cultured on a three-dimensional nanofiber scaffold show altered myelination capacity compared with mMCD cell cultures. We were able to demonstrate higher amounts of oligodendroglial precursor cells, however an overall lower content of mature oligodendroglia and myelinated fibers. In our culture model of myelination dynamics, we were able to show reduced myelination capacity of oligodendroglial cells is in TSC and FCD2B when compared to mMCD. Furthermore, myelin formation seemed to be disorganized.

Conclusions: Our study showed for the first time a more functional proof of oligodendrocytes affected by the malformative process per se rather than being inactive bystanders.

Abstract Number: 822

Title: The effect of inhibition of endocannabinoid system on cytokine expression in the rat brain after lithium-pilocarpine status epilepticus

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Purpose: We investigated the expression of cytokines IL-6, IL-1β, and fractalkine in the hippocampus and cortex of rats in the acute, latent, and chronic periods after lithium-pilocarpine status epilepticus (SE) and the effect of inhibition of the endocannabinoid system early after seizures on the cytokines expression.

Method: The study was carried out on lithium-pilocarpine model of SE in adult rats. Seizures continued for 90 min; 4 h after SE rats were treated with endocannabinoid receptor antagonist AM251 or vehicle. Animals were sacrificed 24 h, 7 days, and 5 months after SE, the left dorsal and ventral hippocampus, somatosensory, entorhinal, and frontal cortices were extracted. The right hemispheres were fixated in paraformaldehyde for the histological analysis. Quantitative PCR was used to analyze the expression of IL-1β, IL-6, and fractalkine in these structures.

Result: The expression of IL-1β was increased in all studied brain structures 24 h and 7 days after SE, while the expression of fractalkine was reduced in the cortex but not in the hippocampus. In the chronic period, no significant changes were found. The inhibition of CB1 endocannabinoid receptors in the acute period after SE caused a significant decrease in the expression of IL-6 in the hippocampus in the chronic period (5 months after SE). This effect did not depend on the development of spontaneous seizures during this period and the degree of neurodegeneration in the hippocampus. Inhibition of endocannabinoid receptors did not affect the expression of IL-1β and fractalkine either in the chronic or in the acute and latent period after SE in any studied brain structures.

Conclusions: Inhibition of the endocannabinoid system after SE reduces chronic inflammation in the hippocampus but does not affect the initial inflammatory response to the prolonged seizures.

This work was supported by the Russian Foundation for Basic Research, project no. 20-015-00468.

Abstract Number: 850

Title: Age-related development of spike-and-wave discharges after PTZ kindling in rats with genetic absence epilepsy

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Purpose: This study aimed to examine whether pentylenetetrazol-induced kindling at early postnatal age influences the development of absence epilepsy in WAG/Rij rats.

Method: 14 days old WAG/Rij rats (n=12) were treated with a subconvulsive dose of PTZ (35 mg/kg) every other day (max. 30 injections). Seizure intensity was observed, and rats were considered kindled when seizures (stage 4,5) occurred after three consecutive PTZ injections. Controls (n=12) received saline. Animals were equipped with monopolar cortical electrodes placed over the frontal cortex. EEG was recorded after 72 day every month: in pre-symptomatic period - PD73, PD90 and in post-symptomatic period - PD120, P150, PD180. SWDs were assessed by the mean duration, asymmetry index, and averaged power spectra.

Result: Experimental animals reached a stage 2-4 but not achieved the kindling progress. The rats PD73, PD90 showed a significantly longer duration of SWDs compared to the control animals. In addition, the asymmetry index was significantly higher in this age group. Morphology analysis of SWDs revealed that discharges for experimental rats PD73, PD90 were more mature compared to control rats of the same age group. Averaged power spectrograms of SWDs revealed significant differences for rats PD73, P90 after PTZ-kindling. In rats PD120, PD150, PD180 (symptomatic period) all data was not significant.

Conclusions: The experimental data shows that there probably is a mechanism in absence epilepsy, which is responsible for the resistance of kindling progress. Although there is, no progress of kindling in the pre-symptomatic period (PD14-PD72), at the age PD73, PD90 WAG/Rij rats showed an aggravation of absence epilepsy. We suggest that abolish the effect after PTZ-kindling at the age PD120, PD150, PD180 related maturation of SWDs, which have an antagonistic action generalization of limbic seizures during the kindling process.

Abstract Number: 862

Title: Striatal degeneration alters absence seizures during epileptogenesis: Is nigro-striatal pathway involved in spike-and-wave discharges?

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Purpose: The increase in the nigrostriatal dopaminergic activity and the generation of spike-and-wave discharges (SWDs), which are typical absence seizures, show an inverse proportion (1,2). We aim to investigate the effect of degeneration of the nigro-striatal pathway on SWDs, during the development process- epileptogenesis- of absence epilepsy, which is characterized by non-convulsive seizures.

Method: 8 µg dose of 6-hydroxydopamine (6-OHDA) was injected to degenerate the striatum of 30-day-old rats with genetic absence epilepsy (GAERS) (striatum two injections; AP: -0.5 mm/ -1.0, ML: -3.0 mm, V: -6.0 mm). In the control group, saline was administered to the same areas (Sham). At the third week, behavioral tests were performed with apomorphine injection. Stereotaxic surgery under ketamine and xylazine anesthesia were performed in 6-OHDA and sham group GAERS with positive rotation behavior when they were three months old, and EEG recording electrodes were placed over the skull. After a one-week recovery period, basal EEGs were recorded from the animals and SWD parameters were evaluated.

Result: As a result of 6-OHDA administration to the striatum, the cumulative duration ($F(2,11)=9.287$; $P=0.004$) and mean duration ($F(2,11)=6, 396$; $P=0.014$) of SWDs were statistically lower comparing to the control groups. Striatum injections caused a deterioration in the form of SWDs.

Conclusions: The loss of striatal dopaminergic neurons seem to lead an impairment in SWD formation. It is known that the striatum may be an intermediate step in the generalization of seizures. In light of these findings, it is aimed to evaluate the SWD properties with advanced analysis.
Supported by TUBITAK-SBAG218S653.
1-Birioukova LM, et al. Compensatory Changes in the Brain Dopaminergic System of WAG/Rij Rats Genetically Predisposed to Absence Epilepsy. Bull Exp Biol Med. 2016 Sep;161(5):662-665.
2-de Bruin NM, et al. Dopamine characteristics in different rat genotypes: the relation to absence epilepsy. Neurosci Res. 2000 Oct;38(2):165-73.

Abstract Number: 878

Title: Early epileptiform activity may be involved in distant hippocampal damage in lateral fluid percussion model of brain injury in rats

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Purpose: Long-term effects of traumatic brain injury (TBI), such as cognitive impairment, depression and epilepsy, are closely associated with damage to the hippocampus. The aim of the study was to search for an early electrophysiological marker of acute hippocampal damage.

Method: Lateral fluid percussion (LFPI) or sham-operation were modelled in 44 male Sprague-Dawley rats. ECoG and local field potentials in thedentate gyrus (DG) were recorded for 7 days before and 7 days after TBI. Brain sections were stained by Nissl and anti-IBA staining.

Result: The number of high amplitude spikes in the rat hippocampus increased at day 7 after TBI as compared to the background and sham-operated rats. The degree of histological changes in the hippocampus (neuronal loss in DG and microglial activation) significantly correlated with the number of spikes 7 days after TBI. The number of neurons in DG was lower and the number of microglial cells was higher in rats with significant electrophysiological changes. After TBI, the number of spike-wave discharges increased in 50% of rats, while the hippocampal damage was detected in all animals.

Conclusions: Neuronal loss and microglial activation in DG may reflect early mechanisms underlying the development of late posttraumatic pathology. Epileptiform activity may serve as invasive biomarker of early distant hippocampal damage.
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Abstract Number: 882

Title: Activity-dependent Gene Therapy for Intractable Epilepsy

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Purpose: Epilepsy remains one of the commonest serious neurological diseases. 30% of people with epilepsy are refractory to pharmacological treatment, and surgical resection of the focal brain area remains the best option. Gene therapy is currently the most promising candidate replacement for surgical treatment of pharmaco-resistant focal epilepsy. However, current experimental gene therapies do not discriminate between neurons involved in seizure generation and 'healthy' surrounding neurons. Here, we use activity-dependent promoters to drive a therapeutic transgene that attenuates neuronal excitability only in pathologic hyperactive neurons. Once seizures resolve, the gene therapy tool automatically turns off. Self-time-limited expression of the transgene and specificity for over-active neurons argue that the treatment should be better tolerated.

Method: We initially tested different immediate early genes (IEG) driving either the potassium channels KCNA1 or KCNJ2, *in vitro* (using MEA) and *ex vivo* (using patch-clamp). Then, as proof-of-principle, we used the promoter of an extensively characterised IEGs, *cfos*, to drive the expression of *KCNA1* in an animal model of intractable epilepsy. We also performed behaviour experiments to assess the effect of our innovative treatment on memory and learning.

Result: *In vitro* results showed that activity-dependent gene therapy is efficient in decreasing neuronal activity using different combinations of promoters and transgenes. *In vivo* results showed that cfos-KCNA1 reduces network activity and seizures in a mouse model of intractable epilepsy (intra-amygdala kainic acid). Furthermore, our data shows that the activity-dependent gene therapy is self-regulated, it is switched-off when seizures were fully rescued. We also observed no behaviour deficits with mice treated with the activity-dependent gene therapy. *In vivo* testing of other promoter-transgene combinations is ongoing with encouraging preliminary results.

Conclusions: Activity-dependent gene therapy is a very promising innovative approach for the treatment of intractable epilepsy with great potential for translation into clinic in the near future.

Abstract Number: 974

Title: Comparison of thyrosine hydroxylase and parvalbumin immunoreactivity in striatum and substantia nigra

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Purpose: The role of various type of neurotransmitters such as gamma aminobutyric acid (GABA) or dopamine across cortico-thalamic circuit and basal ganglia in the absence seizure mechanisms has been previously examined by several studies. The ontogenesis of spike-and-wave discharges (SWDs) of absence epilepsy change with age in which cortical maturation completes at around 3 to 4 month-old genetic absence epilepsy rats. We aimed to compare the immunoreactivity (ir) of dopaminergic and GABAergic neurons in the striatum and

substantia nigra (SN) of the 2 month-old non-epileptic Wistar control and genetic absence epilepsy rats from Strasbourg (GAERS).

Method: Wistar rats and GAERS were anesthetized with ketamine and xylazine and transcardially perfused with saline followed by 10% paraformaldehyde. Coronally cut free-floating sections (40 µm-thick) of striatum and SN were used for immunohistochemical procedures of thyrosine hydroxylase (TH, dopaminergic neurons) and parvalbumin (PRV, GABAergic interneurons). Photomicrographs captured *via* an Olympus DP72 microscope (Tokyo, Japan) were used for densitometric analysis (Image J software, USA). Data were expressed as mean±standard error of mean and analyzed by using GraphPad Prism.

Result: Comparison of TH-ir in the striatum and SN pars compacta and PR-ir in the striatum and SN pars reticulata between Wistar and GAERS was found not to be statistically significant. Also there was no difference between the groups for mean number of PRV positive GABAergic interneurons of striatum or SN pars reticulata.

Conclusions: Our findings on dopaminergic and GABAergic transmission in the basal ganglia for the underlying mechanisms of epileptogenesis in the absence epilepsy provide insight into the mechanisms of epileptogenesis in absence epilepsy.
This study was supported by the Scientific and Technological Research Council of Turkey (TUBITAK-SBAG-218S653).

Abstract Number: 977

Title: Unveiling small RNA signature after experimental traumatic brain injury

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Purpose: Neuroinflammation is a long-lasting secondary injury mechanism that evolves in the brain for months after traumatic brain injury (TBI). The control of neuroinflammation may lessen the risk of developing comorbidities, like epilepsy. Previously microRNAs (miRNAs) have been identified as key regulators of inflammation after brain injuries. In this work, our objective was to identify an altered small RNA signature chronically after TBI. We hypothesized that altered signature play a role in modulating post-TBI neuroinflammation.

Method: At 2months post-TBI, adult male rats (n=22) underwent T2-w MRI, to identify perilesional cortical inflammation (n=13/22). At 3months post-TBI, small RNA sequencing was performed on samples from ipsilateral thalamus and perilesional cortex of selected TBI rats (n=6/13), and sham operated controls (n=6). Deregulated miRNAs were validated with droplet digital PCR and deregulated transfer RNA fragments (tRFs) with qPCR.

Result: Small RNA-Seq identified deregulation in 2 and 19 miRNAs, in the thalamus and cortex respectively (FDR<0.05). The 2 candidates from thalamus and the top 10 from cortex were selected for the technical validation. In the thalamus, elevated miR-146a-5p (FC=2.01, p<0.05) and miR-155-5p (FC=2.34, p<0.01) levels were validated after TBI. In the cortex, elevated miR-375-3p (FC=3.44, p<0.01) and miR-211-5p (FC=1.45, p<0.05) levels were validated after TBI. Surprisingly, we found 16 and 13 dysregulated tRFs in the thalamus and cortex respectively (FDR<0.05). From these we validated upregulation of 3'tRF-LysTTT in both brain areas (Cortex, FC=6.85, p<0.01; Thalamus, FC=5.20, p<0.05).

Conclusions: Our data indicate that both pro-inflammatory (miR-155) and anti-inflammatory (miR-146a) miRNAs are elevated in the thalamus at a chronic time post-TBI. However, the inflammatory role of the deregulated miRNAs in the perilesional cortex is not well known. This study revealed a novel class of small

RNAs, tRFs, involved in post-TBI pathophysiology. Whether the role of tRFs is pro-inflammatory or anti-inflammatory remains to be explored.

Abstract Number: 1017

Title: Understanding the nuclear mis-localization of miRNAs in Temporal Lobe Epilepsy

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Purpose: Mesial temporal lobe epilepsy (mTLE) is a chronic neurological disease characterized by recurrent seizures. The pathogenic mechanisms underlying TLE involve defects in post-transcriptional regulation of gene expression. MicroRNAs (miRNAs) are a class of non-coding RNAs that control gene expression at the post-transcriptional level, and can modulate complex gene expression networks that govern the process of epileptogenesis. Previously, we have shown that a significant number of miRNAs are de-regulated in hippocampal tissue of human mTLE patients, and few of those miRNAs showed subcellular mis-localization with aberrant enrichment in the nucleus (Kan et al., 2012. Cell Mol Life Sci). In the present study, we are investigating the mechanisms that lead to the mis-localization of miRNAs into the nucleus and their contribution towards mTLE pathogenesis.

Method: We have performed subcellular fractionations of hippocampal tissue from mTLE patients and controls, and compared the nuclear and cytoplasmic distribution of miRNAs by RNA-seq and in situ hybridisation. Immunostainings were performed for nucleolar proteins.

Result: Several miRNAs were found to be specifically enriched in the nucleus of hippocampal cells from patients compared to the controls, where *miR-92b-3p* (a miRNA-enriched in neurons) was the most de-regulated nuclear miRNA. Using *in situ* hybridization, we observed *miR-92b-3p* hippocampal sub region-specific mis-localization into neuronal nucleoli both in human and experimental TLE. Further analysis of the nucleolus in TLE tissue indicated broad nucleolar stress; indicated by changes in nucleolar size and shape (based on nucleophosmin (NPM1) immunostainings), and by reduced expression of nucleolin.

Conclusions: Localization of miRNAs to nucleolar regions in TLE could influence ribosomal RNA synthesis and thereby protein production leading to neuronal dysfunction. We are currently investigating the consequence of the mis-localization of *miR-92b-3p* to nucleolus by *in vitro* target finding approaches and are further characterizing the functional role of this microRNA in nucleoli.

Abstract Number: 1028

Title: Acute and chronic medium-chain triglyceride administration alters neurotransmitter levels in specific brain areas – a possible antiseizure mechanism

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Purpose: Medium-chain triglyceride (MCT) enriched diets help in the management of cognitive dysfunction and epilepsy in humans and dogs. However, the functional mechanisms of MCTs remain not fully elucidated. The aim of the current study was to investigate the effect of MCTs on neurotransmitter metabolism in different brain regions, in cerebrospinal fluid (CSF) and serum in canines.

Method: Dogs were fed in a randomised, crossover trial with a commercial hypoallergenic diet (control), which was either supplemented with one dose of MCT-oil (9% of caloric requirement) 2 h prior to measurements (acute) or daily for two weeks, with measurements conducted >10 h after last feed (chronic). Proton Magnetic Resonance Spectroscopy (1H-MRS) with a 3-Tesla MRI scanner was used to measure neurotransmitter concentrations in four brain regions (parietal, piriform, occipital lobe, thalamus). Immediately after MRI, CSF and blood were collected and analysed via high-performance liquid chromatography.

Result: Paired data from eight healthy Beagle dogs were compared across the three feeds. Glutamine concentration was reduced 2 h after MCT in the piriform cortex [P = 0.0349] and glutamate concentration after two weeks of MCT [P = 0.0184], respectively. Thalamic gamma-Aminobutyric acid (GABA) concentrations were increased 2 h after MCT [P = 0.0492]. Serum and CSF analysis did not reveal any significant changes between groups.

Conclusions: MCT enriched diets have a direct effect on canine brain neurotransmitter levels in specific brain regions that may be important for seizure generation and propagation. Reduction of glutamate and increase of GABA might represent one of the anti-seizure mechanisms of MCTs.

Abstract Number: 1035

Title: gene variants involved in the glutamate and calcium pathway in the epileptic model hamster gash/sal.

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Purpose: The GASH/Sal hamster is a model of audiogenic epilepsy of genetic origin whose epileptogenic focus is the inferior colliculus (IC). Goals. To evaluate the mutations found in the Gash/Sal hamster exome analysis related to glutamate and calcium pathways.

Method: Using the Sanger sequencing technique, the mutations found in the GASH/Sal hamster exome related to glutamate and calcium pathways were validated; images of three-dimensional structures of the mutated proteins were created in the Pymol program. An immunohistochemical and Western blot analysis was performed where the difference in the protein expression of the *Mesocricetus auratus* control hamster vs. the GASH/Sal hamster was located and evaluated. Finally, its expression was observed by RT-qPCR.

Result: The *Grik1* and *Cacna2d3* genes showing a relationship with the formation of the kainate receptor involved in the glutamate pathway and the corresponding α2β3 subunit of the calcium channel CaV2.1 were validated. When carrying out the three-dimensional design of the protein structure of *Grik1* and *Cacna2d3*, it is observed that the substitution could affect the intramolecular contact and the stability of the protein. Regarding the immunohistochemical analysis, Western blot and RT-qPCR, an increase in the expression of *Grik1* was evidenced in GASH/Sal vs. control hamster in the inferior colliculus.

The intensity of immunostaining in certain regions, such as the cerebellum, hippocampus and cortex, is weaker in the GASH/Sal than in the control for both proteins. However, in the brainstem, the immunostaining pattern is reversed, being higher in the GASH/Sal than in the control.

Conclusions: The mutations found in the *Grik1* and *Cacna2d3* genes may be contributing to a changes in the excitatory balance that facilitates the status epilepticus.

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Abstract Number: 1113

Title: Are all status epilepticus the same? A comparative study of pilocarpine and kainic acid intrahippocampal administration in mice.

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Purpose: Systemic administration of pilocarpine (PL) and kainic acid (KA) can lead to sustained status epilepticus (SE) with long-lasting consequences in rodents. While local application of KA has been used, few studies have investigated the effects of PL's intrahippocampal administration. Here, we compared the acute and chronic effects of unilateral intrahippocampal administration (iHPC) of PL and KA in mice.

Method: Male adult C57BL/6J mice received one of four possible doses of PL (70, 245, 400, and 700 µg/site) or saline (SAL) in the right hippocampus during isoflurane anesthesia. Positive controls included iHPC of KA (20 mM/site) and the intraperitoneal administration of PL (sPL, 290mg/kg). Video-monitoring and electrophysiological recordings were used to quantify seizure and SE severity. One month after SE, the Barnes maze test and saccharin consumption were used to evaluate hippocampal-dependent spatial learning and anhedonia, respectively. Histopathological alterations were scored by Nissl staining.

Result: iHPC of PL (iPL) led to orofacial automatisms, rearing, falling, and wild-running in a dose-dependent manner. Seizures evolved faster in iPL compared to KA-treated animals. None of the iPL developed tonic seizures, and the mortality rate in this group was significantly lower compared to sPL. Epileptiform discharges occurred in both hippocampi after iPL and KA. Weight loss in the week following SE positively correlated with the dose of iPL (R2=0.98). Chronically, only animals treated with the highest dose of PL or KA developed generalized motor seizures. KA-, but not PL-treated, animals showed impaired performance in the Barnes maze test and reduced saccharin consumption. Histological analysis revealed severe degeneration of the ipsilateral hippocampus in KA- but not in PL-treated animals.

Conclusions: While demonstrating that not all SE are equal, the present study indicates that cognitive impairment and hippocampal degeneration are independent of SE severity and may serve as a temporal lobe epilepsy model without hippocampal sclerosis.

Abstract Number: 1120

Title: Dual role of stimulation and discharges in seizure dynamics is a generic phenomenon

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Purpose: Dual role of inter-ictal discharges or external stimulation with respect to the seizure dynamics has been discussed, with two competing mechanisms, previously considered contradictory, having been recently reunited. It was shown that both the proconvulsive role by initiation of seizures and anti-convulsive role (longer inter-seizure intervals with inter-ictal discharges), can be observed in single scenario represented by simple phenomenological model. Here we show the mechanism is generic (Pérez-Cervera A & Hlinka J. PLOS Comp. Biol. 2021;17(3):e1008521).

Method: We perform theoretical analysis of phase response (that is delay or advancement of the quasi-periodic dynamics of switching between inter-ictal and ictal state) of general mathematical slow-fast dynamical oscillating system, modelling the slow buildup of excitability (epileptogenicity/seizure propensity) and fast transitions to/back from seizure state. The theory is supported by computational simulation of the perturbation effect in computational models.

Result: We show both initiation and delay of seizures by perturbations are a generic phenomenon in such slow-fast systems, with the enigmatic delaying effect depending crucially on dynamics of the excitability variable. The simulations further illustrate how depending on perturbation amplitudes, frequency and timing, train of perturbations causes an occurrence increase, decrease or complete suppression of seizures. Quite intuitively, the delaying effect of perturbations is most prominent in models with prominent reactivity of excitability to mean firing rate, in particular when even transient increase in firing rate triggers feedback decreasing excitability.

Conclusions: While our mathematical analysis is valid for any planar slow-fast oscillator, in epilepsy it helps to elucidate the mechanistic role of both external and internal perturbations (such as inter-ictal discharges and therapeutical stimulation) in seizure dynamics. It shows that both triggering and delay of seizures is to be expected within the same tissue, and provides computational framework to predict the outcome based on the properties of the tissue and the perturbations.

Abstract Number: 1139

Title: Prolongation of cortical sleep spindles during hippocampal interictal epileptiform discharges in epilepsy patients

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Purpose: Impairment of memory function is a common problem in individuals with epilepsy. The hippocampo-neocortical information transfer is critical for the slow wave sleep (SWS) related memory consolidation; it is coordinated by the temporal coupling of the hippocampal sharp wave ripple (SPW-r) and neocortical sleep spindle activity. Hippocampal interictal epileptiform discharges (IEDs) are considered to be the pathological exaggeration of the SWRs. Although IEDs are known to correlate with impaired memory consolidation, it remains unknown how they interact with the physiological processes of the memory network. The present study focused on characterizing the influence of the hippocampal IEDs on cortical spindles.

Method: We analyzed the data of 21 pharmacoresistant epilepsy patients who underwent scalp-foramen ovale (FO) video EEG monitoring. We investigated relationship of hippocampal IEDs detected with FO electrodes and cortical spindles detected in the scalp electrodes during a whole night sleep.

Result: Scalp spindles co-occurring with hippocampal IEDs lasted longer (mean duration difference was 0.134s (SD=0.062), $p<0.0001$), had higher amplitude (mean amplitude difference 3.87µV (SD=0.97), $p<0.0001$) and

their frequency range shifted towards the higher frequencies (frequency bins remaining significant after correction were observed between 13.5 and 15.5 Hz (corrected p< 0.005). "Altered" spindles only emerged when they co-occurred with IEDs irrespectively of the hippocampal structural damage or the epileptic focus. In more than half of our subjects (52%) we also observed temporal correlation between hippocampal IEDs and cortical spindles.

Conclusions: Altered spindles emerged when they co-occurred with IEDs. We propose that IEDs negatively affect spindle formation; moreover we reckon that IEDs generate a pathological oscillatory coupling with sleep spindles. These findings support the hypothesis that IEDs could impair memory through the derailment of physiological mechanisms of the hippocampo-cortical coupling; epileptic spiking contributes more to memory disturbances in MTLE than we had expected earlier.

Abstract Number: 1246

Title: Perinatal exposure to PM2.5 can cause long-lasting changes in neurotransmission and neuroinflammation, and predispose to epileptic seizure.

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Purpose: Exposure to air pollution during early life can represent a risk factor for neurological diseases such as stroke and epilepsy. Exposition to fine particles (< 2.5µm; $PM_{2.5}$) can induces oxidative stress and neuroinflammation, both factors involved in triggering seizures. Our goal was to verify if the perinatal exposure of rats to $PM_{2.5}$ would be able to induce molecular changes in the brain, predisposing to epileptic seizures in adulthood.
Method: Seven-day-old rats were exposed to a polluted air chamber (POL-group) or filtered air (CT-group), 1h/day for 30 days (N=7/group). The POL-group inhaled about 600 µg/m³ of $PM_{2.5}$ in the compartment of a Harvard Ambient Particle Concentrator (HAPC) every day. After the exposure period, rats were subjected to PTZ kindling protocol (20mg/kg, followed by of 10 mg/kg every 10 min), to determine the susceptibility to seizures. Rats were euthanized, and the hippocampus removed for analysis of proinflammatory cytokines (IL-1β, IL-6, TNFα), and markers of GABAergic (GABA-B, GAD67, Parvalbumin) and glutamatergic (mGluR2/3, GluR5-7, NMDAR1, NMDAR2B) neurotransmission.

Result: The POL-group was more susceptible to exhibit seizures induced by PTZ than control group. In the POL-group the seizures started in 1 minute after the first injection of PTZ (20 mg / kg) and were more severe (stage V of the Racine scale) compared to the control group that presented milder seizures (stage III-IV of Racine) with higher doses of PTZ (32±5 mg / kg), and greater latency (22 min). POL-group also showed a significant increase in the levels of cytokines and in the density of kainate receptors (GluR5-7), with a reduction of GABA-B (-30%), PV (-30%) and mGLUR2/3 (+33%).

Conclusions: Our data indicate that perinatal exposure to $PM_{2.5}$ for 30 days, induces long-term changes such as neuroinflammation and imbalance between glutamatergic and GABAergic neurotransmission, predisposing rats to neuronal hyperexcitability in adulthood.

Abstract Number: 1284

Title: G3bps tether the TSC complex to the lysosome: Validation of role in zebrafish

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Purpose: The mTORC1 complex stimulates anabolic and inhibits catabolic processes at the lysosome. During times of stress its activity needs to be suppressed by upstream regulators. One of these regulators is the TSC complex consisting of TBC1D7 and the tumor suppressor genes TSC1 and TSC2, encoding hamartin and tuberin, respectively. Loss of function mutations in the TSC genes hyperactivates the mTOR pathway resulting in tuberous sclerosis complex (TSC), a neurodevelopmental disease where patients suffer from brain malformations and epilepsy. While their role in regulation of mTORC1 is well known, its lysosomal anchoring mechanism is unknown.
In this work, we show that G3BP1 and G3BP2 (Ras-GTPase activating protein SH3 domain binding proteins 1 and 2) are the lysosomal tether for the TSC complex *in vitro*. Hence, they are involved in the regulation of the mTOR pathway and thus mutations in these genes might give rise to TSC-alike phenotypes *in vivo*.

Method: We generated a G3bp1 morphant zebrafish model to investigate the resulting phenotype *in vivo* by behavioral, electrophysiological and calcium imaging assays and structural imaging of the brain.

Result: With a G3bp1 morphant zebrafish model we demonstrate that loss of *g3bp1* results in hyperactivity of mTORC1 *in vivo* and is thus involved in the regulation of mTORC1s activity. Moreover, it also results in ectopic localization of neurons and abnormal brain activity and therefore mimics the brain malformations and seizures observed in TSC patients. Besides, the abnormal brain activity as detected by behavioral, electrophysiological and calcium imaging assays could be restored by the mTOR inhibitor rapamycin and thus emphasizes its involvement in the regulation of mTORC1.

Conclusions: Taken together, we discovered a new role for the g3bps, whose loss of function might be involved in mTOR-related diseases such as TSC.
Reference including full list of coauthors:
Cell. 2021 Feb 4;184(3):655-674.e27.
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Abstract Number: 1314

Title: Combining bispectral magnitude and entropy measures to improve classification of preictal and ictal iEEG

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Purpose: The complex and nonstationary nature of mechanisms driving ictogenesis circumscribes our understanding of epilepsy and limits algorithms from decoding intracranial electroencephalography (iEEG). Unlike traditional preictal iEEG biomarkers, bispectrum, a higher-order spectral representation, measures nonlinear phase and amplitude cross-frequency coupling (CFC). While our group has demonstrated that bispectrum features are promising for explaining preictal mechanisms and for classifying epileptic iEEG, features are kept separate, and all available channels are used. This work explores bispectrum feature-channel combination selection to optimize classification of preictal and ictal iEEG in the only long-term human database [1].

Method: iEEG recordings of seizures with 60 preictal seconds from 12 patients were obtained online from the Melbourne University Seizure Prediction Data [1]. Bispectrum plots were computed from 16 contacts of 1195 seizures using 30-sec segments (n=29186). From these, average magnitude (Mave), entropy (E1) and squared entropy (E2) were extracted. To evaluate what feature-channel combinations best distinguish preictal and ictal segments, the minimum redundancy maximum relevance algorithm ranked the 48 combinations in order of importance. Patient-specific support vector machines were trained to classify segments based on varying numbers of the most important combinations.

Result: Overall, combining magnitude and entropy features yielded the highest classification accuracy (86.1%) compared to separate features (Mave: 83.9%, E1: 85.2%, E2: 81.2%). For all patients, the 2 most important feature-channel combinations consisted of one entropy and one magnitude measure which suggests that these features are complementary.
Conclusions: This work demonstrated that combining bispectral magnitude and entropy features can capture complex brain dynamics underlying seizure activity and can classify ictal and preictal segments better than individual features. These results support the idea that features which measure nonlinear CFC can better explain seizures and preictal mechanisms.

References: [1] Cook MJ et al. Lancet Neurol 2013;12(6):563-71.

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Abstract Number: 1358

Title: The antiseizure potential of plinabulin, a microtubule destabilizing agent in clinical trials

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Purpose: Using zebrafish-based screening we previously identified two new antiseizure compounds, i.e., the 2,5-diketopiperazine halimide, which was isolated from the marine-derived fungus *Aspergillus insuetus* IBT 28433, and its semi-synthetic analogue plinabulin (PCT patent publication WO2019043012 (PCT/EP2018/073147), Copmans D., et al.). Plinabulin is a microtubule destabilizing agent that is currently in phase III trials for the prevention of chemotherapy-induced neutropenia and treatment of non-small cell lung cancer, in combination with docetaxel. Since 30% of epilepsy patients are resistant to currently available

antiseizure drugs, we investigated the potential of plinabulin against drug-resistant seizures in the larval zebrafish ethyl ketopentenoate (EKP) seizure model and the mouse 6-Hz psychomotor seizure model.

Method: Behavioral and electrophysiological antiseizure analysis of plinabulin in the zebrafish EKP seizure model was performed using automated video recording (Zebrabox, ViewPoint, France) and non-invasive local field potential recordings (optic tectum), as previously reported (WO2019043012), after a treatment of 18 hours via water immersion. Behavioral antiseizure analysis of plinabulin in the mouse 6-Hz psychomotor seizure model was performed as described before (WO2019043012), 30 minutes after administration via i.p. injection.

Result: Within the zebrafish EKP model of drug-resistant seizures, plinabulin was observed to significantly lower EKP-induced seizure behavior at 1.25, 2.5, 5, and 10 µM ($p \leq 0.0001$) in a concentration-dependent manner and to significantly lower EKP-induced epileptiform brain activity at 10 µM ($p \leq 0.0001$). Moreover, within the pharmacoresistant mouse 6-Hz psychomotor seizure model, plinabulin treatment significantly shortened the duration of electrically-induced seizures at 10, 20, and 40 mg/kg ($p \leq 0.001$, $p \leq 0.01$, and $p \leq 0.01$, respectively).

Conclusions: Plinabulin was found to be active against seizures in two distinct drug-resistant animal seizure models. It is therefore of interest to further investigate its antiseizure efficacy and mode-of-action, exploring its repurposing potential for the treatment of epilepsy.

Abstract Number: 1366

Title: A novel KCNA2 variant in a patient with cerebellar ataxia and epilepsy: functional characterization and sensitivity to 4-aminopyridine

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Purpose: Kv1.2 channels, encoded by the *KCNA2* gene, are localized in the central and peripheral nervous system, where they regulate neuronal excitability. Recently, heterozygous mutations in *KCNA2* have been associated with a spectrum of symptoms extending from epileptic encephalopathy, intellectual disability and cerebellar ataxia. *In vitro* studies allowed to stratify mutations into three subgroups according to the functional defect (GoF, LoF and GoF/LoF) and provided evidence for a significant genotype-phenotype correlation in *KCNA2* disorders. Patients are treated with a combination of antiepileptic drugs, sometimes with limited benefit. The possibility to offer 4-aminopyridine (4-AP), a known Kv blocker, as treatment option to specific cases can be, therefore, appealing. We identified a novel mutation in *KCNA2*, E236K, in a Serbian proband with non-progressive congenital ataxia and early onset epilepsy, treated with sodium valproate. The aim of this study was to functionally characterize Kv1.2 mutant channel and assess the effect of 4-AP on channel activity.

Method. To this aim, we transfected HEK 293 cells with Kv1.2 WT or E236K cDNAs and recorded potassium currents through whole-cell patch-clamp. *In silico* analysis supported electrophysiological data.

Results. E236K channels showed voltage-dependent activation shifted towards negative potentials, slower kinetics of deactivation and activation compared with Kv1.2 WT. Heteromeric Kv1.2+E236K channels, resembling the condition of the heterozygous patient, confirmed a mixed GoF/LoF biophysical phenotype. 4-AP

inhibited both Kv1.2 and E236K channels with similar potency. Homology modeling studies of mutant channels suggested a reduced interaction between the residue K236 in the S2 segment and the gating charges at S4.

Conclusion. Overall, the biophysical phenotype of E236K channels correlates with the mild end of the clinical spectrum reported in patients with GoF/LoF defects. The response to 4-AP corroborates existing evidence that *KCNA2*-disorders could benefit from variant-tailored therapeutic approaches, based on functional studies.

Abstract Number: 1371

Title: Pericardial injection of kainic acid induces a chronic epileptic state in larval zebrafish

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Purpose: In rodents, injection of kainic acid (KA) leads to the development of spontaneous epileptic seizures, reminiscent of neuropathological characteristics as seen in patients with temporal lobe epilepsy (TLE). Although this model has significantly contributed to better understanding of epileptogenesis, it is technically demanding and costly, hence not suitable for high-throughput screening of anti-epileptic drugs (AEDs). Zebrafish, a vertebrate with complementary advantages to rodents, is an established animal model for epilepsy research. Here, we generated and functionally and pharmacologically validated a novel KA model in zebrafish larvae.

Method: KA was administered by pericardial injection at an early zebrafish larval stage. The epileptic phenotype induced was examined by quantification of seizure-like behaviour using automated video tracking, and epileptiform brain activity measured by local field potential (LFP) recordings. We also assessed GABAergic and glutamatergic neurons in double transgenic KA-treated zebrafish larvae, and examined GABA and glutamate levels in the larval heads by liquid chromatography with tandem mass spectrometry detection (LC-MS/MS). Finally, KA-injected larvae were exposed to five commonly used AEDs by immersion for pharmacological characterization.

Result: Shortly after injection, KA induced a massive damage in the zebrafish larval brain and seizure-like locomotor behavior. After 48 hours, epileptogenic disorganization of the brain was observed, resulting in continuous epileptiform brain activity. Neuronal cell counts and titration of neurotransmitter levels revealed a decrease in the GABAergic and glutamatergic networks. Three out of five AEDs tested rescued LFP abnormalities but did not affect the seizure-like behavior.

Conclusions: In summary, pericardial injection of KA in zebrafish larvae induces spontaneous recurrent seizures after a short latency period, as seen in rodent models. For the first time, we describe a chemically-induced larval zebrafish epilepsy model suitable for high-throughput AED screening purposes.

Clinical Neurophysiology

Abstract Number: 63

Title: Validity measures of direct cortical stimulation for seizure onset zone localization

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Purpose: Direct cortical stimulation (DCS) of the human brain is a common technique during intracranial explorations for presurgical evaluation in drug-resistant epilepsy (DRE). Variations of the technique, methods and parameters are used for a variety of goals. In accordance with the French protocols this technique can be used to delineate the seizure onset zone (SOZ). Few studies have reported levels of concordance between spontaneous seizure generators and elicitable seizures during DCS. However, no studies have systematically reported the validity measures of DCS. The present study reports the validity measures of DCS for detecting the SOZ during stereoelectroencephalography (SEEG).

Method: consecutive patients at our epilepsy center between 2013 and 2019. Results were analyzed using contingency tables. Radiofrequency thermocoagulation (RF-TC) and/or resective surgery were performed after intracranial explorations. Validity measures of the diagnostic test were afterwards calculated for the Engel Class I group.

Result: Fifty-eight patients were evaluated with intracerebral electrodes and DCS. One hundred forty-one clinical seizures were elicited with DCS. True positive seizures showed a high specificity (97.5%) for the detection of the seizure onset zone in Engel Class I patients. Sensitivity was low (24.2%) and a high percentage of false negative stimulations was documented in the SOZ. The accuracy was 87.5%.

Conclusions: DCS is a low sensitivity technique. Specificity is high. Results of DCS should be taken into account to bulid the RF-TC targets and the resection hypothesis.

Abstract Number: 122

Title: Quantitative analysis of heart rate variability before focal epileptic seizures in temporal lobe epilepsy

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Purpose: We used the heart rate variability generated by the fluctuating balance of sympathetic and parasympathetic nervous systems to predict focal epileptic seizures in patients with temporal lobe epilepsy.

Method: 30 video-EEG with simultaneous ECG, and recorded seizure during presurgical evaluation were analyzed retrospectively. Regarding the fact that heart rate variability (HRV) signals are nonstationary, our analysis focused on linear features in the time domain such as R-R interval (RRI), quantitative analyses of Poincaré plot features (SD1, SD2, and Cardiac Sympathetic Index CSI=SD1/SD2). The calculations were made in minute intervals, starting from tenth minute before the seizures.

Result: Significant changes of CSI values were observed in the time intervals (10-9min, 8-7min, 7-6min, 6-5min, 5-4min, 4-3min, 3-2min, $p< 0.005$) in relation to the first minute before the clinical attack 3.69 ± 2.28. The increase in the CSI parameter in the second and first minute before the clinical attack was observed. The average value of the CSI coefficient is 3.03 in the second minute before the seizure, 3.69 in the first. This was the largest mean values calculated for each one-minute interval preceding the clinical seizure and suggest that the average CSI value increases 1-2 minutes before clinical seizure. There were 22 such cases, so the seizure prediction rule would work correctly in 73% of cases. The results of the number of patients and the significance of p calculated for the chi-square test suggest that the distribution is not random. For intervals 10-9, 8-7, 7-6 , 6-5, 4-3, 3-2 minutes the significance is $p < 0.05$.

Conclusions: Our results give the impression that it is possible to use the cardiac sympathetic index for detection or even several minutes before, prediction the focal epileptic seizure.

Abstract Number: 145

Title: Entropy on routine EEG: a fingerprint of recent seizure activity?

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Purpose: Multiscale entropy (MsEN) can evaluate at multiple time scales the degree of complexity of non-linear time series such as EEGs. We sought to assess if MsEN of routine EEG could reflect recent seizure activity.

Method: Charts of all patients undergoing an outpatient EEG between January and March 2018 were reviewed to: a) confirm (or not) the diagnosis of epilepsy (based on information collected before and 2 years after the EEG), and b) assess seizure occurrences in the year preceding the EEG. EEGs with excessive artifacts and patients for whom diagnosis remained uncertain even after 2 years of follow-up were excluded. 9s-EEG segments were extracted at pre-specified time-points. MsEn was calculated for all channels and values aggregated at the 25th percentile (Richman et al., 2004). We performed a multivariate zero-inflated analysis to test the association between MsEn and occurrence of seizures in the one-year interval preceding the EEG, after controlling for age, presence of abnormal slowing, and presence of a focal brain lesion.

Results: 269 EEGs were screened and 159 met inclusion criteria (112 patients). 94 EEGs (59%) were from patients with epilepsy, of which 53 had at least one seizure within year preceding the EEG. Remaining EEGs were from patients who were deemed not to have epilepsy at last follow-up. 28 EEGs (18%) had spikes. Each one standard-deviation (1SD) decrease in MsEn was associated with an OR of 1.43 of having at least one seizure in the preceding year (p=0.032). In patients with more than one seizure in the preceding year, each 1SD decrease in MsEn was associated with an increase in seizure frequency of 1.19/year ($p < 0.001$). Seizure frequency between epileptic patients with and without spikes was similar (p=0.52).

Conclusion: MsEN of EEG is a potential objective method to assess contemporary seizure occurrence.

Abstract Number: 238

Title: Data-driven electrophysiological atlas of normal resting state intracranial EEG

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Purpose: While the electrophysiological footprint of brain activity in the scalp EEG is well known, the similar knowledge in intracranical EEG (iEEG) is limited. Currently, the only available iEEG atlas is based on manually selected iEEG from a limited dataset. The purpose of this work is to investigate whether creation of an electrophysiological atlas by means of automated processing is feasible.

Method: We have investigated resting state iEEG sampled at 5 kHz in 39 epileptic patients with unilateral, drug-resistant, focal epilepsy who underwent implantation of stereotactic electrodes. The anatomical

structures were labeled according to Talairach atlas. The channels ipsilateral to seizure onset zone and channels in the irritative zone were removed from analysis. This resulted in a total of 743 analyzed channels in 28 distinct anatomical areas. The signal power was calculated in 1 second sliding window for delta (1-4 Hz), theta (4-8 Hz), alpha (8-12 Hz), beta (12-20 Hz), low gamma (20-45 Hz), high gamma (55-80 Hz), ripple (80-250 Hz) and fast ripple (250-600 Hz) frequency bands.

Result: The highest proportion of signal power was found in the occipital lobe the lowest in the frontal lobe. Parietal lobe showed increased power in the theta and high gamma bands, occipital lobe in the alpha band, while there was no distinct peak for frontal and temporal lobe. The regions exhibiting specific peaks were: gyrus precentralis (low gamma activity), gyrus frontalis inferior (ripple band), cingulate gyrus (theta activity), cuneus (theta), precuneus (high gamma).

Conclusions: We have shown differences in resting state iEEG band power in different brain structures. The proposed methodology is easy to implement and the data-driven approach can be applied on extensive data sets from multiple institutions. The created atlas can be used as a reference for clinicians and research studies.

Abstract Number: 289

Title: Parieto-Premotor functional connectivity changes during parietal lobe seizures are associated with motor semiology

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Purpose: Parietal lobe seizures (PLS) are characterized by multiple clinical manifestations including motor signs (Francione S et al. Epileptic Disord 2015; 17: 32–46.). The mechanisms underlying motor sings in PLS remains imperfectly known. The objective of this work was to understand this mechanism with the help of functional connectivity (FC) analysis during PLS.

Method: We retrospectively selected patients affected by drug-resistant epilepsy who underwent Stereoelectroencephalography (SEEG) for pre-surgical evaluation and in whom the seizure onset zone (SOZ) was located in the parietal cortex. The SOZ was defined visually and quantitatively by the epileptogenicity index (EI) method (Bartolomei F et al. Brain 2008; 131: 1818–1830.) Two groups of seizures were defined according to the presence ("motor seizures") or the absence ("non-motor seizures") of motor signs. FC estimation was based on pairwise nonlinear regression analysis (h^2 coefficient) (Wendling F et al. Clin Neurophysiol 2001; 112: 1201–18.). For studying the FC changes between parietal, frontal and temporal regions, for each patient, z-score values of 16 cortico-cortical interactions have been obtained comparing h^2 coefficients of pre-ictal, seizure onset and seizure propagation periods.

Result: We included 22 patients, 13 with "motor seizures" and 9 with "non-motor seizures". motor seizures". A resective surgery was performed in 14 patients, 8 patients had a positive surgical outcome (Engel's class I and II). Z scores computed between the onset and the propagation of discharges were significantly higher in "motor seizures", between lateral pre motor area and precuneus (p=0,01), lateral pre motor area and superior parietal lobule (p=0.03) and between inferior parietal lobule/posterior cingular gyrus and supplementary motor area (SMA)(p=0.04).

Conclusions: Our study shows that motor semiology in PLS are underline by an increase of FC between parietal and premotor cortices, significantly different than what is observed in PLS without motor semiology.

Abstract Number: 310

Title: Eye Closure Sensitive Idiopathic Generalized Epilepsy Investigation of Blink Reflex and Recovery Curve

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Purpose: In this study, we aimed to investigate whether the brain stem excitability contributes to the pathophysiology of the brain stem by blink reflex and recovery curve electrophysiologically in patients who are followed by the diagnosis of idiopathic generalized / genetic epilepsy with and without eye closure sensitivity in EEG examinations.

Method: The study included 20 healthy controls, 20 eye closure sensitivity idiopathic generalized / genetic epilepsy (IJE) patients, 20 non-eye closure sensitivity idiopathic IJE patients. The electrophysiological responses of the blink reflex were recorded to all participants. In each inter stimulus intervals (200-300-500-700-800-1000 ms), the amplitude and area values of R2 responses (R2t and R2) formed after the conditioning and test stimuli were measured for each trace pair obtained.

Result: In the study group, there was no statistically significant difference in R2 latency (right p = 0.732, left p = 0.392) and R2 amplitude (right p = 0.253, left p = 0.513) obtained with the first conditioning stimulus compared to the control group. Second, in our study, there was no significant difference in the recovery of the R2 component in the patient group at 200,300,500, 700, 800, 1000 ms inter stimulus intervals compared to the control group. However, it was observed that the R2 recovery curves of the IJE group with eye closure sensitivity remained higher than normal. In the R2 recovery curve, bilaterally 200 ms inter stimulus interval, statistically significant difference was found in the IJE group with eye closure sensitivity compared to the control group (right p = 0.044 and left p = 0.006).

Conclusions: The findings in our study suggest that there is a decrease in inhibitory mechanisms in IJE patients with eye closure sensitivity, although it is not statistically significant.

Abstract Number: 321

Title: EEG as a biomarker in neonatal onset Maple Syrup Urine Disease

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Purpose: maple syrup urine disease (MSUD) is a rare autosomal recessively inherited metabolic disorder characterized by a defect in the catabolic pathways of branched-chain amino acids, in particular leucine. In the neonatal period MSUD, onset is typically in the first days of life with non-specific symptoms such as irritability/lethargy, stereotyped movements and seizures. Early diagnosis and restricting dietary treatment are essential to prevent long-term sequelae. Although a unique EEG pattern, the so called Comb-like pattern, has been associated with MSUD, its occurrence, specificity and temporal evolution remains poorly defined.

Method: retrospective search of the EEG database and the metabolic database from 2002 to 2020 at GOSH (UK). All patents with a confirmed diagnosis of MSUD and at least 1 EEG were included and their EEGs analysed.

Result: 24 EEGs were analyzed from a cohort of 15 patients (5 females) aged 6-83 days. EEG background activity was abnormal in all with variable degree of dysmaturity. Electrographic-only seizures were recorded in 2 patients (on day 8 and 15), involving parasagittal regions, with low seizure burden. Comb-like pattern were found in 11 patients (76% of EEGs in neonatal period, 67% of all EEGs). They showed unique evolution: in the first days of life comb-like pattern seemed less marked and confined to the midline; the incidence increased in the first 2 weeks, becoming better defined with spread to the central regions. During the resolution an opposite trend was observed with less spread. No comb-like pattern were seen outside neonatal period. After their disappearance, transients and later a rhythmic delta-theta activity could be seen in the same regions.

Conclusions: Comb-like patterns are seen in the majority of neonatal onset MSUD, limited to the neonatal period and have a typical temporal evolution. Findings indicate that EEG is a valuable biomarker for the early diagnosis of MSUD.

Abstract Number: 368

Title: Artificial Intelligence outperforms Quantitative EEG Assessment for Seizure Detection of ICU Patients

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Purpose: To compare performance of an artificial intelligence (AI) based computer algorithm to visual assessments of quantitative EEG panels for classification of seizure versus seizure-free EEG segments recorded from critical care patients.

Method:
Retrospective EEG recordings from 45 ICU patients with a duration of 4h each were reviewed independently by two authors (CBS, SRS) to determine timepoints of electrographic seizures [1]. EEGs were split into 180 non-overlapping 1-hour segments and defined as seizure-segment (one or more seizures included) or as seizure-free segment (no seizures included). Two approaches not involving full EEG review were compared to the results of the full EEG review: 1) Quantitative EEG (qEEG) panels interpreted by medical staff 2) A deep neural network trained on an independent training dataset [2], (2) Per-patient sensitivity and specificity were assessed and average values including confidence intervals were calculated for both classification schemes.
Result:
The AI was able to classify 1-hour segments as seizure or seizure-free with a sensitivity of 91.4% (84.2–95.6) and a specificity of 91.7% (81.1–95.8). Visual assessment of qEEG panels resulted in a sensitivity of 84.1% (82.4–85.8) and a specificity of 68.9% (66.3–71.5). Comparison of both methods showed superior performance of the AI based approach in both sensitivity (+7.3%) and specificity (+22.8%).
Conclusions:
An artificial intelligence outperforms visual assessment of quantitative EEG panels for classification of seizure or seizure-free 1-hour EEG segments from ICU patients. Our results show that computer-based interpretation of neurophysiology data is beneficial to traditional approaches involving visual assessment of quantitative EEG by experts.
[1] Swisher CB et al., Diagnostic Accuracy of Electrographic Seizure Detection by Neurophysiologists and Non-Neurophysiologists in the Adult ICU Using a Panel of Quantitative EEG Trends. J Clin Neurophysiol. 2015
[2] Shah, V. et al., The Temple University Hospital Seizure Detection Corpus. Frontiers in Neuroinformatics. 2018

Abstract Number: 383

Title: Increased power at low-alpha frequencies is an endophenotype of Juvenile Myoclonic Epilepsy.

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Purpose: Abnormal EEG features are a hallmark of epilepsy, and abnormal frequency and network features are apparent in EEGs from people with Genetic Generalised Epilepsy in both ictal and interictal states. Here, we characterise differences in the resting-state EEG of individuals with juvenile myoclonic epilepsy (JME).

Method: We collected EEG data from 147 participants with JME through the Biology of Juvenile Myoclonic Epilepsy (BIOJUME) study. 95 control EEGs were acquired from two independent studies (Chowdhury et al. (2014) and EU-AIMS Longitudinal European Autism Project). We extracted frequency and functional network-based features from 10-20s epochs of resting-state EEG, including relative power spectral density (PSD), peak alpha frequency, network topology measures and Brain Network Ictogenicity (BNI): a computational measure of the propensity of networks to generate seizure dynamics. Each feature was tested between JME and controls using univariate, multivariable and receiver operating curve (ROC) analyses. P-values were corrected for multiple comparisons.

Result: Univariate analysis showed significant differences in PSD in delta (2-5Hz) ($p=0.0007$, hedges' $g=0.55$) and low-alpha (6-9Hz) ($p=2.9\times10^{-8}$, $g=0.80$) frequency bands, peak alpha frequency ($p=0.000007$, $g=0.66$), mean degree of networks ($p=0.0006$, $g=0.48$) and BNI ($p=0.00006$, $g=0.56$) between JME and controls. Since mean age ($p=0.009$) and epoch length ($p=1.7\times10^{-8}$) differed between the two groups and were potential confounders, we controlled for these covariates in multivariable analysis where disparities in EEG features between JME and controls remained. ROC analysis showed low-alpha PSD was optimal at distinguishing JME from controls, with an area under the curve of 0.72.
Conclusions: Individuals with JME have increased power of neural oscillatory activity at low-alpha frequencies, along with a decreased peak alpha frequency compared to controls, supporting evidence from studies in other epilepsies. Further, since low-alpha PSD remained elevated in JME in each analysis and was not influenced by covariates, supports its use as an endophenotype of JME.

Abstract Number: 402

Title: Evaluation of ENCEVIS in Automatic Seizure Detection. Primary Results

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Purpose: To evaluate the digital system ENCEVIS (Austrian Institute of Technology) for automatic seizure detection and consider diagnostic value of the system

Method: Prospective evaluation of all long-term recordings (4hrs and longer) at SEIN-SKUH Epilepsy and Sleep Centre in the one- year period from June 1/2018 to June 1/2019 was carried out. All recordings containing at least one documented clinical seizure were included into the study. Comparative EEG analyzes - Visual vs ENCEVIS was carried out according to the protocol, which was elaborated for this study: visual detection by 2 independent experts and detection by ENCEVIS. Data were added to the data table developed based on the SCORE standardized EEG reporting system. True, false positive and false negative seizure detection by ENCEVIS was taken into consideration.

Result: Total 214 long term video-EEG recordings were carried out. Out of them 39 recordings with documented seizures were included into the study. Patients were grouped according to localization of seizure onset. Temporal lobe epilepsy (TLE) - 16, frontal lobe epilepsy (FLE) - 8, occipital lobe epilepsy (OLE) - 1 and parietal lobe epilepsy (PLE) – 2, generalized epilepsy (GE) - 9 and unclassified – 3. ENCEVIS appeared to be most sensitive in generalized epilepsy (100%) and temporal lobe epilepsy - 86.4%. In frontal lobe seizures, which often were EEG negative, the program sensitivity was much lower - (23.8%). In general, ENCEVIS was sensitive in 73% of all cases.

Conclusions: According to preliminary results, ENCEVIS is a promising tool for seizure detection in temporal lobe epilepsy and epilepsy with generalized tonic clonic seizures. The system requires further refinement for detection of brief seizures with minimal EEG manifestation. Further study, involving more recordings is required to assess possibilities of ENCEVIS clinical application.

Abstract Number: 485

Title: High-frequency oscillations recorded with surface EEG in neonates with seizures

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Purpose: Neonatal seizures are often the first symptom of perinatal brain injury. High-frequency oscillations (HFOs; ripples: 80-250 Hz; fast ripples: 250-500 Hz) are promising new biomarkers for epileptogenic tissue and can be found in intracranial and surface EEG. To date, we cannot reliably predict which neonates with seizures will develop childhood epilepsy. We questioned whether epileptic HFOs can be generated by the neonatal brain and potentially predict epilepsy.

Method: We selected 24 surface EEGs sampled at 2048 Hz with 175 seizures from 16 neonates and visually reviewed them for HFOs. Interictal epochs were also reviewed.

Result: We found HFOs in thirteen seizures (7%) from four neonates (25%). 5025 ictal ripples (rate 10 to 1311/min; average frequency 135 Hz; average duration 66 ms) and 1427 fast ripples (rate 8 to 356/min; average frequency 298 Hz; average duration 25 ms) were marked. Two neonates (13%) showed interictal HFOs (285 ripples and 25 fast ripples). All HFOs co-occurred with sharp transients. We could not yet find a relationship between neonatal HFOs and clinical outcome.

Conclusions: The neonatal brain can generate epileptic ripples and fast ripples, particularly during seizures, and they co-occur with ictal and interictal sharp transients. The occurrence of neonatal HFOs is not common and their potential clinical value not evident yet.

Abstract Number: 507

Title: Automatic sleep scoring from depth EEG recordings

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Purpose: To develop an algorithm for automatic sleep scoring based exclusively on depth EEG recordings.

Method: Forty-four consecutive epilepsy patients undergoing combined polysomnography/stereo-electroencephalography investigation were included. Polysomnography was comprised of electrooculography, chin electromyography and scalp EEG. Sleep was visually scored independently by two neurophysiologists according to standard criteria.
Automatic sleep scoring was carried out through machine learning, using 33 patients for development and training and 11 as hold-out set for testing. The automatic scoring requires exclusively a night of depth EEG. No further information (location or epileptogenicity of channels, EOG, EMG, scalp EEG) is used. Forty-eight features were computed for each 30s epoch based on band power, transient fluctuations, and characteristics of the non-oscillatory part of the spectrum. Based on these features, channels from the training set were separated into 20 clusters (unsupervised k-means algorithm), and a multiclass decision tree was fitted for each cluster (maximum 2000 splits).

Result: We considered the automatic detector made a correct prediction for an epoch when it coincided with at least one of the human raters. The median (range) per-patient epoch-by-epoch agreement was 70(42-77)% between automatic and visual scoring, and 86(75-92)% between the human raters. The median (range) per-patient sensitivity of the automatic detector was W=91(84-99)%, N1=0(0-0)%, N2=80(41-94)%, N3=70(43-99)%, R=18(0-86)%, and the specificity W=47(27-78)%, N1 undefined, N2=74(50-96)%, N3=90(55-99)%, R=96(15-100)%. To compare human raters, each was considered the ground-truth in turn, yielding equal sensitivity and specificity of W=96(76-99)%, N1=56(37-84)%, N2=81(64-92)%, N3=87(49-95)%, R=96(67-99)%. Not a single epoch in any patient was automatically classified as N1. The specificity for N3 and R was high, but sensitivity for R was low.

Conclusions: Automatic sleep scoring does not reach the performance of visual scoring when considering five stages but can be used to reliably identify segments of N3 and R without requiring EOG/EMG or scalp EEG.

Abstract Number: 523

Title: EEG as a biomarker in neonatal Molybdenum Cofactor Deficiency

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Purpose: Molybdenum cofactor deficiency (MoCD) is a rare autosomal recessive inborn error of metabolism, in which deficiency of the molybdenum cofactor dependent enzymes leads to an accumulation of neurotoxic metabolite (sulfite) and the deficit of the product (sulfate). Neonatal presentation is characterized by encephalopathy with intractable seizures. EEG background abnormalities in neonates with MoCD are typically characterized by burst-suppression pattern or encephalopathy with multifocal epileptiform discharges but to date no specific EEG findings have been described.

Method: retrospective search of the EEG database and the metabolic database from 2002 to 2020 at GOSH (UK) and Ferrara (IT). Patents with a confirmed diagnosis of MoCD and at least 1 EEG were included and their EEGs analysed.

Result: eleven infants with MoCD (6 males) aged 1-120 days were included (7 within 28 days of life). In the neonatal period the background activity was abnormal in all with burst-suppression (n=4), excess discontinuity (n=3) and/or multifocal discharges over the parasagittal regions (n=6). Seizures were recorded in all neonates (n=7) at 1-18 days which were electrographic-only in 6 and electro-clinical in 1, with high seizure burden and resistant to treatment. Ictal EEG pattern consisted predominantly of rhythmic delta frequencies with recruitment, arising independently from the central regions. Infants outside the neonatal period had lower seizure burden. A unique Delta-crown pattern (high amplitude delta transients with ripples of superimposed fast activity) was observed in 7 patients between 3 and 74 days of life. Delta-crowns were seen over the central regions and frequency increased at times of seizures.

Conclusions: EEG is a valuable biomarker in MoCD with abnormal background activity, a characteristic delta-crown pattern and a high seizure burden which is often electrographic-only.

Abstract Number: 545

Title: Safety and efficacy of cathodal transcranial direct current stimulation in patients with Lennox Gastaut Syndrome

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Safety and efficacy of cathodal transcranial direct current stimulation in patients with Lennox Gastaut Syndrome

Purpose: Lennox-Gastaut Syndrome (SLG) is a severe form of childhood refractory epilepsy. Only one pilot study has been conducted using cathodal transcranial direct current stimulation (c-TDCS; 2mAx30minx5days) in LGS with promising results (-99% seizure reduction at 5 day). Our aim was to assess the efficacy and safety of 10 sessions of c-tDCS in SLG.

Methods: We conducted a doble blind placebo-controlled randomized clinical study to treat LGS patients with ten consecutive days (with 2-day rest during weekend) of c-tDCS (2mAx 30 min), over highest amplitude epileptiform discharges areas based in a EEG recording without changes in their pharmacological treatments. The tDCS device used was Enobio EEG® (Neuroelectrics, Barcelona, Spain). Assessment of seizure frequency was performed using SZs diaries before, during the 2 weeks of treatment, and then on a 4 and 8 weeks of follow-up. Descriptive statistics and Wilcoxon signed rank test and two-way ANOVA were used.

Results: Twenty-eight patients were enrolled. Mean age was 10.1 ±5.9 years-old and 75% male. All the patients had severe mental retardation and abnormal neurological examination. In the c-TDCS group we found a significant median percentual seizure frequency reduction: -61% (p=<0.001) at 1 week of c-TDCS, -74.1% (p=<0.001) in the second week, -53.6% (p=<0.02) a month after therapy and -77.6% (p=<0.003) at 2 months; mainly tonic and atonic seizure were reduced significantly in all the times. Only mild self-limited side effects were recorded in the c-TDCS group mainly itching and erythema in the application zone.

Conclusion: Ten sessions of c-tDCS in combination with pharmacologic treatment in LGS is safe and appear reduce significatively seizure frequency at 2 months of follow-up.

Abstract Number: 587

Title: Fully-Automated Spike Detection and Dipole Analysis of Epileptic Magnetoencephalograms Using Deep Learning

Masayuki Hirata[1], Ryoji Hirano[1,2], Takuto Emura[2], Otoichi Nakata[2], Toshiharu Nakashima[2], Miyako Asai[2], Kuriko Shimono[1], Haruhiko Kishima[1]

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Purpose:
Magnetoencephalography (MEG) is a useful tool for clinically evaluating the localization of interictal spikes. Neurophysiologists visually identify spikes from the MEG waveforms and estimate the equivalent current dipoles (ECD). However, presently these analyses are manually performed by neurophysiologists and are time-consuming. Another issue is that spike identification from MEG waveforms largely depends on neurophysiologists' skills and experiences. Combined, these issues cause poor cost-effectiveness in clinical MEG testing. Here, we fully automated spike identification and ECD estimation using a deep learning approach to overcome these issues: fully automated AI-based MEG interictal epileptiform discharge identification and dipole estimation (FAMED).

Method: We applied a semantic segmentation method, which is an image processing technique, to identify the appropriate times between spike onset and peak and to select appropriate sensors for ECD estimation. FAMED was trained and evaluated using clinical MEG data with spikes analyzed by neurophysiologists acquired from 375 patients. FAMED training was performed in two stages: the first stage was to learn a waveform classification network, and the second stage was to learn a segmentation network that extended the classification network.

Result: Regarding the classification network, the AUC was 0.987 ± 0.005 (10-fold patient-wise cross-validation), and the sensitivity and specificity were 0.795 and 0.997, respectively. The median distance between the dipoles estimated by the neurophysiologists and the dipoles estimated using FAMED was 0.43 cm.

Conclusions:
The performance of FAMED is comparable to that of neurophysiologists, and it can contribute to the efficiency and consistency of MEG dipole analysis.

Abstract Number: 617

Title: Electrophysiological effects in the first 48 hours after withdrawal of perampanel and levetiracetam in refractory epilepsy patients

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Purpose: Assessment of electrophysiological effects of withdrawal of the anti-seizure drug (ASD), perampanel (PER) and levetiracetam (LEV), in refractory epilepsy patients. Because of the longer half-life of PER (around 105h) compared to LEV (6-8h), we hypothesize more electrophysiological changes in LEV withdrawal than in PER withdrawal.

Method: Eighteen patients treated with PER (n=9) or LEV (n=9) were selected from the LTM database of Geneva University Hospital and Oslo University Hospital. Inclusion criteria were: >18y old, PER or LEV tapered during the LTM and EEG duration >48 hours after the last dose. Automated spike detection was performed and the baseline corrected spike rate at night 1, day 1, night 2 and day 2. Quantitative spectral analysis was performed to investigate changes in EEG spectral activity.

Result: There was no significant change in spike rate between the LEV and PER group. Nevertheless, the median spike rate rises at day 2 in the LEV group, while it remains stable in PER group. When comparing spectral activity we found a significant statistical difference at night 2 in the delta (p=0.005), theta (p=0.018)

and alpha band (p=0.048). The power in the delta and theta band increased in LEV patients while it remained constant in PER patients. This increase in LEV patients corresponds with an earlier study that showed a decrease in delta and theta power when patients were treated with LEV (Cho JR et al. Clin Neurophysiol. 2012).

Conclusions: This study shows that quantitative EEG analysis can provide insights into changes in brain activity after drug withdrawal. Despite the low number of patients in the study, the results suggest that smaller changes are seen in the EEG of PER patient compared to LEV patients after drug withdrawal, which could be related to longer half-life.

Abstract Number: 627

Title: Seizure-onset EEG patterns in malformations of cortical development: a systematic review

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Purpose: Malformations of cortical development (MCDs) are a large, heterogenous group of disrupted cerebral cortex formations often associated with drug-resistant epilepsy. MCDs may not be recognised on MRI resulting in significant delay in epilepsy surgery in suitable candidates. Characteristic EEG features can guide MCD identification. We systematically reviewed studies reporting scalp or intracranial EEG seizure-onset patterns in MCDs, aiming to assess the predictive value of specific patterns across different types of MCDs.

Method: We searched databases for English publications on scalp or intracranial EEG seizure-onset patterns in MCDs. Two reviewers independently screened title and abstracts and reviewed full-text articles. A third reviewer resolved discrepancies. For the first three publications, data were extracted by two independent reviewers to ensure consistency in the data extraction process. Data from the remaining papers were extracted by one author. Due to the wide variability in reported EEG patterns, a classification framework was implemented to group different descriptions in specific predefined patterns. Multinomial logistic regression was used to predict the probability of MCD types for each EEG pattern.

Result: Of 1568 publications identified, 13 studies comprising 354 MCD patients were included. Five scalp EEG and six intracranial EEG seizure-onset patterns were defined. Of the scalp EEG patterns, repetitive epileptiform discharges had higher predictive probabilities for focal cortical dysplasia (FCD) (0.33, corrected-p=0.006) and tuberous sclerosis (0.24, corrected-p=0.04) than polymicrogyria (<0.001), while rhythmic slow activity had a higher predictive probability for heterotopia (0.65) than polymicrogyria (0.06, corrected-p=0.03). Of the intracranial EEG patterns, spike-and-wave activity had higher predictive probability for FCD (0.67) than tuberous sclerosis (0.20, corrected-p<0.001), heterotopia (0.13, corrected-p<0.001) and polymicrogyria (<0.001, corrected-p <0.001).

Conclusions: MCD types share similar EEG patterns reflecting some degree of similarity in their underlying biological structure. However, certain EEG patterns can aid in diagnosing specific MCD types, specifically in MRI-negative cases.

Abstract Number: 695

Title: Surgery-Related Changes in Sleep Spindle Activity of Children with Drug-Resistant Epilepsy

Assia Chericoni[1,2], Lorenzo Ricci[3], Georgios Ntolkeras[1,4], Joseph Madsen[4,5], Phillip Pearl[4,6], Alexander Rotenberg[4,7], Ellen Grant[1,4], Eleonora Tamilia[1,4]

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Purpose: Sleep spindles (waxing-and-waning 10–16 Hz oscillations) are considered the EEG hallmark of non-REM sleep. Several studies showed that non-REM sleep facilitates epileptic activity in the brain; however, it is rather unknown whether or how an epileptogenic focus (*epi-focus*) alters the generation of spindles. Here, we examined children with drug-resistant epilepsy (DRE), who became seizure-free after surgery, with the purpose of evaluating spectral and spatial evolution of sleep spindles before and after successful surgery, in relation to the epileptogenic focus (*Epi-Focus*).

Method: We included 19 children who had epilepsy surgery at Boston Children's Hospital. For each patient, we analyzed N2-sleep EEG (19-24 channels) collected before and after surgery. We identified spindles and labelled them as *slow* or *fast* based on their power spectrum (**Fig.1A**). We estimated the cortical source of each spindle through electrical source imaging (ESI; **Fig.1B**). We delineated each child's *Epi-Focus* (**Fig.1B**) by identifying the resection on the post-op MRI and performed ESI on interictal spikes to localize *spiking-areas*. For each spindle, we computed distance from *Epi-Focus* ($distance_{EpiF}$) and from spiking-area ($distance_{Spikes}$). We tested effect and interaction of two factors (spindle type: slow/fast; phase: pre-surgery/post-surgery) on spindle characteristics using two-way ANOVA.

Result: We observed surgery-related changes in power and frequency of slow-spindles (**Fig.2A**), but not fast-spindles. Similarly, the spatial extent decreased after surgery for slow-spindles ($p<0.001$) but not for fast-spindles. Slow-spindles presented shorter $distance_{EpiF}$ and $distance_{Spikes}$ compared to fast-spindles before surgery, but not after surgery ($p<0.001$, **Fig.2B**). Finally, a higher percentage of slow-spindles than fast-spindles co-localized with spiking-areas (**Fig.2C**; $p=0.02$).

Conclusion: We present first evidence of surgery-related changes in the cortical generation of sleep spindles in children with DRE. Our data suggest spatial relationship between slow-spindle generators and epileptogenic generators that is not seen for fast-spindles, which do not present surgery-related changes in their characteristics.

Figure 1. Spindle labelling (slow vs. fast) and source localization

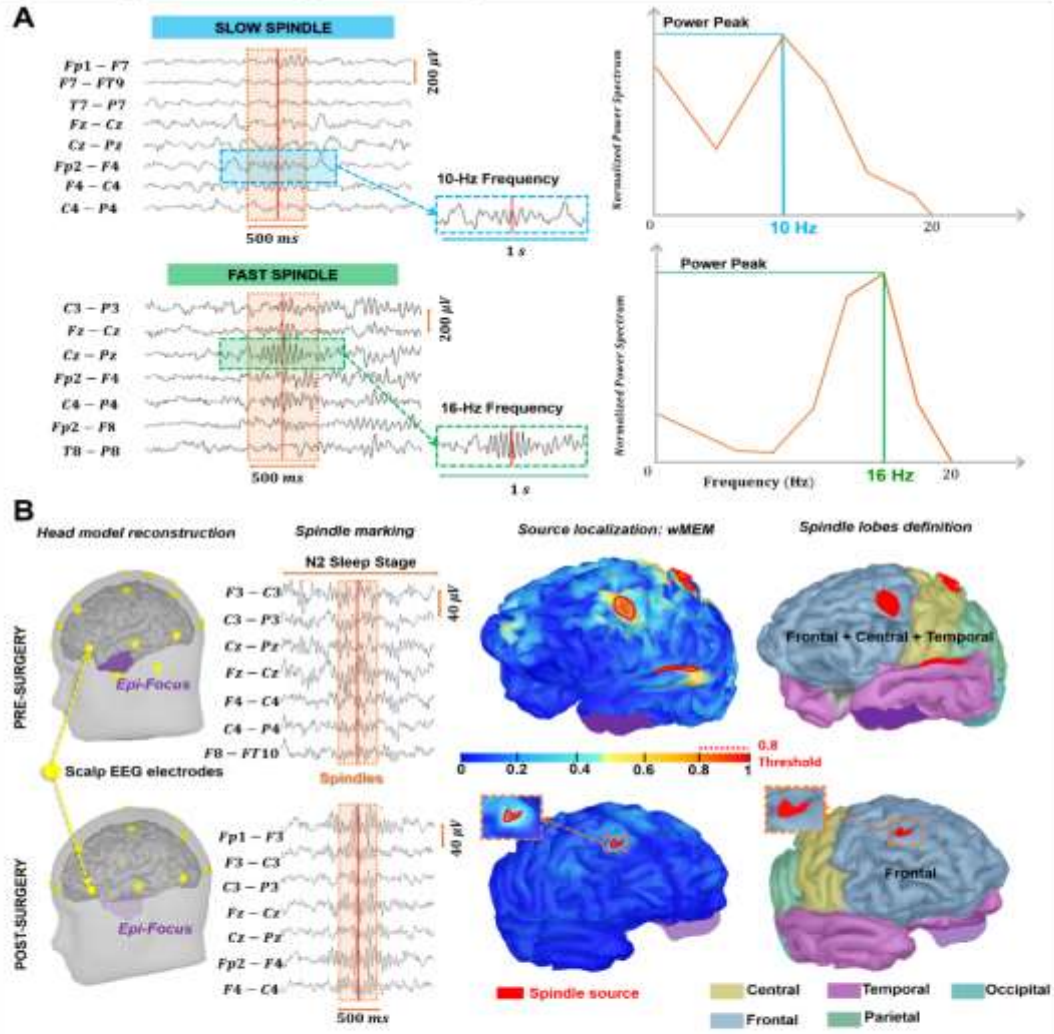

Figure 1: **A.** Visual marking of spindles on bipolar montage and their power spectrum (averaged across channels). Top spindle is classified as "slow" having a power peak at 10 Hz, while the bottom spindle is classified as "fast" (power peak at 16 Hz); **B.** 3D electrodes reconstruction on the child's head, before and after the surgery. Each marked spindle is localized on the cortex using the *Wavelet Maximum Entropy of the Mean* (wMEM), where activation values are associated to each cortical vertex (middle panels). The highest amplitude vertices (i.e., normalized amplitude > 0.8) delineate each spindle cortical source, which is then assigned to a cortical anatomical area (central, frontal, temporal, parietal or occipital).

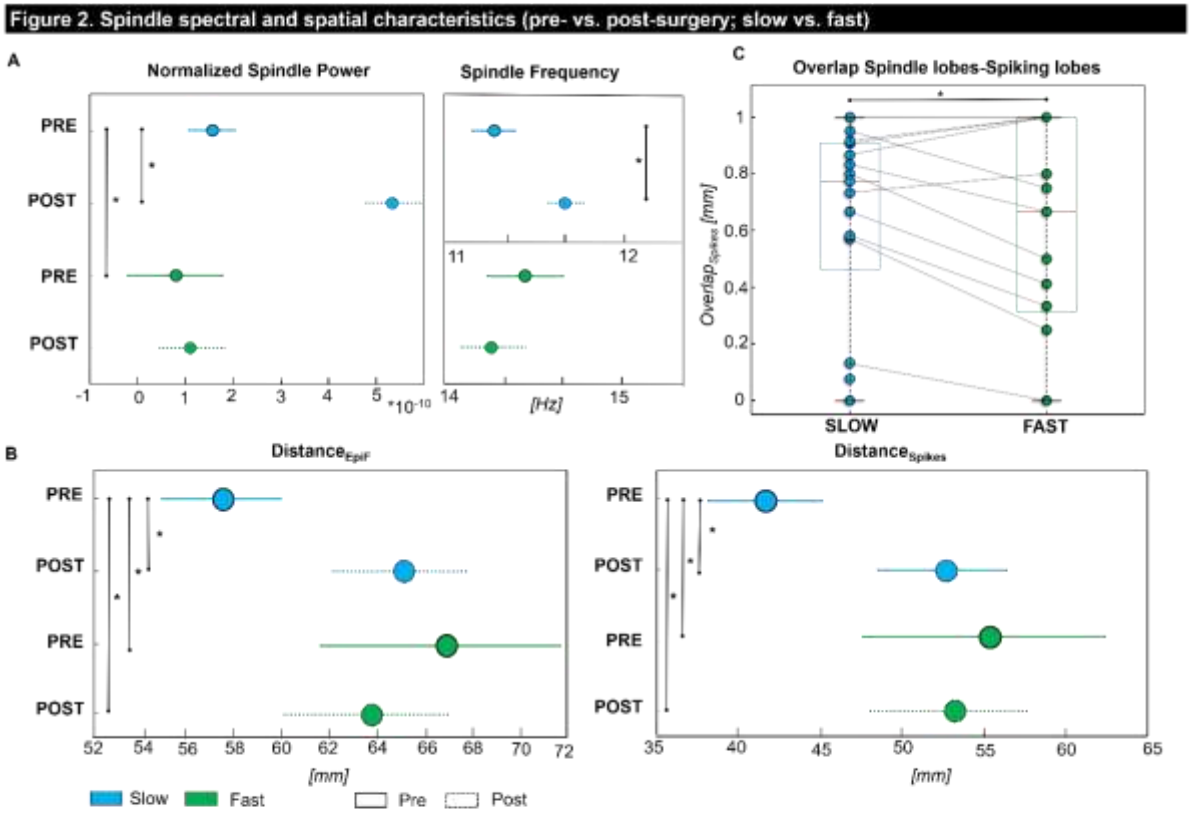

Figure 2: **A.** Interaction between the effects of type (slow vs. fast) and phase (pre vs. post) on spindle power and frequency: power increase is seen between pre- and post-surgery only for slow spindles ($p<0.001$), frequency increase between pre- and post-surgery was seen just for slow spindles ($p=0.0037$); **B.** Slow spindles are closer to the epi-focus (shorter $Distance_{EpiF}$) than fast spindles before surgery ($p<0.001$), but not after surgery. The same results were obtained for $Distance_{Spikes}$ ($p=0.0167$). **C.** The percentage of spindle generators in the proximity of the epi-focus is greater before than after surgery for slow spindles only ($p=0.02$).

Abstract Number: 716

Title: Non-invasive Electrophysiological Signatures of the Epileptogenic Zone in Children with Focal Drug-Resistant Epilepsy

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Purpose: Children with drug-resistant epilepsy (DRE) need neurosurgery for seizure control. To delineate the epileptogenic zone multiple techniques are used, among which conventional scalp EEG is the most widely used across all epilepsy centers. Interictal EEG is traditionally reviewed seeking visually identifiable epilepsy biomarkers (i.e., spikes); however, sophisticated EEG analysis can provide additional information on the

underlying epileptogenicity albeit not visibly identifiable by the human reader. Our purpose is to identify novel non-invasive EEG measures that characterize the epileptogenic tissue in children with DRE via phase-amplitude coupling (PAC) and regional connectivity (rConn) analysis at the source level.

Method: We analyzed sleep scalp-EEG (19-24 channels) from 19 children who had successful epilepsy surgery (Engel1). We distinguished between EEG epochs with and without spikes (spike-epochs vs. silent-epochs, **Fig.1A**). We defined Epileptogenic-Tissue (*EpiTissue*) as the area resected during surgery and *Non-EpiTissue* as the homotopic region in the contralateral hemisphere (**Fig.1B**). Using source localization, we reconstructed the activity of *EpiTissue* and *non-EpiTissue* (virtual sensors placed 20-mm apart, **Fig.1C**). We computed rConn within *EpiTissue* and *non-EpiTissue* (in delta, theta, alpha, beta and gamma bands) as well as their PAC (between delta and gamma). PAC and rConn values were compared between *EpiTissue* and *non-EpiTissue* for silent-epochs and spike-epochs (*Wilcoxon-sign-rank*).

Result: We found increased beta rConn in the *EpiTissue* compared to *non-EpiTissue* in silent-epochs (p=0.01) and spike-epochs (p=0.007, **Fig.2A&B**)**,** and increased gamma rConn in spike-epochs (p=0.009). In both *EpiTissue* and *non-EpiTissue*, rConn (p<0.001, p=0.02, **Fig.2B**) and PAC (p<0.001, p<0.001) were higher, and showed more variability, during spike-epochs compared to silent-epochs. We also found increased PAC in the *EpiTissue* compared to *non-EpiTissue* in silent-epochs (p=0.014, **Fig.2C**).

Conclusions: Non-invasive measures of increased regional connectivity and PAC (estimated via scalp-EEG source imaging) can help identify the *EpiTissue* in children with focal DRE using non-ictal EEG

recordings with or without spikes.

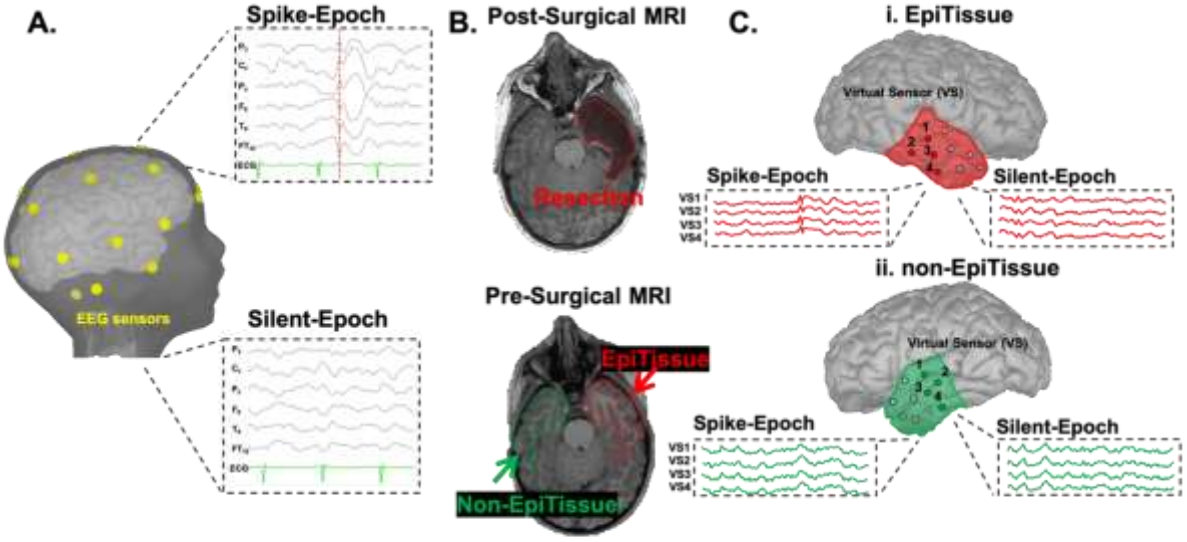

Figure 1: A. 3D-reconstruction of scalp EEG Electrodes on the child's head. Signals were segmented in 2-sec epochs including a spike (Spike-Epoch) or without spikes (Silent-Epoch). **B.** Post-surgical MRI showing the resected area that was used to define the EpiTissue and the contralateral healthy brain region (non-EpiTissue) in the pre-surgical MRI. **C.** Virtual sensors placed in the EpiTissue **(Ci.)** and non-EpiTissue **(Cii.)** and corresponding activity reconstructed via electrical source imaging.

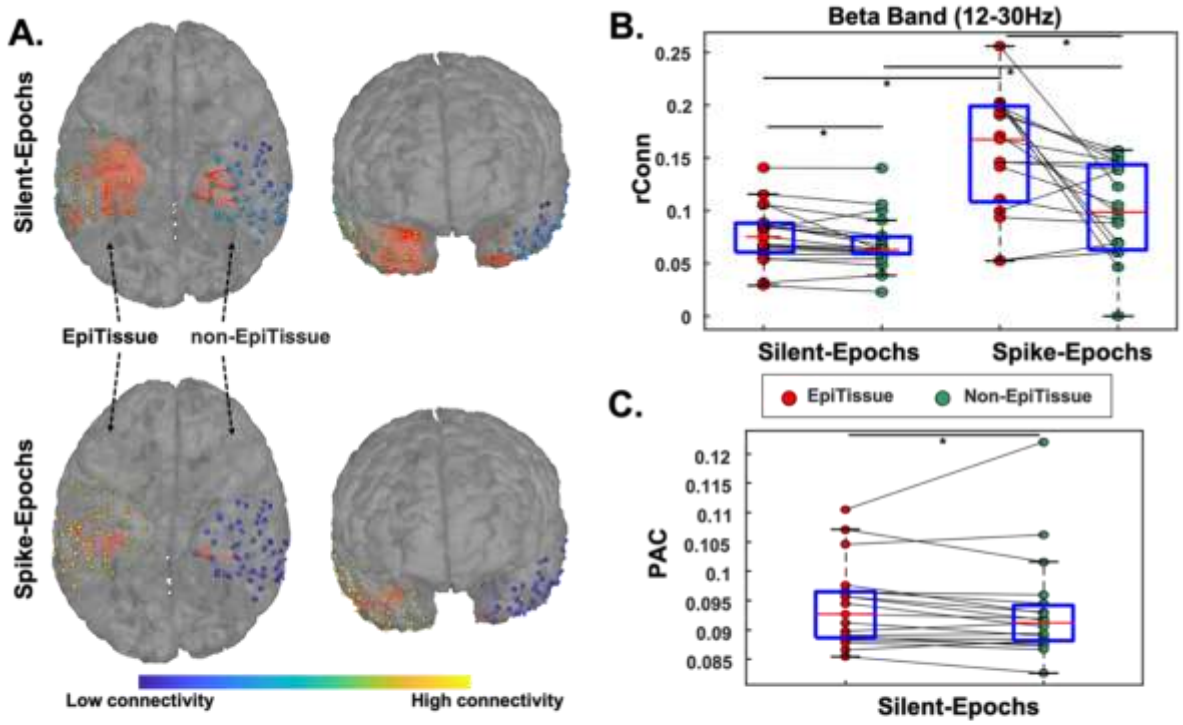

Figure 2: A. Virtual sensors placed in EpiTissue and non-EpiTissue in the same patient. Colormap shows regional connectivity (rConn) in Silent-Epochs (left) and Spike-Epochs (right). Warm colors (yellow-orange) correspond to higher, while cold colors (blue) to lower rConn. Orange lines show connections between sensors that overpass 80% of maximum rConn within that region. Spike-Epochs have fewer virtual sensors overcoming 80%-threshold in comparison with silent-epochs representing a higher variability in rConn within the region. **B.** Regional connectivity in Beta band (12-30Hz) in EpiTissue (red) and non-EpiTissue (green) **C.** Phase-amplitude coupling (PAC) in the Beta band (12-30Hz) in EpiTissue and non-EpiTissue

Abstract Number: 718

Title: Overdiagnosis of epileptiform discharges in patients in the postoperative period (misinterpretation of breach-rhythm)

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Purpose: to study the significance of breach-rhythm in the interpretation of EEG results in patients with epilepsy and craniotomy defect in the postoperative period.

Method: we analyzed the results of video-EEG monitoring in the preoperative period and after neurosurgical treatment in 7 patients with structural focal epilepsy (5/7 patients - removal of meningeoma, 2/7 - removal of brain tumor) and compared different EEG results in the postoperative period.

Result: in the EEG in the preoperative period 3/7 patients had a constant regional slowing, 4/7 patients had persistent regional slowing, 4/7 patients - regional epileptiform discharges in the area of structural brain damage. After neurosurgical treatment, all patients were monitored by neurologist at the polyclinic, and 3

months later, 5/7 patients made routine outpatient EEG, and 2/7 patients made video-EEG monitoring. In all cases, according to the conclusions, epileptiform discharges were described like regional spikes, spike-and-wave complexes and slow spike-and-wave complexes. During video-EEG monitoring in Federal Center for Brain Research and Neurotechnologies, breach-rhythm was recorded in 6 cases. Only 3/7 patients have epileptiform discharges – 2/7 in combination with breach-rhythm, 1/7 without it.

Conclusions: breach-rhythm is an artifact in the form of high-voltage waveforms of the alpha, beta range, which develops near skull defects (Cobb WA et al., ElectroencephalogrClinNeurophysiol. 1979; 47(3):251-271). Our clinical experience shows the difficulty of interpretation of EEG results in patients with structural focal epilepsy and craniotomy defect. Breach-rhythm is not related to epileptiform discharges, but can mimic it (Brigo F. et al., ClinNeurophysiol. 2011; 122(11):2116-2120). In 4/7 patients (57.1% of cases), high-amplitude waves with spike-like morphology, caused by breach-rhythm, were mistakenly regarded as epileptiform discharges. For correct interpretation of EEG results, clinical neurophysiologists need information about medical history (including head injury and neurosurgical treatment).

Abstract Number: 723

Title: Seizure detection using a reduced number of channels

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Purpose: The aim is to validate a channel ranking and selection model in a subset of patients with scalp electroencephalogram (EEG). We expected that the model's performance would decline as we reduced the number of analysed channels.

Method: We used our validated random forest classifier on the EPILEPSIAE surface EEG data (30 patient subset) to rank the EEG channels in order of their contribution to the detection of a given seizure. The patients' epilepsy type was a mix of complex partial, secondary partial, secondary generalised and unclassified. Next, we used the automatic channel selection (ACS) algorithm to select the 10 most important channels per patient. For seizure detection, we fed the complete number of channels per patient into our seizure detection model. Next, the top 10 channels across the entire group of 30 patients were selected and fed into our seizure detection model. Lastly, we selected a subset of the top 6 channels from the top 10, and fed those into our model.

Result: The average AUC score for seizure detection on 19, 10, and 6 channels was 98.03, 91.57, 92.25, respectively. We attributed the slightly higher average AUC for the 6-channel condition to several patients with improved performance compared to the 10 channels condition. However, the number of false positives remained a challenge.

Conclusions: Although the electrode selection model was promising for some patients, the overall results illustrate the difficulty in achieving optimal performance with a reduced number of channels. Despite the model producing favourable results for some, performance declined for most patients when the number of channels reduced from 19 to 6. A limitation was the small dataset for model training. Future works could benefit from further refinement of the model using extensive data for model training and validation.

Abstract Number: 753

Title: Network analysis of impaired awareness in mesial temporal lobe epilepsy in foramen ovale and scalp EEG co-registration

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Purpose: Seizures with impaired awareness (SIA) significantly affect the quality of life of people with temporal lobe epilepsy. Whereas a large number of researches focused on network alterations characterizing TLEs, very few studies investigated connectivity modifications underlying SIA. This paper aimed at investigating hub's network alterations of subjective manifestations without impaired awareness (auras) and SIAs in mesial TLE with foramen-ovale and scalp-EEG co-registration.

Method: One *aura* and one SIA event were selected from each of the six patients enrolled in the study. Network temporal dynamic among 4 different time epochs, as well as the differences between aura and SIA, were analyzed through a linear multivariate index (partial directed coherence) and six graph theory-based indexes of "centrality".

Result: Regarding the auras temporal evolution, fronto-parietal (FP) regions showed decreased connectivity with respect to the interictal period, in both epileptogenic (EZ) and non-epileptogenic zone (nEZ). During SIAs, temporal dynamic showed more changes than auras: centrality of mesial temporal (mT) regions changes during all conditions, and nEZ FP centrality showed the same dynamic trend of the aura (decreased centrality), until the last epoch, close to the impaired awareness, when showed increased centrality. Comparing SIA with aura, in proximity of impaired awareness, increased centrality was found in all the regions, except in nEZ mT, which showed reduced connectivity in SIA with respect to aura.

Conclusions: Our findings suggested that the impairment of awareness is a dynamical process that requires different steps and has a clear relationship with functional hubs alterations. Network hubs changes occur mainly and earlier in neocortical regions than in the mesial ones and most of these connectivity changes, leading to SIA, start when awareness is still retained and before visible scalp EEG and clinical alterations. The analysis of 'hub' alteration can represent a suitable biomarker for scalp EEG-based prediction of awareness impairment.

Abstract Number: 797

Title: Characteristic occipital epileptiform EEG pattern in ADCK3-related mitochondrial disease

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Purpose: ADCK3-related disease is a mitochondrial disorder associated with an abnormality of coenzyme Q_{10} metabolism. Ataxia and epilepsy are common, and the phenotype overlaps with other mitochondrial

encephalopathies, particularly POLG related disease. CoQ_{10} supplementation may be beneficial. We have noted a remarkable epileptiform pattern in ADCK3-related encephalopathy, and since EEG studies in this rare condition are limited, we wished to assess the evolution of EEG characteristics in patients with this disorder.

Method: All EEG recordings of the four known patients from Mid Norway were systematically reviewed. EEG graphoelements were classified according to the standardized computer-based organized reporting of EEG (SCORE) and international glossary terms. The evolution of EEG features was assessed. A total of 96 recordings spanning over 15-32 years were available, mean 24 per patient (range 17-28). Altogether, 50 digital recordings were reviewed, including four long term and 46 selected paper segments.

Result: In three patients, EEG showed prominent bilateral asynchronous and synchronous epileptiform discharges in occipital and posterior-temporal regions. This intense activity included multiple epileptiform graphoelements, which occurred continuously, nearly continuously or in prolonged runs. The findings remained stable over many years.

Conclusions: Although the number of patients is small, we suggest that interictal EEG findings of continuous/nearly continuous bi-occipital spike-waves may serve as a biomarker for this potentially treatable condition. This peculiar EEG pattern might help to differentiate ADCK3- related disease from the more common POLG related disease, which is usually characterized by lateralized or focal slowing with more sporadic epileptiform elements of similar topography.

Abstract Number: 803

Title: Objective and subjective assessment of the effect of Levetiracetam on daytime sleepiness in patients with epilepsy

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Purpose: The purpose of our study is the subjective and objective assessment of the effects of 2000 mg Levetiracetam (LEV) monotherapy over a 3-month period on daytime sleepiness in patients with epilepsy.

Method: The subjective assessment of daytime sleepiness was made through Epworth sleepiness scale (ESS), and the objective assessment - through 4 naps MSLT, preceded by a PSG. All procedures were performed at baseline and after a 3-month period of LEV treatment. The dynamics in ESS score, the dynamics in the mean sleep latency for all naps and sleep stage were evaluated.

Result: Twenty nine patients participated in our study. The subjective and objective assessment of daytime sleepiness matched in only 5 of them. In none of the patients ESS score was worsened after therapy. There was a statistically significant difference between the subjective assessment at baseline and after therapy. There was no statistically significant difference between the objective assessment of daytime sleepiness at baseline and after therapy. The patients with prolonged mean sleep latency reached a deeper sleep stage after therapy. The daytime sleepiness assessment correlated only with seizure frequency - patients with < 1 seizure a year had more constant mean sleep latency.

Conclusions: LEV 2000 mg/day does not worsen the subjective and the objective assessment of daytime sleepiness in patients with epilepsy.

Abstract Number: 818

Title: The influence of the abundance and morphology of epileptiform discharges on diagnostic accuracy: How many spikes you need to spot in an EEG

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Purpose: The operational definition of interictal epileptiform discharges (IEDs) of the International Federation of Clinical Neurophysiology (IFCN) described 6 morphological criteria. Our objective was to assess the impact of pattern-repetition in the EEG-recording, on the diagnostic accuracy of using the IFCN criteria. For clinical implementation, specificity over 95% was set as target

Method: Interictal EEG-recordings of 20-minutes, containing sharp-transients, from 60 patients (30 with epilepsy and 30 with non-epileptic paroxysmal events) were evaluated by three experts, who first marked IEDs solely based on expert opinion, and then, independently from the first session, evaluated the presence of the IFCN criteria for each sharp-transient. The gold standard was derived from long-term video-EEG recordings of the patients´ habitual paroxysmal episodes.

Result: Presence of at least one discharge fulfilling 5 criteria provided a specificity of 100% (sensitivity: 70%). For discharges fulfilling fewer criteria, a higher number of discharges was needed to keep the specificity over 95% (5 discharges, when only 3 criteria were fulfilled). A sequential combination of these sets of criteria and thresholds provided a specificity of 97% and sensitivity of 80%.

Conclusions: Pattern-repetition and IED morphology influence diagnostic accuracy, and systematic application of these criteria will improve quality of clinical EEG interpretation.

Abstract Number: 825

Title: A biomarker for benign adult familial myoclonus epilepsy: High-frequency activity in giant SEPs

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Purpose:
To elucidate the pathophysiology and establish reliable biomarkers including high-frequency oscillations (HFOs) with giant somatosensory evoked potentials (SEPs) for the diagnosis of benign adult familial myoclonus epilepsy (BAFME).

Method: This retrospective case study included 49 consecutive cortical myoclonus (CM) patients (16 BAFME and 33 other CM patients) who exhibited giant P25 or N35 SEPs. The SEPs were processed by a band-pass filter of 400–1000 Hz to analyze HFOs. Clinical and SEP findings were compared between (1) BAFME and other CM groups and (2) the presence and absence of P25-HFOs (HFOs superimposed on giant P25). The diagnostic power of each factor for BAFME was calculated.

Result: All 16 BAFME patients showed SEP P25-HFOs with significantly higher occurrence ($p < 0.0001$) compared with that of other CM groups. The presence of P25-HFOs significantly correlated with a BAFME diagnosis ($p < 0.0001$) and high SEP P25 and N35 amplitudes ($p = 0.01$ and $p < 0.0001$, respectively). BAFME was

reliably diagnosed using P25-HFOs with high sensitivity (100%), specificity (87.9%), positive predictive value (80%), and negative predictive value (100%), demonstrating its superiority as a diagnostic factor compared to other factors.

Conclusions: P25-HFOs with giant SEPs is a potential biomarker for BAFME diagnosis. P25-HFOs may reflect cortical hyperexcitability partly due to paroxysmal depolarizing shifts (PDS) in epileptic neuronal activities and higher degrees of rhythmic tremulousness than those in ordinary CM.

Abstract Number: 837

Title: Clinical and Neurophysiological Characterisation of Ictal and Sleep Pattern in Alternating Hemiplegia of Childhood

Josie Poole[1,2], Sara Zagaglia[1,2], Fiona Farrell[1,2], Matthew C. Walker[1], Sanjay Sisodiya[1,2], Umesh Vivekananda[1], Simona Balestrini[1,2,3]

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Purpose: Our aims were to: 1) characterise the sleep phenotype of Alternating Hemiplegia of Childhood (AHC), a rare monogenic neurological condition characterised by unilateral or bilateral hemiplegic and other paroxysmal events, including dystonic spells and refractory epileptic seizures; 2) explore potential sleep-wake alterations in brain states, as the remission of hemiplegia with sleep is a clinical diagnostic feature of AHC.

Method: Retrospective clinical phenotyping and electroencephalography (EEG) spectral analysis were carried out in 5 adults with AHC. 10-minute samples of wake, light sleep and deep sleep from clinical video-EEGs for each AHC patient were compared with 12 age-/gender-matched control patients with well-controlled epilepsy and no epileptiform abnormality on EEG. Additional 5-minute epochs pruned before, during, and after hemiplegic episodes were analysed where available. Arousals were counted per hour of sleep and divided by the total number of hours of sleep-EEG available.

Result: Preliminary spectral analysis suggests: 1) reduced alpha and beta power and increased delta and theta power during wake in AHC versus controls; 2) intra-individual hemispheric differences in ictal power (p=0.024), with increased power contralateral to the clinically affected side, when lateralising signs were identified, during 10 hemiplegic episodes from 2 AHC patients; this was most prominent in the pre-attack phase. There were 97% more arousals in the AHC group versus controls (p=0.00032) and the sleep-EEG was further interrupted by epileptiform activity and clinical events in 60% of the AHC group.

Conclusions: Sleep is disrupted in adults with AHC. Given the risks associated with seizures from sleep, such as sudden unexpected death in epilepsy, and the restorative benefit of sleep in AHC, it is imperative that this is explored further. The presence of pre-ictal hemispheric differences in spectral power provides a novel insight into the neurophysiological signature of hemiplegia in AHC and a potential predictive tool for hemiplegic episodes.

Abstract Number: 859

Title: A deep learning method is useful for seizure detection before or at early ictal stage in hypersynchronous EEG pattern.

Masahiro Gotoh[1], Shunsuke Kajikawa[1], Katsuya Kobayashi[1], Masao Matsuhashi[2], Kiyohide Usami[2], Akihiro Shimotake[1], Takefumi Hitomi[3], Yamao Yukihiro[4], Kikuchi Takayuki[4], Kazumichi Yoshida[4], Ryosuke Takahashi[1], Akio Ikeda[2]

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Purpose: Seizure detection methods before or at early ictal stage is important for epilepsy monitoring examination of high degree of safety and for responsive seizure abortion therapy. We experienced a patient with temporal lobe epilepsy (TLE) showing repetitive, sharply contoured, high-amplitude discharges called hypersynchronous pattern (HYP) at hippocampus in stereo-electroencephalography (SEEG). Two types of HYP were identified: (1) HYP leading to subclinical ictal activity (defined as pre-ictal HYP) and (2) HYP not leading to ictal activity (defined as aborted-ictal HYP). The power spectrogram revealed that each HYP discharge was accompanied by high frequency activity (HFA) and the HFA in pre-ictal HYP tended to increase toward ictal activity. Based on these findings, we utilized deep learning to distinguish pre-ictal and aborted-ictal HYP.

Method: In 1 patient with TLE by SEEG, each HYP was divided into 5 segments in time course. The pre-ictal HYP discharges in segment 3 and 4 showing increased HFAs were labeled as red, and the aborted-ictal HYP discharges were labeled as green. We collected 555 discharges for both red and green, and each signal (-0.3 to +0.3 s from the peak) was converted to spectrogram by fast Fourier transformation. We applied convolutional neural network to distinguish the two. The model was validated with another dataset.

Result: In the validation dataset (20 HYPs for each pre-ictal and aborted-ictal, 224 red and 420 green discharges), the correct red/green discrimination rate (accuracy) was 81.1%. The rate of red-predicted discharges in HYP was 61.1% for pre-ictal and 13.3% for aborted-ictal. Setting presumably a seizure prediction threshold as 8 red discharges in HYP, the correct prediction rate was 82.5%.

Conclusions: In this TLE patient with pre-ictal and aborted-ictal HYP, deep learning effectively distinguished 2 types of HYP. Thus, deep learning focusing on spectrogram of HYP discharges may be useful for future seizure prediction.

Abstract Number: 863

Title: Usefulness of 24-hour Ambulatory EEG Monitoring in the Diagnosis of Typical Absences

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Purpose: Voluntary hyperventilation (VH) is believed to be highly successful to elicit typical absences (*TAs*), especially in patients with genetic generalized epilepsies (GGE) and absences, including childhood and juvenile absence epilepsy (CAE and JAE) respectively. Failure in recording *TAs* may lead to diagnostic uncertainties and therapeutic difficulties in clinical practice. Thus, the aim of this study was to evaluate the diagnostic yield of 24-hour ambulatory EEG monitoring (EEG/DIN) compared with VH, in patients with suspected or definite *TAs*/GGE. We also evaluated if any clinical factors might influence VH efficacy.

Method: The study group included 108 consecutive individuals (53 women, mean age 12.6±5.4 years) clinically suspected of having TAs, who were enrolled between January 2011 and December 2018. All underwent EEG recording with VH for 4-5 min of maximal effort from the subject, with monitoring of respiratory excursions and encouragement by the EEG technologist. If standard EEG was uninformative, they were investigated with EEG/DIN.

Result: Three distinct groups were defined on the basis of HV and EEG/DIN findings: -ì. In 61/108 (56%) subjects (41/61 with CAE, 20/61 with JAE, 43/61 on antiepileptic drugs [AEDs]), HV triggered TAs. -ii. In 36/108 (34%) individuals (17/36 with CAE, 19/36 with JAE; and 26/36 on AEDs), HV was unsuccessful, but EEG/DIN showed TAs or electrophysiological hallmarks of them. -iii. The remaining 11/108 patients had normal EEG with HV and EEG/DIN, and the diagnosis of TAs/GGE was ruled out in 9/11 of them. AED was discontinued in 2/4 individuals on therapy at the time of the study.

Conclusions: The results of this study have illustrated a higher diagnostic yield of EEG/DIN than HV in individuals with *TAs*/GGE. Moreover, HV was less effective in JAE, regardless of AED therapy. Overall, these findings give evidence that EEG/DIN greatly help establish the diagnosis and monitor *TAs*, especially in JAE.

Abstract Number: 886

Title: Bi-hemispheric synchrony in childhood absence epilepsy

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Purpose: Epilepsy with a genetic etiology and an onset in early childhood commonly is characterized by a bilateral distribution of synchronously occurring (generalized) epileptic discharges in the EEG, the so-called Spike-and-Wave Discharges (SWDs). This type of difficult to treat epilepsies often goes along with impairment of the child's cognitive development. In the current research project, a mobile EEG device was used to evaluate a novel EEG biomarker, which might be related to the impact on cognition of patients with frequently occurring generalized SWDs.

Method: For the recording of the SWDs recently introduced C-shaped EEG grids (cEEGrids) with ten electrodes, which are mounted behind the ears (http://ceegrid.com/home/), were used together with a wireless EEG amplifier (SAGA: TMSi ®, Oldenzaal, Netherlands). In this study we calculated the Mean Phase Coherence (MPC) for distinct frequency bands of EEG signals recorded, respectively, behind the left and right ear using the algorithm of Mormann et al. [Physica D: Nonlinear Phenomena, 2000; 144(3):358–369].
Result: In the cEEGrid recordings of three of the patients studied four distinct generalized SWDs occurred with a length of 3 s or more. The MPC was computed during the evolvement of the SWDs indicating a significant increase for the delta-frequency band in the first 500 ms after the onset of the SWDs. The significant increase with next a flattening at the maximum of the MPC-curve was observed for all cEEGrid-electrode configurations, between EEG signals recorded, respectively, behind the left and right ear.

Conclusions: The significant increase up till a maximum occurs indicates that in all cEEGrids signals synchronous behavior arises approximately 500ms after the onset of the SWDs. A next step is to study whether the synchronous behavior of the cEEGrid-recordings coincides with the occurrence of the characteristic clinical signs during absence seizures.

Abstract Number: 904

Title: Phantom Sleep Jerks: An Adult Myoclonic Epilepsy Case Report

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Purpose: In children, both benign and epileptic sleep myoclonia are prevalent and seen predominantly in benign myoclonus of early infancy and West syndrome, respectively. In adults, non-epileptic sleep myoclonia are common, while epileptic sleep myoclonia reports appear scatter. Here, we present a case of sleep myoclonic seizures in an adult.

Case report: A 28-year old right-handed otherwise healthy male patient admitted to Clinical Neurophysiology Department with several seizure types in history. His seizures manifested at the age of two years with brief head nodding, arm elevation, and simple vocalization. At the age of ten, seizures with impaired awareness, behavioral arrest, staring, falling, and bilateral tonic-clonic convulsions emerged. The latter seizures completely resolved at the age of 14, and the head-nodding seizures completely resolved at the age of 21. Later on, he noted "sight trembling" (oscillopsia in oculoclonia?) on sleep deprivation. The patient denied myoclonic phenomena, including drowsiness jerks. Since 12 years of age, the patient takes valproate with current daily dose of 1000 mg.

Method: We performed a complete-protocol overnight video-EEG with two additional deltoid electromyography [EMG] leads.

Result: A total of five myoclonic seizures were recorded in sleep – two in stage 2 non-REM sleep and three in stage 3 non-REM sleep. Single myoclonic EMG bursts immediately followed single generalized spike-/polyspike-slow-wave complexes on EEG. Myoclonia involved brief right arm extension, right-side neck flexion, and diaphragm jerk (inspiration abruption); according to EMG, left deltoid activation occurred as well with a delay of 5 ms following right deltoid contraction. No seizure caused arousal or awakening. Additionally, three generalized spike-wave discharges with no EMG or clinical correlates were observed in non-REM sleep.

Conclusions: In this unique case, the patient appears to suffer from previously unreported adult epilepsy syndrome – sleep myoclonic seizures, towards which the patient is completely oblivious, combined with transient oculomotor disturbances.

Abstract Number: 935

Title: Discrimination of interictal epileptiform discharges and sharp wave ripples in SEEG recordings in patients with temporal lobe epilepsy

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Purpose: Interictal epileptiform discharges (IEDs) and Sharp Wave ripples (SWR) are pathological and physiological events in patients with temporal lobe epilepsy. We study a group of epilepsy patients implanted with sEEG depth electrodes (DE) to identify interictal abnormalities IEDs, and differentiate them from SWRs using a new algorithm. IEDs demonstrate a state of hypersynchronous depolarization of neuronal activity. SWRs are known as the most synchronous neuronal activity evoked by the hippocampus. Although these two events may display similar temporal frequency patterns, they carry different energy in different frequency bands. Our algorithm uses these frequency-specific IED and SWR waveforms to detect and discriminate them.

Method: We analyzed the SEEG recordings obtained from patients with medically-resistant epilepsy (MRE) implanted with DE at the Western University Hospital Epilepsy Unit. The data were cleaned, denoised, montaged and segmented based on the clinical annotations, such as sleep intervals and observed Ictals. For event detection, the signal waveform and its power were extracted symmetrically in non-overlapping intervals of 500 ms. Each waveform's power across all detected spikes was computed and clustered based on their energy distributions.

Result: The recordings included thirteen sessions of 24 hours of extracellular recordings from two patients with 312 hours extracted from four hippocampus electrodes anterior and posterior hippocampus. Our results indicate that SWRs energy distribution is significantly more stationary than IEDs in non-sleep periods. IEDs

carrying the most energy in the bands [30-45] Hz, SWR, on the other hand, are distributed between and [25-40] Hz and [90-110]Hz.

Conclusions: Our algorithm was able to detect and successfully distinguish IED from SWRs based on their carrying energy during non-sleep periods with accuracy 70% during interictals. The waveforms' energy is more significant in sleep than awake (non-ictal) periods, but didn't increase the accuracy of discriminating both events.

Abstract Number: 966

Title: Diagnostic Yield Of Five Minutes Compared To Three Minutes Hyperventilation During Electroencephalography In Children

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Purpose: To investigate whether hyperventilation (HV) for 5 minutes increases the diagnostic yield of electroencephalography (EEG) compared to 3 minutes HV and to determine whether performing HV for 5 minutes is feasible and safe in children.

Method: Data were evaluated from 579 children aged less than 18 years, referred to EEG for epilepsy evaluation. Occurrence of seizures, HV induced interictal epileptiform discharges precipitation and potentiation and adverse events if any were noted during the first 3 minutes and last 2 minutes of HV separately.

Result: 398 children (68.7%) completed 5 minutes HV. Seizures were precipitated during the first 3 minutes of HV in 2 children, and during the last 2 minutes in one more child. Inter-ictal EEG abnormalities were precipitated in the first 3 minutes of HV in 31 children, and during the last 2 min in 4 more children. All 398 children completed HV during the last 2 minutes successfully and no adverse events occurred during the last 2 minutes of HV

Conclusions: 33.33 % of seizures and 11.5 % of inter-ictal EEG abnormalities triggered by HV occurred during the last 2 min of HV. This finding supports the utility of prolonged hyperventilation for 5 minutes. Prolonged HV for 5 minutes increases the diagnostic yield of EEG in paediatric population and it is safe and feasible.

Abstract Number: 967

Title: Spike Wave Discharges Detection in Animal Models and Epilepsy Patients with Genetic Generalized Epilepsy and Absence Seizures

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Purpose: Spike and wave discharges (SWDs) are the electrographic hallmark of absence seizures in patients with genetic generalized epilepsy (GGE), which serves as a major diagnostic criterion and treatment biomarker. As one of the most well-validated models to study absence epilepsy, the Genetic Absence Epilepsy Rat from Strasbourg (GAERS) characterizes seizures with SWDs. The large volume of prolonged EEG now being acquired in laboratories and clinics makes the marking and quantification of the SWDs impractical. Conversely, the large-

sized data can benefit the deep learning technique. We developed a detection algorithm with a graph neural network (GNN), which can embed both characteristics of EEG traces and brain connectivity networks.

Method: The EEG data of GAERS model was recorded with four epidural electrodes, while the patient data was recorded from the scalp-EEG using the standard 10-20 system. We constructed a graph network for 2-second EEG epochs, for which graph nodes and edges were EEG electrodes and their correlation coefficients, respectively. The animal GNN detector was trained on four animals with 24-hour EEG, while the patient SWDs detection was performed with the leave-one-out cross-validation across 24-hour data of six patients.

Result: The GNN detection algorithm of SWDs on GAERS rats was validated on recordings of 36 GAERS animals, which included 192 sessions of 24-hour data with 89,888 SWDs annotated. The GAERS SWDs detector achieved a sensitivity of 100% with a false positive (FP) rate of 1.26/hour. The patient SWDs detector achieved the median sensitivity of 99.1% across six patient prolonged ambulatory EEG recordings with range [96.0%, 100%], where the median FP rate was 4.76/hour with range [0.53, 6.72].

Conclusions: We developed an automatic SWDs detector for GAERS and patients with GGE and absence seizures which shows promising sensitivity and specificity that can be useful in basic and clinical research, and potentially clinical practice.

Abstract Number: 981

Title: Accuracy of automated interictal source localisation based on high-density EEG

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Purpose: EEG source localisation of interictal epileptic spikes is a valuable non-invasive tool for presurgical epilepsy evaluation. However, manual marking and averaging of spikes is tedious and time-consuming, and automated analysis has been validated on long-term low-density recordings. We aimed at evaluating feasibility and accuracy of automated interictal source localisation based on presurgical high-density EEG.

Method: Thirty patients with pharmacoresistant focal epilepsy and >3 hours of 257-channel EEG prior to a first resective brain surgery were retrospectively included. To compare high- to low-density EEG, recordings were virtually downsampled to 25 channels and analysed separately. Per patient and EEG setup, up to 4 clusters of spikes were automatically detected, followed by expert review. Source localisation was based on individual structural MRI, a finite element head model, and a distributed source model. The source maximum at the averaged spike's half-rise was compared to resected zone. Sublobar concordance was assessed and related to 12-month postsurgical seizure outcome.

Result: Among all detected clusters, 38% were epileptic spikes, 46% were artefacts, 9% were physiological EEG patterns, and 7% were polyspikes or rhythmic patterns which were discarded. Twenty-one patients (70% of those included; 12 with favourable postsurgical outcome, ILAE 1+2; 9 with unfavourable outcome, ILAE 3-5) had at least one spike cluster. In these, based on sublobar concordance, sensitivity of EEG source localisation was 75% (257 channels) and 67% (25 channels). Specificity was 67% for either setup; overall diagnostic accuracy was 71% (257 channels) and 67% (25 channels). Differences between high- and low-density EEG were statistically not significant ($p>0.05$).

Conclusions: Automated interictal source localisation from high-density EEG is feasible in the majority of patients, with EEG-expert review to discard false-positive patterns. Validated by site of resection and postsurgical seizure outcome, results of automated source localisation are fairly accurate but not significantly different from low-density EEG.

Abstract Number: 990

Title: Increased spike rate is a marker of increased seizure risk

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Purpose: In the present study, we determined the influence of antiseizure drugs (ASDs) withdrawal on interictal scalp-EEG spikes and we investigated changes of spike frequency during the 3 hours before a seizure occurred, a period of time that can be considered prodromal at the onset of seizures.

Method: We included 35 adult unifocal epilepsy patients admitted for presurgical evaluation in the EEG and Epilepsy Unit of Geneva between 2016 and 2019, monitored for at least 5 days. ASDs was individually tapered down and automated spike detection was performed using Epilog Diagnostic (Epilog NV, Belgium, Ghent). We first compared observed 24 h spike rate at day 1 when patients were on full dose medication, with 24 h spike rate at the day with the lowest dose of medication. In a second step, we analysed the spike rate in the 3 hours preceding a seizure and in a 3-hour period at day 1, taken as baseline. We then investigated the cumulative effect of seizures on spike rate.

Result: Our results showed a significant increase in spiking activity in the day of lowest drug load if compared to the 24 h spike rate at day on full medication ($p < 0.001$). We revealed also a significant increase in spiking activity in the three hours preceding a seizure (pre-ictal period) when compared to the homologous circadian profile ($p < 0.001$). With increasing number of seizures, the spike rate increased as well before the next seizure ($p<0.001$).

Conclusions: Our results suggest that spike changes occur during medication withdrawal and in particular before seizures. This effect becomes even more pronounced with increasing number of seizures. Drug withdrawal facilitates seizures and increase spike rates: spiking rate is therefore an important biomarker suggestive that the patient is at risk of seizure.

Abstract Number: 1000

Title: Automated ictal EEG source imaging: a retrospective, blinded clinical validation study

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Purpose: Interictal EEG source imaging (ESI) is a validated tool in the presurgical evaluation of drug-resistant epilepsy patients to localize the epileptogenic focus. Ictal ESI, however, is more difficult because the EEG contains more artefacts and it requires specialized expertise to interpret it. In this study, an automated ictal ESI pipeline is proposed and is validated blinded in a retrospective cohort.

Method: The study was performed in fifty consecutive patients having refractory epilepsy (Dianalund, Denmark). In the EEG recording, the epileptologist marked the electrographical onsets and indicated the frequency band in which the ictal activity occurred. Time-frequency analysis of the ictal epoch between the onset and 3s after was performed to compute the time-frequency window (TFW). For ESI, a patient specific headmodel with 6 tissues and more than 13.000 distributed dipoles was generated. The gray matter was

segmented into 25 sublobes per hemisphere. After applying ESI, signals at dipole-level were generated. Principal component analysis was then used to make sublobar signals. Spectral analysis was performed in sublobes and the one with the highest activity in the TFW was identified as seizure onset zone (SOZ). For evaluation, the estimated SOZs were compared to the post-operated MRI at sublobar level. By knowing the surgical outcome after 1-year follow-up, the method performance was quantified by calculating the accuracy, sensitivity, specificity, PPV and NPV.

Result: Six patients having too noisy data were excluded from the analysis and depending on their outcome they were classified as true(n=2)/false(n=4) negative. The analysis led to a sensitivity, specificity and accuracy of 64.52%(45.37-80.77%), 89.47%(66.86-98.70%), and 74%(59.66-85.37%), respectively. PPV and NPV were 90.91%(72.43-97.44%) and 60.71%(48.41-71.80%). The pipeline accuracy in the 16 patients with normal MRI was 87.50%.

Conclusions: Automated ictal ESI has a high accuracy for SOZ localization and therefore it has potential to be used during the presurgical evaluation.

Abstract Number: 1015

Title: Signal quality and power spectrum analysis of remote ultra long-term subcutaneous EEG

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Purpose: Ultra long-term subcutaneous EEG (sqEEG) monitoring is a new modality with great potential for both health and disease. However, little is known about the long-term quality and consistency of the sqEEG signal, which is the objective of this study.

Method: A multicenter cohort was analysed, including fourteen patients with epilepsy (King's College London, United Kingdom and Zealand University Hospital, Denmark) and twelve healthy subjects (Hospital of South West Jutland, Denmark), implanted with a sqEEG device (24/7 EEG™ SubQ), and recorded from 23 to 230 days (median 42 days), with a median adherence of 75% (17.9 hours/day). We examined the median power spectral density plots of each subject, including diurnal and nocturnal periods, and investigated any long-term trends in signal impedance and power spectral features through time.

Result: sqEEG spectrograms showed an approximately 1/f power distribution. Diurnal peaks in the alpha range and nocturnal peaks in the sigma range were seen in the majority of subjects. Signal impedances remained low and frequency band powers were highly stable throughout the recording periods.

Conclusions: The spectral characteristics of minimally-invasive, ultra long-term sqEEG are similar to scalp EEG, while the signal is highly stable. Subcutaneous EEG is a promising modality for diverse clinical applications, from long-term monitoring in epilepsy to brain-computer interfaces.

Abstract Number: 1033

Title: Enhanced fluctuations of high-frequency activities may be an important factor for clinical seizures: a single-pulse electrical stimulation study

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Purpose: We recently presented that decrement of high-frequency activity (HFA) at the stimulus site by single-pulse electrical stimulation (SPES) was larger on the seizure onset zone (SOZ) than that on the normal cortices (Kajikawa et al., 2020). We also presented that delayed responses (DRs), considered as a marker of epileptogenicity evoked by SPES, tended to appear around the end of HFA decrease on the SOZ. Based on these interictal characteristics of responses to SPES, we here investigated the pre-ictal HFA changes and DRs by SPES leading to induced seizures.

Method: We enrolled 4 patients with intractable focal epilepsy who underwent intracranial EEG (iEEG) recording and presented induced clinical seizures by 1-Hz SPES (IRB#C1192/C1212). iEEGs were recorded with a time constant 2 or 10 s and a sampling rate 1000 or 2000 Hz. For the session of repetitive SPES leading to seizures, we evaluated the HFA (> 80 Hz) power changes after each SPES by Hilbert transform. We also investigated the presence of DRs and the overriding HFAs by calculating the integral of instantaneous power.

Result: Clinical seizures were induced by stimulating SOZ in 3 patients and the site remote from SOZ in 1 patient. The initial EEG changes in all induced seizures started from the SOZ or early spread area of spontaneous seizures. In the electrodes with initial EEG changes in induced seizures, all patients showed HFA decrease after SPES. DRs appeared in the early or middle of the session in 2 patients, while DRs were seen only just before seizure in the remaining 2 patients. The integral of instantaneous HFA power on DRs tended to be larger before seizure in all patients.

Conclusions: SPESs preictally produced HFA decrease and following HFA increase on DRs toward the induced-seizure, which may imply the vulnerability of the cortical excitability leading to seizures.

Abstract Number: 1036

Title: Sleep-wake temporal distribution of spike-and-wave discharges in drug-naïve adult patients with idiopathic generalized epilepsy

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Purpose: To assess sleep-wake temporal distribution of generalized spike-and-wave discharges (GSWDs) in previously untreated patients with idiopathic generalized epilepsy (IGE).

Method: We reviewed our database of patients who referred to our department for diagnostic overnight EEG during the last three years and selected a group of 50 patients diagnosed with IGE who had previously not received any antiseizure medications. Mean age was 26 years (range 18–53), mean age at disease onset – 18.4 years (range 6–34). Overnight EEG started approximately at 9 p.m. and ended at 7 a.m., with photic stimulation and hyperventilation tests performed in the evening and morning. GSWDs and sleep stages were scored manually. Time to first GSWD (latency) was measured in minutes. Spike-and-wave index (SWI, discharges per hour), was calculated for wakefulness and each sleep stage. SWI estimation for night and morning awakenings which lasted less than 60 minutes was additionally performed.

Result: Median latency to first GSWD was 33 minutes (range 1–315). In 44 patients, first GSWD was observed during evening wakefulness, including four on hyperventilation and two on photic stimulation. In the remaining six patients first GSWD occurred during sleep. Median GSWD count per record was 98 (range 7–1410). In 25 patients, highest SWI was observed during night or morning awakenings; in 23 patients – during evening wakefulness; and in two patients – in sleep.

Conclusions: Total number of GSWD is highly variable among IGE patients. For studies starting in the evening, first discharge can be captured within 30 minutes in half of drug-naïve adult patients. In some patients GSWD might emerge in sleep or on awakening. Unlike focal epileptiform discharges, GSWDs in IGE have uneven distribution over the sleep-wake cycle, with highest SWI observed during awakenings in half of all patients.

Abstract Number: 1049

Title: Effect of sleep stages on bitemporal interictal epileptiform discharges

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Purpose: The prevalence of bitemporal independent epileptiform discharges (BIEDs) in patients with temporal lobe epilepsy reaches 35%. The aim of our work was to study effect of sleep on BIEDs and variability of BIED side-to-side ratio across different sleep stages.

Method: 31 long-term video-EEG (LTM) recordings with BIEDs were included in the analysis. All discharges as well as sleep stages were scored manually. BIED index (discharges per hour) in wakefulness and each sleep stage~~s~~ was calculated for left and right side separately. Side with a larger discharge index was defined as leading side (LS); accordingly, the other side was defined as non-leading side (NLS). Afterwards, the predominance of LS discharges was determined as LS discharge percentage of the sum of discharge indices from both sides. Predominance was calculated for the whole recording and separately for wakefulness and each sleep stage. Finally, we compared the predominance of LS discharges in each sleep stage to the predominance during the whole recording.

Result: Maximal index of BIEDs was observed in N3 sleep stage, being minimal in wakefulness and REM. Correlation of LS discharge predominance in each sleep stage with predominance during the whole recording was the strongest and statistically significant only for stage N2 ($p<0.02$). In REM sleep, 64% of recordings had discharges only on LS with no cases of epileptiform activity solely on NLS.

Conclusions: LS discharge predominance varies across wakefulness and sleep stages. Despite the fact that the largest epileptiform discharge index was observed in slow wave sleep, N2 sleep stage seems to be the most demonstrative in estimating side-to-side ratio of the bitemporal epileptiform activity. If all interictal temporal discharges in REM sleep are strictly unilateral, these discharges are more likely to point to the LS of BIEDs.

Abstract Number: 1061

Title: Detecting epilepsy from apparently normal EEG at the first seizure: a new insight from topographies, a pilot study

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Purpose: Detecting epilepsy at the first seizure is challenging since EEG show epileptiform abnormalities in less than half of the cases. In the present pilot study we focused on the signal's topographies and tried to disentangle epileptic patients from controls based on the results of microstates analyses.

Method: we studied a group of 35 chronic focal epilepsy patients with 256 electrodes EEG as well as 21 healthy controls. Recordings of resting EEG with eyes closed for at least 20 seconds without evident epileptic spikes were selected. EEGs were inspected again visually by an expert EEG reader and artifacts were excluded. A segmentation based on a K-means algorithm was applied to extract the microstates for each patient and at a group level. The so identified microstates were backfitted to the individual EEG signals of each patient. Differences in microstates duration and global explained variance were assessed statistically.

Result: a set of 4 to 6 microstates were obtained at a group level, corresponding to previously observed microstates classes in normal subjects described in the literature. Microstates from the patients and control groups were similar in topographies and duration, but a specific microstate (A) explained significantly more variance of the control group while the opposite pattern was observed for a different map (C).

Conclusions: the results of this pilot study suggest that patients and controls share the same microstates, except for 2 maps labelled "A" and "C". The underlying source of "A" reflects a left-hemispheric based network, more active in the control group. "C" represents the saliency network involving the anterior and posterior cingulate cortex, more active in patients, perhaps as compensatory mechanism. Further studies in a larger patient population with early onset epilepsy, and controls will determine if this finding is specific to epilepsy patients and present already at the disease onset.

Abstract Number: 1110

Title: On the Role of the REM sleep microstructure in the ESES syndrome

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Purpose: The Electrical Status Epilepticus during Sleep (ESES) is a rare epileptic encephalopathy and it represents the extreme condition of epileptiform abnormalities (EAs) activation during sleep. EAs can be present in up to 85% of the whole sleep EEG in these patients. It is well established that the two main sleep stages – NREM and REM – have opposite effects on epileptic spiking: NREM sleep promotes the spread and propagation of EAs, while REM sleep has a suppressive effect. Recently, it has been shown that the suppressive effect is mainly related to the phasic REM, the phase characterized by rapid eye movements. This study aims at assessing whether the inhibitory effect of phasic REM is prevailing even in a type of epilepsy characterized by an extremely high frequency of EAs during sleep.

Method: The study included 9 patients affected by ESES, who underwent long-term EEG monitoring with 16 EEG, 1 ECG, 2 EMG and 4 EOG channels. In addition to traditional sleep scoring proposed by the AASM in 2007, REM sleep was subdivided into phasic and tonic states, differentiated by presence/absence of rapid eye movements. EAs count was carried out on all EEG channels using a semi-automatized method and EAs rate was calculated as the ratio between the number of EAs in a given sleep stage and the time (seconds) spent in that stage.

Result: The EAs rate was higher in NREM sleep than in REM sleep. In REM sleep, EAs rate was significantly lower in phasic than in tonic REM (mean values (± SD): 0.069 ± 0.084 vs 0.249 ± 0.218); these results seem to be independent of EAs topographic distribution.

Conclusions: Our data point out that phasic REM has a greater suppressive effect on epileptic activity even in a type of epilepsy with an extreme EAs activation during sleep.

Abstract Number: 1133

Title: MEG and foramen ovale co-registration in difficult to lateralize temporal lobe epilepsy: source reconstruction and network analysis

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Purpose: Ten percent of pre-surgical patients suffer from temporal epilepsy with unclear lateralisation of epileptogenic foci and require invasive evaluations (SEEG or foramen ovale electrodes, FOE). The aim of our study was to investigate the reliability of non-invasive magnetoencephalography (MEG) in determination of epileptic foci in case of mesial temporal epilepsies (MTLE).

Method: To this purpose, interictal properties of co-registered MEG/FOE were analysed while ictal activity recorded with FOE identified the epileptogenic lobe. Five patients with DL-TLE who underwent MEG/EEG/FOE co-registration were used in this preliminary study.

Result: Our results confirmed that mesial interictal activity detected on FOE is not easily visible on MEG sensor and EEG data probably due to the low signal-to-noise ratio. On the other side, using MEG source data, we could demonstrate the ability of MEG data to detect deep brain pathological activity with different approaches. First of all, we reconstructed the activity of MEG sources in correspondence of interictal activity on FOEs achieving a correct identification of the epileptic lobe. Successively, we used the beamformer approach to reconstruct MEG source activity at the same positions as the FOE. Comparing the reconstructed and FOE signals, we found good agreement for low-frequency activities, while beta and gamma activity appeared more prominent on MEG data. Moreover, some of the spikes detected on FOE could be visible also on the reconstructed MEG data. Finally, to study the lateralisation, we performed connectivity analysis using Imaginary coherence and graph-theory on MEG data including also healthy subjects. Results highlighted that MTLE patients with right epileptogenic focus differ from the left and healthy subjects comparing hemispheric differences of graph indices in beta and theta band.

Conclusions: Our study demonstrates how MEG can contribute to the characterization and determination of the affected side in patients with MTLE

Abstract Number: 1208

Title: Interictal spike frequency predicts attenuated overnight slow wave activity decline in adult drug-refractory epileptic individuals

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Purpose: Analysis of slow wave activity (SWA, delta power, 1-4 Hz) is a promising instrument to estimate the impact of epileptic spikes on neuronal excitability and its overnight decline is a reliable marker of homeostatic decrease in synaptic strength. In animal studies, neuronal burst firing triggered by interictal spikes (IS) may prevent synaptic downscaling, while in children with ESES and in adult patients with epilepsy they lead to reduced SWA decline. Our purpose is to confirm this neurophysiological and clinical background by assessing the impact of IS during sleep on SWA overnight decline in a larger cohort of patients with epilepsy.

Method: 50 patients with drug-refractory epilepsy underwent overnight high-density EEG recordings (HDEEG, 256 electrodes). After sleep scoring using AASM criteria, HD-EEG data were filtered between 0,5 and 40 Hz, artifact rejection was performed using custom Matlab scripts and N2-N3 stage epochs were selected. Both focal and generalized IS were manually marked by a certified epileptologist (MB) and a square root transform was applied to make the data distribution near to the Gaussian. The SWA overnight decline was computed using a Fourier transform. For statistical analysis we used Statistical Parametric Mapping (SPM) and Statistical Non-Parametric Mapping (SnPM) as well as random effects approach to take into account inter-subject variability. Results were corrected for multiple comparisons using SPM and SnPM family wise error (FWE).

Result: Both parametric and non-parametric Random effects analysis revealed a significant negative correlation between IS frequency and SWA decline in right parieto-temporal area and frontal regions bilaterally (cluster-level FWE corrected SPM p=0.022, SnPM p=0.025).

Conclusions: These results confirm that interictal epileptiform discharges during sleep has a direct impact on synaptic down-scaling and therefore on cortical excitability and synaptic plasticity.Future studies will compare the effect of focal versus generalized IS and their impact on different sleep rhythms.

Abstract Number: 1294

Title: Short-term heart rate variability predicts sudden unexpected death in epilepsy

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Purpose: Aberrant heart rate variability (HRV) strongly predicts sudden death in heart disease patients, but whether it is a risk factor for sudden unexpected death in epilepsy (SUDEP) remains unclear. We compared HRV between SUDEP cases and living epilepsy controls.

Method: This international, multicenter, nested case-control study analyzed patients admitted for video-EEG monitoring (VEM) between January 1, 2003, and December 31, 2014. Cases subsequently dying of SUDEP and matched living epilepsy controls were identified. Time-domain and frequency-domain components were extracted from five-minute interictal electrocardiogram recordings during sleep and wakefulness from SUDEP cases and controls.

Result: We identified 31 SUDEP cases and 56 living epilepsy controls. Normalized low-frequency power (LFP) during wakefulness was lower in SUDEP cases (median 42.5, IQR 32.6–52.6) than controls (55.5, IQR 40.7–68.9; *p*=0.015, critical value=0.025). In the multivariable model, normalized LFP was lower in SUDEP cases than controls (contrast -11.01, 95% CI: -20.29–-1.73; *p*=0.020, critical value=0.025). There was a negative correlation between LFP and survival duration (as measured by the time latency from VEM admission to SUDEP), where each 1% incremental reduction in normalized LFP conferred a 2.7% decrease in the time to SUDEP (95% CI: 0.95–0.995; *p*=0.017, critical value=0.025). Longer survival duration from VEM admission to SUDEP was associated with higher normalized high-frequency power (HFP; *p*=0.002, critical value=0.025). The predictive model of normalized LFP in SUDEP cases had a C-statistic of 0.66 (95% CI: 0.55–0.77), which was associated with a small and non-significant increase with the addition of normalized HFP (C-statistic 0.70, 95% CI 0.59–0.81; *p*=0.209).

Conclusions: Reduced short-term LFP, a validated biomarker for cardiac sudden death, predicts SUDEP. Increased HFP appears to be associated with longer survival and may be cardioprotective in SUDEP. Integration of HRV into multimodal risk-stratification models may help identify patients at greatest SUDEP risk.

Abstract Number: 1304

Title: Usefulness of extended EEG electrode placement in nocturnal Polysomnography to detect epileptiform abnormalities

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Purpose: Standard nocturnal video assisted Polysomnography (PSG) includes only 4-6 channels of EEG, which is insufficient to identify epileptiform abnormalities. Even though many sleep machines have the provision of simultaneous recording of video EEG and PSG. Only few sleep laboratories uses the extensive EEG recording in addition to the common PSG channels. PSG combined with standard 10-20 EEG electrode placement system may be a useful diagnostic tool in patients suspecting nocturnal paroxysmal events.
The aim of this study was to determine the usefulness of combining PSG with standard 21 channels EEG in patients suspecting seizure disorders or paroxysmal nocturnal events

Method: All patients who had undergone combined PSG- video EEG studies from March 2015 to April 2019 were included. Detailed demographic data, provisional diagnosis, sleep and clinical history were tabulated. Each patient data's were analyzed in standard PSG montages and Video EEG montages separately. Various sleep disorders and epileptiform abnormalities were evaluated. EEG abnormalities were sub classified into non-specific and epileptiform abnormalities.

Result: Out of 154 patients, around 89% were diagnosed primary sleep disorder; most of them were obstructive sleep apneas followed by 20% patients had periodic limb movement syndromes and 1% parasomnia. None of them showed epileptiform abnormalities in conventional PSG montages. Reanalyzing with standard 21 channel EEG montages 12 patients (7.8%) showed epileptiform abnormalities.

Conclusions: Combined PSG – video EEG is very useful technique to detect epileptiform abnormalities in patients with history of nocturnal paroxysmal events or seizure disorders. It is a cost effective method to detect focal epileptiform abnormalities during routine sleep studies.

Abstract Number: 1313

Title: Lateralization of interictal delta slowing in the magnetoencephalography (MEG) in patients with focal epilepsy and its relation to cognitive functions

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Purpose: To investigate the hemispheric occurrence of interictal delta slowing in patients with left (LFE) and right focal epilepsy (RFE) as well as healthy controls (HC) and to evaluate its lateralization value. Further, to evaluate the interrelation between delta slowing and cognitive functioning.

Method: Resting state MEG was recorded from 15 patients with LFE and 11 patients with RFE as well as 10 HC. Epilepsy diagnosis was determined during video-EEG-monitoring. Using non-parametric tests, data was analysed regarding hemispheric group differences in absolute delta power between (1) epilepsy patients and healthy controls, (2) patients with LFE and RFE, and (3) the hemispheres within patients with LFE and RFE. Spearman rank correlations between delta power and semantic as well as phonemic verbal fluency were evaluated.

Result: (1) Compared to HC, patients with focal epilepsy showed higher delta power in the hemisphere ipsilateral (p = .027) and contralateral to the epileptic focus (p = .037). (2) Patients with LFE and RFE did not differ in either of the hemispheres. (3) Patients with RFE showed higher delta power in the ipsilateral-to-focus right than the contralateral-to-focus left hemisphere (p = .016). Patients with LFE did not show a significant difference between the hemispheres. Besides, a significant negative Spearman rank correlation was found between delta power and phonemic (r_s = -0.59, p = .008) but not semantic verbal fluency.

Conclusions: Focal epilepsies constitute complex network diseases of the brain that may be associated with changes in neuronal activity even beyond the epileptic hemisphere. LFE and RFE seem to have similar interictal dynamics, but unique neuronal activity changes in the hemisphere contralateral to the epileptic focus. This could be related to the hemispheric dominance. Besides, differences in the correlation of semantic and phonemic verbal fluency with delta power suggest that delta slowing could indicate executive dysfunction.

Abstract Number: 1330

Title: Comparison antiepileptic drugs influence based on EEG

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Purpose: Understanding the correlation between clinical and neurophysiological effects has been receiving appreciation in clinical epileptology more recently. Electroencephalography is thought to be an efficient not only controlling ongoing effectiveness of the treatment but also to be an efficient tool to predict potential clinical and psychocognitive adverse effects of the treatment. Vallproate acid(VPA) and Carbamazepine (CBZ) are widely used antiepileptic drugs (AED).Selection of AED is determined by the type of seizures, effect on basic neurophysiological processes of CNS is not fully investigated. The aim of study was to compare the effect of CBZ and VPA on EEG to assess both epileptic activity and overall functional state of the brain.

Method: Epileptic patients aged 3 to 9 years were examined. 53 patients treated by VPA and 47- by CBZ. Patients underwent EEG recording for three- times: before administration of AED in 3-4 and 6-8 months after the initiation of treatment. EEG signals were digitally recorded using scalp electrodes according to International 10–20 system.10-15 fragments for each patient were performed for the evaluation of background activity also spectral analysis absolute value of power (AVP).

Result: Qualitative characteristics of EEG under VPA revealed reduce the degree of disorganization of basic rhythmicity EEG of reduction of high amplitude mono-poly-morph waves in low frequency range. VPA appears significantly reduce AVP spectra practically in all zones brain especially in parietal and occipital areas.VPA efficient to suppress spike-wave complex with substrate in thalamus. During CBZ therapy increase of AVP dynamics is caused by growth of the low frequency range, predominantly in the parietal-occipital areas. CBZ mostly affect the neural population of the cortex.
Conclusions: In summary, the difference in the effect this drugs on bioelectrical activity of the brain could be related to region-specific differences within the loci of maximal neuropharmacological effect.

Abstract Number: 1342

Title: Characteristics and risk factors associated with DSM-5somatic symptom disorder in patients with epilepsy: a retrospective case-control analysis.

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Purpose: Somatic symptom and related disorders (SSD), a new disorder newly defined in the Diagnostic and Statistical Manual Fifth Edition (DSM-5) was rarely reported in people with epilepsy (PWE). The study is to determine the prevalence, clinical features and risk factors of SSD in PWEs.

Method: Adult PWEs attending our epilepsy center from 2020.7 to 2021.10 were screened for inclusion in this study. We underwent a structured interview to identify SSD in PWEs. Patients were divided into two groups depending on the presence of SSD. Clinical data including social/demographic, epilepsy-related, psychiatric status variables, quality of life, disability and direct health care costs were compared between the two groups. Least absolute shrinkage and selection operator (LASSO) was employed to identify risk factors of SSD in PWEs. A nomograph was generated for assessing SSD occurrence.

Result: One hundred twenty six of 524 PWEs comorbid SSD 24.05%. PWEs with SSD showed significantly higher WHO DAS 2.0 total scores (81.0 ± 24.3 & 60.9 ± 25.8, P <0.001), higher direct costs (75679.2 ± 96632.9 & 45295.0 ± 88892.7, P <0.001) and lower QOLIE-31 total score (46.8 ± 12.3 & 64.6 ± 16.1, P<0.001). More of them experience current frequent seizures (more than once a month, 38.9% & 25.9%, P =0.005) and RE (48.4% & 31.7%, P <0.001), showing significantly higher NHS3 total scores (9.2 ± 6.5 & 6.7 ± 6.4, P<0.001). Using LASSO regression analysis, presence of hippocampal sclerosis, number of somatic symptoms, GAD-7 score, seizure worry, medication effects, QOLIE-31 total score were identified as risk factors of SSD occurrence. The receiver operating characteristic (ROC) curve revealed a satisfactory performance (area under the curve, AUC=0.929).

Conclusions: This study provides first insights into the prevalence, clinical characteristics and risk factors of SSD in PWEs.

Abstract Number: 1345

Title: Brain network reconstruction of abnormal functional connectivity in Lennox-Gastaut syndrome according to drug responsiveness

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Purpose: Lennox-Gastaut syndrome (LGS) shows abnormal functional connectivity. This study aimed to clarify if drug responsiveness in LGS could alter the network reconstruction of brain connectivity by comparing LGS with healthy control.

Method: Thirty-seven patients with LGS and forty healthy controls were enrolled in this study. Patients with LGS were classified into drug-unresponsive LGS and drug-responsive group. The graphic theoretical analysis was applied to reveal the brain connectivity using resting-electroencephalography (EEG). Follow-up EEG was obtained in only 24 patients with LGS (drug responsive: drug unresponsive=13:11). The different network measurements in brain connectivity are investigated between each group.

Result: Network measurements were statistically significant between patients with LGS and healthy control. In both frontal areas in patients with LGS, betweenness centrality was significantly reduced compared to healthy controls. Differences between drug responsive and unresponsive LGS group were not significant in brain connectivity using initial EEG. The drug-unresponsive LGS group (n=11) showed enhanced local and global connectivity by comparing initial and follow-up EEG. The drug-responsive LGS group (n=13) had no significant difference in brain connectivity between the initial and follow-up EEG. Compared to healthy controls, drug-unresponsive LGS group showed enhanced local and global connectivity, while drug-responsive LGS group showed no difference from healthy controls.

Conclusions: LGS patients have different brain connectivity and decreased hubs in frontal areas compared to healthy control. Brain connectivity in drug responsive LGS reconstructs brain connectivity in a pattern similar to that of healthy controls.

Abstract Number: 1370

Title: Electroclinical features in an adult patient within Dravet spectru

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Electroclinical features in an adult patient within Dravet spectrum

Purpose: To describe electro-clinical features of a 20-years-old naive patient who had delayed psychic development, resulting in mild cognitive retardation. At 3-4 years he had simple febrile convulsions . Since childhood he showed distal hyperkinesia at the upper limbs. At 15 years he had a first afebrile seizure during sleep. A second seizure recurred four years later always during sleep, described as generalized tonic-clonic.

Method: Neurophysiological evaluation included an EEG-EMG recording , and somatosensory evoked potentials (SEP). Genetic analysis was performed with a next-generation sequencing (NGS) panel.

Result: EEG showed diffuse sequences of slow waves on fronto-temporal regions, but not clear epileptic abnormalities. Intermittent photic stimulation showed photo-myoclonic response from 10 to 20 Hz, without clear photo-paroxysmal response. EMG recording showed repeated brief bursts synchronous on antagonist

muscles during action, consistent with myoclonus. Corticomuscular coherence analysis supported the cortical origin of the jerks. SEP showed increased cortical responses.
The patient harboured c.3924A>T (p.Glu1308Asp) *SCN1A* mutation, inherited from the healthy mother.

Conclusions: *SCN1A* gene is frequently involved in genetic epilepsies, showing a wide range of phenotypic manifestations. Our patient had atypical phenotype including predominant developmental encephalopathy and myoclonus but rare seizures. In Dravet spectrum, cortical myoclonus is a characteristic sign, while photomyogenic response is not typical probably depending from the activation of brainstem reflex circuit. Phenotypic heterogeneity and incomplete penetrance of the mutations may delay the diagnosis; the present report expands the Dravet spectrum.

Comorbidities

Abstract Number: 140

Title: Prevalence of Vitamin B12 Deficiency and Hyperhomocysteinemia in Patients with Epilepsy

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Purpose: To evaluate prospectively the prevalence of vitamin B12 deficiency and hyper-homocysteinemia as well as their associated factors in Thai patients with epilepsy.

Method: One hundred and forty nine patients were admitted to epilepsy monitoring unit, National Neurological Institute from 6th January 2020 to 28th February 2021. Fifty-six patients were excluded due to receiving vitamin supplement and having the diagnosis of psychogenic nonepileptic seizures. The remaining of 93 patients were enrolled. Vitamin B12 deficiency, defined as a level of vitamin B12 lower than 187 pg/ml and hyper-homocysteinemia, defined as a level of homocysteinemia higher than 15.4 μmol/L.

Result: Mean age of patients was 34 years (SD, 5). Mean epilepsy duration was 14 years (SD, 12). Mean number of antiepileptic drugs was two (SD, 1). None of the patients had vitamin B12 deficiency. Eleven patients (11.8%) had hyper-homocysteinemia (19.0±2.8) and all had no folate supplement. Despite normal homocysteine level, the group received no folate supplement (n=47) had higher homocysteine level than the group received folic supplement (n=35) (11.5±2.0 vs 8.8±2.4, p<0.001). In the group received no folic supplement, there was a higher proportion of phenobarbital used in the subgroup of hyper-homocysteinemia (36.4% vs 6.4%, p=0.02). No difference of vitamin B12 and homocysteinemia levels between patients who received monotherapy and polytherapy.

Conclusions: The prevalence of vitamin B12 deficiency was 0% and the prevalence of hyper-homocysteinemia was 11.8% in patients with epilepsy. Folic supplement play a major role in homocysteine level. Significant higher proportion of phenobarbital used was found in patients with hyper-homocysteinemia.

Abstract Number: 301

Title: Seizure predictors after liver transplantation: a single-center study

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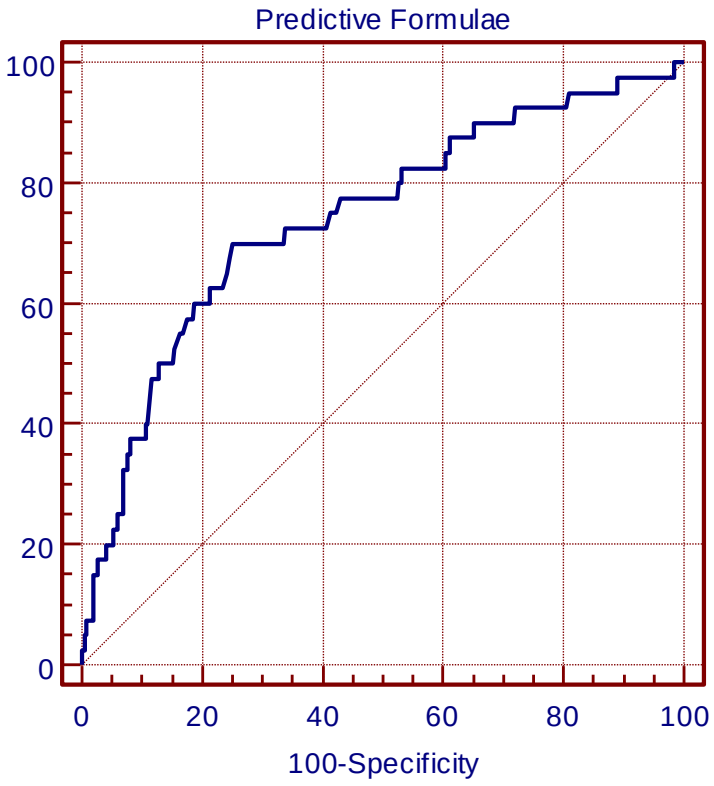
Purpose: Seizures after liver transplantation (LT) are common (Ghaus N et al. J Neurol. 2001; 248:1042-1048), multiple etiologies underlie its physiopathology (Wszolek ZK et al. Seizure. 1997; 6:31-39; Choi EJ et al. Eur Neurol. 2004; 52:230-236). We aimed to determine the role of different perioperative factors in seizure development after LT in adult population.

Method: We performed a single-center retrospective analysis study including LT from 2009 to 2019. Medical history, peri-surgical variables were compared among those who developed seizure and those who did not, during the first 30-days after surgery. We performed a multivariate logistic regression analysis to predict seizure.

Result: We included 376 consecutive LT, 40 developed seizures (11%). Female 59%, median age 57 y.o. (IQR 49-64), 15% admitted for emergency transplant. Associated factors with seizures were: chronic hyponatremia (35% vs 21%, p<0,05), epilepsy (18% vs 3%, p<0,0002), acute symptomatic seizures history (8% vs 1%, p<0,02), acute on chronic liver failure (23% vs 6%, p<0,0002), portosystemic encephalopathy (PSE) (50% vs 30%, p<0,02) and sepsis on admission (20% vs 10%, p<0,042). Seizures group had more graft rejection (35% vs 8%; p<0,002), required surgical re-intervention (38% vs 18%; p 0,005) with a longer in-hospital stay (28 vs 12 days, p<0,005). In multivariate logistic regression, epilepsy (OR 8.73, p<0,0002), PSE (OR 2.07, p<0.9), acute on chronic liver failure (OR 4.63, p<0,002) and older age (OR 1.04, p 0.62) predicted seizures after LT (Specificity 75%; Sensitivity 70%, ROC curve=0,742, IC 0,695-0,786).

Conclusions: Multiple factors were related to seizures after LT. We propose a predictive model for seizure development during the first month with a good sensitivity/specificity that should be evaluated in prospective and multicenter studies.



Abstract Number: 389

Title: Effects of high fat diet in the WAG/Rij rat model of epileptogenesis, absence epilepsy and neuropsychiatric comorbidities.

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Purpose: Studies reported metabolic syndrome (MetS) may precipitate and/or worsen seizures [1]. In this light, we decided to study the effects of MetS on absence seizures and neuropsychiatric comorbidities in WAG/Rij rats [2].

Methods: WAG/Rij rats were fed with normo-caloric-diet (NCD) or high-fat-diet (HFD) up to 16 weeks, in order to develop MetS [3]. After 16 weeks of dietary manipulation, an intraperitoneal glucose tolerance test (IPGTT) and insulin tolerance test (ITT) were performed. Subsequently, NCD and HFD rat groups were further divided. Two subgroups of rats, for type of diet, were respectively subjected to EEG recordings and several behavioral tests. Simultaneously, a subgroup of HFD fed rats was switched to NCD for 12 weeks. During this period EEG recordings were assessed. At the end of the switch period behavioral tests were performed also in this group.

Results: HFD fed rats showed a non-significant weight gain in comparison to NCD group. Likewise, IPGTT and ITT analysis, performed in both groups, did not show any significant difference. At odds, HFD significantly increases both the number (nSWDs) and total duration (dSWDs) of spike-wave discharges (SWDs) in comparison to NCD fed rats. Moreover, HFD fed rats showed an increased depressive-like behavior in comparison to NCD groups. Likewise, HFD fed rats in comparison to NCD fed rats showed an altered working memory. Regarding switch group, we only noticed a reduction of dSWDs and an increased depressive-like behavior.

Conclusions: Our data indicate that HFD diet can worsen both epilepsy and their related comorbidities, although, in this strain, we did not notice any altered glycometabolic profile. Finally, we are investigating the role of gut microbiota and other molecular mechanisms.

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Abstract Number: 490

Title: Maternal methyl-enriched diet alters absence seizures, depression-like comorbidity and DNMT1, HCN1 and TH gene expression in adult offspring

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Purpose: Emerging evidence suggests that developmental exposure to maternal methyl-enriched diet (MED) may lead to epigenetic and phenotypic effects in offspring through modification of DNA methylation and gene expression. This study was designed to determine whether maternal MED can alter absence seizures, comorbid

depression, DNA methyltransferase 1 (DNMT1), HCN1 ion channel and thyrosine hydroxylase (TH) gene expression in adult WAG/Rij offspring. The WAG/Rij rat strain is a genetic model of absence epilepsy with depression-like comorbidity. Reduced expression of the HCN1 ion channels in the somatosensory cortex (SSC) and the mesolimbic dopamine deficiency is thought to be associated with the genesis of spike-wave discharges (SWDs) and depression comorbidity.

Method: Females of WAG/Rij rats were fed MED (choline, betaine, folic acid, vitamin B12, L-methionine, zinc) or control diet for a week prior mating, during pregnancy and for a week after parturition. EEG and depression-like behavior were analyzed in 7 months old male offspring. The expression of the DNMT1, HCN1 and TH genes in the SSC, hippocampus (HIP), nucleus accumbens (NAC) and hypothalamus (HYP) was assessed using qPCR.

Result: Animals born to mothers fed MED had significantly less number of SWDs and exhibited decreased immobility time in the forced swimming test and increased sucrose preference compared with animals born to mothers fed control diet. Maternal MED also delayed the occurrence of SWDs. Disease-modifying effects of MED were associated with increased expression of the DNMT1 and HCN1 genes in the SSC and HIP, as well as DNMT1, HCN1 and TH genes in the NAC. No changes in gene expression were detected in the HYP.

Conclusions: The results point to a new epigenetic therapeutic strategy for preventing the development of genetic absence epilepsy and comorbid depression in offspring, based on maternal diet. This study was funded by RFBR, project N 20-015- 00327A.

Abstract Number: 540

Title: Comorbidities in patients with Unverricht–Lundborg disease (EPM1)

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Purpose: The clinical course of progressive myoclonus epilepsy type 1 (EPM1) is variable but typically leads to accumulating disability and early retirement. There are little data on comorbidities but identifying and treating them could improve the prognosis.

Method: Comorbidity data were derived from neurological, surgical, internal medicine and intensive care patient records for the previously reported 135-person (54% women) national cohort of persons with EPM1 in Finland in 1998- 2016.

Result: At least one comorbidity was observed in 108 patients (80% of the cohort, median per patient 2, range 0-11). The most common single comorbid diagnoses in the entire cohort were a fracture of the ankle (27 in 25 individuals or 19% of the entire cohort), diabetes which was observed in 18 patients (13% of the cohort) and depression which had been recorded for 17 patients (13% of the cohort). In total, there were 48 bone fracture diagnoses in 27 individuals (20% of the cohort), an endocrine or metabolic diagnosis had been recorded in 41 individuals (30% of the cohort) with nine patients (7%) having more than one and 39 individuals (29% of the cohort) had at least one diagnosis of a mental or a behavioural disorder. Alcoholism was observed in 13 patients (10%) and abuse of other substances in three. There had been seven patients (5%) with a malignant neoplasm but no specific organ clustering. Hypertension had been diagnosed in 15 patients (11%) and atrial fibrillation in three. Two patients had a diagnosis of coronary disease, but no myocardial infarctions were observed. Specific diagnoses of infectious disease were few.

Conclusions: Comorbidities are common in patients with EPM1. Especially the risk of trauma, diabetes, mental health disorders and substance abuse should be noted.

Abstract Number: 544

Title: HypoAware: An alternative Focus

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Purpose: Drug resistance is common in epilepsy, affecting 20-40% of patients. Confirming the diagnosis is an important step in management. Our patient, a 42-year-old man, was misdiagnosed with drug resistant focal epilepsy due to recurrent hypoglycemic episodes, on a background of Type 1 Diabetes Mellitus. We reviewed the literature to identify other cases of recurrent hypoglycemia misdiagnosed as epilepsy

Method: A literature search using specified criteria identified 473 studies, 20 of which were relevant to this review, including a total of 22 cases. The majority are isolated case reports given the rarity of this entity.

Result: An underlying insulinoma (n=20) is the most common reason for hypoglycemic episodes to be misdiagnosed as epilepsy. Early morning seizures are common (n=9). Video EEG monitoring in our case resulted in the correct diagnosis. During a 21 day admission to the epilepsy monitoring unit, a typical event was captured. Objectively, he became unresponsive and clammy. He was disorientated in place and unable to follow commands. This was followed by confusion and bizarre speech, repeatedly calling out inappropriate phrases such as "chicken out of the bed" and "chicken at the window." Subtle oral automatisms were observed. EEG showed progression from theta to delta bihemispheric slowing, with intermixed bihemispheric frontal-maximal sharp complexes. As the slowing enhanced, bi-hemispheric frontal-predominant periodic sharp and slow wave complexes (BiPEDS) occurred, in-keeping with an evolving severe metabolic encephalopathy. The blood glucose was 1.1mmol/L. The diagnosis was revised, and he has been seizure-free for 6 years now.

Conclusions: We report the first case of recurrent hypoglycemia from exogenous insulin, misdiagnosed as focal epilepsy with an available video EEG. The unusual presentation appeared clinically indistinct from recurrent focal seizures. Although rare, hypoglycemia is an important differential diagnosis for drug-resistant epilepsy, and an underlying insulinoma is the most common aetiology published in the literature.

Abstract Number: 616

Title: 7-year-incidence of clinical fractures in institutionalized adults with refractory epilepsy and intellectual disability

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Purpose: To determine the incidence of clinical fractures over 7-years of follow-up in adults with refractory epilepsy and intellectual disability (ID) residing at a long-stay care facility.

Method: In 2009, all institutionalized patients aged 18 years or older (n=261) were invited to undergo a Dual-energy X-ray Absorptiometry (DXA) measurement and a Vertebral Fracture Assessment (VFA). In 2016, DXA and

VFA were repeated. If indicated, patients were prescribed anti-osteoporosis treatment according to the Dutch guidelines.
The patients' medical files were screened for radiology reports and staff notes to gather information on clinical fractures. Data collection started at the day of the first DXA scan and ended after the second DXA scan. When a patient deceased during the study period or moved out from the care facility, data collection was stopped at the day of deceasing or moving out.

Result: A total of 205 patients (124 male, 60.5%) aged between 18 and 88 years old (mean age 46.8±16.6 years) were enrolled in the study. At baseline, 38 patients (18.5%) had a normal BMD, 92 patients (44.9%) were classified as osteopenic and 65 (31.7%) as osteoporotic. In ten patients (4.9%), the scan results were missing. Between 2009 and 2016, 30 patients (14.6%) deceased and 3 patients (1.5%) moved out from the care facility. During follow-up, a total of 156 clinical fractures were reported in 82 patients (40.0%). Thirty-eight patients (18.5%) had at least one major osteoporotic fracture. Overall, we found an incidence rate (IR) of 11.6 fractures per 100 person-years. About half of the fractures (48.1%) occurred during treatment with bisphosphonates.

Conclusions: This study demonstrated that 40% of institutionalized adults with refractory epilepsy and ID had at least one clinical fracture during seven years of follow-up, despite adequate anti-osteoporosis treatment.

Abstract Number: 704

Title: Epilepsy and Depression – a Bidirectional Relationship that is Not Explained by Berkson's Bias

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Purpose: Epilepsy and depression have a bidirectional relationship, but part of this may be explained by Berkson's bias, i.e., increased risk of obtaining an additional diagnosis for persons with a chronic disorder, through more frequent medical contacts. We investigated the risk of depression following epilepsy and vice versa, addressing Berkson's bias by comparing to the risks of depression or epilepsy following a diagnosis with another chronic disease (asthma).

Method: In a nation-wide register-based cohort study, we identified all individuals who received a first diagnosis of epilepsy, depression, or asthma, from 1 Jan 1980 to 31 Dec 2016. We used Cox-regression to estimate the risk of epilepsy after depression and vice versa, and the risks of epilepsy or depression following asthma, comparing to healthy reference persons matched on age and sex, and adjusting for medical comorbidity, substance abuse, and calendar time.

Result: In a population of 8,741,955 individuals, we identified 144,420 persons with epilepsy (54% males) with a median age at diagnosis of 42 years (IQR 17-65 years), 227,633 persons with depression (37% males) with a median age at diagnosis of 43 years (IQR 29-60 years), and 364,171 persons with asthma (49% males) with a median age at diagnosis of 29 years (IQR 6-56 years). The adjusted HR (aHR) of depression following epilepsy was 1.91 (95 % CI: 1.85-1.98), and the aHR of epilepsy following depression was 2.37 (95 % CI: 2.29-2.47). The aHR of depression following asthma was 1.40 (95% CI: 1.36-1.44), and the a HR of epilepsy following asthma was 1.23 (95% CI 1.18-1.28).

Conclusions: The risks of depression following epilepsy and vice versa were higher than those of epilepsy or depression following asthma, suggesting that Berkson's bias cannot fully explain the relationship between epilepsy and depression.

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Abstract Number: 713

Title: Changes in cardiac ion channels and cardiac structure in post-status epilepticus models of epilepsy

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Purpose: There is a wealth of evidence that cardiac dysfunction is common in epilepsy and may contribute towards an increased risk of premature mortality. However, knowledge about the underlying pathophysiological mechanisms are limited. This study investigated the time course of structural cardiac abnormalities and changes in ion channel expression in different models of epilepsy at acute and chronic timepoints.

Method: We used the kainic acid (KA) induced post-status epilepticus (SE) model of temporal lobe epilepsy (TLE) in male Wistar rats and the electrical-stimulated self-sustained status epilepticus (SSSE) in male mice. Sham groups were handled the same way but did not receive epileptogenic insult. Heart tissue was collected at acute (1-week post-SE) and chronic (3-4 months post-SE) timepoints from both models. Histological analysis of cardiac fibrosis and quantitative PCR of ion channel expression were performed. Statistical analysis was performed using student's t-test, one-way ANOVA and the Kruskal-Wallis test.

Result: On structural level, significant cardiac hypertrophy was found in 1-week post-SE animals compared to sham (n=16/group, p=0.0018) in SSSE mice. In the KA-induced chronic epileptic rats, cardiac fibrosis was 86% greater, compared to sham rats (n=4/group, p=0.018). For ion channel expression, both KA (12 weeks post-SE) and SSSE (1-week post-SE) animals exhibited increased of *NCX1* mRNA in the left ventricle (p=0.018 and 0.0019, respectively). KA (12 weeks post-SE) animals also had an increase of *Nav1.5* mRNA in the right atrium (p=0.005).
Conclusions: Acute and chronic experimental epilepsy is associated with an increased risk of cardiac abnormalities, which are evident at both the structural and molecular levels and might contribute to the elevated risk of cardiac dysfunction and mortality in epilepsy. Future studies should examine mechanisms underlying this, and whether interventions aimed at reducing seizure frequency and/or cardio-protection lessen the degree of cardiac abnormalities.

Abstract Number: 787

Title: Enzyme-Inducing Antiseizure Drugs associate with Low Bone Mineral Density in Men with Epilepsy

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Purpose: Despite the knowledge about enzyme-inducing antiseizure drugs (EI-ASD) and the reduction of Bone Mineral Density (BMD), little is known about its impact on men with epilepsy (MWE).

To evaluate the BMD in MWE with previous or current usage of EI-ASDs (phenytoin, carbamazepine and phenobarbital) and its relationship with the duration of epilepsy.

Method: We evaluated BMD from 74 consecutive MWE (median age (range), 52.5 (25-74) years) with previous or current EI-ASDs, at the outpatients' epilepsy clinics, from the University of Campinas-Brazil. Individuals were split into two groups (young-group, 31 individuals [age range 25-49]; older group, 43 subjects, [age range 50-74]). The BMD test evaluated t-score indexes from the femoral neck, whole femur and lumbar spine. Osteopenia was defined with a negative t-score of -1.0 to -2.4; osteoporosis was considered with T-scores lower than -2.5. Clinical data were extracted from the medical records. We analyzed data with SPSS22 and performed chi-square tests for categorical variables. We also applied a partial correlation test (controlled for age) between BD scores and duration of epilepsy.

Result: BMD was reduced in 49/74 men (66.2%; 21 osteoporosis, 28 osteopenia). Surprisingly, young and older groups presented equivalent proportions of BMD abnormalities (p=0.087) (young-group [14/41 normal (45%), 12/31 osteopenia (39%), 5/31 osteoporosis (16%)]; older-group [11/43 normal (26%), 16/43 osteopenia (37%), 16/43 osteoporosis (37%)]. The BD measures did not correlate with the duration of disease or age of onset.

Conclusions: BMD reduction is highly prevalent in MWE exposed to EI-ASD, including young individuals. Our data suggest that exposure to EI-ASD in young men may associate with early BMD reduction, which can evolve to osteopenia and osteoporosis. We believe that examination of BMD in MWE and appropriate treatment for osteopenia and osteoporosis (and switch of ASD) may be necessary to reduce fractures' risk.

Abstract Number: 1003

Title: Problem gambling behaviours in people with frontal lobe epilepsy

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Purpose: Poor impulse control and impaired decision making processes can have a significant impact on the lifestyle choices of some people with epilepsy, particularly those with frontal lobe dysfunction. Given the marked increase in gambling opportunities associated with the proliferation of online gambling platforms and smartphone apps in recent years, we wanted to examine the participation rates of people with epilepsy in regular gambling activities.

Method: Lifestyle questions, including the Lie/Bet screening questionnaire were administered to 250 consecutive attendees at a neurology clinic. Valid data was available for 174 adults with epilepsy and 65 adults with other neurological conditions.

Result: As a group, people with epilepsy were not significantly more likely to participate in gambling than those with other neurological conditions (16.4% vs 11.5 %: χ^2 (1, n= 232) =0.84, p>0.05). The rates in both groups were significantly lower than the national average of 47%. However, within the epilepsy group there was a significant association between the epilepsy classification and gambling participation (χ^2 (4, n= 171) =28.0, p<0.001). Gambling behaviours were significantly more frequent in the FLE group than those with other types of epilepsy. People with FLE did not differ from those with other epilepsy classifications with respect to markers of other excessive behaviours such as Body Mass Index (t= (112) =0.31, p>0.05) or intake of harmful levels of alcohol (χ^2 (1) =0.02, df 1, p>0.05). Neither did they differ from the other epilepsy groups controls with respect to rates of smoking (=χ^2 (1)= 1.4, p>0.05) or exercising (χ^2 (1) =0.5, p>0.05).

Conclusions: : People with FLE may have a heightened vulnerability to participation in gambling behaviours. The role of the neurological consultation in managing the risks associated with escalating gambling behaviours is discussed.

Abstract Number: 1157

Title: Correlation between objective sleep measures and sleep complaints in Dravet Syndrome

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Purpose: The presence of sleep disorders in Dravet Syndrome (DS) is a known clinical feature, along with the recurrence of several seizures types during sleep which can last well into adulthood. However until now few patients were studied by means of objective measures. We evaluated the sleep-wake cycle and sleep quality both in a subjective and objective way in a population DS patients.

Method: The presence of sleep complaints was assessed in 15 patients with DS via the Sleep Disturbance Scale for Children (SDSC). We measured objective sleep-wake cycle and sleep parameters of all patients for a minimum of 5 days using wearable fitness bracelets and elaborated the data using SleepActa™ neural network. A subgorup of 7 patients also underwent single nocturnal polysomnography (PSG). All variables were analyzed along with demographic and clinical data.
Result: SDSC scores had z-score >2 in 26.7% of cases, in particular the subscale Disorders of Arousal (DA) was above the 2SD cut-off in 66.7% of cases. Sleep Efficiency (SE) was below 85% in 14,3% of patients both considering neural network derived measures and PSG data. SDSC scores and its subscales do not correlate significantly with PSG measures. On the contrary, significant correlations ($p<0.05$) were found between quantitative measures derived by wearable devices and SDSC. In particular, the Number of Wakefulness Episodes (NWE) correlates with the total SDSC score, while the Movement Fragmentation Index (MFI) correlates with the DA subscale of the SDSC.

Conclusions: We confirm the presence of a high proportion of patients with DS complaining sleep disorders. In our cohort the most frequent complaint is DA. The multimodal approach we used allowed us to identify that objective measures derived from long term wearable accelerometric device recordings strongly correlate with self-reported sleep problems, thus offering a non-invasive, cost-effective method to assess sleep disturbances in DS.

Abstract Number: 1186

Title: eeg findings in migraine patients with genetic generalized epilepsy

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Purpose: The purpose of this prospective study was to investigate the EEG changes in a sample of migraineurs patients with genetic generalized epilepsy (GGE)

Method: This cross-sectional study was conducted in the department of neurology, at the Faculty of Medicine, Karadeniz Technical University in Trabzon, Turkey. We administered face-to-face structured questionnaires investigating the presence of migraine as well as its characteristics in GGE patients. Migraine was diagnosed and classified according to the International Classification of Headache Disorders, third edition (ICHD-III). A total of 22 migraine patients with GGE between the ages of 10-57 were included in this study.

Mean±standard deviation for non-quantitative data and Chi square test for quantitative data were used in SPSS software version 18.

Result: Twenty two migraine patients with GGE were evaluated. The distribution of headache diagnosis according to migraine subtypes were as follows; 12 (54.6%) with migraine without aura (MwoA), 9 (40.9%) with migraine with aura (MwA), 1 (4.5%) with migraine with brainstem aura. Of the twenty two studied patients 19 were having abnormal electroencephalographic (EEG) findings. All patients with MwA have abnormal EEG (100%), while in patients with MwoA, 9 of them have abnormal EEG (75%). 1 patient with migraine with brainstem aura has abnormal EEG finding. Slow waves were found in 3 patients (13.6%), sharp waves in 6 (27.2%), and spikes in 10 patients (45.5%). 3 (13.6%) of patients with migraine have normal EEG findings.

Conclusions: In this prospective study no difference was found in terms of EEG findings between MwA and MwoA

Abstract Number: 1268

Title: Hippocampal and Septal 5-HT1A Receptor Expression in Rat Models of Temporal Lobe Epilepsy and Stress

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Purpose: Experimental and clinical data suggest an impact of serotonergic neurotransmission on stress response and seizure susceptibility in patients with epilepsy as well as on epilepsy-associated comorbidities. In this context, 5-HT_{1A} receptor expression is discussed as a biomarker candidate for monitoring epilepsy-associated comorbidities.

Method: 5-HT_{1A} receptor binding potential was investigated by [^{18}F]MPPF-µPET studies in one chemical and one electrical post-status epilepticus (SE) model (n=24 and n=21 animals, respectively) and for direct comparison in one restraint stress model (n=32 animals) in rats. Seizure parameters and behavioral alterations were documented and correlated with µPET data. Based on µPET data, 5-HT_{1A} receptor expression in septum and hippocampal sub-regions was analyzed by stereological principles using immunohistochemically stained brain sections.

Result: µPET studies revealed an increased uptake of [^{18}F]MPPF in the septum of post-SE animals in the chemical post-SE model ($p<0.001$), the electrical post-SE model ($p<0.05$) and the hippocampus of animals experiencing transport as a stressor ($p=0.016$). Stereological analysis revealed a reduced optical density of 5-HT_{1A} receptor expression in hippocampal sub-region CA3 in the electrical post-SE model ($p=0.0449$) and in CA1 in the restraint stress model ($p=0.0343$). In the chemical post-SE model, expression rates were comparable in the evaluated brain regions. Correlation analysis pointed to a potential connection between 5-HT_{1A} receptor expression and ictogenesis, seizure termination and behavioral patterns.

Conclusions: The findings do not suggest widespread alterations of 5-HT_{1A} receptor expression in the analyzed brain regions. µPET data and stereological analysis suggest reduced serotonin levels and a reduction of the competitive inhibition by this endogenous ligand rather than enhanced receptor density as an explanation for increased [^{18}F]MPPF binding. However, this conclusion requires further confirmation by direct analysis of extracellular 5-HT concentrations by microdialysis.

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Abstract Number: 1315

Title: Anticipation of severe chronic venous disease in Genetic Generalized Epilepsy

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Purpose: Genetic generalized epilepsies (GGE) have a genetic susceptibility. The interaction between genetics, epilepsy and comorbidities has been studied. There is evidence for the contribution of genetic factors in the etiology of chronic venous disease. However, its association with epilepsy has never been studied. The aim of this study was to evaluate the association between severe chronic venous disease(SCVD) in two types of epilepsy: GGE and mesial temporal lobe epilepsy with hipocampal sclerosis(MTLE-HS).

Method: Retrospective analysis of patients with GGE and MTLE-HS followed at Centro Hospitalar Universitário do Porto, between 01/2016 and 12/2020 with the diagnosis of SCVD. SCVD was defined as the presence of varicose veins in the lower limbs in which the Vascular Surgeon proposed surgical treatment according to Clinical practice guidelines of the Society for Vascular Surgery and the American Venous Forum. Clinical characteristics, presence of generalized tonic-clonic seizures (GTCS), family history, age at SCVD diagnosis and venous surgery were reviewed. The significance of differences between groups was assessed using the Mann-Whitney or Fisher tests, as appropriate.

Result: In a population of 465 GGE and 245 MTLE-HS patients, SCVD was identified in 18(3.9%) GGE patients and in 9(3.7%) MTLE-HS patients(p=0.538). In both groups, SCVD was more prevalent in women. The median age at SCVD diagnosis was 35 years(IQR 31-48) in GGE and 54(IQR 45-64) in MTLE-HS(p=0.001). In GGE patients, surgical reintervention was required in one third of patients and no patient with MTLE-HS was reinterventioned. SCVD was not associated with the presence GTCS(p=0.970 in GGE, p=1.0 in MTLE).

Conclusions: This is the first study describing an anticipation of almost two decades in the presence of SCVD in GGE patients, probably by sharing reciprocal genetic factors. GGE must be looked not only as a brain disease, but also as a genetic susceptibility disorder associated to other systemic diseases.

Abstract Number: 1356

Title: Anxiety, Depression and Quality of life in Juvenil Myoclonic Epilepsy

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Purpose: Evaluate factors influencing depression, anxiety and Quality of Life (QOLIE) in Juvenile Myoclonic Epilepsy (JME).

Method: 108 patients (age 15-71, mean 31.3; 34.3% males, 65.7% females) with JME were evaluated during 2018-2019 in Hospital Virgen de la Victoria (Málaga, Spain). Inclusion criteria were age > 15 years, normal IQ, and clinical diagnosis of JME. Analysis included age of seizure onset, seizure control in the last month and year,

antiseizure medication (ASM) used, employment, socioeconomic and family status. For assessment of psychological outcome we analysed Beck-II Depression Inventory (BDI-II), Stay-Trait Anxiety Inventory (STAI), and for Quality of life (QOL) Side Effect and Life Satisfaction Inventory (SEALS). Clinical data were compared with psychological and QOL questionnaires. SPSS V.25 was used for statistical analysis.

Result: Mean age of seizure onset was 13 years (SD 5.08), epilepsy duration 18.25 years (SD:14.08). Myoclonic and bilateral tonic - clonic seizures were present in 76 (70.37%), absences in 6 (5.55%), both in 26 (24.07%). 96 (88.9%) were seizure free for the last year, 85.2% were on monotherapy and 11.1% in bitherapy. Depressive symptoms and QOL were similar to the general population, but anxiety was more frequent (STAI-S 25%, STAI-R 30.6%) and there were higher rates of wariness and uncertainty (69.4%). There was no correlation between depression, anxiety and QOL with seizure frequency but QOL was lower in relation to number of ASM used and depressive symptoms.

Conclusions: In this series most JME patients had adequate seizure control and low depression rates. Anxiety was higher. QOL was similar to general population except for increased wariness and uncertainty. Depressive symptoms had a correlation with longer disease duration, higher number of ASM and lower QOL, but not with recent seizure control.

Drug Therapy

Abstract Number: 34

Title: Treatment of patients with prolonged course of medial temporal epilepsy

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Purpose: The aim of the study was to evaluate the efficacy of treatment in patients with prolonged duration of medial temporal epilepsy.

Method: We studied cases of 93 patients with history of medial temporal epilepsy lasted more than 10 years. Among the patients there were 52 women and 41 men that reflects a lack of connection with gender.

Result: The frequency of seizures in most patients was one or more times a month, and 1/5 of the patients had seizures daily. Medial temporal epilepsy is often characterized by drug resistance. Selection of drugs for the treatment of patients with medial temporal epilepsy is a difficult task. In our study, the first drug used rarely immediately had a positive effect. Patients have to try different medications before the effective one is found (in 12% of cases, patients tried 5-7 different medicines). Nevertheless, in 48.4% of patients, pharmacotherapy is ineffective. According to our findings, patients with an early medial temporal epilepsy debut and those with an epileptogenic focus (by electroencephalography and magnetic resonance imaging data) in the medial temporal zone are most likely to have treatment-resistant epilepsy.

Conclusions: If therapy is ineffective, it is necessary to direct patients for pre-surgical evaluation, as therapy often does not help patients with medial temporal epilepsy and can lead to side effects.

Abstract Number: 96

Title: Cognitive performance and retention after 12-month adjunctive brivaracetam in difficult-to-treat patients with epilepsy in a real-life setting

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Purpose: Evaluate retention and cognitive performance in patients aged ≥16years with focal seizures after 12-month adjunctive brivaracetam treatment in real-world practice.

Method: Patients received brivaracetam per clinical practice in a prospective, non-interventional post-marketing study in Europe (EP0077/NCT02687711). Outcomes: brivaracetam retention, treatment-emergent adverse events (TEAEs), cognitive assessment (EpiTrack).

Result: 544/548 enrolled patients received ≥1 brivaracetam dose (=safety set [SS]; mean age: 43.6years; 52.8% female; mean time since epilepsy diagnosis: 22.7years; median number of focal seizures/28days at baseline: 3.7; mean number of lifetime antiepileptic drugs [AEDs] [=historical AEDs+AEDs taken at entry]: 7.3; 77.9% had ≥2 concomitant AEDs at entry). Median brivaracetam exposure duration was 355.0days (range1–603) (SS). Twelve-month brivaracetam retention was 57.7% (95%CI 53.4–61.9%) in full analysis set (FAS; all SS patients not receiving brivaracetam before entering EP0077; n=541), 60.3% (54.6–65.8%) in modified FAS (represents brivaracetam use per SmPC; n=310). In FAS patients with available data, the proportion of patients reporting mildly or significantly impaired cognitive performance (EpiTrack) was lower at 12months (4.9%, 36.1%; n=61) versus baseline (14.8%, 49.3%; n=142); the proportion with excellent or average cognitive performance was higher at 12months (6.6%, 52.5%) versus baseline (2.8%, 33.1%). Trends were similar in modified FAS. 23.0% of patients reported significant improvement (increase of ≥4) in total EpiTrack score from baseline to 12months (n=61); 67.2% remained unchanged (change of −2 to 3); 9.8% reported worsening (decrease of ≥3) (FAS). 41.2% of SS patients experienced ≥1 TEAE; 25.9% discontinued study due to TEAEs; 36.0% experienced TEAEs considered drug-related by investigator (≥5%: drug ineffective [11.4%], seizure [6.3%]). Two deaths (0.4%) were reported (relationship to brivaracetam: one unavailable, one unrelated).

Conclusions: In this real-world study in difficult-to-treat patients with epilepsy, >50% remained on brivaracetam for 12months. Two-thirds reported no significant change in cognitive function (EpiTrack); one-quarter improved. Brivaracetam introduction was well-tolerated.

Funding: UCB Pharma-sponsored

Abstract Number: 97

Title: Effectiveness and tolerability of adjunctive brivaracetam in patients with secondary generalized (focal to bilateral tonic-clonic) seizures in Germany

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Purpose: Assess real-world effectiveness and tolerability of adjunctive brivaracetam (BRV) in patients with secondary generalized seizures (focal to bilateral tonic-clonic seizures [FBTCS]).

Method: Post-hoc analysis of a retrospective study conducted in specialized epilepsy centers across Germany (EP0104). Patients with confirmed epilepsy diagnoses who initiated adjunctive BRV between February and August 2016, reported FBTCS during 3-month Baseline, and took ≥1 BRV dose were analyzed.

Result: 141 (28%) of 506 patients who took ≥1 BRV dose reported FBTCS during Baseline (mean age 40.7 years; 53.2% male; mean epilepsy duration: 25.3 years; median lifetime AEDs [previous + ongoing at BRV initiation]: 7.0; median Baseline seizure frequency/28 days: 3.9 all seizures, 1.2 FBTCS). Most common reasons for BRV initiation were lack of efficacy (74.5%) or behavioral side-effects (12.8%) of current treatment. Median BRV dose was 100 mg/day (n=141) at initiation and 200 mg/day (n=97) at last assessment. At 3- and 6-months after BRV initiation, 87.9% and 53.9% patients, respectively, continued BRV. At 6 months (n=97), 50.5% and 23.7% patients had ≥50% and 100% decrease from Baseline seizure frequency, respectively (all seizure types). 39.7% patients reported ≥1 treatment-emergent adverse event (TEAE; 32.6% during first 3-months; 5.7% during second 3-months); most (87.5%) were mild/moderate in intensity. Most common (≥5% patients) TEAEs were fatigue (7.1%) and aggression (6.4%). 24.1% patients had drug-related TEAEs; 10.6% discontinued due to TEAEs. During 3-month Baseline, 10.6% patients reported behavioral adverse events (most commonly aggression [7.1%]). Following BRV initiation, 9.2% patients reported behavioral TEAEs during the first 6 months (8.5% and 0.7% in first and second 3-months, respectively).

Conclusions: In this difficult-to-treat subpopulation of patients with secondary generalized seizures (FBTCS) requiring treatment change, adjunctive BRV was generally well-tolerated and effective; 24% patients achieved seizure-freedom at 6 months. Incidence of behavioral adverse events was similar before and during BRV treatment.

Funding: UCB Pharma-sponsored

Abstract Number: 98

Title: Pharmacokinetics, safety, and tolerability of intravenous brivaracetam in pediatric patients with epilepsy: an open-label trial

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Purpose: Evaluate the pharmacokinetics, safety, and tolerability of brivaracetam (BRV) as 15-minute intravenous infusion and bolus (up to 2-minute injection).

Method: Phase 2, multicenter, open-label trial (EP0065/NCT03405714) in patients ≥1 month to <16 years old with epilepsy. Patients received ≤5mg/kg/day BRV, not to exceed 200mg/day. Enrollment was sequential by descending age, dependent on safety review. Outcomes included plasma concentration of BRV before and

after intravenous administration, treatment-emergent adverse events (TEAEs), and discontinuations due to TEAEs.

Result: Fifty patients enrolled, received BRV, and completed the trial (mean age: 8.3 years [patients ≥2 years old, n=37], 11.4 months [patients <2 years old, n=13]; 52.0% male). Twenty-six (52.0%) patients received BRV as 15-minute infusion and the remaining 24 (48.0%) received bolus injection; 20 (40%) were previously BRV-naïve. Most (40 [80.0%]) patients received 1 dose intravenous BRV. In the 15-minute infusion group, geometric mean (GeoMean) BRV concentrations 15±2 minutes (n=21) and 3 hours (±15 minutes) (n=21) post-dose were 1903.0ng/mL (geometric coefficient of variation [GeoCV]:60.7%) and 1130.3ng/mL (GeoCV:58.8%), respectively. In the bolus group, GeoMean BRV concentrations ≤1-hour pre-dose (n=22) and 15±2 minutes (n=19) and 3 hours (±15 minutes) (n=21) post-dose were 120.5ng/mL (GeoCV:1222.5%), 1704.8ng/mL (74.5%) and 1383.9ng/mL (85.0%), respectively. Overall, 14 (28.0%) patients had TEAEs (15-minute infusion: 8 [30.8%]; bolus: 6 [25.0%]), most commonly (≥5% of patients) somnolence (3 [6.0%]). Ten (20.0%) patients had drug-related TEAEs (15-minute infusion: 6 [23.1%]; bolus: 4 [16.7%]). No patients discontinued due to TEAEs and there were no deaths.

Conclusions: Intravenous BRV was well-tolerated in patients ≥1 month to <16 years old at doses up to 200mg/day, regardless of whether BRV was administered as 15-minute infusion or bolus. There were no unexpected pharmacokinetic differences observed between infusion groups. Results were consistent with the known safety profile of oral BRV; no new safety concerns were identified.

Funding: UCB Pharma-sponsored

Abstract Number: 100

Title: Tolerability and efficacy of brivaracetam in adults with focal seizures by concomitant antiepileptic drug use: post-hoc analysis

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Purpose: Evaluate the tolerability and efficacy of brivaracetam (BRV) in patients on 1 or 2 concomitant antiepileptic drugs (AEDs) and in patients on 1 specific concomitant AED.

Method: Post-hoc analysis of double-blind trials (N01252/NCT00490035, N01253/NCT00464269, N01358/NCT01261325) in adults with focal seizures randomized to BRV (50-200 mg/day) or placebo with concomitant AED regimen unchanged throughout the 12-week double-blind Evaluation Period. Outcomes were analyzed in patents on 1 or 2 concomitant AEDs, and in those on concomitant carbamazepine (CBZ), lamotrigine (LTG), oxcarbazepine (OXC), or valproate (VPA) only. Efficacy analyses excluded patients on concomitant levetiracetam.

Results: Patients on 1/2 concomitant AEDs, respectively, on BRV (n=181/n=557) or placebo (n=95/n=331), reported similar incidence of treatment-emergent adverse events (TEAEs; 68.0%/66.4% [placebo: 60.0%/60.7%]), drug-related TEAEs (41.4%/41.5% [placebo: 32.6%/30.2%]), TEAEs potentially associated with behavioral disorders (3.9%/4.3% [placebo: 4.2%/1.2%]), TEAEs leading to discontinuation (6.6%/5.4% [placebo: 2.1%/4.5%]), and similar incidences of somnolence (16.0%/15.4% [placebo: 6.3%/9.1%]), fatigue (6.1%/8.8% [placebo: 4.2%/3.6%]), dizziness (9.4%/12.0% [placebo: 5.3%/6.9%]), and headache (11.6%/8.6% [placebo: 9.5%/10.3%]). In patients on 1/2 concomitant AEDs, respectively, the 50% responder rate was higher with BRV (42.3%/36.8%; n=175/n=511) vs placebo (18.3%/19.5%; n=93/n=298); corresponding seizure freedom (all seizure types): 6.9%/3.7% [placebo: 2.2%/0]. For patients taking BRV or placebo on concomitant CBZ (BRV

n=54[placebo n=34]), LTG (n=30[n=13]), OXC (n=27[n=10]), or VPA (n=27[n=15]), TEAEs were reported by 70.4%[61.8%], 60.0%[61.5%], 70.4%[50.0%], 59.3%[53.3%] patients, respectively; drug-related TEAEs: 35.2%[32.4%], 43.3%[46.2%], 48.1%[30.0%], 29.6%[33.3%]; TEAEs potentially associated with behavioral disorders: 5.6%[5.9%], 3.3%[7.7%], 7.4%[0], 0[6.7%]; discontinuations due to TEAEs: 1.9%[5.9%], 10%[0], 7.4%[0], 3.7%[0]. For patients taking concomitant CBZ, LTG, OXC, or VPA, 50% responder rates for BRV[placebo] were 31.5%[17.6%], 30.0%[7.7%], 40.7%[20.0%], 70.4%[33.3%]; corresponding seizure freedom: 3.7%[0], 6.7%[0], 7.4%[0], 11.1%[6.7%].

Conclusions: Consistent with the clinical program, therapeutic doses of BRV were efficacious and well-tolerated regardless of concomitant AED (CBZ, LTG, OXC, VPA), or number of concomitant AEDs (1 or 2).

Funding: UCB Pharma-sponsored

Abstract Number: 104

Title: Adjunctive lacosamide as treatment for primary generalized tonic-clonic seizures (PGTCS): efficacy and tolerability by baseline PGTCS frequency

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Purpose: Time-to-event design of the SP0982 trial allowed inclusion of patients with lower Baseline PGTCS frequency, better reflecting usual clinical practice. This post-hoc analysis assessed efficacy and tolerability of adjunctive lacosamide in patients with primary generalized tonic-clonic seizures (PGTCS) by Baseline PGTCS frequency.

Method: Post-hoc subgroup analysis of phase 3, double-blind, randomized, placebo-controlled trial (SP0982/NCT02408523) of adjunctive lacosamide (≤12 mg/kg/day or ≤400 mg/day) in patients (≥4 years) with idiopathic generalized epilepsy (IGE) and uncontrolled PGTCS taking 1–3 concomitant antiepileptic drugs. Outcomes during 24-week treatment were analyzed by Baseline PGTCS frequency/28 days (≤2, >2).

Result: Median Baseline PGTCS frequency/28 days was 1.0 in patients with ≤2 PGTCS/28 days (n=190; mean age 27.7 years; 58.4% female) and 3.3 in patients with >2 PGTCS (n=52; mean age 27.9 years; 59.6% female). 88.4% patients on lacosamide with ≤2 PGTCS (n=95) completed the study vs 73.1% with >2 PGTCS (n=26) (PBO: 92.6% vs 84.6%, respectively [n=95 and 26]). In ≤2 PGTCS subgroup, numerically higher proportion of patients on lacosamide than placebo had ≥50% (72.3% vs 48.4%) or ≥75% (61.7% vs 40.0%) reduction from Baseline in PGTCS frequency/28 days (n=94 and 95, respectively), or freedom from PGTCS during treatment (28.7% [n=87] vs 15.6%; [n=90]). Similarly, in >2 PGTCS subgroup, numerically higher proportion of patients on lacosamide than on placebo had ≥50% (52.0% vs 38.5%) or ≥75% (40.0% vs 23.1%) reduction in PGTCS frequency (n=25 and 26, respectively) or freedom from PGTCS (22.7% [n=22] vs 4.2% [n=24]). Incidence of treatment-emergent adverse events was similar for patients with ≤2 (lacosamide: 80.0%, placebo: 64.2%) and >2 PGTCS (76.9%, 69.2%).

Conclusions: Adjunctive lacosamide was generally well-tolerated and demonstrated efficacy in PGTCS in patients with IGE, independent of Baseline PGTCS frequency. Overall, patients with lower PGTCS frequency, more representative of clinical practice, had numerically higher efficacy response.

Funding: UCB Pharma-sponsored

Abstract Number: 135

Title: Long-term Safety and Efficacy of Add-on Cannabidiol for Treatment of Seizures Associated with Tuberous Sclerosis Complex in an Open-Label Extension

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Purpose: In this 2nd interim analysis of an open-label extension (OLE) trial GWPCARE6/NCT02544763), we report safety and efficacy of add-on cannabidiol (CBD) for treatment of seizures associated with tuberous sclerosis complex (TSC).

Method: Patients who completed a randomised controlled trial (RCT) received GW Pharmaceuticals' formulation of plant-derived highly purified CBD (100 mg/mL oral solution) in the OLE (titrated to 25 mg/kg/day, or up to 50 mg/kg/day). Primary endpoint: safety. Secondary endpoints: percent change in TSC-associated (countable focal or generalised) seizures, responder rates, and Subject/Caregiver Global Impression of Change (S/CGIC).

Result: Of 201 patients who completed the RCT, 199 (99%) entered the OLE. Median (range) age: 10.7 (1.1–56.8) years. Baseline median TSC-associated seizure frequency/28 days: 57 seizures. At this analysis, 12% of patients had completed treatment, 31% had withdrawn, and 57% were ongoing. OLE median (range) treatment time: 372 (18–1127) days. Mean (SD) modal dose: 28 (9) mg/kg/day. AE incidence: 94%; serious AE incidence: 26%; 8% discontinued treatment due to AE(s). Most common AEs (≥20%): diarrhoea (45%), seizure (28%), decreased appetite (23%), pyrexia (21%), and vomiting (20%). Seventeen (9%) patients had elevated ALT/AST >3×ULN; 12 were on concomitant valproate. No patient met Hy's law criteria for severe liver injury. One death occurred due to cardiopulmonary failure and was not deemed treatment-related. Median reductions in TSC-associated seizures (12-week windows through 72 weeks): 53%–75%. Seizure reductions were 54%–80% for patients with a modal dose ≤25 mg/kg/day (n=145). ≥50%, ≥75%, and 100% responder rates were maintained up to 72 weeks, ranging 52%–63%, 29%–51%, and 6%–19%, across 12-week windows). Improvement on S/CGIC was reported by 85% and 89% of patients/caregivers at 26 and 52 weeks.

Conclusions: Add-on CBD treatment was well tolerated and produced sustained reductions in TSC-associated seizures for up to 72 weeks.

FUNDING: GW Research Ltd.

Abstract Number: 141

Title: Time to Onset of Cannabidiol Treatment Effect and Resolution of Adverse Events in Tuberous Sclerosis Complex Randomised Controlled Trial (GWPCARE6)

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Purpose: Add-on cannabidiol (CBD) significantly reduced seizures associated with tuberous sclerosis complex (TSC) across the 16-week double-blind treatment period in GWPCARE6 (NCT02544763). A post hoc analysis was conducted to estimate time to onset of CBD treatment effect and resolution of adverse events (AEs).

Method: Patients received GW Pharmaceuticals' formulation of plant-derived highly purified CBD (100 mg/mL oral solution) at 25 mg/kg/day (CBD25) or 50 mg/kg/day (CBD50), or placebo for 16 weeks. Treatment started at 5 mg/kg/day for all groups, reaching 25 mg/kg/day on Day 9 in CBD25 and 50 mg/kg/day on Day 29 in CBD50. Percentage change from baseline in primary endpoint TSC-associated seizures (countable focal or generalised) was calculated by cumulative day (i.e., including previous days). Time to onset and resolution of AEs were evaluated.

Result: Overall, 224 patients were randomised 1:1:1 to CBD25 (n=75), CBD50 (n=73), and placebo (n=76). The median (range) age was 11 (1–57) years. Patients had discontinued a median of 4 antiepileptic drugs (AEDs) and were currently taking a median of 3 AEDs. Differences in seizure reduction between CBD and placebo emerged on Day 6 (when titration reached 15 mg/kg/day) and became nominally significant ($p<0.05$) by Day 11 (CBD50) or Day 12 (CBD25). Over 90% of patients had an AE, with onset during the first 2 weeks of the titration period in 63%. AEs resolved within 4 weeks of onset in 42% of placebo and 27% of CBD patients and by end of study in 78% of placebo and 51% of CBD patients; most frequent AEs—diarrhoea, somnolence, decreased appetite—resolved in 69–88% of CBD patients.

Conclusions: Findings suggest that onset of treatment effect (efficacy and AEs) occurred within the first 2 weeks. AEs lasted longer for CBD vs. placebo but resolved within the 16-week study in most patients.
FUNDING: GW Research Ltd.

Abstract Number: 174

Title: Switch from enzyme-inducing antiepileptic drugs to new antiepileptic drugs in patients with epilepsy

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Purpose: The enzyme-inducing antiepileptic drugs (carbamazepine, phenytoin, and phenobarbital) have many metabolic side effects, such as osteoporosis, hyperlipidemia, hypothyroidism, cardiovascular disorders, and hyponatremia. To avoid the metabolic risks, we have switched from the enzyme-inducing antiepileptic drugs to new antiepileptic drugs in 41 patients with epilepsy.

Method: Forty-one patients with epilepsy whose medicines were switched from the enzyme-inducing antiepileptic drugs to the new antiepileptic drugs (28 males and 13 females, aged from 2 to 57 years; median, 21.9 years) were enrolled this study from April 2015 to March 2021. Patients without seizures were 22. Patients with yearly, monthly, weekly, and daily seizures were 4, 8, 4, and 3, respectively. Clinical records of the patients were analyzed retrospectively.

Result: Carbamazepine (CBZ) taken by 21 patients, phenytoin (PHT) by 12, and phenobarbital (PB) by 10 were switched to the new antiepileptic drugs at first. Seventeen patients took levetiracetam (LEV), 16 lacosamide (LCM), 4 lamotrigine (LTG), and 4 perampanel (PER) as the new antiepileptic drugs at first. The new

antiepileptic drugs taken finally were LEV in 20 patients, LCM in 19, LTG in 6 and PER in 6. The epileptic seizures of 6 patients (15%) were worsened transiently during the switch. The comparisons of epileptic condition of the patients before and after the switch were improvement in 8 (20%) patients, no change in 32 (78%), and a change for the worse in 1 (2%).

Conclusions: The epileptic seizures of 15% of the patients were worsened transiently during the switch similar to the previous reports. Taking various metabolic side effects of the enzyme-inducing antiepileptic drugs, the switch to new antiepileptic drugs should be considered.

Abstract Number: 183

Title: Safety of Diazepam Nasal Spray (Valtoco®) in Patients With Epilepsy: Final Results From a Phase 3, Open-Label, 12-Month, Repeat-Dose Safety Study

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Purpose: Benzodiazepines are the mainstay of rescue therapy for seizure clusters. Diazepam nasal spray [Valtoco®, Neurelis, Inc.] is a proprietary formulation with n-dodecyl beta-D-maltoside and vitamin E that is approved for acute treatment of seizure clusters in patients with epilepsy aged ≥6 years. The long-term safety of diazepam nasal spray was evaluated in a 12-month, phase 3, repeat-dose, open-label study.

Method: Caregivers and patients were trained to administer doses of 5, 10, 15, or 20 mg, based on age and weight; if needed, a second dose was to be administered 4–12 hours later. Seizures, drug administration, and treatment-emergent adverse events (TEAEs) were recorded. Study visits included physical/neurological examinations, vital signs, and laboratory tests.

Result: Of 175 patients enrolled, 163 received diazepam nasal spray (mean age 23.1 years; range: 6–65; 3853 total seizure clusters). The majority of patients (81.6%) had duration of exposure ≥12 months; 52.8% of patients averaged ≥2 doses per month. A total of 134 (82.2%) patients had ≥1 TEAE. Serious TEAEs were recorded in 50 (30.7%) patients; none was deemed treatment-related. TEAEs assessed as being possibly treatment-related were seen in 30 (18.4%) of patients, most commonly nasal discomfort (6.1%). Of note, there were no TEAEs of cardiorespiratory depression. There were no trends in vital signs or laboratory tests. Forty-six patients discontinued; 19 withdrew, 11 were lost to follow-up, 1 died (not deemed treatment related), 1 discontinued due to an adverse event (not deemed treatment-related), and 14 discontinued for other reasons.

Conclusions: In this phase 3 long-term, repeat-dose safety study of diazepam nasal spray for patients with seizure clusters, safety was consistent with the established profile of rectal diazepam. Treatment-related TEAEs were reported in 18.4% of patients. Exposure was ≥12 months in 81.6% of patients, and the retention rate was high (71.8% [117/163]).

Abstract Number: 187

Title: Complementary and alternative treatment of epilepsy in childhood – a survey study

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Purpose: To study the use of complementary and alternative treatment (CAT) for epilepsy in children and its consequences on patient management.

Method: Using an internet questionnaire we determined the proportion of patients who use CAT, the profile of these patients in terms of course of epilepsy, the level of awareness about CAT, the effectiveness of CAT and the attitudes towards conventional antiepileptic treatment.

Result: Of 139 respondents, 68 (48.9%) admitted the use of CAT. CBD derivates (43/59, 72.9%), phytotherapy other than CBD (16/59, 27.1%) and fish oil (15/59, 25.4%) were the most used. Before starting or during CAT, 6.9% of children (4/58) took one antiepileptic drug (AED), 27.6% (16/58) two AEDs and 65.5% (38/58) three or more AEDs. The duration of epilepsy until the onset of CAT was <2 years in 45.5% (30/66) of cases and ≥2 years in 54.5% (36/66). The parents reported an insufficient response to conventional AEDs (51/65, 78.5%) and adverse drug reactions (19/65, 29.2%) as the most common reasons for initiating CAT. 34.9% (23/66) of parents reported a reduction of seizures of ≥50% and 6.1% (4/66) seizure free state after started CAT. 50% of parents (17/34) observed side effects of CAT.
According to 51.1% of parents (23/45), CAT met their expectations. On the other hand, 37.2% (16/43) of parents disclosed they were not sufficiently informed about possible side effects of CAT, 24.1% (13/54) did not inform their doctor about the use of CAT, and 28.2% (11/39) changed classic antiepileptic treatment arbitrarily after starting CAT.

Conclusions: The results clearly show the high popularity of CAT in children with epilepsy, especially in drug-resistant cases. We perceive as insufficient the level of awareness about possible side effects of CAT, as well as communication between parents and doctors about CAT, what can carry a consequent negative impact on patient management.

Abstract Number: 228

Title: Plasma Concentrations/Clinical Effects of Perampanel 4mg/day Monotherapy for Focal-Onset Seizures (FOS): Post Hoc Analysis by Body Mass Index (BMI)

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Purpose: FREEDOM (Study 342; NCT03201900) is an open-label, Phase III study of perampanel monotherapy in patients (aged 12-74 years) with newly diagnosed/currently untreated recurrent FOS, with/without focal to bilateral tonic-clonic seizures. We explored the association between perampanel plasma concentrations and clinical efficacy/tolerability following perampanel 4 mg/day based on BMI.
Method: The Core Study comprised 6-week Titration and 26-week Maintenance Periods; patients received perampanel 4 mg/day (8 mg/day following seizure). Blood samples for pharmacokinetic assessments were collected at Weeks 6 (Titration), 10 and 20 (Maintenance). Perampanel plasma concentrations are summarized in the modified Intent-to-Treat (mITT) population (patients in the
4-mg/day Maintenance with ≥1 post-dose efficacy assessment). Results (4-mg/day Maintenance) were stratified by BMI, seizure-free status and treatment-emergent adverse events (TEAEs).

Result: Overall, 73 patients were included in the mITT population. Mean (standard deviation [SD]) perampanel plasma concentrations at Week 20 by BMI (kg/m^2) and seizure-free status were: BMI <18, 194.5 (275.1; n=2) ng/mL in seizure-free patients (no non-seizure-free patients); BMI 18-25, 358.9 (211.1; n=29) ng/mL in seizure-free vs 688.4 (1042.9; n=5) ng/mL in non-seizure-free patients (*P*=0.520); BMI >25, 394.2 (227.0; n=14) ng/mL in seizure-free patients (no non-seizure-free patients). Mean (SD) perampanel plasma concentrations at Week 20 by BMI and TEAE incidence were: BMI <18, 194.5 (275.1; n=2) ng/mL in patients without TEAEs (no patients with TEAEs); BMI 18-25, 372.9 (260.0; n=16) ng/mL without TEAEs vs 438.1 (542.9; n=18) ng/mL with TEAEs; BMI >25, 492.9 (194.6; n=7) ng/mL without TEAEs vs 295.6 (226.1; n=7) ng/mL with TEAEs. There was large inter-subject variability in perampanel concentrations, regardless of BMI, seizure-free status or TEAE incidence.

Conclusions: Most patients receiving perampanel 4 mg/day achieved seizure freedom. There was no association between perampanel plasma concentrations and BMI, seizure control or TEAE incidence, suggesting dosing should be personalised based on individual clinical response/tolerability.

Funding: Eisai Co., Ltd.

Abstract Number: 255

Title: Exploring the Impact of Need for a Second Dose of Rescue Therapy for Seizure Episodes on Healthcare Utilization

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Purpose: Seizure clusters may last 24 hours or more. Approved outpatient rescue therapies have differing profiles that may affect multiple aspects of healthcare utilization. A review of large, long-term, open-label studies in seizure clusters was conducted to examine the impact of second doses of rescue therapy on cost burden. Proportions of seizure episodes requiring a second dose of rescue medication and serious treatment-emergent adverse events (TEAEs) are reported.

Method: For 3 large, long-term studies of approved seizure-cluster treatments (ie, diazepam nasal spray, rectal diazepam, intranasal midazolam), percentage of episodes controlled by the initial dose was compared with those requiring a second dose before 6, 12, and 24 hours. Serious TEAE data were collected.

Result: For diazepam nasal spray, no second dose was administered in 94.2% (3629/3853) of seizure episodes within 6 hours of the initial dose, 91.7% (3535/3853) within 12 hours, and 87.4% (3368/3853) within 24 hours. For rectal diazepam seizure control ≥12 hours after treatment, 77% of administrations (1215/1578) prevented further seizures (second doses not reported). For intranasal midazolam, measuring seizure control 10 minutes to 6 hours after treatment, 55.5% (1108/1998) of seizure-cluster episodes were successfully treated; second doses were not administered in 61.5% of seizure episodes (1229/1998).
For diazepam nasal spray, serious TEAEs occurred in 50 patients (30.7%), and none was considered treatment related. For diazepam rectal gel, 16 of 363 seizure clusters were subsequently treated in the emergency department. For intranasal midazolam, 4 patients had 1 serious TEAEs possibly treatment related (association with second dose not reported).

Conclusions: Across these noncomparative open-label studies, need for a second dose ranged from <10% to <40% at 6, 12, and 24 hours. Differences among approved therapies appear to have the potential to impact healthcare burden and should be considered when selecting rescue therapy for seizure clusters.

Abstract Number: 257

Title: Patient-Reported Experience With Diazepam Nasal Spray for Seizure Clusters: Exit Survey Results From a Phase 3, Open-Label, Repeat-Dose Safety Study

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Purpose: Ideal rescue treatments for patients with epilepsy should be easy for nonmedical individuals to use; therefore, it is important to assess user perceptions of these treatments. Diazepam nasal spray [Valtoco®, Neurelis, Inc.] is indicated for acute treatment of seizure clusters in patients with epilepsy aged ≥6 years. Patient responses to a survey from a phase 3 safety study of diazepam nasal spray were analyzed.

Method: Patients and caregivers were trained to administer age- and weight-based doses of 5, 10, 15, or 20 mg. A survey was distributed to patients and caregivers at study end or patient completion/discontinuation. Data were collected on comfort using diazepam nasal spray outside the home, timing of administration, and comfort of use compared with rectal diazepam. Safety was assessed.

Result: Of 175 patients enrolled at interim cutoff, 158 received diazepam nasal spray; 67 responded to the survey (66 with safety data). Thirty-two of 53 patients with prior rescue medications (60.4%) reported past use of rectal diazepam.
Most patients were very comfortable doing activities outside the home if they had diazepam nasal spray available (78.8%); 87.9% of patients/caregivers carried diazepam nasal spray outside the home, and 84.5% of patients were very or extremely comfortable carrying diazepam nasal spray. Diazepam nasal spray was primarily administered at the first signs of a seizure (46.2%). Compared with diazepam nasal spray, 86.7% were not at all comfortable having rectal diazepam publicly administered.
Fifty-one patients (77.3%) had treatment-emergent adverse events (TEAEs). Seventeen (25.8%) had a serious TEAE; none were treatment related. The 4 mild and 1 moderate report of nasal discomfort were assessed as treatment related.

Conclusions: In this survey, patients were comfortable with diazepam nasal spray outside the home and were more comfortable being treated in public than with rectal diazepam. Safety was consistent with rectal diazepam.

Abstract Number: 281

Title: Effectiveness, Safety and Tolerability of Perampanel in Adolescents with Focal and Generalised Seizures: Evidence from Clinical Practice

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Purpose: To assess the real-world effectiveness, safety and tolerability of perampanel (PER) when used to treat adolescent patients in everyday clinical practice.

Method: Adolescent patients (aged ≥12 – <18 years) treated with PER for focal or generalised seizures were identified from an interim pooled analysis of data from 18 clinical practice studies/work groups. Retention was assessed after 3, 6 and 12 months of PER treatment. Effectiveness was assessed by seizure type at the last visit. Effectiveness assessments comprised seizure freedom rate (no seizures since at least the prior visit), responder rate (≥50% seizure frequency reduction). Safety and tolerability were assessed by evaluating adverse events (AEs).

Result: A total of 112 adolescent patients (54.1% male; mean age, 15.2 years; mean number of previous antiepileptic drugs, 4.7) were included. Effectiveness was assessed for 101 patients and safety/tolerability for 91 patients. Seizure types at baseline were focal only (68.0%), generalized only (28.2%), and focal and generalised (3.9%). PER was used as adjunctive therapy in 94.5% of patients and as monotherapy in 5.5% of patients. Mean (standard deviation) PER dosage was 2.5 (1.2) mg/day at baseline and 6.9 (2.3) mg/day at the last visit. Retention rates at 3, 6 and 12 months were 92.2%, 77.5% and 60.2%, respectively. Mean (95% confidence interval) time under PER treatment was 10.0 (9.1–11.0) months. At the last visit, seizure freedom rates in patients with focal and generalised seizures were 12.7% and 57.7%, respectively, and corresponding values for responder rates were 48.1% and 80.8%, respectively. AEs were reported for 53.8% of patients; most common AEs were behavioural (aggression/anger/irritability; 25.3%), dizziness/vertigo (17.6%) and somnolence (12.1%). Overall, 13.7% of patients discontinued due to AEs.

Conclusions: PER was effective and generally well tolerated when used to treat adolescent patients with focal and generalised seizures in everyday clinical practice.

Study supported by Eisai

Abstract Number: 285

Title: Effectiveness and Safety of Perampanel in Elderly Epilepsy Patients (aged ≥65 Years) Treated in Everyday Clinical Practice

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Purpose: To evaluate the real-world effectiveness and safety/tolerability of perampanel (PER) in epilepsy patients aged ≥65 years treated in clinical practice.

Method: Patients aged ≥65 years were identified from an interim pooled analysis of 18 studies/work groups that collected clinical practice data on patients treated with PER for focal or generalised seizures. Retention was assessed after 3, 6 and 12 months of PER treatment. Effectiveness was assessed by seizure type. Effectiveness assessments included seizure freedom rate (no reported seizures since at least the prior visit) and responder rate (≥50% reduction in seizure frequency) at the last visit. Tolerability was assessed by evaluating adverse events (AEs).

Result: Data from 256 patients aged ≥65 years were included in the analysis (50.8% female; mean age 72.4 years; mean number of previous antiepileptic drugs [AEDs], 4.6). The majority of patients (77.4%) had focal seizures only; 6.7% had generalised seizures only and 6.0% had both focal and generalised seizures. At

treatment initiation the majority of patients were on 1 or 2 concomitant AEDs (1.2% initiated PER as monotherapy). The mean (standard deviation) PER dosage was 2.6 (1.4) mg/day at baseline and 5.7 (2.5) mg/day at last visit. Retention rates at 3, 6, and 12 months were 87.6%, 74.1% and 58.4%, respectively. The main reasons for discontinuation were AEs (20.7%), lack of efficacy (6.0%) and both (2.3%). At the last visit, seizure freedom rates in patients with focal and generalised seizures were 35.0% and 42.9%, respectively; the corresponding values for 50% responder rates were 68.7% and 83.3%, respectively. AEs were experienced by 52.0% of patients; most common were dizziness/vertigo (16.3%), somnolence (11.3%) and behavioural AEs (10.4%).

Conclusions: PER was effective for both focal and generalised seizures and was generally well tolerated when used to treat elderly patients in clinical practice.

Study supported by Eisai

Abstract Number: 288

Title: Perampanel in Adult Epilepsy Patients Treated in Everyday Clinical Practice: Results from an Interim Pooled Analysis of Real-World Studies

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Purpose: To evaluate the effectiveness and safety/tolerability of perampanel (PER) in adult epilepsy patients treated in clinical practice.

Method: Adult patients (aged ≥18 to <65 years) treated with PER for focal and/or generalised seizures were identified from an interim pooled analysis of data from 18 clinical practice studies/work groups. Retention rate was evaluated at 3, 6 and 12 months. Effectiveness was assessed by seizure type at last visit. Effectiveness assessments included seizure freedom rate (no seizures since at least the prior visit) and 50% responder rate (≥50% reduction in seizure frequency) for focal and/or generalised seizures and responder rate (seizures under control) for status epilepticus. Tolerability was assessed by evaluating adverse events (AEs).

Result: Overall, 2922 adults were included (50.8% female; mean age 39.5 years; mean number of previous antiepileptic drugs [AEDs], 5.9). Patients had focal seizures (74.7%), generalised seizures (12.2%), both focal and generalised seizures (12.2%) and status epilepticus (0.9%). At treatment initiation the majority of patients were on 2 or 3 concomitant AEDs (1.3% initiated PER as monotherapy). The mean (standard deviation) PER dosage was 2.3 (1.1) mg/day at baseline and 6.6 (2.6) mg/day at last visit. Retention rates at 3, 6, and 12 months were 91.2%, 79.4% and 62.3%, respectively. Mean retention time on PER treatment was 10.3 months. At the last visit, seizure freedom and responder rates in patients with focal seizures only were 12.3% and 43.4%, respectively; corresponding values in patients with generalised seizures only were 47.4% and 76.0%, respectively. Among patients with status epilepticus, 40.7% responded to treatment. AEs were reported for 55.4% of patients; most common AEs were dizziness/vertigo (17.6%), behavioural AEs (15.7%), and somnolence (12.3%). Overall, 13.9% of patients discontinued due to AEs.

Conclusions: PER was effective and generally well tolerated in adult patients with focal and generalised seizures.

Supported by Eisai

Abstract Number: 290

Title: Perampanel for the Treatment of Focal and Generalised Seizures in Patients with Epilepsy with Tumour Aetiology: Evidence from Clinical Practice

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Purpose: To assess the real-world effectiveness and safety/tolerability of perampanel (PER) when used in patients with epilepsy with tumour aetiology in everyday clinical practice.

Method: Patients with epilepsy with tumour aetiology were identified from an interim pooled analysis of 18 clinical practice studies/work groups in which patients with focal and generalised seizures were treated with PER. Retention was assessed after 3, 6 and 12 months of PER treatment. Effectiveness was assessed by seizure type at the last visit. Effectiveness assessments included 50% responder rate (≥50% seizure frequency reduction) and seizure freedom rate (no seizures since at least the prior visit) for focal and/or generalised seizures, and responder rate (seizures under control) for status epilepticus. Safety/tolerability was assessed by evaluating adverse events (AEs).

Result: Overall, 51 patients with focal and/or generalised seizures with tumour aetiology were identified (mean age, 49.7 years; mean number of previous antiepileptic drugs, 2.5). Seizure types at baseline were focal only (82.4%), generalised only (5.9%), focal and generalised (11.8%), and status epilepticus (11.8%). All patients received PER as adjunctive therapy. Mean (standard deviation) PER dosage was 3.0 (1.9) mg/day at baseline and 6.3 (2.2) mg/day at the last visit. At 3, 6 and 12 months, retention rates were 99.7%, 90.5% and 79.5%, respectively. Mean (95% confidence interval) time under PER treatment was 10.7 (9.9–11.6) months. At the last visit, seizure freedom rates in patients with focal and generalised seizures were 37.5% and 33.3%, respectively, and corresponding values for 50% responder rate were 85.0% and 100%, respectively. Among patients with status epilepticus, 33.3% were responders. AEs were reported for 38.5% of patients (most frequent: dizziness/vertigo [12.8%] and somnolence [12.8%]); 6.8% of patients discontinued due to AEs.

Conclusions: PER was effective and generally well tolerated in patients with epilepsy with tumour aetiology in clinical practice.

Supported by Eisai

Abstract Number: 292

Title: Real-World Experience of Treating Patients Aged <12 years with Perampanel

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Purpose: To assess the real-world effectiveness, safety and tolerability of PER when used in everyday clinical practice in epilepsy patients aged <12 years.

Method: Patients aged <12 years with focal or generalised epilepsy who were treated with PER were identified from a pooled analysis of 44 prospective, retrospective and cross-sectional clinical practice studies and work groups. Retention was assessed after 3, 6 and 12 months of PER treatment. Effectiveness assessments comprised responder rate (≥50% seizure frequency reduction), seizure freedom rate (no seizures since at least the prior visit), and the proportions of patients with unchanged or worsening seizure frequency. Safety and tolerability were assessed by evaluating adverse events (AEs).

Result: A total of 64 patients aged <12 years were identified. Retention was assessed for 48 patients, effectiveness for 50 patients, and safety/tolerability for 55 patients. Mean (standard deviation) PER dose was 2.0 (0.5) mg/day at baseline and 4.6 (2.7) mg/day at the last visit. Retention rates at 3, 6 and 12 months were 89.6%, 77.8% and 58.8%, respectively. The most common reasons for discontinuation included lack of efficacy (17.6%), AEs (5.9%), both lack of efficacy and AEs (2.9%), and seizure worsening (5.9%). Mean (95% confidence interval) time under PER treatment was 9.4 (8.2–10.6) months. At the last visit, responder and seizure freedom rates were 54.0% and 24.0%, respectively. At the last visit, the proportions of patients with unchanged and worsening seizure frequency were 26.0% and 6.0%, respectively. AEs were reported for 34.5% of patients and psychiatric AEs were reported for 21.8% of patients.

Conclusions: In this pooled analysis of clinical practice studies, PER was effective and generally well tolerated when used in patients aged <12 years with focal and generalised seizures.

Study supported by Eisai

Abstract Number: 293

Title: Perampanel as Early Add-on Therapy for Epilepsy Patients with Focal and Generalised Seizures Treated in Clinical Practice

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Purpose: To assess the real-world effectiveness, safety and tolerability of perampanel (PER) when used as early add-on therapy in everyday clinical practice.

Method: Patients treated with PER as early add-on therapy for focal and/or generalised seizures were identified from an interim pooled analysis of data from 18 clinical practice studies/work groups. Retention was assessed after 3, 6 and 12 months of PER treatment. Effectiveness was assessed by seizure type at the last visit. Effectiveness assessments comprised seizure freedom rate (no seizures since at least the prior visit), responder rate (≥50% seizure frequency reduction). Safety and tolerability were assessed by evaluating adverse events (AEs).

Result: Data from 430 patients treated with PER as early add-on therapy for focal and/or generalised seizures were included (52.1% male; mean age, 41.9 years). Seizure types at baseline were focal only (85.0%), generalised only (14.3%), and focal and generalized (0.7%). Patients had been treated with a median of 1 previous antiepileptic drug (AED) and were receiving a median of 1 concomitant AED at baseline and at the last visit. Mean (standard deviation) PER dosage was 3.3 (1.7) mg/day at baseline and 5.7 (2.2) mg/day at the last visit. At 3, 6 and 12 months, retention rates were 94.4%, 86.1%, and 79.3%, respectively. Mean time under PER treatment was 12.0 months. At the last visit, seizure freedom rates in patients with focal and generalised seizures were 34.8% and 56.1%, respectively, and the corresponding responder rates were 80.2% and 80.7%, respectively. AEs were reported for 40.9% of patients; most frequent AEs were: behavioural AEs (aggression/anger/irritability; 15.1%), somnolence (12.9%) and dizziness/vertigo (10.6%). Overall, 13.4% of patients discontinued due to AEs.

Conclusions: PER was effective and generally well tolerated when used as early add-on therapy in patients with focal and/or generalised seizures in clinical practice.

Study supported by Eisai

Abstract Number: 295

Title: Perampanel Monotherapy in Epilepsy Patients with Focal and Generalised Seizures: Real-World Experience

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Purpose: To assess the real-world effectiveness, safety and tolerability of perampanel (PER) when used as monotherapy in everyday clinical practice.

Method: Patients treated with PER monotherapy for focal and/or generalised seizures were identified from an interim pooled analysis of data from 18 clinical practice studies/work groups. Retention was assessed after 3, 6 and 12 months of PER treatment. Effectiveness was assessed by seizure type at last visit. Effectiveness assessments included seizure freedom rate (no seizures since at least prior visit) and responder rate (≥50% seizure frequency reduction). Safety and tolerability were assessed by evaluating adverse events (AEs).

Result: A total of 111 patients treated with PER monotherapy at baseline (first line or conversion to monotherapy) were identified (51.4% male; mean age, 32.1 years; mean number of previous antiepileptic drugs 4.0). Seizure types at baseline were focal only (54.7%), generalised only (42.2%), and both focal and generalised (3.1%). Mean (standard deviation) PER dosage was 2.0 (0.0) mg/day at baseline and 6.5 (2.5) mg/day at last visit. At last visit, 54.2% of patients were being treated with concomitant antiepileptic drugs. Effectiveness was assessed for 35 patients and safety/tolerability for 38 patients. At 3, 6 and 12 months, retention rates were 94.4%, 88.9% and 55.6%, respectively. Mean (95% confidence interval) time under PER treatment was 9.5 (7.8–11.2) months. At last visit, seizure freedom rates in patients with focal and generalised seizures were 20.0% and 47.6%, respectively; corresponding 50% responder rates were 50.0% and 100.0%, respectively. AEs were reported for 60.5% of patients; most common AEs were behavioural AEs (aggression/anger/irritability; 26.3%) and dizziness/vertigo (21.1%). Overall, 11.1% of patients discontinued due to AEs.

Conclusions: PER monotherapy was effective and generally well tolerated in patients with focal and/or generalised seizures treated in everyday clinical practice.

Study supported by Eisai

Abstract Number: 312

Title: Dosage of DOACs concomitantly intaken with AEDs in real life: a retrospective study

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Purpose: The medical treatment of epilepsy involves prescription of anticonvulsant drugs (AEDs). The primary goal is to ensure the best possible quality of life that is compatible with the nature of the patient's seizure disorder and with any associated mental or physical disabilities. Direct oral anticoagulants (DOACs) used in prevention of arterial embolism in atrial fibrillation (AF) and treatment of venous thromboembolism (VTE) are now plenty prescribed improving the quality of life of patients since the management is more simple. There are few data in real life about the interactions between old and new AEDs and DOACs, but there are some warnings to use them together. We investigated patients that concomitantly intake AEDs and DOACs.

Method: we collected consecutively patients in concurrent tratment with AEDs and DOACs.

Result: We report 14 patients taking DOACs and AEDs: 5 patients in apixaban, 4 rivaroxaban, 3 dabigatran and 2 edoxaban. Five patients were receiving levetiracetam, 5 valproic acid, 3 phenobarbital and 1 phenytoine. Plasma levels of DOACs were in range, as also concomitant AEDs dosage. During a follow-up period of at least 6 months, no adverse events were reported.

C**onclusions:** We recommend physicians before to think to change AEDs to assess dosage of DOACs (peak and trough) and be careful to posology and compliance of patients.

Abstract Number: 313

Title: Global pooled analysis of perampanel in epilepsy patients treated in routine clinical practice: the PERMIT study

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Purpose: To assess effectiveness, safety and tolerability of perampanel (PER) when used in everyday clinical practice to treat patients with focal and generalised epilepsy.

Method: The PERMIT study is a pooled analysis of real-world data from 44 studies/work groups in which patients with focal and generalised epilepsy were treated with PER. Retention was assessed after 3, 6 and 12 months. In patients with focal and/or generalised seizures, effectiveness assessments included 50% responder rate (≥50% seizure frequency reduction) and seizure freedom rate (no seizures since at least the prior visit); in

those with status epilepticus, effectiveness was assessed as responder rate (seizures under control). Safety and tolerability were assessed by evaluating adverse events (AEs).

Result: Full Analysis Set included 5193 patients (50.5% female; mean age, 39.7 years; mean number of previous antiepileptic drugs, 4.9). Baseline seizure types were focal only (81.4%), generalised only (12.6%), focal and generalised (4.5%) and status epilepticus (1.5%). Most patients were treated with PER as adjunctive therapy; 5.5% were treated as monotherapy at baseline. Mean (standard deviation) PER dosage was 2.4 (1.1) mg/day at baseline and 6.3 (2.6) mg/day at last visit. Effectiveness was assessed for 4392 patients and safety/tolerability for 4617 patients. At 3, 6 and 12 months, retention rates were 90.5%, 79.8%, and 64.2%, respectively. Mean time under PER treatment was 10.7 months. At last visit, responder and seizure freedom rates in patients with focal and/or generalised seizures were 50.0% and 20.5%, respectively, and 52.7% of patients with status epilepticus were responders. AEs were reported for 49.9% of patients; most frequent AEs were: dizziness/vertigo (15.2%) and somnolence (10.6%). Overall, 17.6% of patients discontinued due to AEs.

Conclusions: PER was effective and generally well tolerated when used to treat a large cohort of patients with focal and generalised epilepsy in everyday clinical practice.

Supported by Eisai

Abstract Number: 324

Title: Comparative effectiveness of fenfluramine vs cannabidiol for the treatment of seizures in Dravet syndrome (DS): a network meta-analysis (NMA)

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Purpose: Fenfluramine is a recently licensed add-on therapy to standard of care antiepileptic drugs to treat the frequent, severe seizures of DS. Although an alternative to cannabidiol, there are no comparative trials of these therapies. We assessed the comparative effectiveness of licensed fenfluramine (with/without concomitant stiripentol) to cannabidiol (with/irrespective of concomitant clobazam, per respective European/US licenses), using robust indirect comparison methods.

Method: We systematically searched for randomised controlled trials (RCTs) of licensed add-on therapies for DS published to 28 June 2020. Outcomes of interest were relative, placebo-adjusted reductions from baseline in monthly convulsive seizure frequency (MCSF), and proportion of patients achieving ≥50% (clinically meaningful) and ≥75% reductions in MCSF. Comparative efficacy was assessed where possible using Bayesian NMA. Adverse events were considered descriptively.

Result: For both interventions we identified two placebo-controlled RCTs. When comparing fenfluramine 0.7mg/kg/day (without concomitant stiripentol) and fenfluramine 0.4mg/kg/day (with concomitant stiripentol) versus cannabidiol (maintenance dose: 10mg/kg/day, irrespective of clobazam use) the mean differences in placebo-adjusted reduction from baseline in MCSF were 46.8% (95%CrI: 19.7, 64.7), and 35.1% (1.0, 57.5), respectively. Comparing fenfluramine 0.7 and 0.4mg/kg/day to the European licensed regimen of cannabidiol 10mg/kg/day plus clobazam, the mean differences were 37.2% (2.0, 59.7) and 23.5% (-20.2, 51.3), respectively. For these outcomes, and for the proportion of patients achieving ≥50% and ≥75% reductions in MCSF, Bayesian treatment ranking indicated ≥98% probability that fenfluramine is the most effective therapy versus <2% probability for cannabidiol 10 or 20mg/kg/day (maximum recommended dose), with/irrespective of concomitant clobazam. Fenfluramine had lower rates of somnolence and no increase in weight loss, valvular heart disease or pulmonary hypertension versus cannabidiol.

Conclusions: NMA using RCT data indicates fenfluramine provides more effective convulsive seizure control than cannabidiol across all licensed dose regimens. Fenfluramine is comparatively well-tolerated and provides a much-needed step change in DS seizure management.

Abstract Number: 348

Title: Cenobamate as Adjunctive Therapy in Adults With Uncontrolled Focal Seizures: Time to Onset of Efficacy During Titration

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Purpose: Cenobamate is a new antiseizure medication (ASM) approved in the US for uncontrolled focal seizures in adults. Two international, double-blind, placebo-controlled trials (C013/C017) demonstrated cenobamate efficacy and safety. Here we report time to onset of efficacy during titration of cenobamate in these studies.

Method: Adults with uncontrolled focal seizures and taking 1-3 concomitant ASMs were enrolled in Studies C013/C017. Concomitant ASM changes were not allowed during the double-blind period. Time to onset of cenobamate efficacy was evaluated during the 6-week cenobamate titration (C013: 50mg/day initial dose, increased 50mg/week every 2 weeks to the 200mg/day target dose. Amended C017: 50mg/day initial dose, increased 50mg/week until target dose of 100 or 200mg/day; patients randomly assigned to 400mg/day were up-titrated by 100mg/day per week after the 200mg/day dose). Post-hoc analysis of efficacy examined the percent reduction in seizure frequency from baseline to each week during titration using a Wilcoxon rank-sum test (C013) or an ANCOVA model fit to ranked values of baseline seizure rate and treatment group (C017).

Result: Patients receiving cenobamate had significant reductions in median percent seizure frequency versus placebo starting from the first 1-2 weeks of cenobamate titration at the initial dose of 50mg/day (C013: -26.7% cenobamate vs -15.1% placebo, $P<0.05$; C017: -36.4% cenobamate vs -20.0% placebo, $P<0.05$). Sustained significant decreases in seizure frequency versus placebo were seen throughout the 6-week titration in both studies, reaching -39.5% versus -12.8% at week 6 in C013. Median reduction in seizure frequency was progressively higher with cenobamate doses of 100 (-39.0%), 200 (-52.2%), and 400mg/day (-55.5%) versus -12.5% at week 6 in C017.

Conclusions: Onset of cenobamate efficacy in significantly reducing seizure frequency occurs early and at lower doses than the target dose for maintenance therapy; efficacy improves at higher doses.
Studies sponsored by SK Life Science; analyses supported by Arvelle Therapeutics.

Abstract Number: 358

Title: Safety of Adjunctive Cenobamate in Adults With Uncontrolled Focal Seizures: Time to Onset, Duration, and Severity of AEs

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Purpose: Cenobamate is a new antiseizure medication (ASM) approved in the US for uncontrolled focal seizures in adults. Two international, double-blind, placebo-controlled trials with open-label extensions (OLEs; C013/C017) and a large international open-label safety study (C021) demonstrated efficacy and safety. Here we characterize the most common adverse events (AEs) in these studies**.**

Method: Adults with uncontrolled focal seizures taking 1-3 concomitant ASMs were enrolled (C013/C017/C021). Concomitant ASM changes: not allowed during double-blind; allowed during OLEs (C013/C017) and C021 (patients taking phenobarbital/phenytoin only after titration). C021 titration started lower (12.5mg/day) and up-titrated slower (to 200mg/day over 12 weeks) than C013/C017 double-blind 6-week titration (C013: 50mg/day initial dose, increased 50mg/week every 2 weeks to 200mg/day target dose; Amended C017: 50mg/day initial dose, increased 50mg/week until target dose of 100 or 200mg/day; patients randomly assigned to 400mg/day up-titrated by 100mg/day per week after the 200mg/day dose) or OLEs (C013 4-week/C017 2-week titration). Time of first onset (pooled C013/C017 double-blind and OLEs; C021), AE duration (pooled C013/C017 double-blind), and severity (pooled C013/C017 double-blind; C021 first 18 weeks) of somnolence, dizziness, and fatigue were examined**.**

Result: First onset of the most common AEs emerged throughout the double-blind and OLE, mostly during titration. In C021 the peak occurred when dosing reached ≥50mg/day. Median duration in days (double-blind, all occurrences) was: somnolence 32 cenobamate versus 22 placebo, dizziness 11 cenobamate versus 8 placebo, and fatigue 34 cenobamate versus 20.5 placebo. AEs in the double-blind were primarily mild or moderate, with few severe AEs. In C021, more patients reported mild AEs and fewer reported moderate and severe AEs.

Conclusions: Onset of the most common AEs occurred primarily during titration; AEs were generally self-limited in duration and mainly mild or moderate. Slower titration reduced the severity of AEs.
Studies sponsored by SK Life Science; analyses supported by Arvelle Therapeutics.

Abstract Number: 441

Title: Anti-seizure efficacy of carbamazepine in randomized controlled trials: a meta-analysis

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Purpose: Carbamazepine (CBZ) has been successfully used to prevent seizures since the 1970s, and has become the gold standard in randomized clinical trials (RCT) for anti-seizure drugs (ASM). Our aim was to evaluate the anti-seizure efficacy of CBZ across clinical trials and its variability.

Method: We conducted a literature search according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement via PubMed, Cochrane library and EMBASE. We included randomized, blinded or unblinded, monotherapy clinical trials that compared the efficacy of CBZ (as retention rate (RR) or seizure freedom rate (SFR)) to placebo or other ASMs in patients >12 years old with epilepsy. Meta-regression was performed to estimate the proportion of the RR and SFR with CBZ. Pooled proportion estimates were calculated using fixed and random-effects models adjusted for the follow-up times (FU) of the individual studies. We tested the significance of heterogeneity between studies using the Q test and I2 statistic.

Result: Our combined search results comprised 571 studies. After screening, 27 studies were included in the final analysis. FU ranged from 3-24 months. The efficacy of CBZ expressed as SFR varied from 21% to 85%, and from 37% to 75% when expressed as RR. There was significant heterogeneity between studies (I2=89,9% among the 8 studies that expressed efficacy as RR, I2=92,2% among the 26 studies that used SFR). The pooled estimated SFR was 56% at six months and 50% at 12 months. The time-adjusted average RR was 52%.

Conclusions: Published RCTs evaluating the anti-seizure efficacy of CBZ are very heterogeneous and consequently yield highly variable results. Nevertheless, our results show that CBZ is effective, with pooled RR and SFR >50%. A systematic effort to unify study design and outcome reporting is needed to homogenize ASM efficacy results, enabling better comparisons between ASMs and clinical decision-making.

Abstract Number: 469

Title: N-of-1 trial Recommendations for Precision Treatments in Monogenic Epilepsies

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Purpose: Up to a quarter of severe childhood epilepsies result from single-gene mutations. This discovery has laid the groundwork for precision medicine targeting the underlying genetic etiology in these epilepsies. While several centers offer precision treatments to individual patients, a common therapeutic or monitoring approach is lacking and clinical trials are hampered by interpatient heterogeneity and low disease prevalence. N-of-1 trials may leverage this problem by considering individual patients as the sole unit of observation in establishing the efficacy or side-effect profiles of different interventions.

Methods: A retrospective study including patients with monogenic epilepsies who have been treated with precision therapies will be performed in collaboration with the European Reference Network for rare and complex epilepsies, EpiCARE. This registry will help define patient populations that could benefit from precision treatments and assist in the design of future efficacy studies. Monogenic epilepsies selected for this registry will include syndromes associated with mutations of the following genes: GABRB3, KCNT1, NPRL2/NPRL3/DEPDC5, amongst others. The outcome of precision treatments in relation to clinical and laboratory variables will be assessed. Based on the results of this survey, an n-of-1 methodological framework tailored to different monogenic epilepsy phenotypes and treatment characteristics will be developed.

Results: This abstract concerns the study setup. The expected result of this project will be a methodological framework for the use of tailored n-of-1 trial approaches. This will include a set of eligibility criteria, treatment regimens, as well as, pre-defined baseline and outcome measurements. Implementation of this framework will harmonize data collection for monogenic epilepsies and allow pooling of safety and efficacy data of precision treatments.
Conclusions: The results of this project will provide a basis for the choice of appropriate trial designs for precision therapies in monogenic epilepsies in order to provide high-quality evidence for treatment recommendations.

Abstract Number: 497

Title: Drugs for Dravet syndrome: a novel computational method for predicting effective and aggravating drugs

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Purpose: To facilitate the identification of drugs that could be repurposed for the treatment of seizures in Dravet syndrome (DS), we have developed a genomics-based computational method for predicting the relative efficacy of drugs against seizures in this syndrome.

Method: Our prediction method is based on the following precept: drugs are more likely to be effective for seizures in DS if (1) they are better at correcting the protein abundance changes underlying DS, and (2) they affect the function of more proteins underlying epilepsies more like DS. Data for changes in abundance of genes occurring in DS were obtained from a published mouse model study. From published studies of gene mutations discovered in people with epileptic encephalopathies, we collated genes underlying epileptic encephalopathies, in particular the epileptic encephalopathies that clinically resemble DS. Existing ('connectivity mapping') and novel computational methods were used to predict the relative ability of drugs to affect the protein products of these genes. We validated our method and results *in silico*.

Result: Our top 20 predicted drug are 68-fold more enriched with the antiseizure drugs that are known to be clinically effective for DS than expected by chance. Also, our method correctly predicts the detrimental effect of the antiseizure drugs that are known to aggravate seizures in people with DS. Furthermore, antiseizure drugs that are poorly effective but not aggravating are predicted to be so. This accurate pattern of drug predictions is unlikely to occur by chance (p= 0). Our method predicts the effective compounds from a large-scale drug screen in the zebrafish model of DS.

Conclusions: We present a novel method that can potentially lead to significant savings in the time and cost of drug discovery for DS, and present promising predicted candidate drugs for DS. This method could potentially be adapted for other monogenic epilepsies.

Abstract Number: 543

Title: Effectiveness and tolerability of perampanel in children and adolescents (own experience of Svt. Luka's Institute of Child Neurology & Epilepsy)

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Purpose: Analysis of effectiveness and tolerability of perampanel in children and adolescents with epilepsy in Svt. Luka's Institute of Child Neurology & Epilepsy.

Method: We conduct an observational, open trial including 46 patients (4-18 years), divided into two groups: children (4-11 years, n=29) and adolescents (12-18 years, n = 17). Etiology of epilepsy: structural focal epilepsy – 24; genetic epilepsy – 19 (Lafora disease, PCDH19, PHACTR1, SCN1A, CDKL5, etc.) and idiopathic generalized

epilepsies 3 patients. Perampanel was used in polytherapy (44), in final monotherapy (2), in dose 4-12 mg at night. Effectiveness assessed as median reduction in seizure frequency >50%.

Result: In children (4-11 years, n=29) prolonged or temporary remission (effectiveness 75-100%) was achieved in 3 (10.5%), effectiveness 50-75% in 14 (48%), effectiveness < 50% or without effect - 10 (34.5%), aggravation of seizures - 2 (7%) of patients. In adolescents (12-18 years, n = 17): remission (effectiveness 75-100%) - 5 (29.4%), effectiveness 50-75% - 10 (58.8%), effectiveness < 50% or without effect – 1 (5.8%), aggravation - 1 (5.8%) of patients.
Effectiveness of perampanel: in children (4-11 years, n=29) (remission + effectiveness 50-75%) = 17 (58.6%); in adolescents 12-18 years, n = 17 (remission + effectiveness 50-75%) = 15 (88%); in general group (children and adolescents 4-18 years, n=46) (remission + effectiveness 50-75%) = 32 (69.5%); significant reduction of epileptiform activity index in 43% of cases.
Side effects were observed in 8 of 46 (17%) patients, including excitability, aggression, insomnia, drowsiness, psychosis, in 4 out them perampanel was canceled due to poor tolerance.
The retention rate for therapy with perampanel for more than 12 months was 56% (26/46)!

Conclusions: Perampanel was highly effective in 69.5% of children and adolescents with genetic and structural epilepsies, well tolerated and conveniently dosed. Perampanel should be used not only for resistant epilepsies, but much wider.

Abstract Number: 555

Title: Machine learning based prediction model for initial antiseizure medication selection in newly diagnosed epilepsy

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Purpose: Under current guidelines an antiseizure medication (ASM) is selected based on broad seizure type (focal vs. generalized onset). However, for each type of seizure, many ASMs have demonstrated similar efficacy when analysed on a group basis. For a given patient, it is not possible to predict which particular ASM will be most effective. The study aimed to develop a machine learning based prediction model to aid ASM selection.

Method: The model was trained and tested on a development cohort of adults with newly diagnosed epilepsy seen in Glasgow, Scotland, between 1982 and 2012. We included 16 routinely available clinical characteristics and investigation findings as model input features. The model was validated on an independent cohort of adult patients newly diagnosed with epilepsy seen at Perth, Australia, between 1999 and 2016. To simulate personalized drug selection, we hypothetically applied the model to each patient in the validation cohort and compared the median probability of seizure freedom with the actual proportion of patients who were seizure-free at 1-year follow up.

Results: The adapted model had an area under receiver operating characteristics curve (AUC) of 0.82 (sensitivity: 83%, specificity: 81%) in predicting treatment success (≥0.55 probability of seizure freedom for 1 year) with the first prescribed ASM in the development cohort (n=1504; median age 42 years, 55% male). The results were validated (AUC 0.78) in the validation cohort (n= 336; median age 41 years, 38.7% male). In the validation cohort, 35.7% (n=120) patients were seizure-free while taking the first prescribed ASM at 1-year of treatment whereas the median predicted probability of 1-year seizure freedom on taking the model-recommended ASM was 0.63 (IQR: 0.56-0.69).

Conclusion: Our proposed model can potentially guide the clinicians to adopt a personalized treatment strategy, and start treatment with the 'right drug' in patients with newly diagnosed epilepsy.

Abstract Number: 582

Title: Formulation Challenges and Technologies to Address Unmet Needs for Rescue Medications

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Purpose: For decades, the only US Food and Drug Administration (FDA)-approved option for out-of-hospital treatment of seizure clusters by nonmedical personnel was diazepam rectal gel. However, the intranasal route offers advantages over rectal administration, including more predictable absorption and convenient, socially acceptable access. To address formulation challenges regarding solubility, bioavailability, and tolerability, Neurelis developed a novel diazepam nasal spray formulation delivered as a therapeutic dose in an acceptable spray volume (≤100 µL) from an easy-to-use portable device.

Method: Intranasal formulations were investigated to optimize diazepam solubility, enhance absorption to achieve high and consistent bioavailability, and exhibit good tolerability**.**

Result: Numerous solvent systems and excipients have been explored to overcome intranasal formulation challenges. One excipient, n-dodecyl beta-D-maltoside [Intravail A3, Neurelis], has been shown to temporarily enhance mucosal permeation of a broad range of proteins, peptides, and small molecule drugs. It is "Generally Recognized as Safe" by the FDA for oral administration and is included in FDA-approved intranasal formulations, including one with sumatriptan [Tosymra®, Upsher-Smith Laboratories]. n-Dodecyl beta-D-maltoside, along with vitamin E to enhance diazepam solubility, are components of diazepam nasal spray [Valtoco®, Neurelis]. The absolute bioavailability of this formulation is 97% and, in healthy volunteers, the mean plasma concentration-time profiles are comparable to rectal and oral diazepam. In a long-term, phase 3 safety study in patients with seizure clusters, safety was consistent with the established profile of rectal diazepam. Diazepam nasal spray is approved for acute treatment of seizure clusters in patients with epilepsy aged ≥6 years.

Conclusions: Technologies for overcoming challenges of intranasal diazepam delivery have been investigated. The use of n-dodecyl beta-D-maltoside, which has a proven clinical safety profile, improves intranasal absorption. Diazepam nasal spray [Valtoco®, Neurelis] rescue therapy is designed to provide a more reliable and socially appropriate option for out-of-hospital treatment of seizure clusters.

Abstract Number: 667

Title: Efficacy and safety of everolimus in patients with tuberous sclerosis complex

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Purpose: Investigate efficacy and safety of the mTOR inhibitor everolimus in patients with Tuberous Sclerosis Complex (TSC) in real life.

Method: Sixty four patients with TSC (0.9-54 years, mean 20, range 0.9-54), treated with everolimus for following indications; epilepsy (n=28), renal angiomyolipomas (n=35), supependymal giant cell astrocytoma (n=5) and lymphangioleiomyomatosis (n=2) were included, (Norway (n=35), Denmark (n=29)). Out of 64 patients, 45 (70%) had epilepsy, with mean duration of treatment 35 months (range 3-106). Retrospective data were collected from medical records and cross-sectional data from patients/parents interviews.

Result: One third of epilepsy patients, 15/45 had ≥ 50 % reduction in seizure frequency last 3 months of treatment, compared with last 3 months before treatment (Denmark 11/19 (58%); Norway 4/26 (15%) (p=0.003)). Seizure reduction ≥50% was not associated with number of seizure types (<3, ≥3), focal to bilateral tonic clonic seizures and median weekly seizure frequency (<7, ≥7), number of antiseizure medications (<3, ≥3) or major change in antiseizure medications. There was a trend towards better efficacy in participants <18 years.
Among 64 patients, most common adverse events first treatment year were infectious episodes; (oral ulceration 28 (43%), upper respiratory tract infection 19 (30%), pyrexia 10 (16%), skin infection 6 (10%), nausea/vomiting 7 (11%), diarrhoea 6 (10%), dermatitis, acne, pneumonia and otitis, all 4 (6%). Laboratory abnormalities with most often clinical implications were hyperlipidaemia 7 (11%) and myelosuppression 6 (10%)). Other adverse effect were fatigue 9 (14%) and amenorrhea/irregular menses 4/21(19%).
Most adverse effects were mild to moderate, but life-threatening conditions were reported in two (cerebral oedema, acute disseminated encephalomyelitis); one reported diabetes, and one immunodeficiency disorder.

Conclusions: Everolimus treatment was associated with ≥50% reduction in seizure frequency among 33% of patients. Most adverse effects were mild /moderate, but life-threatening conditions were reported. This calls for close follow-up of this group.

Abstract Number: 689

Title: Cerliponase alfa for treatment of CLN2 disease in a patient cohort including children <3 years old: Interim results from an ongoing clinical study

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Purpose: CLN2 disease, a rare, inherited, neurodegenerative lysosomal storage disorder caused by TPP1 deficiency, is characterized by seizures, language and motor function loss, blindness, and early death. Open-label studies have demonstrated that biweekly intracerebroventricular (ICV) infusion of 300 mg cerliponase alfa (rhTPP1) for 96 weeks slowed deterioration in motor and language function. We report interim findings from a study to assess safety and efficacy of cerliponase alfa in an expanded cohort including children <3 years (NCT02678689).

Method: Cerliponase alfa was dosed based on age (subjects ≤2 years receive <300 mg). Safety was assessed by adverse event (AE) frequency. The primary efficacy endpoint was rate of decline in score on the motor and language (ML) domains of the CLN2 Clinical Rating Scale, comparing treated subjects with matched historical controls.

Result: As of April 2020, a total of 14 subjects were enrolled (8 female, 6 male); mean (SD) age was 3.0 (1.5) years; 8 subjects were aged <3 years at baseline. Subjects received cerliponase alfa for a mean (SD) of 127.0

(26.9) weeks (range: 64.4-142.6). Mean (SD) ML score was 4.6 (1.7) at baseline. Twelve subjects were matched to historical controls (up to 3:1) on the basis of age, baseline ML score, and genotype: mean (SD) rate of decline in ML score was 0.14 (0.262) points/48 weeks for treated subjects and 1.24 (1.022) points/48 weeks for controls (mean difference: 1.10; 95% CI: 0.69, 1.52). Common AEs included pyrexia, upper respiratory tract infection, gastroenteritis, extensor plantar response, and generalized tonic-clonic seizures. Twelve subjects (86%) experienced ≥1 serious AE, with pyrexia being most frequent. There were no deaths or study discontinuations due to AEs.

Conclusions: ICV-administered cerliponase alfa in children, including those <3 years, has an acceptable safety profile and an efficacy profile comparable to that observed in prior studies.

Funding: BioMarin Pharmaceutical Inc.

Abstract Number: 721

Title: Effect of valproate vs levetiracetam monotherapy on body composition, hormonal profile and physical activity in persons with epilepsy

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Purpose: : This study investigated the changes in body-composition and hormonal profile in person with epilepsy (PWE) after six months of valproate and levetiracetam monotherapy and correlated the same with physical activity score.

Method: PWE of either gender of age group (18-55 years) on montotherapy (<3 months) of valproate or levetiracetam were enrolled in this prospective observational study and followed up for 6 months. The following parameters were recorded at baseline and at follow-up: hormonal status [insulin, HOMA-IR, leptin, adiponectin, and lipid profile], body-composition by bioelectrical impedance analyzer, and physical activity by International Physical Activity Questionnaires (IPAQ). Correlation analysis was done between changes in body composition and hormonal status with physical activity score.

Result: Out of the 105 PWE enrolled, 74 completed follow-up [levetiracetam (n=50) and valproate (n=24)]. Valproate group had significantly lower fat-free mass ($p<0.05$) and higher body weight and muscle mass ($p<0.05$), higher insulin ($p<0.001$), HOMA-IR ($p<0.01$), leptin ($p<0.01$) and lower adiponectin level ($p<0.01$) after 6 months of VPA treatment. Levetiracetam group had no significant change after 6 months of treatment in different parameters except decreased IPAQ score ($p<0.05$). Valproate group had significantly higher total cholesterol ($p<0.05$), insulin level ($p<0.05$) and lower adiponectin level ($p<0.001$), as compared to levetiracetam group after 6 months of treatment. Comparison of % absolute changes revealed significantly higher BMI, fat mass, insulin, HOMA-IR and leptin level and lower adiponectin level and total water in valproate group as compared to levetiracetam after 6 months. IPAQ score did not show any significant correlation with different parameters after 6 months in both groups.

Conclusions: Treatment with valproate resulted in significant changes in body-composition and hormonal biomarkers which may lead to weight gain. Such changes were not evident with levetiracetam therapy. This may be considered for optimizing treatment in PWE with obesity and metabolic dysfunction.

Abstract Number: 726

Title: Use of zonisamide in patients with epilepsy and comorbid migraine

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Purpose: This study focused on the assessing the effectiveness of zonisamide in patients with epilepsy and comorbid migraine.

Method: 12 patients with epileptic seizures and comorbid migraine are women. The average age is from 15 to 21 years. Forms of epilepsy: 3 patients - juvenile myoclonic epilepsy, 6 patients – unknown epilepsy, 3 patients - focal epilepsy. The patients received the following anti-epileptic therapy in monotherapy, while the seizures persisted: carbamazepine - in 1 case, oxcarbazepine - in 1 case, levetiracetam - in 6 cases, lamotrigine - in 4 cases. All the patients had migraine attacks which occurred before the first epileptic seizure and continued while taking AEDs with a different frequency (from 2 to 4 episodes per month), regardless of the frequency of epileptic seizures. Patients were transferred to monotherapy with zonisamide at a dose of 150 to 300 mg/day.

Result: The frequency of epileptic seizures did not correlate with the frequency of migraine attacks. Two months after AEDs taking, 10 patients had a reduction of migraine episodes by 50%, 1 patient, did not have migraine attacks after reaching a dose of zonisamide more than 100 mg per day, in 1 case - no effect. Six months after initiation of zonisamide therapy – in 5 patients the frequency of migraine episodes decreased by 75%, in 7 patients, migraine attacks did not recur.

Conclusions: Migraine is the most represented type of headache in people with epilepsy. Migraine and epilepsy are comorbid disorders that have common pathophysiologic mechanisms. Zonisamide may be effective in patients with epilepsy and comorbid migraine. Greater understanding of the shared mechanisms of epilepsy and migraine can provide a basis for the development of improved treatment approaches that may be applicable to both conditions.

Abstract Number: 727

Title: Evaluation of Effect of Perampanel on Serum Lipid Profile among Young Adults with Epilepsy in duotherapy

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Purpose: To determine if perampanel affected the patients´ cholesterol levels and other key markers in duotherapy with carbamazepine and levetiracetam.

Method: We observed 28 adolescents with focal epilepsy of which 15 patients were receiving levetiracetam in monotherapy, 13 patients were receiving carbamazepine in monotherapy. All patients received perampanel at 8 mg average daily dose as add-on therapy. We have determined serum TC, HDL-C, LDL-C,TG levels before the addition of perampanel and after 6 months of treatment.

Result: The average serum TC, HDL-C, LDL-C and TG levels were 182.5±7.77mg/dl, 71.2±3.14mg/dl, 81.25±7.43mg/dl and 133.7±4.50mg/dl, in the group of patients who received CBZ before addition of PER. After PER therapy serum lipid profile was 179.0±8.79 mg/dl, 68.20±3.40 mg/dl, 86.40±7.32 mg/dl and 129.70±4.51 mg/dl, respectively. The group of patients who received levetiracetam had lipid profiles that were 172.90±8.59 mg/dl, 62.87±3.19 mg/dl, 82.71 ±7.79 mg/dl, 126.67±5.01 mg/dl and after addition of perampanel, they were 170.86±8.36 mg/dl, 64.52±4.19 mg/dl, 81.88±7.65 mg/dl, 124.99±4.72 mg/dl respectively. The group of patients who received CBZ after addition of perampanel has a significant decrease of TC ($p<0.05$), LDL-C ($p<0.001$), 6 months after taking therapy. In the group of patients who received LEV+PER, there were no statistically significant differences between serum lipid profile before and after PER prescribing.

Conclusions: We observed statistically significant high mean TC, HDL-C, LDL-C and TG levels in the group receiving CBZ both before addition of PER, and 6 months after. In the group of patients who received LEV both before and after addition of PER, serum concentration of lipid profile levels did not differ from the norm. We have not found the impact of PER on serum lipid profile, which is extremely important when choosing long-term therapy for the patients with epilepsy and decreasing cardiovascular risk factors.

Abstract Number: 735

Title: Pharmacological Evaluation of Neuroinflammatory TGF-β/non-SMAD Signaling Pathway in the Pentylenetetrazole-induced Epileptogenic Model

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Purpose: Despite extensive research on epileptogenesis, current medications only provide symptomatic control of seizures. Thus, there is high demand in the investigation of new mechanisms and approaches for the development of treatments for 30% of epilepsy cases that prove drug resistant. Inflammation, neural loss, plasticity, mossy fibre sprouting and blood–brain barrier dysfunction are the most common causes of epileptogenesis. Increasing evidence supports that transforming growth factor (TGF-β)/non-SMAD pathway is of utmost importance in neuroinflammation- mediated epileptogenesis. Therefore, exploring TGF-β/ non-SMAD pathway could provide an interesting opportunity to discover and validate targets for novel therapeutics for controlling pharmacoresistant epilepsies.

Method: Male Balb/c mice were categorized into 5 groups i.e., normal-control, Pentylenetetrazole-control, drug control (diazepam and valproic acid) and test group i.e., Isoxylitone (E/Z-2-propanone-1,3,5,5-trimethyl-2-cyclohexen-1-ylidine) abbreviated as (ISOX). Kindling was induced by giving sub-convulsive dose of pentylenetetrazole (PTZ, 40 mg/kg) every alternate day until seizure score 5 develops in the PTZ-control group. Treatments were given to respective groups 30 min prior to PTZ dose. When animals acquired consistent score 5 for at least 3days, experiments were terminated and brain samples were isolated for gene expression studies in cortex and hippocampus samples.

Result: The experimental findings revealed that ISOX (30 mg/kg) not only significantly suppressed the PTZ-induced seizures but also halted the epileptogenesis by altering the non-SMAD associated TGF-β genes. ISOX pre-treatment significantly upregulated the RhoA, ROCK2 and AKT expressions and downregulated the ROCK1, MAPK14, and NFkB expressions as compared to PTZ-control group in hippocampus region, suggesting the disease modifying effect of ISOX and other treatments in epileptogenesis

Conclusions: Our findings suggest that non-SMAD/ TGF-β signaling pathway act as critical target in epilepsy, and also rationalizes the ISOX as a promising newer neuroprotective, anti-inflammatory, and disease-modifying agent in forestalling the epileptogenesis.

Abstract Number: 736

Title: Dysregulated Smad Signalling Cascade, A Compelling Therapeutic Target for Epileptogenesis

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Purpose: Improvement of pharmacotherapy against epilepsy mandates immediate attention towards enhancing knowledge regarding the mechanistic pathogenesis of epileptic seizures. Considering the role of neuro-inflammation and compromised blood brain barrier (BBB) in epileptogenesis and the implications of transforming growth factor-beta (TGF-β) signaling in endothelial-mesenchymal transition, we designed a study to assess the epileptogenic molecular alterations associated with Smad signaling, the downstream cascade for regulating TGF-β mediated cellular processes. Also, keeping in view the seizure-arresting potential of novel antiepileptic compound [*E/Z*] isoxylitones, we aimed to delineate the pharmacological implications of this compound in the regulation of Smad pathway

Method: Pentylenetetrazole (PTZ)-induced kindling model of epileptogenesis in mice was developed. Experimental groups were (a) normal control (b) PTZ control (c) diazepam+PTZ (d) valproate + PTZ, and (e) ([*E/Z*] isoxylitones) + PTZ. PTZ administration was done on the alternate days to PTZ control group and animals in the treatment groups. Experiment was terminated once the PTZ control group exhibited generalized recurrent seizures. Animals were humanely sacrificed, and the brain tissues were harvested for molecular studies

Result: Pretreatment with diazepam, valproate and ([*E/Z*] isoxylitones offered significant seizure protection as compared to PTZ control group. A significant upregulation of key regulators of Smad pathway including SARA, Smad2, Smad3, and Smad4 was observed in both the cortical and hippocampal regions of the epileptic control group. Interestingly, consistent with diazepam and valproate, [*E/Z*] isoxylitones hindered the hyperactivation of Smad pathway as reflected by the downregulation of the aforementioned markers

Conclusions: Bearing in mind the causal relationship between dysregulated Smad pathway and compromised BBB, it is speculated that [*E/Z*] isoxylitones has a promising neuroprotective competence against the detrimental inflammatory cellular changes underlying epilepsy and provides new avenues to hamper epileptogenesis by modulation of signaling cascades.

Abstract Number: 812

Title: Anticonvulsant effect of cannabidiol in males and females in the gash/sal audiogenic epilepsy model.

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Purpose: To determine the possible anticonvulsant effects of 200 mg/kg CBD in the GASH/Sal model in males and females, as well as possible side effects.

Method: 200mg/kg of CBD was administered to GASH/Sal hamsters (8 males and 8 females) acutely and chronically. The effects of drug treatment were evaluated for seizure severity and the Ethomatic software was used to assess the seizure characteristics of the GASH/Sal. We further analyzed the effects of each chronic drug administration (14-days post-treatment) on the body weight as well as on the hematological and biochemical profiles of each experimental group. Using HPLC, we measured the CBD level in the blood and the brain in all experimental groups.

Result: Animals treated with the vehicle were scored with the maximum values in the categorized seizure index (cIS=8) after both acute and chronic vehicle administrations. Acute administration of CBD on females eliminates seizures (cIS=0) in 12% and reduces their severity (cIS=2-5) in 50% of, having no effect on males. At the end of the chronic treatment with CBD, the absence of seizures (cIS=0) was observed in 40% of the females and a decrease in the severity index (cIS=2-5) in 40% of the cases. In males, a decrease in the severity index was observed in 50% (cIS=2-5) and 12% presented absence of seizures (cIS=0), with not changes in the rest of the animals. The GASH/Sal animals showed a steady weight after chronic administration of any of the treatments and no statistically significant differences were found when compared to the baseline pretreatment conditions

Conclusions: Acute and chronic CBD treatment exerts an anticonvulsant effect on GASH/Sal males and females. The effect is greater in chronic administration, being more evident in females. No adverse effects on body weight, hematological parameters and liver function were observed following repeated daily administration.

Abstract Number: 814

Title: In vitro effects of antiseizure drugs on lacosamide concentration at hepatic metabolism level

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Purpose: Therapeutic-drug-level-monitoring is an effective method used for prevention of drug-drug interactions (DDIs) between antiseizure drugs (ASDs) in which minimum drug concentration (Cmin) is the primary and maximum drug concentration (Cmax) is the candidate biomarker. Carbamazepine and phenobarbital have inducing whereas valproic acid has inhibiting effects on hepatic cytochrome P450 (CYP) metabolism enzymes. We aimed to investigate the *in vitro* effects of ASDs on CYP enzymes at mRNA level whether they could alter Cmin or Cmax of lacosamide (LCM).

Method: Human hepatocellular carcinoma (HepG2) cells were treated with carbamazepine, phenobarbital or valproic acid at therapeutic concentrations for 72 hours and LCM was added to wells at Cmin or Cmax levels for 24 hours subsequently. The mRNA expression levels of CYP2C19 or CYP2C9 genes were monitored in triplicate design by real-time PCR, changes in the expression levels were identified with fold change (FC) values and analysed with GraphPad Prism 8. Effects of these ASDs on cell viability of HepG2 cells were also detected by XTT assay.

Result: The highest mRNA expression of CYP2C19 and CYP2C9 genes were detected in the groups where phenobarbital and LCM at Cmax were administered together (FC:2.2 and FC:1.7, respectively) while the lowest expression for valproic acid and LCM at Cmax treated groups (FC:0.3 and FC:0.2, respectively). There was no statistically significant difference in mRNA expression levels for none of the treatment groups compared to their controls. Cell viability increased only in phenobarbital treated groups (112.2±9.35%) and maximum reduction was detected in valproic acid treated groups (68.46±18.19%), although not significant.

Conclusions: Our initial findings suggest that further studies with higher number of samples or different hepatic cell lines which LCM levels are also measured concomitantly are needed to effectively validate our results.
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Abstract Number: 849

Title: Changes in the use of antiseizure medications with focus on children and adolescents in Norway 2009-2018

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Purpose: Changes in the use of antiseizure medications (ASMs) in children/adolescents are poorly described. The purpose was to investigate changes in the use of ASMs over the past decade in Norway in children/adolescents as compared to adults/elderly.

Method: Data from the Norwegian Prescription Database, 2009-2018, was used. Variables included age, gender, drug-specific codes, diagnosis-specific reimbursement codes, number of users and population data. Selected ASMs used for specific indications or subgroups were studied in detail; valproate, ethosuximide, sulthiame, rufinamide, stiripentol and clobazam.

Result: The number of ASM users in children/adolescents (0-19 years) was unchanged, 4.8/1000 over the decade (2009-18), as compared to an increase from18.3 to 21.6/1000 in adults (20-59 years) and 25.1 to 35.2/1000 in elderly (60+ years). Lamotrigine, valproate and levetiracetam were the three most commonly used ASMs in epilepsy in children/adolescents. In adults/elderly carbamazepine was also commonly used. The use of valproate in epilepsy decreased by 15% in girls (15-19 years), which was an expected trend due to safety restrictions, whereas the use in boys (15-19) increased by 8%. The selected ASMs were mainly used in children/adolescents and accounted for 0.7/1000 in 2018 (15%); with significant increases from 2009 in sulthiame (8-fold), ethosuximide (4-fold), clobazam (3-fold), and unchanged use of rufinamide and stiripentol. Limited and stable use of ASMs in non-epilepsy indications (psychiatry, pain) was noted in children/adolescents, accounting for 12.5% of the total use in 2018, in contrast to extensive use, accounting for 65% of total use in both adults and elderly.

Conclusions: The pattern of use of ASMs in children/adolescents demonstrated several differences as compared to adults/elderly, e.g., limited use in non-epilepsy disorders, gender-related change seen with valproate and changes in selected ASMs in children/adolescents. Systematic surveillance especially of new and special ASMs in the pediatric population is important for improved pharmacovigilance and patient safety.

Abstract Number: 889

Title: Reductions in Oculogyric Crisis in Children With AADC Deficiency Treated With Eladocagene Exuparvovec Gene Therapy- Results From 3 Clinical Trials

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Purpose: Aromatic L-Amino Acid Decarboxylase (AADC) deficiency is a rare autosomal recessive disorder resulting in marked dopamine loss, impeding normal motor development. A common symptom of AADC deficiency is oculogyric crises (OGC), which is frequently linked to decreased dopamine levels and characteristic involuntary eye movement. OGCs can also be accompanied by limb stiffness, torso rigidity, and autonomic signs. Eladocagene exuparvovec, a recombinant adeno-associated viral vector containing the human cDNA encoding the AADC enzyme, was studied in 3 AADC clinical trials.

Method: Eladocagene exuparvovec was administered as a bilateral infusion in the putamen of 28 children with AADC deficiency in 3 clinical trials (AADC-CU/1601 [8 patients, completed], AADC-010 [10 patients, ongoing], and AADC-011 [10 patients to date; ongoing]). Patients received a total of 1.8×10^{11} vg (n=21) or 2.4×10^{11} vg (n=7; AADC-011)]. Duration (h/wk) and frequency (episodes/wk) of OGC episodes were calculated at baseline and 3 to 12 months after gene therapy.

Result: Burden of OGC episodes decreased steadily following treatment with eladocagene exuparvovec. At baseline, mean duration of OGC episodes was 12.58 h/wk (n=22). OGC was reduced from baseline by a mean of 2.08 h/wk at 3 months (n=20), 2.24 h/wk at 6 months (n=12), 3.2h/wk at 9 months (n=12), and 3.64 h/wk at 12 months (n=8). At baseline, mean frequency of OGC was 2.63 episodes/wk (n=22). By month 3, the mean frequency decreased to 1.93 episodes/wk (n=20), by month 6, it was 1.9 episodes/wk (n=12), and remained at ~2 episodes/wk from months 9 to 12.

Conclusions: These results indicate a pattern of steady and sustained decrease over time in OGC episodes after PTC-AADC gene therapy. Reduced OGC has the potential to improve quality of life for patients with AADC deficiency and their caregivers by decreasing clinical burden.

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Abstract Number: 945

Title: Anticonvulsant activity of the herbal complex preparation

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Purpose: Study the effect of herbal complex preparation on PTZ-induced seizures in mice.

Method: The complex preparation was prepared from the 70% ethanol extract of radix *Valeriana officinalis L and* leaves *of Leonurus sibiricus L*, ratio was 70:30. The study of the anticonvulsant effect of herbal complex prepatation in the treatment of PTZ- induced seizures performed on C57BL/6 mice. Research subjects were divided into 4 groups with 6 animals each; control group (saline 10 ml/kg), standard group (diazepam 2 mg/kg i.p) and two experimental groups (herbal preparation 750 mg/kg, 1000 mg/kg). To determine onset time, duration of myoclonic and tonic-clonic seizures and mortality rate, the PTZ was injected intraperitoneally at a dose of 70 mg/kg and observed for 30 minutes.

Result: Onset time of myoclonic seizure in the control group was 1.1 times shorter (80.83 ± 3.27 sec) compared to the experimental group 1 (95.33 ± 4.21sec), while in experimental group 2 (104.66 ± 4.38 sec) it was 1.3 times prolonged ($p < 0.05$). Compared to the control group (69.66±3.78 sec), the duration of myoclonic seizure was 1.5 times shorter in experimental group 1 (44.83 ± 4.64 sec) and 3.2 times short ($p<0.05$) in experimental group 2 (21.50 ± 3.19 sec). Comparing to the control group (88.83±3.65 sec), the time of onset of tonic-clonic seizure was 1.8 times prolonged in experimental group 1 (163.5±22.35 sec) and 11 times longer ($p < 0.05$) in experimental group 2 (977.5±367.84 sec).Duration of tonic-clonic seizure was 2.6 times short in experimental

group 1 (36.50±5.32 sec) and 8.5 times short (p <0.05) in experimental group 2 (11.33±5.99 sec) compared to the control group (94.66±5.8 sec).

Conclusions: Herbal complex preparation has anticonvulsant activity on PTZ-induced seizure. Especially when it comes to a tonic-clonic seizure.

Abstract Number: 957

Title: Long term experience with Brivaracetam in Mexico

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Purpose: Brivaracetam is an AEM that is used in several parts of the world. (1-4) The experience in Mexican population has not been reported.

Method: We included 40 patients with at least one year follow-up. Ages ranged from 16 to 63 years The Research and Ethics Committees of the General Hospital Mexico approved the study. Patients were divided into three groups. A: Patients who had brivaracetam as an add-on medication and at least one antiepileptic drug. B: on levetiracetam (LVT) treatment and switched to brivaracetam due to undesirable adverse events. C: naive for antiepileptic treatment.

Result: Best results were found in group B. Irritability and mood swings presented with LVT were the most common reason for exchange medication. These side effects allowed us to administer only low doses of LVT, and we could not increase them to achieve good seizure control. The switch was performed without titration. In group A patients, seizure reduction was observed. Also, other medications could be reduced or discontinued, but none of the patients remained seizure-free on brivaracetam only. The most common and useful combination was with lacosamide. The poorest response occurred more often in group C. This usually happened in patients who initiated brivaracetam in higher doses than 25 mg twice a day. Four patients discontinued use and were reluctant to try titration again. Two of them did not come back for further consultation. The primary adverse effect was a long-lasting drowsy-lethargic state, which impeded patients' daily activities.

Conclusions: Brivaracetam is a good option for patients with irritability and impulsiveness can be particularly benefited. In Mexican population, there is a sensitivity to having sleepiness. Try an initial very low dose (12.5 mg at night) and explain the risk of transitory adverse effects.

Abstract Number: 968

Title: Metformin protects rats against Status Epilepticus associated Cognitive dysfunction by ameliorating neuroinflammation and neuronal death

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Purpose: A plethora of clinical and preclinical evidence highlight the development of cognitive impairment in temporal lobe epilepsy as well as status epilepticus (SE) subjects mostly attributed to the seizure-induced

neuroinflammation, oxidative stress, neuronal death, and aberrant hippocampal neurogenesis. Recently, metformin has shown promising anti-epileptic effects in several animal models of epilepsy. However the effect of chronic metformin treatment over status epilepticus-induced chronic inflammation, neurodegeneration, and memory deficits remain unkown.

Method: 2 month old Male Wistar rats were subjected to SE by systemic administration of lithium (127 mg/kg)-pilocarpine (30 mg/kg). Vehicle/Metformin (200 mg/kg, p.o.) was administered orally for 30 days starting from 60 minutes post SE. Morris water maze was performed to study the spatial learning and memory. Thereafter, rats were euthanized for analyses of neuronal damage (Nissl staining and Fluorojade B, FJB), inflammatory cytokines mRNA levels, and astroglial (GFAP) and microglial (CD-11b) activation status.

Result: Metformin-treated rats performed significantly better than vehicle treated SE rats in the Morris water maze task. SE induced an array of inflammatory events comprised of significant astroglial and microglial activation and elevated IL-1β, IL-6, NFκβ, and COX-2 mRNA levels which were reduced in metformin treated group. Besides, metformin reduced the GFAP immuostaining in the CA1 region, and CD11b staining in CA1, CA3 and thalamic regions. Further metformin treatment also reduced FJB+ cells in CA3 and hilar areas, and restored the hippocampal neuronal density in SE-induced rats.

Conclusions: These results suggest that metformin exerted a protective effect on SE-induced cognitive impairment possibly by ameliorating the neuroinflammation and neurodegeneration.

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Abstract Number: 979

Title: antiepileptic drugs in seizures-free temporal epilepsy at indonesia national referral hospital period of january 2019 - january 2021

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Purpose: To know the efficacy of antiepileptic drugs (AED) in temporal lobe epilepsy (TLE) at Dr Cipto Mangunkusumo Hospital in period of January 2019 – January 2021.

Method: A cross-sectional descriptive study was conducted from January 2019 to January 2021 at Dr Cipto Mangunkusumo General Hospital. Subjects were TLE patients, diagnosed based on semiology and EEG findings, who had taken AED for at least two years. Subjects were classified as seizures-free if had experienced no seizure for at least twelve months consecutively, regardless of monotherapy or polytherapy.

Result: We enrolled 102 subjects in the study, of whom 53.9% were not seizure-free, and 46.1% were seizure-free. Moreover, distribution of seizure-free patients was seen higher in the monotherapy than in two, or three AED group, 65.9%, 31.8%, and 28.6%, respectively (p=0.001). The most common AED used as monotherapy drugs were carbamazepine (43.2%), phenobarbital (18.2%), valproic acid (15.9%), phenytoin (9.1%), topiramate (6.8%), lamotrigine (2.3%), and clobazam (2.3%). The most common combined AED was the combination of valproic acid and phenytoin (11.4%).
Conclusions: There was 46.1% people with TLE were seizure-free with AED for more than 12 months and most of them using monotherapy. Addition of one or more AEDs after single use, only mildly increased the chance of seizure free.

Abstract Number: 1008

Title: Medical treatment of focal epileptic spasms

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Purpose: Focal epileptic spasm (F-ES) is very pharmaco-resistant. Ictal superficial EMG of spasm shows diamond-shaped with high-voltage positive slow waves on EEG, which seems to be a mixture of EMG of tonic seizure and that of myoclonic seizure. This analogy suggests that F-ES might respond to combination of anti-seizure medicines (ASMs) for focal tonic seizures (FT-Sz) and those for focal myoclonic seizures (FM-Sz).

Method: Twenty-five patients with refractory F-ES, aged 7 months to 37 years, were enrolled. F-ES were confirmed by ictal video-EEG with EMG in 16 cases, and judged from ictal symptoms in 9 cases, which looked like tonic or myoclonic seizures with focal epileptiform discharges on interictal EEG but did not respond to full dose of ASMs for tonic or myoclonic seizures. They consisted of frontal lobe epilepsy, epilepsies after West syndrome with focal clinical and/or EEG features, epileptic spasms with focal features, and epilepsy with myoclonic atonic seizures in 8, 8, 7 and 2 cases, respectively. ASMs for FT-Sz and those for FM-Sz were added or increased. The subjects were prospectively followed-up for 1 to 6 years.

Result: At the last evaluation, F-ES had ceased for 0.6 to 5.7 years in 17, and reduced by >75% in 5, by >50% in 2, and <50% in 1 case. Among effective 24 cases, added or increased ASMs for FT-Sz included LTG in 5 cases, ZNS in 2, LTG+(ZNS in 5, PER in 2), ZNS+(PB in 2, PER in 1), LTG+ZNS+(PB in 4, PER in 1), and LTG+PER +(Br in 1, PB in 1), and added or increased ASMs for FM-Sz were CLB, CZP and CLB+CZP in 12,10 and 2 cases, respectively. One ineffective case could not increase LTG, PER and CZP because of agitation and somnolence.

Conclusions: Combination of ASMs for FT-Sz and FM-Sz is effective for refractory F-ES.

Abstract Number: 1092

Title: Efficacy and safety of Cenobamate in adult patients with uncontrolled focal seizures: a real-world study

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Purpose: Cenobamate is a new anti-seizure medication that has been recently approved by the US FDA as add-on therapy for the treatment of focal onset seizures in adults. Here, we evaluate efficacy and safety of add-on Cenobamate in a series of adult patients with drug-resistant epilepsy consecutively enrolled within an Early Access Program (EAP) in two Italian epilepsy centers, in a real-world clinical practice context.

Method: In this prospective, independent, open-label study, Cenobamate was administered as add-on, one daily at an initial dose of 12.5 mg/kg/d titrated up to 400 mg/kg/d or until tolerated dose. Seizures were recorded in a diary. We evaluated focal countable seizures. Adverse events were investigated every month. Concomitant medications were also evaluated.

Result: Forty-seven patients were enrolled, with a median age of 24.9 years (interquartile range [IQR] = 21.1-30.3). Forty-two (89.3%) patients completed the efficacy analysis. The median follow-up was 9.0 months (IQR = 4.2-9.5). We will present data about median reduction in convulsive seizures and responder rate (≥ 50% reduction of convulsive seizures), and most common adverse event. Laboratory, ECG, and neuropsychological evaluation (PM38, TMT A-B, QOLIE 31, PedsQL, ABAS II, Vineland II, CBCL, PHQ9 e GAD7) data will be also presented.

Conclusions: In this real-world study, Cenobamate provided a clinically meaningful reduction in convulsive seizure frequency in the majority of patients and was well tolerated.

Abstract Number: 1119

Title: Sleep disturbances increase the risk of drug resistance in patients with epilepsy

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Purpose: Sleep deprivation increases cortical excitability in epilepsy and induces seizures, while the effect of sleep disturbances on incractable epilepsy is still unclear. In this study, we investigated the role of sleep disturbances on the risk of drug resistance in patients with epilepsy.

Method: Patients diagnosed with newly diagnosed epilepsy at the epilepsy clinic in our clinic between August 2017 and February 2020 were evaluated for eligibility for this study. Pittsburgh Sleep Quality Index (PSQI) was used to assess the sleep quality. Patients with PSQI>5 were included in poor sleep quality group. Cumulative incidence curves for time to seizure freedom were compared for different cohorts by Gray test.

Result: Altogether, 237 patients with epilepsy were included in this study, and the median duration of follow-up was 26 months. The probability of seizure freedom was significantly higher in patients with good sleep quality (n = 123) compared to those with poor sleep quality (n=104, P=0.022). Competing risk regression analysis showed that poor sleep quality significantly
increased the probability of drug resistance (hazard ratio = 1.523, 95% confidence interval = 1.087-2.942, P = 0.031).

Conclusions: Sleep disturbances increase the risk of drug resistance in patients with epilepsy. Improving sleep quality may be an auxiliary means for epilepsy therapy.

Abstract Number: 1122

Title: Anti-epileptic drugs and Seizure Freedom - a real world study with Natural Language AI

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Purpose: Achieving seizure freedom is the primary goal of the treatment and management of epilepsy. Anti-epileptic drugs (AEDs) are the first line of treatment for new-onset epilepsy. However, there is little evidence for the optimal AED order or medication combinations since the possibilities are so numerous that doctors and their patients can't try every permutation.
We aimed to explore the feasibility of using a novel patient data analytics tool (CogStack ecosystem) to extract automatically extract AED prescribing patterns alongside diseases and symptoms at King's College Hospital NHS Foundation Trust (KCH).

Method: To identify our patient cohort, we utilised CogStack to search and retrieve all Neurology clinic letters which contained the word “epilepsy” between 2013-2020. We then used a novel AI-based natural language processing system called the Medical Concept Annotation Tool (MedCAT) to annotate the free-text of each of the epilepsy patients’ neurology clinic letters. MedCAT is a semi-supervised system that leverages the SNOMED CT terminology structure to annotate free-text. Epilepsy specialists were asked to produce training and benchmarking materials for MedCAT through annotating a minimum of 200 documents for all mentions of diseases, symptoms and medications. As well as to label the contextual information of each annotation (Meta-annotation). The trained model of MedCAT was then used to annotate all clinic letters and its performance was evaluated.

Result: CogStack retrieved 36855 documents of 9860 unique patients. From which MedCAT could accurately identify that 4042 patients had epilepsy, 26.6% seizure-free. Levetiracetam followed by Lamotrigine were the most popular AEDs. Polytherapy prescribing patterns were compared in the context of reaching seizure freedom.

Conclusions: Overall automated information extraction techniques of patient records, particularly unstructured data, can provide insights beyond direct patient care and into epilepsy subtypes, treatment strategies, and adverse events. Together this can improve the management of epilepsies through evidence-based decisions.

Abstract Number: 1164

Title: Long-term effectiveness of add-on stiripentol: an observational study in Dravet syndrome and non-Dravet developmental and epileptic encephalopathies

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Purpose: To assess long-term effectiveness and tolerability of stiripentol as adjunctive treatment in Dravet syndrome and non-Dravet refractory developmental and epileptic encephalopathies (RDEEs).

Method: Retrospective observational study of all children and adults with RDEE and prescribed adjunctive stiripentol at Hospital Ruber Internacional (Madrid) from January 2000 to June 2020. Outcomes were retention rate; responder rate (proportion of patients with ≥50% reduction in total seizure frequency relative to baseline); seizure freedom rate; responder rate for status epilepticus; rate of adverse events (AEs) and individual AEs. Outcomes are reported overall, and for Dravet and non-Dravet subgroups.

Result: Of 55 patients, 33 had Dravet syndrome and 22 had non-Dravet RDEE. Median age was 68 months years (interquartile range [IQR] 40.5–162 months), and mean age of epilepsy onset was younger in the Dravet group (5.0 months) than non-Dravet (12.5 months). Median duration of treatment with stiripentol was 28.0 months (IQR 5.5–62.0 months), was longer in the Dravet group (44.0 months) than non-Dravet (10.5 months). At 12 months, the responder rate was 48.9% overall (23/47), 50.0% in the Dravet group (14/28) and 47.4% in non-Dravet (9/19), and no patients were seizure-free for 12 months. There were no statistically significant differences between groups on these seizure outcomes**.** Freedom from status epilepticus was achieved in 60.0% (18/30) at final visit, and this was significantly higher in the Dravet group (20/21, 95.2%) than non-Dravet

(3/9, 33.3%). Adverse events were reported in 83.3% of patients (30/36), most commonly somnolence, anorexia, and irritability.

Conclusions: In this population of patients with epileptic and developmental encephalopathies, outcomes with adjunctive stiripentol were similar in patients with non-Dravet RDEE to patients with Dravet syndrome**.**

Abstract Number: 1204

Title: Comparison of the effects of new anti-seizure drugs (ASDs) on cardiac autonomic control in patients with temporal lobe epilepsy (TLE)

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Purpose: Temporal lobe epilepsy (TLE) is the most common form of focal epilepsy in adulthood. The temporal lobe plays a central role in the regulation of autonomic cardiovascular functions. Lesions in this area are associated with abnormalities in the regulation of heart rate, atrioventricular conduction and ventricular repolarization. Such alterations may play an important role on the risk of Sudden Unexpected Death in Epilepsy (SUDEP). The spectral analysis of the Heart Rate Variability (HRV) represents a useful tool for the evaluation of the impairment of cardio-autonomic control. The aim of this study is to assess, using the spectral analysis of HRV, new anti-seizure medication (ASMs) - Perampanel (PER), Lacosamide (LCS), Eslicarbazepine (ECB) and Brivaracetam (BRV) - effects on autonomic cardiac control in patients with TLE.

Method: Eighty adult patients with diagnosis of TLE were enrolled. According to the specific new add-on anti-seizure therapy, patients were divided into 4 subgroups: PER (20 patients), LCS (20 patients), BRV (20 patients) and ECB (20 patients). Each patient underwent a 20-minute EEG + EKG recording in resting state before and after the introduction of the new ASM. HRV evaluation was performed by a short-lasting analysis with a specific software (Kubios®). Time domain-related and frequency domain-related parameters, were compared between groups. Kruskal-Wallis test was employed to evaluate statistical differences.

Result: PER showed a significant reduction in low frequency (LF) and an increase in high frequency (HF) with a reduction in the low frequency/high frequency ratio (LF/HF). BRV and LCS showed an increased LF and a reduction in HF with a slight increase in the LF/HF ratio. ECB showed an increased LF and a reduction in HF with a reduction in the LF/HF ratio.
Conclusions: Our study demonstrates that the use of PER, compared to other new ASMs, provide the safest modification of cardio-autonomic profile.

Abstract Number: 1273

Title: Marijuana Use in Individuals with Epilepsy Post-Legalization in Canada

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Purpose: Patients with epilepsy may turn to alternative treatments such as marijuana to manage both their epilepsy and medication side-effects. The legalization of recreational marijuana by the Canadian government in

2018 increased accessibility and awareness, despite a lack of evidence that it is beneficial for epilepsy patients. The goal of our study is to review marijuana use in patients with epilepsy in Canada.

Method: A Canadian cross-sectional survey was launched to investigate if marijuana is used, usage habits, and perceptions of marijuana, in patients suffering from epilepsy.

Result: 99 surveys were analysed. 75.8%(n=75) were female and 83.8%(n=83) were completed by the participants. The mean age of the participants was 32.2 years(IQR=24-40). The duration of their epilepsy was over 10 years in 56.1%(n=55) and the most common seizure frequency is once per month 50.5%(n=49). The most common type of seizures is generalized (58.1%). From the total participants, 76.8%(n=76) of participants have used marijuana and 33.9%(n=21) of the users report using marijuana because of their epilepsy. Buying marijuana at a dispensary without a prescription was the most common method of obtaining it (60.7%;n=37). 30%(n=18) of surveyed users smoked marijuana and 7.6 grams(IQR=2-7) is the mean dose per week. 63.2% of marijuana users feel more comfortable using marijuana compared to other pharmaceuticals because it is "natural", though 61.4% have felt the need to hide marijuana usage from others. 55.5%(n=55) discussed marijuana use with his/her neurologist at some point. 51.1%(IQR=15-73) of users reported a beneficial effect after using marijuana. Stigma against people using marijuana was found in 89.7% of users and 68.2% of non-marijuana users.

Conclusions: Marijuana use is a common concern in caregivers and patients with epilepsy. These results suggest that more data is required on the use of marijuana in the Canadian population suffering from epilepsy and clinical counselling is recommended.

Epidemiology

Abstract Number: 40

Title: Optimizing epilepsy treatment: big data from population-wide registers suggest room for improvement in drug selection

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Purpose: The first anti-seizure medication (ASM) is ineffective or intolerable in 50% of epilepsy cases. The choice between more than 25 available ASMs is guided by age and co-morbidities, among others, but randomized evidence for particular patient groups is seldom available. Register data is easier to retrieve, provides long-term follow-up, may contain enough individuals for stratification, and is updated frequently.

Method: We used medical, demographic, and drug prescription data from cohorts derived from comprehensive Swedish registers, containing 6380 observations. By analyzing 381,840 dispensed prescriptions, we describe the retention rates using Kaplan-Meier estimation of first- and second-line ASMs for patients with previous multiple sclerosis (MS), brain infection, dementia, trauma, or stroke.

Result: Using optimal stratification for each brain disease, we quantified the potential improvement of the 5-year retention rate if patients had received the optimal ASM for each of the diseases; MS: 20%, brain infection: 21%, dementia: 14%, trauma: 21%, stroke: 14%. For example, in patients with trauma, optimal stratification was based on sex. Males had a higher retention rate with levetiracetam while females had a higher retention rate with lamotrigine. Patients with epilepsy after trauma had the highest retention rate with levetiracetam which was significantly higher compared to the most commonly prescribed ASM, carbamazepine. Patients with

dementia had significantly higher retention rates with lamotrigine and levetiracetam than with carbamazepine. We also designed a web-based tool showing first- and second-line retention rates of ASMs of user-defined subgroups, which can help clinicians select the right medication.

Conclusions: We demonstrate that big data from national registers offer a feasible and powerful way of determining retention rates for different ASMs based on individual patient characteristics. Our results indicate potential improvement in treatment success if optimal ASM was selected based on characteristics. This indicates a need for tools facilitating optimal ASM selection in clinical care.

Abstract Number: 134

Title: Heterogeneous data-based prediction of quality of life level in patients with epilepsy

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Purpose: Quality of life (QoL) in epilepsy is important to develop economically reasonable treatment and rehabilitation programs, so QoL prediction is necessary to form appropriate funding for treatment and rehabilitation of patients with epilepsy.
Method: The study used results of the QOLIE-31 (Cramer JA et al. Development and cross-cultural translation of a 31-item quality of life questionnaire (QOLIE-31). Epilepsia 1998;39:81-88) and basic demographical (gender, age, domicile, education, employment), anamnestic (age of onset), clinical (epilepsy form, seizure type and frequency, psychiatric diagnosis), and pharmacoeconomic (total direct and indirect medical costs, costs of certain groups of medications) values of 166 patients with epilepsy, including 79 female ones.

Result: . An analysis of the QOLIE-31 results demonstrated a need to divide an indirect integral quality of life index (IIQoLI) prediction and a direct subjective quality of life assessment (DSQoLA) prediction because of a difference in principle of patients' self-assessment. It is impossible to perform an appropriate IIQoLI and DSQoLI ranking, as these parameters are highly depended on patients' personalities. Heterogeneity of objective values in terms of their content and thread affinity disables factorization or classification as regressors reduction methods in prediction. A simultaneous presence of ranked, normally distributed, and categorial objective values denies linear and non-linear prediction models exclusively as relevant methods. Among all the common prediction methods, a quantile regression only formed models with more than "good" prediction quality due to its flexibility in combining of a non-linear prediction for categorial variables with a linear prediction for parametric values (Buchinsky M. Recent advances in quantile regression models: a practical guideline for empirical research. J Human Resources. 1998;33(1):88-126).
Conclusions: A quantile regression is the method of choice to predict QoL levels in patients with epilepsy due to necessity of an evaluation of heterogeneous clinical-anamnestic, pharmacoeconomic, and demographical data simultaneously.

Abstract Number: 180

Title: Care Pathway Mapping for Dravet Syndrome (DS) patients in England – interim results from a pilot study

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Purpose: DS is a rare, life-threating epileptic encephalopathy. Patients experience life-long, frequent convulsive seizures (CS) often requiring emergency hospital admissions. This study examined care, management, and

health care resource use (HCRU) of DS patients in England to explore drivers of HCRU and how CS frequency impacts quality of life (QoL).

Method: Care of patients with DS was discussed with a purposive sample of 16 clinicians (11 sites, 6 regions), using semi-structured interviews and structured quantitative tasks, followed by quantitative validation.

Result: Data showed regional variation in care and service provision. Paediatric services were more likely to follow a 'joined-up' approach in contrast with adult services. Transitioning arrangements between services were felt particularly lacking.
Clinicians reported CS frequency as the primary driver of ongoing and emergency HCRU. Younger patients (ages 2-3) with clinician-reported high seizure frequency (HSF: average ≥7 seizures/month) had more (5.0 Vs 3.3.) annual face-to-face secondary care consultations compared to adults (age 18+) with HSF (average ≥13 seizures/month). Patients with lower CS frequency (average 1 seizure/month) accessed ongoing care less often (average annual consultations: children = 2.7 Vs. adults = 1.5). Children had more ambulance attendances after rescue medications (82.3%), compared with adults (24.5%).
Seizure freedom is rarely achievable. Clinicians reported interventions providing longer CS-free durations, reductions in 'absolute' and 'relative' seizure frequency were clinically important for patient/carer QoL and gaining seizure control. Six of eight clinicians rated a 50% reduction in CS as 'meaningful'.

Conclusions: DS patients and their carers have high care requirements, but experience a varied delivery in England. There is need to reduce regional variations in service provision for DS patients, and improve transitioning arrangements into and adult services. Meaningful reductions in CS frequency, in all patients, could reduce HCRU and improve QoL, which may in turn alleviate current variations in service provision and care.

Abstract Number: 185

Title: The Global Economic Burden of Epilepsy

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Purpose: Global action for epilepsy requires information on the cost of epilepsy, which is currently unknown for many countries and regions of the world. To address this gap in knowledge, the ILAE Commission on Epidemiology formed a Task Force on the Global Cost of Epilepsy to estimate the direct and indirect cost of epilepsy across countries worldwide.

Method: Employing costing methods used for other disease conditions, we searched the epilepsy cost-of-illness literature since 2000 and identified 100 studies from 22 countries that met our inclusion criteria: comprehensive set of direct and/or indirect costs, standard methods of case identification and cost estimation, and data on a representative sample of people with epilepsy. Single study cost estimates of per person costs for a given country or the average of multiple study estimates were adjusted to 2019 PPP US Dollars. For countries with no available cost studies, estimates were imputed based on average per person costs in similar income countries adjusted for healthcare spending and gross domestic product (GDP) per capita. The per

person cost estimates were applied to the latest country-specific data on the prevalence of epilepsy from the Global Burden of Disease Collaborative to estimate total costs.

Result: The average annual per person cost of epilepsy worldwide in 2019 was $4,536, the sum of $1,844 direct (range $0.57 to $13,948) and $2,692 indirect (range $10 to $24,732) costs. The total global cost of epilepsy, assuming average per person costs apply to all people with epilepsy in each country, was $179.4 billion (54.8% direct and 45.2% indirect), but with existing estimates of the treatment gap, total epilepsy costs were $158.7 billion (49.0% direct and 51.0% indirect).

Conclusions The global cost of epilepsy is substantial but varies significantly across countries depending on the prevalence of epilepsy, costs per person, and the treatment gap.

Abstract Number: 303

Title: Prenatal exposure to antiseizure medication and intrauterine growth restriction in offspring of women with epilepsy.

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Purpose: To examine the association between prenatal exposure to antiseizure medication (ASM) and risk of being born small for gestational age in offspring of women with epilepsy.

Method: This prospective population-based register study was based on live-born singleton children in Denmark (1997-2017), Finland (1996-2016), Iceland (2004-2017), Norway (2005-2017), and Sweden (2006-2017), and was carried out within the SCAN-AED project (www.scanaed.org). Women with epilepsy were identified through hospital-based diagnoses, the medical birth registries and reimbursement codes for prescriptions. Monotherapy with valproate, lamotrigine, levetiracetam, carbamazepine, oxcarbazepine, topiramate and clonazepam was defined as any redeemed prescription for each (and no other) ASM from 90 days before pregnancy to birth. We used logistic regression models to estimate the adjusted odds ratio (aOR) and corresponding 95% confidence interval (95% CI) for being born small for gestational age, defined as having a birth weight below the 10th percentile for gestational age, sex, and country.

Result: The SCAN-AED population consisted of 4,493,437 live-born singletons, of whom 33,387 (0.7%) children were born to mothers with epilepsy. After adjustment for maternal characteristics, we found that offspring of women with epilepsy using carbamazepine (aOR=1.30, 95% CI: 1.12-1.50; n=2,650), oxcarbazepine (aOR=1.37, 95% CI: 1.13-1.65; n=1,459) and topiramate (aOR=1.61, 95% CI: 1.10-2.36; n=217) were more likely to be born small for gestational age compared to offspring of women with epilepsy, not using ASM in pregnancy, while no association was found for valproate (aOR=1.09, 95% CI: 0.92-1.30; n=1,943), lamotrigine (aOR=0.97, 95% CI: 0.87-1.08; n=4,679), levetiracetam (aOR=1.13, 95% CI: 0.92-1.39; n=1,019), and clonazepam (aOR=1.38, 95% CI: 0.94-2.03; n=228).

Conclusions: In pregnant women with epilepsy, we found an increased occurrence of intrauterine growth restriction in offspring exposed to carbamazepine, oxcarbazepine and topiramate, but not in offspring exposed to valproate, lamotrigine, levetiracetam, and clonazepam.

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Abstract Number: 320

Title: Hypertension and risk of post-stroke epilepsy

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Purpose: Stroke is the leading cause of epilepsy in the elderly. Hypertension is very common and a well-known risk factor of both haemorrhagic (ICH) and ischemic stroke (AIS). This study aims to evaluate the effect of hypertension on the risk of epilepsy following ICH or AIS.

Method: All strokes in Denmark are registered in The Danish Stroke Registry. The registry further collects information on several risk factors for stroke, including hypertension. We identified all patients with a first stroke between April 1 2004 and December 16 2016 and no prior diagnosis of epilepsy (7 634 ICH patients and 69 899 AIS patients). The patients were followed to the first diagnosis of epilepsy, death, emigration or end of follow-up (December 31 2016). We used a cox regression to estimate the HR of post-stroke epilepsy associated with hypertension.

Result: In persons with ICH, the unadjusted HR was 0.80 (95% CI 0.69-0.92) for epilepsy after stroke in persons with hypertension compared to persons without hypertension. When adjusting for stroke severity, age and sex, the adjusted HR was 0.82 (95% CI 0.71-0.94). In persons with AIS, the unadjusted HR was 0.98 (95% CI 0.91-1.05) for epilepsy after stroke in persons with hypertension compared to the persons without hypertension. After adjusting for stroke severity, gender and age, the HR was 1.03 (95% CI 0.96-1.11).

Conclusions: There was no association between hypertension and the risk of post-stroke epilepsy in persons with AIS. However, in persons ICH, the risk of post stroke epilepsy was lower in persons with hypertension than in persons without hypertension at time of stroke.

Abstract Number: 323

Title: Quality of life and stigma in persons with epilepsy across Europe - the European Study on the Burden and Care of Epilepsy Study

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Purpose: This study estimated quality of life and stigma associated with epilepsy in four European countries representing northern (Denmark), central (Austria), eastern (Romania) and western (Ireland) Europe. The study was conducted under the auspices of ESBACE, the European Study on the Burden and Care of Epilepsy.
Method: Participants were recruited among adult persons with epilepsy without intellectual disability identified living in representative regions in Austria, Denmark, Ireland and Romania. For each of the participating persons with epilepsy, we included information from a control person, identified by the person with epilepsy, who did not have and epilepsy, but otherwise similar demographic characteristics as the person with epilepsy. Both persons with epilepsy and control persons completed the Hospital Anxiety and Depression Scale and the SF36 questionnaire, and persons with epilepsy completed the Liverpool Impact of Epilepsy Scale and the Revised Stigma Scale.

Result: Invitations to participate in the study was sent out to 292 participants who provided consent (235 persons with epilepsy and 57 control persons; Austria: 61, Denmark: 135, Ireland: 74, and Romania: 22), response was received from 220 (75.3%) participants (174 persons with epilepsy and 46 controls). As identified with the Hospital Anxiety and Depression inventory, abnormal scores of anxiety and depression were more prevalent in persons with epilepsy compared to their controls. Similarly the persons with epilepsy scored lower on all aspects of the SF36 measurements of quality of life. In persons with epilepsy, the Liverpool Impact of Epilepsy Scale and the Revised Stigma Scale identified significant problems in persons with epilepsy.
Conclusions: The study identified that epilepsy has an impact on psychiatric well-being and quality of life in countries representing the European Union. Further, there seems to be little reduction in stigma and impact of epilepsy over time.

Funding: Funded by the European Union (grant no. 2014//199564).

Abstract Number: 425

Title: FSD Whole Genome Sequencing Program: A Patient-Lead Initiative to Accelerate Diagnosis of Dravet Syndrome and other Rare Epilepsies

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Purpose: Dravet Syndrome (DS) is one of the most severe congenital epilepsies. Caused by mutations in the SCN1A gene, DS is characterized by frequent and drug-resistant seizures. As the disease develops, patients also show cognitive deficits, motor dysfunction, behavioural problems and language impairment. With a 15% mortality rate and seizures worsened by certain antiepileptic drugs, an early diagnosis is essential for a proper disease management. With the aim of contributing to reducing the time to diagnosis and discovering novel genetic factors causing/affecting DS, Dravet Syndrome Foundation Spain (FSD) launched a pioneer Whole Genome Sequencing (WGS) Program, which offers a free WGS testing and analysis service to patients.

Method: Patients eligible to the program include those of any age suffering from two seizures before the age of six months, presence of frequent, severe or long-lasting partial, hemiclonic or myoclonic seizures induced by vaccination or heat in the first year of life, or febrile seizures persisting beyond the age of five. These eligibility criteria ensure inclusion of people affected by DS, whilst patients with related epilepsies remain unexcluded. Patient's HPO and pharmacological data are also requested for analytical purposes.

Result: Since its launch in September 2020, the free FSD WGS Program has identified DS- and other epileptic disorder-related variants in undiagnosed individuals. General results and interesting cases will be presented at the conference.

Conclusions: This is a pioneer rare epilepsy support program, lead for the first time by a patient organization, shortening the time to diagnosis of DS and related disorders. WGS enables a more precise diagnosis of rare epilepsies, ultimately allowing easier patient access to appropriate disease-specific therapies.

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Abstract Number: 431

Title: Clinical factors related to work disability in patients with epilepsy: analysis of a tertiary referral hospital.

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Purpose: The impact of epilepsy on work disability remains unclear. The aim of this study was to describe the percentage of patients with epilepsy with unemployment, temporary incapacity of work and permanent work disability and to analyze the clinical factors of epilepsy related to work disability.

Method: We performed an observational, cross-sectional study of patients with epilepsy visited in a specialized epilepsy unit of a tertiary referral hospital. We analyzed the percentage of patients who were active at work, unemployed or with work disability (temporary or permanent) and compared these groups of patients in terms of demographic data (age, sex, marital status, job qualifications), clinical data (type of epilepsy, disease duration, monthly seizure frequency, presence of anxiety or depression), treatment variables and quality of life.

Result: 742 patients (53% male, mean age 44.3±13.7 years-old) were included. Of these, 40.5% were employed, 29.2% were unemployed, 19% had a temporary work disability and 11.1% had a permanent work disability. Depression and poorer quality of life were associated to unemployment (OR 2.3, p=0.02 and OR 1.8, p=0.01), temporary incapacity for work (OR 1.4, p=0.05 and OR 1.7, p=0.02) and permanent incapacity of work (OR 1.9, p=0.01 and OR 2.2, p=0.01). Low-skilled work was also a predictor for unemployment (OR 1.9, p=0.04), temporary work disability (OR 2.8, p=0.03) and permanent work disability (OR 1.7, p=0.04). Variables indicative of greater epilepsy severity (higher monthly seizure frequency) were associated with permanent work disability (OR 2.01, p=0.02).

Conclusions: Less than half of our patients with epilepsy are working. Factors associated with unemployment or work disability were higher seizure frequency, low-skilled work, depression and a poor quality of life.

Abstract Number: 452

Title: Challenges in determining the prevalence of epilepsy in Europe: to GDPR and beyond

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Purpose: A retrospective chart review study sought to determine the prevalence of epilepsy in four European countries; Austria, Denmark, Ireland and Romania.

Method: Research teams within each country identified a representative region with a population of approximately 50,000 persons. All hospitals and family physicians supporting patients in these regions were invited to identify eligible patients with epilepsy. Identified patients were contacted by research teams requesting access to medical records. Where local data protection practices allowed, medical records were accessed anonymously on behalf of those who did not return consent. A standardised case report form was developed to gather data on seizure frequency, type, investigations, aetiology, comorbidities and anti-seizure medication. Cases were classified by epileptologists as definite, probable or suspect.

Result: 1,988 (0.8%) potential cases of epilepsy were identified from the combined population of 237,757 in the four regions. Of these potential cases, 39% (n=780) could not be investigated further due to legal and ethical issues. A further 6% (n=113) were found to have insufficient information to be included in the study. The 55% of cases with sufficient information to be investigated were classified as definite (n=706; 64.5%), probable (n=191; 17.4%), suspect (n=153; 14.0%) or not epilepsy (n=45; 4.1%).

Conclusions: The data from these cases provide a unique portrait of the profile of patients with epilepsy within these representative regions in Europe using a standardised methodology. Differences across the four countries are likely to reflect the case ascertainment sites from which cases were recruited, differing clinical practices in different jurisdictions, and the quality and availability of medical records. This study was conducted during the introduction of the General Data Protection Regulation in Europe (GDPR). Concerns regarding GDPR compromised the study's potential to access medical records and more generally raise significant issues regarding the ongoing impact of data protection for epidemiological research.

Abstract Number: 643

Title: Incidence, severity and outcomes of COVID-19 in elderly people with epilepsy in Moscow: case-control study

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Purpose: We aimed to evaluate incidence, severity and mortality of COVID-19 in people with epilepsy (PWE) 60 years and older versus controls from Moscow population (MP).

Method: Subjects were members of a prospectively followed 1:3 age- and gender-matched cohort previously described (Rider F et al. European Journal of Neurology 2020; 27(1), 818). We included 1638 people 60 years and older: 392 PWE (71.5±8.6 years, 229 females) and 1246 MP (70.6±9.1 years, 696 females). We looked at cases and controls, diagnosed with COVID-19 from 01.03.2020 till 01.03.21. Severity was assessed according to WHO clinical classification. Data source was the "Unified medical information analytical system" of Moscow. Pearson's chi-squared test and logistic regression were used.

Result: We found 298 COVID-19 patients, 52 in PWE (73.9±9.5 years, 30 females) versus 246 in MP (70.1±9 years, 135 females). Incidence was 13.3% in PWE versus 19.7 % in MP. Moderate and severe cases were diagnosed in 33 (63.5%) PWE and 152 (61.8%) MP. The proportion of hospitalized patients (59.6% in PWE versus 47.6% in MP) and mortality (17.3 % of PWE versus 11.4% of MP) did not different significantly. The only parameters that significantly affected outcomes in both groups were age (OR 1.08, 95% 1.03-1.12, p=0.000) and number of comorbidities (OR 1.30, 95% CI 1.07-1.57, p=0.006). The combination of hypertension, diabetes

mellitus and obesity was strongly associated with increased risk of mortality in cases and controls (26.3% versus 10.4%, p=0.005).

Conclusions: Epilepsy did not affect severity and outcomes of COVID-19 in elderly population of Moscow. Age, number of comorbidities and especially the combination of hypertension, diabetes mellitus and obesity were the most significant risk factors for mortality in all people 60 years and older.

Abstract Number: 711

Title: Adult-onset epilepsy is defined by phenotypic clusters with unique comorbidities and risks of death

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Purpose: To identify clusters of adult-onset epilepsy with distinct comorbidities and risks of early and late death.

Method: This was a retrospective open cohort study that included all adults meeting a case definition for epilepsy after the Acceptable Mortality Recording date in The Health Improvement Network (THIN) database, inclusive years 2000-2012. Unsupervised agglomerative hierarchical clustering was performed to identify unique clusters of patients based on their predicted risk of early (< 4 years of epilepsy diagnosis) and late (≥ 4 years from diagnosis) mortality and patient-level clinical characteristics.

Result: We identified 10,499 presumed incident cases of epilepsy from 11,194,182 patients. Four phenotypic clusters were identified in the early and late risk periods. Early clusters include older adults with cardiovascular disease and a high risk of death (median predicted risk 20%; interquartile range 'IQR' 9-31%), a group with moderate risk of death and cancer (median predicted risk 6%; IQR 2-15%), a group with psychiatric disease/substance use and few somatic comorbidities (median predicted risk 5%; IQR 2-9%), and one with a younger age of onset and few comorbidities (median predicted risk 4%; IQR 1-11%). There was minimal movement of individuals between clusters for those surviving the early risk period. Age- and sex-standardized 3-year mortality ratios were >6-fold higher than the general population for every cluster, even those primarily comprised of healthy younger adults.

Conclusions: Adult-onset epilepsy is marked by unique clusters of comorbid conditions and elevated risks of death that form discrete populations for targeted therapeutic interventions. These clusters remain relatively stable between the early and late mortality risk periods. Of particular interest are the clusters marked by young and otherwise healthy adults whose SMR is 6-fold higher than general population despite few conventional risk factors for premature death.

Abstract Number: 746

Title: Impact of epilepsy definition on estimates of prevalence, psychiatric co-morbidity and cost - a population-based, cross-sectional study

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Purpose: This study estimated prevalence, psychiatric co-morbidity and costs associated with epilepsy using different definitions of epilepsy.

Method: We used Danish national health registers to identify persons diagnosed with epilepsy and psychiatric disorders and persons using antiseizure medication and drugs for psychiatric disorders.
We calculated the prevalence of epilepsy and co-morbid psychiatric disorders in Denmark on December 31, 2016, using various definitions of epilepsy based on combinations of hospital contacts and use of antiseizure medication. Direct and indirect costs associated with epilepsy were calculated using individual-level data from a range of socioeconomic registers.

Result: There were 5,044,367 persons alive and living in Denmark on December 31, 2016, including 33,628 persons with at least one hospital contact with epilepsy in the previous five years (epilepsy prevalence 0.67%. (0.69% males; 0.65% females)). Among these persons with epilepsy, we identified 12,562 (37.4%) persons with psychiatric disorders as compared with 801,052 (15.9%) persons in the general population. In this population, total annual individual net costs associated with epilepsy were €30,683. The prevalence of epilepsy varied significantly with other definitions of epilepsy; from 0.51% to 1.87%. However, total annual individual net costs varied only slightly between epilepsy prevalence definitions from €28,558 to €34,097.

Conclusions: Epilepsy prevalence varies highly with the definition used, and this has a profound impact on the estimated total cost associated with epilepsy. The main determinant of societal costs associated with epilepsy is the number of persons with the disorder rather than the actual personal cost estimated per person with epilepsy.

Study Funding: This project received funding from the European Unions - SANTE C-Public Health - Directorate General for Health and Food Safety under grant agreement no. 2014//199564.

Abstract Number: 838

Title: Automating the Assessment of First Seizure Care Pathways and Clinical Outcomes using Electronic Health Records

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Purpose: When a person presents with a suspected first seizure episode – an event that can have profound emotional, social, and vocational consequences – they will tend to have frequent and numerous encounters with the healthcare system to help manage their health.

Electronic Health Records (EHR), which record the details of each interaction, are ideal sources of information to provide evidence for the optimisation of health management. However, beyond direct patient care, their use for secondary purposes such as research or service improvement has been limited.
We aimed to explore the feasibility of using a novel patient data analytics tool (CogStack) at King's College Hospital NHS Foundation Trust (KCH) to identify suspected first seizure patients who present to the A&E department between 2017-18 and compare their management against NICE guidelines.

Method: We utilised CogStack to search EHR documents at KCH and used natural language processing (NLP) to identify suspected first seizure patients who attended the emergency department. We then retrieved their subsequent records and extracted information about their symptomatic presentation, final diagnosis, timing of investigations, and specialist appointments.

Result: 226 patients attended the emergency department with suspected first seizures. After investigations, common final diagnoses were Epilepsy (23%), cardiovascular syncope (19%), and single episodes (19%). Our analysis of patient records identified steps in the clinical pathway that frequently fell short of the NICE guidelines.

Conclusions: EHRs are feasible to be mined at scale for the rapid analysis of service demand and monitoring patient health trajectories. The insights of this study have been used to improve first seizure management in KCH, demonstrating the value of NLP application in healthcare, and have informed the development of a prototype NLP platform (MedCAT) performing large-scale data extraction such as diseases, symptoms and medications from unstructured text.

Abstract Number: 896

Title: Sounds of Seizures – Immediate detection and sound recognition of generalized tonic-clonic seizures in canines

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Purpose: Epilepsy is the most common chronic neurological disease in humans and dogs. Seizures greatly impact patients' and caretakers' quality of life. Seizures often remain unnoticed or are noticed late, adding to the worries of caretakers. This leads to the need for reliable detection of seizures in order to apply quick emergency treatment for preventing further seizure evolution. Advances in using artificial intelligence to understand large datasets can help overcome this gap. A crucial step in this direction is the creation of quality datasets and computational tools for investigating seizure-related audio, video and sensor signals.

Method: We collected and annotated a dataset of 42 audio tracks of videos of dogs with generalized tonic-clonic epileptic seizures. Using 138 statistical features, we investigated 9 classifier types using 4474 sound samples with the duration of 1 second each.

Result: We evaluated the obtained classifiers with k-fold cross-validation and automatic hyperparameter tuning, reaching balanced accuracy of above 70%.

Conclusions: Classical machine learning methods show promising results in the detection of epileptic seizure sounds, providing a potential basis for the development of an alert and detection system. Employing more advanced deep learning techniques and neural networks has even greater potential to increase accuracy, however larger datasets need to be obtained.

Funding:

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Abstract Number: 921

Title: Study of the frequency and distribution of epilepsy in 25 regions of Peru in 2019

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Purpose: In Peru we do not have statistical information on the number of people diagnosed with epilepsy. The purpose of the study is to show a first approximation to the number of people with epilepsy from the data registry of those treated for this cause, in public health establishments of the Ministry of Health at the national level. This preliminary information will be useful for further study.

Method: It is a retrospective and descriptive study. Statistical information was obtained from the website of the Ministry of Health, which records the number of patients treated in 2019 for all causes in each of the 25 regions of the country and those with a diagnosis of epilepsy. The total and relative number of people treated for epilepsy that year was obtained.

Result: In 2019, 18,299,782 people were treated for all causes, 9,807 corresponded to people with a diagnosis of epilepsy, which represents 0.053% of the total.

Conclusions: The number of people treated for epilepsy in the public health ministry establishments in 2019 was 0.053% of the total treated, a low percentage that deserves to be evaluated. The study has a sample selection bias because it includes only those patients treated in the hospitals of the Ministry of Health network, and leaves out those who did not attend. In addition, it does not consider those treated at the Social Security hospitals, in the health establishments of the Armed Forces and Police, in the private outpatient clinics because the information is not available on the web.
This information will be useful for subsequent studies that allow us to know the epidemiology of people with epilepsy in the country and to make better future public health planning to improve the diagnosis and treatment people with epilepsy in Perú

Abstract Number: 963

Title: Post – Stroke risk of Epilepsy: A Case-Crossover Analysis

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Purpose: Prior studies have associated acute ischemic stroke (AIS) with risk of subsequent epilepsy. However, risk factors for post-stroke epilepsy remain incompletely characterized. Here, we quantify risk associated with age and sex using case-crossover analysis, to optimally control for confounding factors as each patient serves as their own control.

Method: We used administrative data from the Florida State Inpatient and Emergency Databases from January 2005 to September 2015. Patient were included if their first seizure or epilepsy diagnosis (index event) occurred between January 2007 and September 2015, to allow for 2 years of observation prior to the index event. Diagnoses of seizure, epilepsy and stroke were identified using validated ICD-9-CM codes. In a case-crossover design, we defined the case period as 1-year period before the index event, and the control period as 1-year period prior to the case period. Then we compared the occurrence of stroke during the case period to

the control period using conditional logistic regression. We also performed stratified analysis by gender and age groups.

Result: Among 186,935 patients with index seizure event during the 10-year study period, median age was 44 [IQR 27-61] years, 51% were females, and 64% were white. 2,240 (1.2 %) suffered AIS during the control period compared to 4,285 (2.3 %) in the case period. AIS 1-year before the index event was associated with significantly increased risk of seizure event (OR 2.06 [95% CI,1.95-2.17]). In stratified analysis, males had similar risk as females. When stratified by age groups, risk increased with advancing age (50-60 years: OR 1.80 [95%CI 1.59-2.04] vs. >80 years: OR 2.37 [95% CI [2.11-2.67])

Conclusions: AIS within the previous year was strongly associated with new diagnosis epilepsy, and this effect was most prominent in elderly populations. These findings support education on possible epilepsy development in elderly patients with AIS.

Abstract Number: 1004

Title: Diagnosis of neonatal jaundice and epilepsy – a population-based cohort study

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Purpose: To study the association between diagnosis of neonatal jaundice and epilepsy.

Method: We used the Danish Medical Birth Registry to identify all live born singletons in Denmark between 1 Jan 1997 and 30 Nov 2016. We obtained information on neonatal jaundice and epilepsy from the Danish National Patient Registry. We used proportional Cox regression models to estimate the hazard ratio (aHR) of epilepsy and 95% confidence interval (CI) adjusted for calendar year, parity, maternal age, employment status at time of birth, parental history of epilepsy, sex of child, and gestational age (20-33, 34-36, 37-38,39-41,42-45). Children were followed from day 29 after birth until diagnosis of epilepsy, death, or the end of the study (31 December 2016).

Result: Among the total study population (N=1,186,683), 46,210 (3.9%) children had a diagnosis of neonatal jaundice. We identified 10,716 (0.9%) children with a diagnosis of epilepsy. The incidence rate of epilepsy was 12.8 and 8.8 per 10,000 person-years for children with or without a diagnosis of neonatal jaundice. The aHR of epilepsy among children with a diagnosis of neonatal jaundice was 1.03 (95%CI: 0.92-1.13). The aHR of epilepsy among children diagnosed with neonatal jaundice was 0.87 (95%CI: 0.70-1.09) for children born between 20 and 33 gestational weeks (gw), 0.89 (95%CI: 0.72-1.09) for children born 34-36 gw, 0.97 (95%CI: 0.80-1.17) for children born 37-38 gw, and 1.30 (95%CI: 1.10-1.53) for children born 39-42 gw. The association found among children born 39-42 gw were found only in girls (1.51, 95%CI: 1.17-1.94), not in boys (1.17, 95%CI: 0.94-1.45).

Conclusions: In this population-based study, a diagnosis of neonatal jaundice was associated with an increased risk of epilepsy. The risk was especially high among girls. The results call for further research into possible long-term effects of neonatal jaundice and related factors such as phototherapy and bilirubin levels.

Abstract Number: 1018

Title: Impact of number of anti-epileptic drugs on health-related quality of life in children with epilepsy: observational cohort study

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Purpose: Health-related quality of life (HRQL) is compromised in children with epilepsy. The current study aims to determine whether children exposed to more than one anti-epileptic drug (AED) over the first 2 years after diagnosis have poorer HRQL at 10 years.

Method: Data came from 387 children enrolled in Health-Related Quality of Life in Children with Epilepsy Study(HERQULES). Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55) was completed by parents at the time of diagnosis (baseline), 2- and 10-years later. Total number of AEDs was reported by physicians over the first two years. Variables associated with HRQL at the 10-year follow-up were evaluated using multivariable linear regression, controlling for baseline HRQL, clinical, demographic, and family characteristics. Analyses were repeated controlling for similar variables at the 2-year follow-up (when pattern of AED use determined).

Result: Children (49.5% female) were aged 7.9±2.3 years at epilepsy diagnosis and were reported to have a mean HRQL of 71.2±14, 76.8±14.4, and 78.5±16 at baseline, 2-year and 10-year follow-up, respectively. Clinically meaningful improvement of 7-points in HRQL from 2 to 10 years after diagnosis occurred in over 70% of children. Exposure to more than one AED by two years from diagnosis was only independently associated with poorer HRQL at the 10-year follow-up when adjusting for baseline HRQL (p=.048), and not when adjusting for HRQL, 2 years after epilepsy diagnosis (p=.74). HRQL at baseline and 2-year follow-up was strongly associated with HRQL at the 10-year follow-up.

Conclusion: Exposure to a higher number of AEDs was only independently associated with poorer 10-year HRQL when accounting for baseline HRQL and not when accounting for two-year HRQL. Longitudinal HRQL assessment in children requiring a higher number of AEDs is recommended for comprehensive patient care and to better understand the interplay the two play on long-term HRQL in children with epilepsy.

Abstract Number: 1081

Title: Focal epilepsy due to malformations of cortical development (MCD): long-term outcome and prognosis predictors

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Purpose: : to evaluate the long-term outcome of patients with focal epilepsy and malformations of cortical development (MCD).

Method: retrospective cohort study of patients with epilepsy and MCD due to impaired neuronal migration and post-migration organization. All patients underwent a full electro-clinical assessment; the type of MCD was classified after accurate neuroimaging review by an expert neuroradiologist. The primary outcome was terminal remission (TR), defined as a period of seizure freedom for at least 1 year at the last follow-up. We used Kaplan-Meier estimates to calculate the cumulative time dependent probability of TR from disease onset and to generate survival curves. Baseline variables were evaluated as possible prognostic factors (Cox model)

Result: The cohort included 71 patients with a 24-year median F-U: 35 had heterotopia (periventricular nodular heterotopia or subcortical heterotopia), 5 lissencephaly, 25 polymicrogyria, and 6 the association of two MCD. The mean age at seizure onset was 12±7 years (median: 13 years). At the last follow-up, 30 patients achieved TR (42%). The cumulative time-dependent probability of conversion to TR was 25% by 20 years from inclusion. At the univariate analysis, the absence of intellectual disability (p=0.041) and the unilateral distribution of MCD (p=0.010) significantly correlated with the outcome. In the Cox model, age at onset ≥13 years (HR 2.4, CI 95%: 1.1-5.1), absence of intellectual disability (HR 2.7, CI: 1-7), and unilateral distribution of MCD (HR 3.3, CI: 1.5 - 7.4) were significantly associated with TR.

Conclusions: Patients with epilepsy and MCD showed a cumulative TR rate of the 25% by 20 years from inclusion. Late seizure onset, absence of intellectual disability and unilateral distribution of the malformation are independent predictors of positive prognosis.

Abstract Number: 1145

Title: Spatio-temporal evolution of epilepsy during 15 years in Ecuador

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Purpose: This study explores the spatial and temporal trends of epilepsy in Ecuador, an upper middle-income country in Latin America.

Method: This ecological work is focusing on the hospital admission rates at the local level. Data were obtained from the National Institute of Statistics and Census (INEC). Data from 2005 to 2019 was analysed. Epilepsy and related pathologies were identified using the International Disease Codes, as follows: from G400 to G404 and G406 to G409. The number of specialists, neurologists and neurosurgeons were also analysed at the local level. Georeferenced information was used for spatial analysis for estimating hospital admission rates and the specialists' density across the country. We applied a monotonic trend (Mann-Kendall) test, which measures the degree to which a trend is consistently increasing or decreasing.

Result: A total of 154 neurologists and 145 neurosurgeons are registered to practice in Ecuador up to 2018. These practitioners were mainly located in the largest cities. In rural areas, no such specialist is present. A high rate of hospital admissions is seen in rural areas, especially in the Amazonian region. We found high admissions hotspots with epilepsy diagnoses in major urban conurbations such as Quito, Santa Elena, Cuenca. In contrast, low admissions rates were seen in sparsely populated areas far from major centers, such as La Concordia and Santa Lucia. There is an apparent variation over time with an initial increase in admission followed by a reduction.

Conclusions: Our findings suggest that Ecuador has a gap of specialists in rural areas, as described here. Our results suggest that closing specialists' gap would be necessary for responding adequately to the constant increment of hospital admissions rate. The reasons for the temporal changes are unknown. One possibility is that it could result from policy changes and budgetary restrictions, but this needs confirmations.

Abstract Number: 1199

Title: Epidemiology of acute symptomatic seizures after ischemic stroke in a Stroke Unit

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Purpose: To describe the population with acute symptomatic seizures after ischemic stroke

Method: Retrospective analysis of the clinical data of patients admitted in the Stroke Unit over 5 years with acute symptomatic seizures (ASS) in ischemic stroke context and no previous history of epilepsy. Stroke epidemiology, seizure timing and type, electroencephalogram findings and antiepileptic drug use were evaluated.

Result: 33 cases were included of 1463 cases of ischemic stroke admitted in the corresponding period (2.3%), 61% of them were male, average age of 78 years. ASS occurred in the first 24 hours of stroke in 61% of patients, being the presenting event in 55%. According to seizure semiology, focal motor seizures were more prevalent (56%). Status epilepticus developed in 21% of cases. Total anterior circulation stroke (TACS) accounted for 64% of cases and cardiac embolic source was the most frequent etiology (52%). 76% of patients performed electroencephalogram, periodic lateralized discharges and generalized slow activity were the most prevalent findings (23% and 19% respectively). Antiepileptic drugs were used in 91% of cases (particularly levetiracetam). 27% of patients died in infirmary and 21% of dismissed patients had at least one unprovoked seizure in 1-year of follow-up. We did not found statistically significant differences between patients that did or did not repeat seizures in 1 year follow-up.

Conclusions: According to literature prevalence of acute symptomatic seizure in ischemic stroke rounds 8.9% and risk of developing vascular epilepsy is even smaller (2,5%), with higher risk described for larger stroke and later onset of seizures after ischemic insult. We found a smaller prevalence of ASS in ischemic stroke setting in our Stroke Unit and no statistically significant differences were found between patients with or without unprovoked seizures in 1 year follow-up.

Abstract Number: 1221

Title: The impact of comorbid autism in persons with epilepsy – a retrospective analysis of the National Inpatient Sample

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Purpose: We compared outcomes amongst hospitalized patients coded for epilepsy and autism spectrum disorder (ASD) to those coded for epilepsy without comorbid ASD.

Method: Admissions amongst patients (all ages) coded with epilepsy with ASD as well as epilepsy without ASD were identified in the 2003-14 National Inpatient Sample using previously validated ICD-9-CM case definitions. One patient with epilepsy and ASD was matched by age and sex to three patients with epilepsy alone. Logistic regressions were performed to compare discharge status, in-hospital mortality, mean length of stay (LOS) and cost in persons with epilepsy and ASD to persons with epilepsy alone. Rates of infection, ventilation, and sepsis, determined by the presence of primary CCS codes, were also compared between the groups.

Result: Data were collected on 9,254 hospital admissions in persons with epilepsy and ASD and 27,762 hospital admissions in persons with epilepsy alone. Patients with epilepsy and ASD had lower odds of discharge against medical advice (OR=0.44,95%CI=0.32-0.62,p<0.0001), higher odds of transfer to another facility

(OR=1.09,95%CI=1.00-1.19,p=0.048), higher odds of in-hospital mortality (OR=1.36,95%CI=1.07-1.71,p=0.011), and longer mean LOS (5.63days vs. 5.12days,p<0.0001). No significant difference in cost of hospitalization was observed. Patients with epilepsy and ASD experienced lower rates of infection (OR=0.85,95%CI=0.79,0.91,p<0.0001) and ventilation (OR=0.74,CI=0.66,0.83,p<0.0001). Sepsis was more common in patients with epilepsy and ASD compared to epilepsy alone (4.21% vs 3.08%,p<0.0001).

Conclusions: The presence of ASD in epilepsy was associated with poor in-hospital outcomes such as longer LOS, higher odds of transfer, and higher odds of in-hospital mortality. Rates of infection and ventilation were higher amongst patients with epilepsy alone. However, sepsis, a severe complication of infection, was more common in patients with epilepsy and ASD, and may have driven the poor outcomes we observed. Future interventions should be targeted towards prevention and prompt treatment of sepsis in patients with epilepsy and ASD.

Abstract Number: 1327

Title: Referral trends for epilepsy surgery between 2000 and 2020 in western India

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Purpose: In 2003 American Academy of Neurology practice parameter in drug resistant epilepsy recommended that Class I evidence for good surgical outcome in refractory temporal lobe epilepsy (TLE). The aim of our study was to study the reference trends and whether the recommendations led to a change in referral patterns to our epilepsy center

Method: Data regarding patients with TLE who underwent long-term video electroencephalography monitoring for presurgical evaluation in comprehensive epilepsy care center over 2 decades were analysed retrospectively. All patients diagnosed to be having drug-resistant epilepsy were included. They were divided into 4 groups, each consisting of an epoch of 5-year period . The time epoch was divided so: Group 1 year 2000–2004; group 2 year 2005–2009; and group 3 year 2010–2014, group 4 2015-2020. Referral data with particular focus as to the duration of epilepsy before referral, age at onset of seizures, and number of antiepileptic drugs tried before referral were analysed

Result: A total of 507 patients were operated for drug resistant epilepsy with 302(59.56%) males and 205 (40.43%) females. There were 33 referrals in group 1, 113 in group 2, and 233 in group 3 and138 in group 4. The mean duration of epilepsy before referral was 11.75±10.25 years . The age at onset of seizures had a increase over the epochs which was significant(0.009).A significant increase in the age at presurgical evaluation was marked over the time epochs(0.043). The number of AEDs tried were 2 in maximum patients in Group 1(69.69%) and Group 2(54.86%) and 3 drugs in Group 3(43.67%) and Group 4(47.82%)

Conclusions: There is evidence for delayed referral of patients with refractory TLE to a surgical epilepsy center in this study. More efforts to change the trend of referral pattern for epilepsy surgery is the need of the hour

Epilepsy in Resource-restricted Settings

Abstract Number: 272

Title: Point-of-care EEG-video in northern Nigeria emergency rooms (ERs) utilizing community healthcare workers (CHWs) trained in EEG technology

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Purpose: Childhood status epilepticus (SE) is associated with short-term associated mortality as high as 25% in northern Nigeria, where there is a shortage of trained EEG technologists. Access to standardized SE treatment protocols, with utilization of EEG-video to assist in management of refractory SE, and non-convulsive SE, may improve SE-associated outcomes Prior to enrolling children into the *Childhood Status Epilepticus (SE) and Epilepsy Determinants of Outcome (SEED)* cohort and deep phenotyping of SE we (1) trained 12 community health workers (CHWs) in EEG Technology; and, (2) implemented point-of-care EEG-video in three major pediatric emergency rooms in Kano, Nigeria to perform EEG-video on children with seizures and SE.

Method: Twelve recently trained CHWs were recruited for SEED. All were enrolled in the flipped classroom EEG Tech Training program from Baptist Health Sciences University (Memphis, TN USA), modified for use in northern Nigeria, and received basic epilepsy training developed as part of the *Bridging the Childhood Epilepsy Treatment Gap in Africa (BRIDGE)* project. EEG Tech students were trained to perform point-of-care EEG-video in pediatric ERs, and routine EEG's.

Result: Twelve EEG technology trainees successfully completed 12 of the 12 training modules for EEG Technology. Point-of-care EEG and EEG-video is being initiated in three major pediatric emergency rooms, with EEG data managed for both clinical care readings by local epileptologists and by SEED epilepsy specialists for research interpretations and EEG database entry.

Conclusions: CHWs represent a pool of potential trainees in EEG technology available to scale-up EEG services in northern Nigeria and other low-resource areas of sub-Saharan Africa. A combined on-line and in-person EEG training is feasible in areas like northern Nigeria to train cohorts of new EEG technologists. Point-of-care EEG for SE should help perform deep phenotyping of children with SE in northern Nigeria. (Funding: FIC/NINDS/NIH R01 NS118483.)

Abstract Number: 421

Title: Using health laws to prioritise epilepsy in resource-restricted settings: an African perspective

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Purpose: WHA Resolutions 68.20 and 73.11 implore UN Member States to address epilepsy as a public health imperative by developing and implementing global and national action plans on epilepsy as well as to reinforce human rights based policies and laws for people with epilepsy at national and international levels. Despite several African States committing to international treaties concerning the universal right to health and the protection of the rights of persons with specific health needs, there is still a dearth of specific national policies and laws on epilepsy as well as accompanying monitoring and enforcement mechanisms. This study reflects on how health laws[1] may be used to strengthen the prioritisation of epilepsy in resource-restricted settings, specifically, in the African context.

Method: Twenty-one African States are studied in this research through their international commitments and the hierarchy of their national laws as they relate to epilepsy.[2] Qualitative and quantitative research methods were employed. A desk review of existing international and national policies and laws was systematically conducted together with key informant consultations.

Result: In the countries studied, the implementation rates of general health laws and policies are low. This only pushes epilepsy, as a specific concern, lower on the agendas of duty bearers who were described in survey responses as uninformed or untrained on epilepsy issues. Moreover, as far as inter-sectoral collaboration is concerned, respondents in only two of the countries invited to participate in the survey informed that there is engagement between State and non-State stakeholders on epilepsy matters.

Conclusions: Generally, the existing data on African health laws is not easily accessible and is not comparable between States. In the context of making epilepsy a priority in Africa, the status quo reduces the capacity of key interlocutors to develop national policies, plans and evidence-based responses on epilepsy.

Abstract Number: 629

Title: Epilepsy, between knowledges and beliefs in southern Morocco.

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Purpose: Epilepsy is a neurological disorder that is not well understood. Indeed, major gaps surround its diagnosis, causes and treatments. Especially in low and middle income countries.
Goal: To raise the knowledge and beliefs about epilepsy in southern Morocco considered as a middle-income countries.

Method: This is a descriptive cross-sectional survey using a questionnaire distributed through social networks and door-to-door to a sample of 196 participants from urban and rural areas in southern Morocco. This sample

[1] Defined by WHO as the area of law concerned with the health of individuals and populations, the provision of healthcare and the operation of the healthcare system.
[2] Angola, Botswana, Cameroon, Comoros, the DRC, Eswatini, Kenya, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Nigeria, Rwanda, Seychelles, Sierra Leone, South Africa, Tanzania, Zambia and Zimbabwe.

represented all age groups and educational levels. Of which 5% had epilepsy and 55.3% knew people with epilepsy.

Result: We identified about 20 different appellations for epilepsy, often referring to the supernatural. Only 50% of the respondents knew the types of epilepsy and 67% of them recognized only generalized seizures. Moreover, 26.3% declared as witchcraft and spirits among the causes of epilepsy. In addition, religious therapy through the holy Quran was proposed by 40.6%, with 7.9% suggesting to going to mausoleums and Pious worshippers of Allah. Although the majority of the respondents knew that there are medicines to treat epilepsy, 33.2% of them proposed traditional treatments. Also, more than half % of the respondents do not know how to act in front of an epileptic seizure, of which 20.8% try to stop the patient's movements and 15% put water or honey in the patient's mouth at the time of the seizure.

Conclusions: Influenced by rural origin and illiteracy, the ignorance about epilepsy disorder is very marked in southern Morocco. Furthermore, spiritual and traditional practices occupy in important place in diagnosis and treatment instead of medical ones. Therefore, the health system, media and associations are called to mobilize to promote the medical care.

Abstract Number: 665

Title: Bridging the Childhood Epilepsy Treatment Gap in Africa (BRIDGE): A Cluster Randomized Clinical Trial of Task-Shifted Epilepsy Care.

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Purpose: Conduct the first non-inferiority cluster randomized clinical trial (cRCT) of task-shifted epilepsy care to community health workers (CHWs) versus enhanced usual physician epilepsy care.

Method: Among 399 eligible primary healthcare centres (PHCs) 60 were randomly selected (30 in Kano, 15 in Kaduna and 15 in Zaria); thirty participating PHCs were randomly assigned to a task-shifted protocol (epilepsy diagnosis and treatment by CHWs), and thirty PHCs were randomly assigned to enhanced usual care (EUC) - physician epilepsy care plus primary care by epilepsy-trained CHWs. One hundrid twenty CHWs, two for each of the sixty PHCs, completed a four-month epilepsy training program. About 1800 children with previously untreated epilepsy identified in community-, clinic-, and school-based screenings are being enrolled in the cRCT and are being assigned to the participating PHC closest to their home. Epileptologists who are blinded as to whether the study subjects are receiving task-shifted care or EUC, are evaluating each study subject at 1-, 6-, 18-, and 24-months following enrollment. Electronic case report forms (CRFs) are being used for all study visits, with data uploads to the data coordinating centre at Vanderbilt Institute for Global Health.

Result: The primary outcome will be the percent of children seizure-free in each arm of the cRCT. Implementation and cost-effectiveness of task-shifted care will be studied. Studies of task-shifted care implementation and cost-effectiveness are integrated into the cRCT.

Conclusions: This NIH-funded cRCT of tack-shifted epilepsy care, regardless of outcome, will inform efforts to bring epilepsy care to about 50% of the world's children with epilepsy who are currently without treatment. The BRIDGE cRCT is the first major clinical trial testing the WHO recommendation for addressing the epilepsy treatment gap in low- and middle-income countries of sub-Saharan Africa. Funding: Fogarty International Center and National Institute of Neurological Disorders and Stroke, NIH (R01 NS113171).

Abstract Number: 793

Title: Feasibility and Acceptability of a Modified ketogenic diet for children With drug resistant Epilepsy; a qualitative Study.

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Purpose: Increasing evidence indicates that dietary therapies are efficacious in reducing seizure frequency when offered to children with drug resistant epilepsy. Few patients in Kenya have accessed the Modified ketogenic diet (MKD) and their experiences with this intervention has not been formally evaluated.

Method: This qualitative study utilized in-depth interviews (IDIs) to assess feasibility and acceptability of using the MKD in Kenya among children aged 2-18 years with drug resistant epilepsy and their primary caregivers. IDIs were conducted by an experienced social scientist at a private hospital in Nairobi, and were audio recorded. The study followed six phases of thematic analysis.

Result: Three adolescents aged 9, 14 and 16 years, and 14 adults were interviewed. Duration of epilepsy diagnosis as well as clinic attendance was 1 to 14 years while the duration of MKD utilization ranged from 1 to 24 months. Among ten participants the motivation to start the MKD was the desire to find an alternative therapy for ongoing seizures. Eight participants reported that their expectations for seizure reduction were met, including reduction of seizures and hyperactivity. Factors which contributed to continuation with the diet included support from extended family, reduction in seizures and hope for reduction in anti-seizure medications. Eleven caregivers considered MKD to be a safe intervention for their child. Eight participants reported challenges administering MKD including adherence to the diet, food refusal by the child, cost of the MKD and irregular dietician support. Adolescents reported not having a clear understanding for the need to take the diet.

Conclusions: From this small sample**,** the MKD appeared to be acceptable to families of children with drug resistant epilepsy in Kenya. Feasibility for continuation was hampered by various factors which may be ameliorated through improvement in availability of trained dieticians to support affected families.

Abstract Number: 816

Title: Assessment of the situation of epilepsy in five countries in Sub-Saharan Africa using the WHO's Assessment Instrument for Mental Health Systems

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Purpose: Epilepsy is a serious neurological disorder that affects over 70 million people worldwide. Highest prevalence of epilepsy and the largest treatment gap are in low- and middle-income countries. The World Health Assembly resolution 73.11 (2020) on the global burden of epilepsy highlighted the need to identify factors affecting access to epilepsy care and to facilitate a comprehensive epilepsy care response. We present the results of a situation analysis carried out in Uganda, Malawi, Eswatini, Mauritius and Zimbabwe to assess access to care.

Method: Data collection was done between August 2020 and January 2021 using WHO's Assessment Instrument for Mental Health Systems Version 2.2. The study used (i) qualitative interviews with existing support arrangement and service providers in country; (ii) quantitative analysis of facility records and in the public domain.

Result: Existing diagnostic, educational services and support for people with epilepsy are limited across the 5 countries. The pooled prevalence across the 5 countries was 1.7% and ranged from 1.2%in Eswatini to 2.3% in Malawi. Mortality rates for epilepsy were highest in Eswatini (11.03/100,000 population) and lowest in Malawi (2.08/100,000 population). Of the 5 countries, only the Uganda health policy is partially aligned to the WHO Resolution 68.20. There is a lack of specialized health workers, with 12 neurologists in total, for the 5 countries; a population of 79 million. The highest neurologist to patient ratio is in Malawi (1:80 0000) and lowest in (Eswatini 1:1169).The is high shortage of drugs across the countries. Awareness and educational activities are mainly done by NGOs.

Conclusions: Services and support for epilepsy are not prioritized in sub-Saharan Africa leading to large treatment gaps. There is an urgent need to increase resources allocated to epilepsy care, and policies, plans and legislations need to be developed or updated.

Abstract Number: 901

Title: Accuracy of Phase I Presurgical evaluation in a sample of Egyptian people with focal drug resistant epilepsy.

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Purpose: To evaluate the concordance using the available non-invasive assessment (neurophysiological, and neuroradiological assessment) with clinical semiology in Egyptian patients with focal drug resistant epilepsy in an example of limited resource country. In addition, lateralize dominant hemisphere by available resources.

Method: 118 patients with focal drug resistant epilepsy were recruited from Kasr Alainy hospital, epilepsy outpatient clinic. These patients clinical history data was collected, all patients undergo Interictal Electroencephalograph (EEG) and ictal EEG recorded. MRI epilepsy protocol was done. Collected data were analysed and concordance identified in each patient. Complete concordance defined as when all the 3 modalities localize and lateralize the hypothetical epileptogenic focus to the same site; and partial concordance when only 2 modalities localize and lateralize to the same site. when none of the 3 modalities show concordance, it is considered as non-concordance.
Digit dichotic listening (DDL) was done for 95 patients, and Edinburgh handedness inventory questionnaire (EHIQ) was done for 118 patients, and correlated with patients' handedness.

Result: Among recruited patients, ictal EEG could be recorded in only 44 patients. brain lesion could be localized in only 95 patients. Complete concordance could be achieved in 29 (24.6%) patients, and forty-five (37.3%) patients had partial concordance. Forty-four patients needed further investigation (Non-concordance). Dominant hemisphere could be identified by DDL in 67/95 (70.5%) patients which was concordant with handedness in 58/95 (61.1%) patients. While EHIQ could identify dominant hemisphere in 100 (84.7%) which was concordant with handedness in 107/118 (90.7%) patients.

Conclusions: In limited resource where invasive monitoring is not available, however concordance of investigations with seizure semiology could be achieved in up to (61.9%). This finding would pave the way for surgical treatment of this group of patients. DDL lateralize dominant hemisphere in only 70.5% of patients, therefore another modality might be needed.

Abstract Number: 927

Title: Prevalence of epilepsy in Rural Gujarat in India

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Purpose: To find the prevalence of epilepsy in the rural community of Anand district [Gujarat state] in India. To assess treatment-seeking behaviour, epilepsy care and seizure control.

Method: A cross-sectional two step survey-based study was conducted across 10 villages in the district. Initially a door-to-door survey, using trained health care workers, utilizing pre-designed pre-validated questionnaire was done to identify patients with seizures. The screened-positive [suspect] individuals were evaluated by physician by doing medical camps in the villages. Absentees were evaluated by house visit. The cases were reviewed by neurologist to confirm the diagnosis. A validated structured questionnaire was used to collect demographic details, diagnosis treatment seeking behaviour, seizure control, cost and details of therapy.

Result: Of 5590 households surveyed, [total population 25858] 18896 were adults [9158 male]. 81 persons were screened positive by questionnaire, out of which 59 [38 males] [mean age 39.8 years] people were confirmed to have epilepsy, 16 were false-positive [syncope /PNES] while 6 had inadequate information. The mean duration of epilepsy was 9.7 years (SD=9.4, SE=1.22). Amongst these, only 9 were seizure free for >1 year. 33 had >1 seizures in the last month. 13 required hospitalization for seizures in the last year. The mean cost of treatment was Rs 463/ month [Rs 5351 yearly]. 17 took treatment from private hospital,9 from trust hospital and none from a government hospital. 33 patients did not seek formal treatment. Only 2 patients had an EEG before, 57 patients underwent no investigation. Only 14 of 59 were taking regular anti-seizure drugs. Conclusions: Prevalence of epilepsy is 31.2/10000 in rural Gujarat. Major gaps in seeking health care, investigation and treatment of seizures with poor seizure control were found in the study population.

Abstract Number: 961

Title: Epilepsy education via Hausa-language radio broadcasts: a key component of Bridging the Childhood Epilepsy Treatment Gap in Africa (BRIDGE) project

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Purpose: Enhance community epilepsy education and enrolment in the first non-inferiority cluster randomized clinical trial (cRCT) of task-shifted epilepsy care to community health workers (CHWs) versus physician epilepsy care.

Method: Prior to launching enrolment in a cRCT in three cities in northern Nigeria (Kano, Kaduna, and Zaria), a community epilepsy education and awareness campaign, featuring weekly radio broadcasts in the local language (Hausa) were produced and broadcast for four consecutive weeks. The single over-riding communication objective of the broadcasts was to emphasize that seizures and epilepsy, often undiagnosed and untreated, are treatable with medication, and screening and diagnosis of epilepsy is available via the BRIDGE project. The radio broadcasts featured questions from mothers of children with answers from a panel of physicians with epilepsy expertise. Local government and health system leaders were informed of the cRCT prior to the radio broadcasts.

Result: BRIDGE investigators planned to enroll about 1530 children over 24 months. Following the radio broadcasts, a large number of parents of children with possible epilepsy contacted the study sites at community-based primary healthcare centres (PHCs). The BRIDGE enrolment target was increased to 1800 children, an enrolment goal achieved in approximately 12 months.

Conclusions: Epilepsy educational programs utilizing radio broadcasts in a local language are an effective tool for both education and community engagement, and seemed to play an important role in meeting enrolment goals in a large cRCT in northern Nigeria. [Funding: Fogarty International Centre and National Institute of Neurological Disorders and Stroke, NIH (R01 NS113171).]

Abstract Number: 1194

Title: The ketogenic diet for epilepsy in Africa: a solution with its own problems

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Purpose: The ketogenic diet has become a staple recommendation in refractory epilepsies. However, implementation in resource-limited countries remains challenging. This work reviews the literature on ketogenic diet implementation in Africa in order to find limiting factors to its initiation and success.

Method: We searched key words such as “ketogenic”, “diet”, “epilepsy” in medical databases (e.g., Medline and Embase). We also included geographic regions: “Africa”, “Algeria”, “Angola”…entering each African country individually. Two independent reviewers screened abstracts for pertinence. Out of a total of 56 papers, only 22 concerned the subject of ketogenic diet proper. After further cropping, only 8 papers were of pertinence to our subject.

Result: There were only 5 countries in Africa (9%) with published data on ketogenic diet implementation in patients with epilepsy.
Only one study (13%) entailed a clinical trial conducted in Africa. One paper (13%) described a first-time implementation in a patient. Two papers (25%) reported the experience of a tertiary-level children’s hospital. A paper (13%) was published on the activities of a humanitarian association focusing on dietary therapeutics for epilepsy. All the studies reported seizure remission or a reduction in seizure frequency. However, in one study, adherence proved to be challenging.

Limited means and access to healthcare have made implementation difficult. Many countries lack neurologists. The International League Against Epilepsy (ILAE) Task Force on Dietary Therapy had to convene in 2014 for this very reason to find solutions to the problem.

Conclusions: The ketogenic diet is a feasible therapeutic armament in epilepsy management, and dedicated efforts should be made to implement its use in epilepsy in African countries.

Abstract Number: 1210

Title: A report on Electroencephalographic (EEG) Study in Neonatal Seizure Cases

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Purpose: Recording EEG (electroencephalography) in a neonate has some special consideration. This test is usually done to rule out seizure and structural damages. The maturational process is progressive and changes occur with increase of gestational age. Identification of maturational patterns from the dysfunctional and seizure patterns is very important.
Aim of the study is to review normal EEG patterns in wake and sleep state at different gestational age and electrographic features in neonates presented with neonatal seizure.

Method: We have complied retrospectively 164 EEG neonatal recordings from our registry. Study period was from January'18 to June'19. The clinical presentations, birth related informations and EEG findings were correlated. Data was analyzed using SPSS software, version 17.

Result: Among total 164 neonates there was male preponderance (62.5%). The majority was born at term (86.6%) in hospital; about 60% was delivered by caesarean section. Home delivery was reported in 19%. The common reasons for EEG advice were definite seizures (42.68%), jerky movement (22%) and inconsolable crying (18%). The EEG findings were categorized as epileptiform discharges in 45.3%, focal train of activity in 18.3% and majority of the records, 55% were normal.

Conclusions: Typical epileptiform discharges are not a common feature in neonatal recording and there are other markers for identifying cerebral dysfunction and seizure disorder. As most of the seizures were subtle in nature, EEG was helpful for early case detection.

Abstract Number: 1220

Title: Experiences of infantile spasms management in a limited resource institution

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Purpose: While the standard treatment for infantile spasms is adrenocorticotropic hormone, oral steroids and vigabatrin, some institution utilizes other treatment due to unavailability of the standard treatment. Here, we aimed to compare the treatment and phenotypic features of patients with infantile spasms with and without hypsarrythmia in a limited resource institution.

Method: A retrospective study was conducted using medical records of patients with suspected infantile spasms who underwent EEG recording between January 2020 to March 2021 in Dr. Sardjito Hospital, a tertiary referral hospital for Yogyakarta and southern part of Central Java provinces, Indonesia.

Result: We involved 17 clinically suspected infantile spasms, with 11 males and 6 females. Mean of age of onset was 3.8±4.5 months. Seventy percent (12/17) of confirmed infantile spasm patients had hypsarrythmia. The incidence of hypsarrythmia was not significantly associated with sex, mean age and preexisting developmental delay or epilepsy (p>0.05). Although all patients underwent a basic metabolic screening test, however, no patients had an amino acid and organic acid screening test due to facility and financial constraint, neither genetic test. All patients underwent a MRI examination. Most patients received valproic acid (58.8%) and phenobarbital (52.9%), while the remaining patients had other antiepileptic drug, including clonazepam, levetiracetam and phenytoin. All infants did not receive pyridoxine. Moreover, 9/17 (52.9%) patients had oral prednisone. Although not statistically significant (p=0.131), infants with hypsarrythmia were tend to receive prednisone with the OR of 8.0 (95% CI=0.66-97.32)

Conclusions: Here, we show the management of infantile spasms in a limited resources institution, revealing that the infants with hypsarrythmia were more likely to receive prednisone. It implies that the procurement of the standard treatment for infantile spasms in limited resources institution is necessary and important to improve long-term neurodevelopmental outcome

Abstract Number: 1309

Title: Late onset Lafora disease presenting as ictal hypersalivation

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Purpose: Lafora disease is an autosomal recessive genetic disorder which forms a part of progressive myoclonic epilepsy complex. It generally presents in childhood or adolescence and is characterized by myoclonic jerks along with other seizure types and progressive cognitive decline ultimately leading to death. We describe an atypical case of Lafora disease from India.

Method: A 26 year old female presented in Psychiatry with episodes of altered awareness with excessive salivation. She was referred to Neurology for evaluation of organic cause for it. History revealed episodic hypersalivation, GTCS and myoclonic jerks for last 2 years which had been increasing in frequency. Also, there had been a steady decline in her cognitive domains with behavioural changes for last 1 year. She was evaluated accordingly for progressive myoclonic epilepsy

Result: 1.5 Tesla MRI did not show any structural abnormalities. EEG was suggestive of generalized slowing without any focal epileptiform activity. Axillary skin biopsy was performed, in which, cytoplasm of lining epithelial cells showed PAS positive granular material suggestive of Lafora bodies. Considering her being in reproductive age group, patient was started on Levetiracetam with partial relief in her seizure episodes. She was also counselled as a part of behavioural therapy and occupational therapy. She is planned to be in regular follow-up for periodic EEG monitoring to look for any focal (temporal/occipital) epileptiform activity appearing in future.

Conclusions: Lafora disease is a disease of childhood but can present in late adolescence/ early youth too. Apart from classical myoclonic jerks and GTCS, there can be other presentations too including ictal hypersalivation which is a feature of temporal lobe epilepsy. Meticulous history and examination are must for proper diagnosis and management for all such cases.

Epilepsy in the Elderly

Abstract Number: 322

Title: A real-world study of perampanel as treatment of seizures in elderly

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Purpose: The management of epilepsy in the elderly is challenging, and clinical data about the newer antiseizure medications (ASMs) in this population are limited. The aim of this retrospective, multicentre study was to evaluate the effectiveness, tolerability and safety of perampanel given as adjunctive treatment of seizures in elderly patients according to routine clinical practice.

Method: Patients aged ≥65 years who were prescribed to adjunctive perampanel at 12 Italian epilepsy centers and were on stable treatment with ≥1 ASM were retrospectively identified. Data on seizure occurrence, adverse events (AEs), and drug withdrawal were collected. The main endpoints were seizure response (≥50% reduction in baseline monthly seizure frequency) and seizure freedom. The rates of treatment withdrawal and AEs were assessed. Subgroup analyses by concomitant ASMs and comorbidities were performed.

Results: The study cohort comprised 92 patients with a median age of 69 (66-73) years. Perampanel was added to a median of 2 (1-2) concomitant ASMs. The median dose of perampanel at 12 months was 6 mg/day. At one year from starting treatment, 53 (57.6%) patients had a ≥50% reduction in baseline seizure frequency and 22 (23.9%) were free from seizure from at least the six preceding months. There were more responders to perampanel among patients who were concomitantly taking non-enzyme-inducing ASMs than in those taking enzyme-inducing ASMs. Treatment discontinuation occurred in 20 (21.7%) patients. The most common AEs included irritability (8.7%) and somnolence (4.3%). The risk of behavioral and psychiatric AEs was higher in patients with history of psychiatric comorbidities, whereas there were no differences according to concomitant administration of levetiracetam and presence of cognitive impairment.

Conclusions: Perampanel given as adjunctive treatment in a real-life setting improved seizure control and was associated with a favorable tolerability profile in a cohort of elderly patients with epilepsy.

Abstract Number: 449

Title: Prescribing trends in elderly with epilepsy

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Purpose: Elderly with epilepsy are the population with the highest incidence of epilepsy. Antiseizure medications (ASMs) are usually lifelong treatment for epilepsy in elderly and should be selected according to

their individual needs concerning their age-dependant physiological changes, health condition and comorbidities. The aim is to evaluate the prescribing trends of ASMs for elderly with epilepsy.

Method: 64 elderly with epilepsy with seizure onset over the age of 65 years, 34 males, 30 females were evaluated concerning ASMs prescription.

Result: Most prescribing ASM was carbamazepine (CBZ) from the first generation ASMs, and lamotrigine (LTG) from the second generation ASMs, as both are effective for focal epilepsy treatment although LTG and gabapentin (GBP) are evidence-based recommended treatments for epilepsy in the elderly. Most of the elderly with epilepsy, 45 of them were treated with monotherapy, 29 of them were treated with first generation ASMs and only 16 with second generation ASMs. 19 elderly with epilepsy were treated with combination of two ASMs, seven of them with fist generation ASMs, 2 of them with second generation ASMs, usually LTG and LEV and 10 elderly with epilepsy were treated with combination of first generation and second generation ASMs. Despite the better pharmacokinetic profile of newer generation of ASMs, that are better option for treatment of epilepsy in elderly, the trend of prescribing first generation of ASMs dominates still. Newer generation ASMs are prescribed for only one third of elderly with epilepsy. There is a warning for the use of LTG, oxcarbazepine as some adverse effects may affect safety of elderly and opinions that levetiracetam, lacosamide, eslicarbazepine are effective for epilepsy in elderly, but it takes time updating evidence-based recommendations.

Conclusions: Increasing the awareness for selecting appropriate ASMs, concerning age-related needs for treatment of epilepsy in the elderly will improve their health care.

Abstract Number: 675

Title: People With Epilepsy Face Ageism in Getting Specialist Care

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Purpose: The second National Audit of Seizure management in Hospitals (NASH2) in 2013 identified that older people were less likely to be referred to specialist services following an emergency seizure presentation. Here, we report the third round (NASH3) to assess whether that issue remains.

Method: NASH3 assessed the prior, immediate, and onward care of adult patients attending Emergency Departments with seizures across the UK. Sites provided anonymous data on 30 consecutive cases via a web-based database during 2018. A logistic regression model was used to assess the relative factors associated with accessing care from a specialist, both prior to their presentations and on their subsequent referral.

Result: 3,030 presentations across 125 sites in England (median age = 44 (IQR 28 to 60), 53% male) were analysed. Of the 2,212 (73%) with an existing diagnosis of epilepsy, the likelihood of being under specialist care prior to the emergency presentation reduced over 4 age groups (age >60 *vs* age <30: OR 0.41, p<0.001) with a similar pattern of referral to neurology post seizure (age >60 *vs* age <30: OR 0.69, p=0.018). Other demographic characteristics, including gender and socio-economic deprivation, had no effect. Presence of a co-morbidity reduced onward specialist referral (OR 0.76, p=0.016), but the age effect persisted even with this control. For the 818 (27%) with a suspected first seizure the age effect on referral was also significant (age >60 vs age <30: OR 0.38, p<0.001) – despite the national guideline indicating referral within 2 weeks.

Conclusions: 6 years on from the second NASH audit, the results from NASH3 show that age-related inequalities in access to specialist neurology staff have not changed. The reasons behind this are unclear but ensure that older people are continuing to receive an inappropriate level of care.

Funding:
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Abstract Number: 697

Title: EPILEPSY SURGERY IN ELDERLY ADULTS: experience in a spanish center.

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Purpose: epilepsy surgery is a proved effective treatment in properly selected drug-resistant epilepsies (DRE). The objective of this study is to assess the efficacy of epilepsy surgery and neuropsychological results in adults over 50 years old at our center.

Method: patients with DRE over 50 years old who have undergone surgery in a period of 10 years (2009-2019) in our hospital have been selected. A retrospective analysis of the results in terms of seizure control, complications and neuropsychological results was carried out after a minimum follow-up of one year.

Result: 20 patients (55% women) were identified with a median age of 55 years old at the moment of surgery. They had a long-standing refractory epilepsy with a mean evolution time of 40 years. All patients had a lesion in neuroimaging with a predominance of mesial temporal sclerosis (65%). An anterior temporal lobectomy with amigdalohypocampectomy was performed in 85% of cases. An Engel I was achieved in 70%, an Engel II in 15%, and an Engel III in 15%. Therefore, 85% of patients achieved a satisfactory surgical result (Engel I + II). 10% of cases presented an early and transitory post-surgical complication, and 20% presented a mild persistent complication. We have postoperative neuropsychological evaluation in half of the patients, of which 40% presented worsening in verbal memory and 10% in visual memory. 40% presented improvement in some of the evaluated cognitive functions.

Conclusions: epilepsy surgery in older adults (≥50 years) is an effective treatment and with an acceptable complication rate. An exhaustive neuropsychological study and assessing the cognitive implications in decision making is mandatory.

Abstract Number: 728

Title: Late onset epilepsy in cerebral amyloid angiopathy patients: a case control study.

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Purpose: Sporadic cerebral amyloid angiopathy (CAA) is characterized by amyloid deposition in the walls of leptomeningeal and cortical arteries, arterioles of the central nervous system (1). To date, epileptic seizures at CAA onset have rarely been reported and its prevalence is unknown. In reason of the high frequency of CAA in

the elderly population and of the expected epileptogenic role of cortical hemorrhagic lesions, it may be hypothesized that CAA can explain a proportion of late-onset epilepsies with unknown etiology. This study aims to assess the possible correlation between CAA and late onset (>55 years) epilepsy.

Method: We have consecutively included patients with late-onset epilepsy (defined as seizure onset after 55 years) and age-matched controls who underwent brain MRI for reasons different from epileptic seizures. All subjects underwent 1.5 Tesla MRI including: axial T1-weighted, T2-weighted, 3D fluid-attenuated inversion recovery (FLAIR), DWI images, Gradient-echo and/or SWI images. In patients with epilepsy, MRI has to be performed within 30 days from epilepsy onset. In order to evaluate differences between groups, Chi-squared test is performed.

Result: To date, we have included 20 patients with late onset epilepsy (15 males, mean age 73 ± 8 years) and 44 age-matched controls (15 males, mean age 69 ± 8 years). CAA is significantly more frequent (p=0.01) in patients with late onset epilepsy (4/20) than in controls (1/44).
Conclusions: These preliminary data demonstrate that CAA is more frequent in patients with late onset epilepsy than in age-matched controls.

References: Weber SA, Patel RK, Lutsep HL. Cerebral amyloid angiopathy: diagnosis and potential therapies. Expert Rev Neurother. 2018 Jun;18(6):503-513. doi: 10.1080/14737175.2018.1480938.

Abstract Number: 1359

Title: New onset seizures beyond sixties - Sexagenarians to Nonagenarians !

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Purpose: The rapid growth in elderly population worldwide parallels the rise in new onset seizures in elderly population and also forms the second most common leading cause of mortality and mortality. The study has aimed to assess the clinical characteristics and outcome of new onset seizures beyond sixty years of age.

Method: The study was conducted in Sree Chitra Tirunal institute of medical sciences and technology, Trivandrum, Kerala, obtaining data from electronic medical records from January 2010 to December 2020. The entire study population was divided into four groups consisting of Sexagenarians - Group A (60-69 years), Septuagenarians - Group B (70-79 years), Octogenarians - Group C (80-89 years) and Nonagenarians - Group D(>90 years). The data was analysed using appropriate statistical methods.

Result: A total of 311 patients consisting of 65.9% males were included in the study. 49.8% belonged to Group A, 25.7% to Group B, 18.6% to Group C and 5.7% to Group D. Focal seizure (55.5%) was the most common seizure type and focal motor with impaired awareness (45.5%) was its common subtype. The majority (65.3%) presented with localisation related epilepsy syndrome. Overall, post stroke seizure was the most common etiology of seizure presenting in 34.7% individuals. Imaging was corroborating in 57.5% and specific EEG abnormality was identified in 39.2% patients. The all cause mortality of individuals presenting with new onset seizure was 13.8%.

Conclusions: New onset seizures in elderly population are unique in their way of presentation, response to treatment and outcome in its own way. Hence, clinical context must be judged judiciously in order to avoid both over-treatment and under-treatment.

Epilepsy Surgery

Abstract Number: 67

Title: Outcomes of drug - resistant epilepsy surgery

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Purpose: To determine the outcomes of drug - resistant epilepsy (DRE) surgical treatment.

Method: A retrospective analysis of medical data from 43 patients who underwent presurgical evaluation for DRE at Epilepsy center of Hospital of Lithuanian University of Health Sciences Kauno Klinikos has been done. Nineteen patients were operated. Data of operated patients was analyzed according to etiology of epilepsy: hippocampal sclerosis group (HSG) and other etiology group (OEG). Epilepsy duration before operation, severity and frequency of seizures before and after surgery, time and recurrence of seizures after surgery were analyzed between groups.

Result: Mean duration of DRE before surgical treatment was 14.4 ± 8.6 years. Epilepsy duration prior to surgery was 18.3 ± 6.9 years in HSG and 9.1 ± 8.1 years in OEG ($p < 0.05$). During follow-up period (from 1 to 46 months) after surgical treatment 12 (63.2%) subjects were seizure free and 7 (36.8%) had recurrence of seizures: 3 (27.3%) in HSG and 4 (50.0%) in OEG ($p>0.05$). Seizures recurred after 18.3 ± 22.9 mth. in HSG and after 0.8 ± 1.5 mth. in OEG ($p>0.05$). After surgical treatment there was a reduction of severe and very frequent (≥1 per week) seizures in whole group of operated patients and HSG ($p < 0.05$), there was no significant seizure reduction after surgery in OEG.

Conclusions: The delay from onset of epilepsy to surgical treatment was very long and even longer for patients with hippocampal sclerosis. Time period from surgery to recurrence of seizures in HSG was longer than in OEG. Epilepsy surgery was effective in major proportion of patients with DRE, especially in hippocampal sclerosis patients.

Abstract Number: 110

Title: Epilepsy surgery in children with minimal presurgical video-EEG monitoring

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Purpose: Epilepsy surgery can potentially cure drug-resistant epilepsy, but careful presurgical evaluation is vital to select patients who will profit from such an intervention. Many epilepsy surgery programs offer extensive presurgical evaluation including several days of video EEG monitoring. Non-lesional epilepsy cases are rare upon epilepsy surgery patients. We therefore set up a lesion-orientated pediatric epilepsy surgery program for patients with clearly localized lesions that involved only minimal presurgical diagnostics, particularly with max. 48 hours of non-invasive EEG monitoring that did not necessarily include ictal EEGs.

Method: We evaluated retrospectively the outcome of patients who were operated within our epilepsy surgery program with respect to seizure freedom and cognition.

Result: Of 135 patients evaluated for epilepsy surgery, 36 children and adolescents underwent a resective procedure at a mean age of 8.37±4.7 years (range 0.35-18.78). The most frequent surgery was a

hemispherotomy. Overall seizure freedom was 73.9% after 12 months and 77.8% at a current median observation period of 16.5 months. Seizure frequency was reduced <50% in all other patients. After surgery, IQ values increased slightly from mean 59.87±26.29 to 63.46±28.71. In patients who had lost IQ points after surgery, no developmental regression occurred. These patients developed more slowly than children with an average development speed. Individually they achieved better results than preoperatively or stagnated.

Conclusions: Despite the limits due to the patient selection, our findings highlight the high success rate using a lesion-orientated epilepsy surgery approach with reduced presurgical video EEG monitoring in the pediatric epilepsy population.

Abstract Number: 158

Title: Endoscopic and Radio-frequency Techniques for Hemispherotomy

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Purpose: The authors present their experience with endoscopic hemispherotomy along with its limitations and also describe a new “bloodless” technique for minimally invasive robotic thermocoagulative hemispherotomy (ROTCH).

Method: Endoscopic hemispherotomy (EH) was performed using a robotic guidance as described earlier. For ROTCH: robotic system was used to plan 5 different trajectories: anterior disconnection, middle disconnection, posterior disconnection, corpus callosotomy, temporal stem disconnection, and amygdalar disconnection. Coregistration with O-arm images ensured good accuracy. Radiofrequency ablation was performed at 75°C–80°C for 60 seconds. Surgical procedures were performed with multiple twist drills.

Result: EH: (n=40; males: 42), mean age:8.72±6.41, Seizure frequency/day:8±6.9, for 5.2±4.3years. Number of drugs/patients:4.7±1.6;post-infarct encephalomalacia:14,Rasmussen’s syndrome:7,hemimegalencephaly:7, hemispheric cortical dysplasia:4, post-encephalitis sequelae:2, Sturge-Weber syndrome:1. Mean follow-up 40.16+17.3 months, 4 underwent repeat surgery for residual temporal stem, 36/40(90%) had favorable outcome (ILAE 1&2). Significant improvement seen in secondary outcomes, Blood loss (p=0.02), hospital stay (p=0.049) were less in EH. **ROTCH**: (n= 6) Pathologies: Rasmussen’s encephalitis (n = 2), hemispheric cortical dysplasia (n = 2), posttraumatic encephalomalacia(n = 1), and perinatal insult(n = 1). The mean ± SD (range) age was 6.7 ± 3.6 years(5-10.2 years). Mean seizure frequency: 7.4 ± 5.6 seizures/day. Mean trajectories:15.3 ± 2.5, mean lesions:108 ± 25.8. Mean trajectories/lesions for middle disconnection were 7.1 ± 1.7 and 57.5 ± 18.4, respectively. All but 1 patient had class 1 outcomes according to the ILAE Outcome Scale at follow-up of 13.5 ± 1.6 (12–16) months; one had class 2 outcome. Estimated blood loss < 5 ml. Complications included repeat surgery (after 2 weeks) for a “skip” area (n = 1) and small temporal hematoma (n = 1), which resolved.

Conclusions: EH is an established minimally invasive technique for hemispherotomy while ROTCH appears to be a safe, feasible, and bloodless procedure, with a low morbidity and promising outcomes.

Abstract Number: 190

Title: Combining Intracranial EEG Measures of Brain Connectivity and Excitability to Plan Epilepsy Surgery in Children

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Purpose: Epileptogenicity is a complex brain property depending on both excitability and connectivity. In children with drug-resistant epilepsy (DRE), identifying the epileptogenic zone in the brain can be challenging, even when using intracranial-EEG (icEEG). Here, we propose a novel twofold approach to optimize icEEG interpretation, that is able to quantify both *brain excitability* (via *phase-amplitude coupling*, *PAC*) and *functional connectivity* (*FC*), using interictal data. Our purpose is to develop a new tool to boost icEEG and improve surgical planning in children with DRE, without requiring evocation of seizures.

Method: We studied icEEG from 32 children who had epilepsy surgery at *Boston Children's Hospital* (21 became seizure-free). Figure1A-B shows how, for each electrode, we computed measures of excitability (PAC) and connectivity (through FC and graph-analysis). We quantified the ability of each individual measure to identify the brain tissue resection that predicts seizure-freedom (*Fisher's-exact-test*). Finally, we designed a *fuzzy-inference-system* that combined connectivity and excitability measures into one "*epileptogenicity-index*" (Figure2A). We tested whether our *fuzzy-inference-system* predicted postsurgical outcome -based on each patient's resection- and compared it with support vector machine (SVM).

Result: We found that removing the tissue identified by our *fuzzy-inference-system* as the 'most epileptogenic' predicted postsurgical outcome with 88% accuracy (p-value<0.001), outperforming SVM (which presented 66% accuracy and failed to predict poor outcome), as shown in Figure2B. Using individual measures of FC and PAC, we predicted outcome with a maximum accuracy of 75% (p-value<0.05). Table1 shows PAC and FC measures that were higher inside than outside the resection in seizure-free patients only (*Wilcoxon-signed-rank*).

Conclusions: We proposed an innovative methodology that predicts a patient's post-surgical outcome based on novel icEEG characteristics (beyond typical identification of epileptiform discharges). This may provide the surgical team with a complementary tool to assess resection strategies and estimate prognosis, which is independent of interictal or ictal discharges.

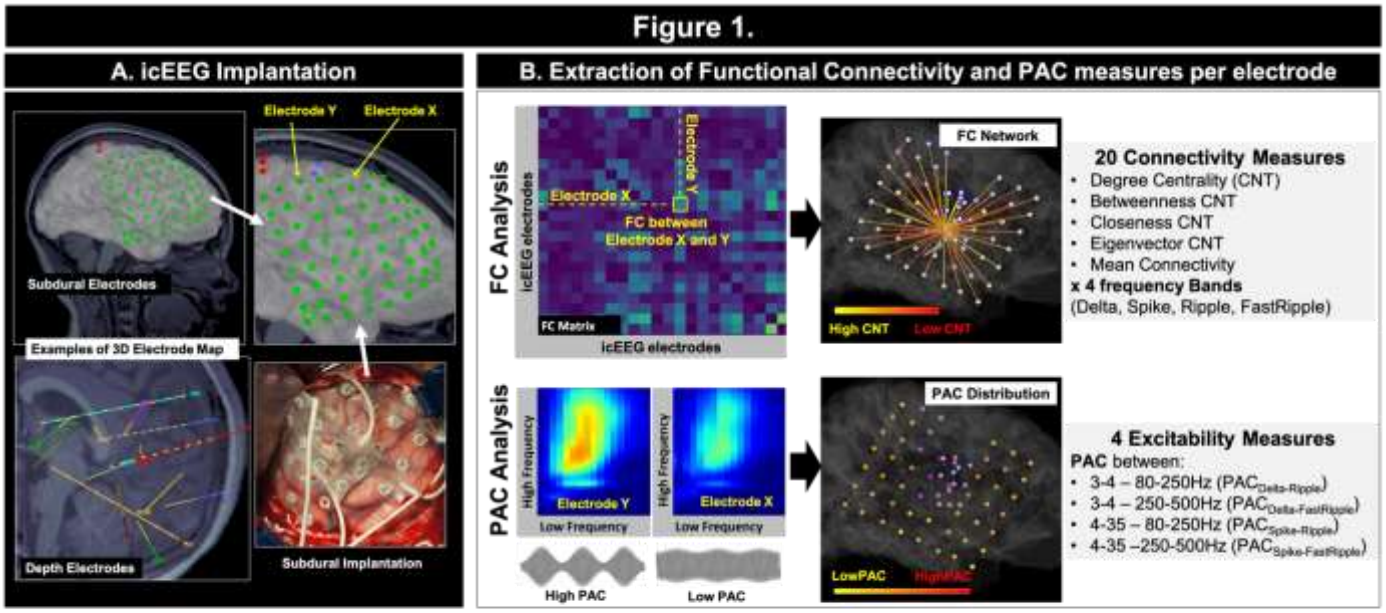

Figure 1. A) Examples of icEEG electrodes (subdural or depth) and their 3D reconstruction in the patient's MRI space. **B)** Overview of the proposed pipeline for the extraction of several icEEG measures of brain connectivity (functional connectivity, FC) and excitability (PAC) from each icEEG contact.

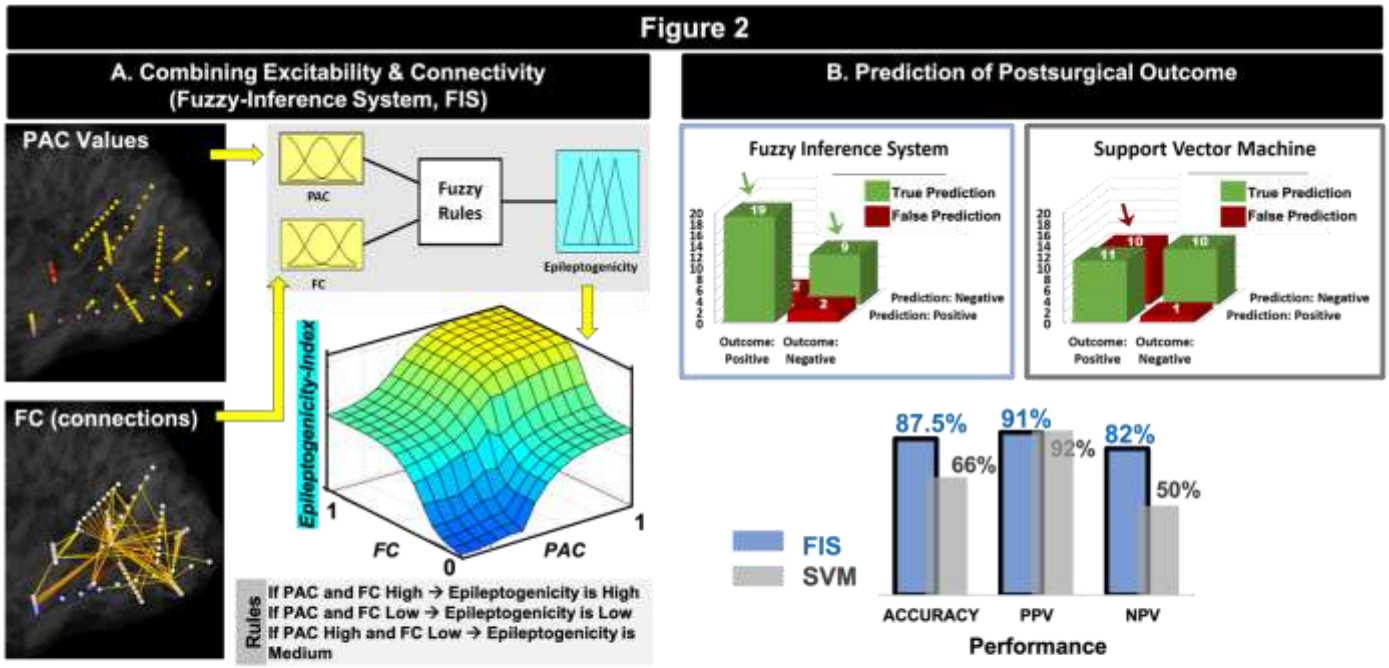

Figure 2. A) Overview of the design of our *fuzzy-inference-system*, which takes as inputs one measure of FC and one measure of PAC per electrode and computes an overall «Epileptogenicity-Index» (based on three fuzzy-rules). The spatial distrubution of this index across electrodes and its overlap with resection was used to predict patient's post-surgical outcome. **B)** Outcome prediction performance of the proposed unsupervised fuzzy-inference-system (FIS, light blue) compared to a supervised support vector machine (SVM, in grey). While the FIS predicts both positive and negative outcome with very high performance (91% and 82%), SVM fails to predict negative outcome (50%).

	Table 1. Comparison Inside vs. Outside Resection (*Wilcoxon sign-rank test**)		
	icEEG Feature	Sz-free (n=21)	Not Sz-free (n=10)
PAC	$PAC_{3-4/80-250Hz}$	p=0.001	p=0.232
	$PAC_{4-35/80-250Hz}$	p<0.001	p=0.375
	$PAC_{4-35/250-500Hz}$	p=0.011	p=0.232
FC	Degree $CNT_{80-250Hz}$	p=0.007	p=0.846
	Degree CNT_{4-30Hz}	p=0.028	p=0.625
	Betweenness CNT_{4-30Hz}	p=0.004	p=0.922
Sz: Seizure; CNT: Centrality			

Abstract Number: 275

Title: Hypothesis: Decrease of mesial temporal sclerosis due to vaccination against Haemophilus influenza?

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Purpose: The number of temporal lobe epilepsy surgeries declined in the last two decades despite high-class evidence of its efficacy and expert advice. Several studies reported a decrease because of a rarefication of patients with mesial temporal sclerosis (MTS). Since the etiopathogenesis of MTS has remained elusive yet, it is particularly challenging to explain its decrease over time. Here, we propose the hypothesis that the vaccination programs to eradicate Haemophilus influenza (HI) may be the cause.

Method: Search of the literature for incidence and prevalence of MTS and HI between 1970 and 2020. Evaluation of the main pathogenic concepts of MTS. Attempt to correlate the decline of MTS with the decrease of HI.

Result: The etiopathogenesis of MTS is not clear. An infectious, especially viral, origin has suspected among other factors. However, the results of PCR studies for herpesviridae yielded inconsistent results. Independent of these considerations, the incidence and prevalence of MTS declined from 1990 to 2008 although the prevalence of viral infections did not decrease at the same rate. HI vaccination programs started in 1986 in the US and Europe in order to prevent early infantile meningoencephalitis and reduce clinically asymptomatic/subclinical HI transmission. If one suspects that exposure to HI may cause MTS by a subacute to chronic postinfectious autoimmune process of several years, then the decline in MTS would just start some years after the start of immunization and then parallel the reduction of HI meningoencephalitis incidence what in fact is the case.

Conclusions: There is a clear temporal association of declining MTS incidence and reduction of HI meningoencephalitis after the initiation of vaccination programs at the mid/end 1980ties. However, this association does not prove a causative relation. Further epidemiological, immunological and neuropathological studies may either support or reject the hypothesis presented.

Abstract Number: 284

Title: Outpatient vagus nerve stimulation surgery in patients with drug-resistant epilepsy with severe intellectual disability

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Purpose: Vagus nerve stimulation (VNS) implantation is increasingly proposed in outpatient procedure. Some epilepsy syndromes are associated with severe neurodevelopmental disabilities (intellectual disability, autism) and often motor or sensory handicaps, making ambulatory surgery more complex.

Method: We prospectively assessed the feasibility and safety of outpatient VNS implantation in 26 adult patients with drug-resistant epilepsy with severe intellectual disability between December 2017 and October 2020 at the Pitié-Salpêtrière University Hospital (Paris, France).

Results: The male-to-female ratio was 0.9 and the mean age on surgery day was 23.1 years. Seventeen patients (65.4%) suffered from epileptic encephalopathy, 7 (26.9%) from cryptogenic or genetic generalized epilepsy, and 2 (7.7%) from severe multifocal epilepsy. Postoperatively, all patients were discharged the day of surgery. No patient was admitted to a hospital or have consulted within one month due to postoperative complications. There was no surgery-related complication during patients' follow-up. Out of 22 guardians, 77.3% were very satisfied and 22.7% were satisfied with the outpatient management.

Conclusion: Our study highlights safety and feasibility of VNS surgery in an outpatient setting among 26 patients with severe intellectual disability. Developmental disability or associated multiple handicaps should not be an exclusion criterion when considering ambulatory VNS implantation. Development of this outpatient procedure makes it possible to offer VNS surgery to more patients in this particular group whose families may be reluctant to traditional hospitalization in the neurosurgery department.

Abstract Number: 286

Title: Intraoperative Ultrasound Shear-Wave Elastography in Focal Cortical Dysplasia Surgery

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Purpose: Previous studies reported interest in intraoperative shear-wave elastography (SWE) guidance for brain-tumor and epilepsy surgeries. Focal cortical dysplasia (FCD) surgery is one of the most appropriate indications for using SWE guidance. The aim of this study was to evaluate the efficacy of ultrasound SWE techniques for the intraoperative detection of FCDs.

Method: We retrospectively analyzed data from 18 adult patients with drug-resistant epilepsy associated with FCD who had undergone SWE-guided surgery.

Results: Conventional B-mode images detected FCD in 2 patients (11.1%), while SWE detected FCD in 14 patients (77.8%). The stiffness ratios between MRI-positive and -negative cases were significantly different (3.6 ± 0.4 vs. 2.2 ± 0.6, respectively; $p < 0.001$). FCDs were significantly more frequently detected by interoperative SWE in women (OR 4.7, 95% CI (1.7–12.7); $p = 0.004$) and in patients in whom FCD was visible on magnetic

resonance imaging (MRI; OR 2.3, 95%CI (1.3–4.3); p = 0.04). At 1 year after surgery and at last follow-up (mean = 21 months), seizure outcome was good (International League Against Epilepsy (ILAE) Class 1 or 2) in 72.2% and 55.6% of patients, respectively.

Conclusion: Despite some limitations, our study highlighted the potential of SWE as an intraoperative tool to detect FCD. Future technical developments should allow for optimizing intraoperative surgical-cavity evaluation from the perspective of complete FCD resection. Interobserver reliability of SWE measurements should also be assessed by further studies.

Abstract Number: 291

Title: Vagus nerve stimulation improves psychomotor functions in patients with severe drug-resistant epilepsy

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Purpose: Patients with severe drug-resistant epilepsy suffer from psychomotor disorders. Our study aimed to assess psychomotor outcome after vagus nerve stimulation (VNS) in this population.

Method: We prospectively evaluated psychomotor functions in 17 adult patients with drug-resistant epilepsy who were referred for VNS at the Pitié-Salpêtrière University Hospital (Paris, France) between October 2017 and March 2018. Psychomotor functions were examined, in the preoperative period and at 12 months post-surgery, by a psychomotor therapist using a full set of the following specific tests: theRey–Osterrieth complex figure (ROCF) test, the Zazzo's cancelation task (ZCT), the Piaget-Head test and the paired images test.

Results: Age at VNS surgery was 29 +/- 6.7 years and the female/male ratio was 2.4. 11 patients had epileptic encephalopathy and 6 had multifocal epilepsy. At 12 months post-surgery, Piaget-head scores increased by 3 percentage points (p=0.008) compared to the baseline. Performances were also improved for ROCF test both in copy (+2.4 points, p=0.001) and recall (+2.0 points, p=0.008) tasks, for the efficiency index of ZCT both in single (+25.1 points, p=0.005) and dual (+15.1 points, p<0.001) tasks, and for the paired images test (+0.14 points, p=0.03). 76.5% of patients achieved a ≥50% seizure frequency reduction at 12 months. The median percent seizure reduction was 60%. Quality of life was improved in 88.2% of patients.

Conclusion: Patients with severe drug-resistant epilepsy treated by VNS experienced improved performance on global psychomotor functions and, more selectively, in assessments exploring perceptual organization and visuospatial memory (ROCF test), laterality awareness (Piaget-Head test), sustained attention, concentration, visual scanning (ZCT), inhibition, and impulsivity (paired images test).

Abstract Number: 444

Title: Comparison of the real-world effectiveness of vertical versus lateral functional hemispherotomy techniques for pediatric drug-resistant epilepsy

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Purpose: Surgical technique is an important modifiable factor that may impact postoperative seizure outcomes following hemispheric surgery for drug-resistant epilepsy. Our goal was to determine whether the vertical parasagittal approach or the lateral peri-insular/peri-Sylvian approach to hemispheric surgery is associated with superior rates of long-term seizure freedom.

Method: We analyzed data for 702 participants who underwent a vertical parasagittal, lateral peri-insular, or lateral peri-Sylvian hemispherotomy. Time to seizure recurrence was assessed using Kaplan-Meier survival analysis with log-rank test. Multivariate mixed-effects regression models controlling for technique and HOPS score determined independent predictors of time to first postoperative seizure and covariates independently associated with seizure freedom.

Result: Seventy-four participants (10.5%) underwent vertical parasagittal hemispherotomy and 628 (89.5%) underwent lateral peri-insular or peri-Sylvian hemispherotomy. The probability of seizure freedom for the entire hemispherotomy cohort was 89.1% (95% CI=86.4-91.3%), 74.4% (95% CI=69.9-78.4%), and 62.4% (95% CI=53.5-70.2%) at 1-, 5-, and 10-years, respectively. The probability of seizure freedom at 1-year follow-up was 89.2% (95% CI=86.3-91.5%) for the lateral cohort and 88.8% (95% CI=78.9-94.3%) for the vertical cohort. At 5- and 10-year follow-up, seizure freedom for the vertical subgroup persisted at 85.5% (95% CI=74.7-92.0%), whereas it decreased in the lateral subgroup to 72.1% (95% CI=66.9-76.7%) and 57.2% (95% CI=46.6-66.4%), respectively. Vertical hemispherotomy was associated with more durable seizure-free progression (p=0.01). Additionally, the lateral subgroup had a shorter time-to-seizure recurrence (HR=2.56; 95% CI=1.08-6.04; p=0.03) and increased seizure recurrence odds (OR=3.67; 95% CI=1.05-12.86; p=0.04).

Conclusions: The vertical hemispherotomy technique demonstrated greater durability of seizure freedom compared to lateral peri-insular or peri-Sylvian techniques. Further studies are required to determine whether the vertical approach provides superior long-term seizure outcomes.

Abstract Number: 448

Title: Comparing VNS and resective surgery outcomes in patients with epilepsy with and without autism: a population-based study

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Purpose: Autism and epilepsy commonly co-occur. Understanding trends in healthcare utilization and hospital outcomes in patients with autism and epilepsy can help optimize care. We compared hospital outcomes amongst patients undergoing VNS and resective/disconnective surgery with autism and epilepsy to those with epilepsy alone.

Method: Elective admissions amongst patients with epilepsy alone and co-occurring autism and epilepsy were identified in the 2003-14 National Inpatient Sample (NIS). The NIS is the largest US all-payer nationally representative database and includes patients and hospital level variables. Two cohorts were examined: one patient with co-occurring epilepsy and autism was matched to three epilepsy patients without autism for age, sex and 1) VNS and 2) resective/disconnective surgery. Differences in discharge status, in-hospital mortality, mean length of stay (LOS), cost and surgical/medical complications were examined. Multinomial logistic regressions were performed to examine the outcomes of interest in persons with comorbid autism and epilepsy to persons with epilepsy alone.

Result: The following cohorts were identified: 1) VNS-52 hospital admissions in persons with comorbid autism and epilepsy (mean age:12.79±1.03; 19.27% female) and 156 matched controls with epilepsy alone (mean age:12.84±0.71; 19.31% female); 2) resective/disconnective surgery-113 with comorbid autism and epilepsy (mean age:12.99±0.84; 24.55% female) and 339 matched controls with epilepsy alone (mean age:13.37±0.68; 23.86% female). Patients with autism and epilepsy who underwent VNS and resective/disconnective surgery showed no differences in discharge status, in-hospital mortality, mean length of stay, mean cost of hospitalisation and surgical/medical complications compared to patients with epilepsy alone.

Conclusions: We have shown the feasibility and safety of epilepsy VNS and resective surgery in those with ASD do not differ with those with epilepsy alone. Contrary to the prevalent concern that epilepsy surgery in patients with ASD may have limited utility, we have found that in-hospital outcomes do not differ from those with epilepsy alone.

Abstract Number: 462

Title: Apparent Diffusion Coefficient As a Novel Predictor of Seizure Outcome after Laser Interstitial Thermal Therapy for Mesial Temporal Lobe Epilepsy

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Purpose: Apparent diffusion coefficient (ADC) is an MRI sequence that delineates pathological processes. ADC may help identify refractory mesial temporal lobe epilepsy (mTLE) patients who may respond better to laser interstitial thermal therapy (LiTT) by highlighting epileptogenic tissues that localize to the mesial temporal region. We sought to determine whether pre-operative ADC intensities in the mesial temporal structures, and the extend of laser ablation of tissues with altered ADC signal are associated with long-term seizure outcome.

Method: Thirty-nine mTLE patients were included in the study. Demographics, clinical, and radiographic data were retrospectively collected. ILAE outcome scale was used to assess seizure outcome, and good outcome was defined as ILAE I and II. For each patient, pre-operative and post-ablation intra-operative T1 sequences were used to generate volumetric segmentation of the target mesial temporal structures (i.e., hippocampus, amygdala, and piriform cortex), final ablation zone, and their mean voxel-wise z-scored ADC intensities.

Result: Mean age at surgery was 36 years and mean follow-up duration was 1.85 years. A total of 31 patients (79%) had evidence of mesial temporal sclerosis. The two outcome groups had similar total ablation volume and proportions of ablated hippocampus, amygdala, and piriform cortex. Good seizure outcome was associated with significantly higher ADC intensities in the mesial temporal structures. Significantly higher pre-operative ADC values of the ablated tissues were associated with good outcome (mean z-scored ADC = 0.009, p = 0.009). There were no difference between the two outcome groups with regard to ADC values of the residual mesial temporal structures following ablation.

Conclusions: Elevated pre-operative ADC in the mesial temporal structures ipsilateral to the seizure onset zone is associated good long-term seizure outcome following LiTT for medically resistant mTLE. ADC may be useful in improving patient selection to enhance LiTT's therapeutic efficacy and durability.

Abstract Number: 470

Title: Utility of Stereo-EEG in the presurgical evaluation of patients with focal epilepsy; our experience over 9 years

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Purpose: In patients with medically refractory focal epilepsy, stereo-electroencephalography (SEEG) can be used to establish surgical candidacy, when non-invasive studies have not been successful in localizing the epileptogenic zone (EZ). We aimed to determine the effectiveness of SEEG in identifying EZ, the number of patients proceeding to surgical resection and the post-operative outcome over a 9 year period.

Method: Between November 2010 and November 2019, 121 patients underwent SEEG implantation at the National Hospital for Neurology and Neurosurgery. Demographics, seizure semiology, results of non-invasive tests (MRI, scalp-EEG, PET, ictal SPECT, MEG), SEEG implantation and analysis, complications and resective surgery outcome were retrospectively collected.

Result: Mean age at time of SEEG was 34.0 ± 9.5 years, 69 patients were male. MRI showed an abnormality in 72 patients (59.5%). 1171 electrodes (mean 9.7 per patient) were implanted. 3 haemorrhages associated with persistent deficit occurred in 2015, following which there was evolution of technique and improved accuracy, and there have been none since. Seizure onset zone was identified in 95 patients (78.5%). 81 patients were considered suitable for surgical intervention with 66 (55%) patients accepting the proposed surgery, and 58

having undergone surgery to date. Within this cohort, 21 patients (32%) were non-lesional. The epileptogenic origin was found most frequently in the temporal lobe (50%), with hippocampal sclerosis being the most common pathological finding (24.2%) and overlapped with results of non-invasive investigations in the majority (PET 58%, Ictal SPECT 65%, MEG 76%). The median follow-up time was 26 months with 31 patients (48%) being seizure free (Engel Class 1).

Conclusions: SEEG is an effective and relatively safe method in identifying the epileptogenic zone in patients where non-invasive investigations have not localised seizure onset, though these can aid implantation strategies. Resective surgery in these patients may lead to seizure freedom in a significant proportion.

Abstract Number: 495

Title: Rapid stimulation cycles of vagus nerve stimulator are associated with a good response in patients with refractory epilepsy.

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Purpose: To assess the efficacy of the vagus nerve stimulator (VNS) in reducing the frequency of seizures, the number of antiseizure drugs (ASDs) and the impact on quality of life at 6 and 12 months and to evaluate the existence of factors associated with a good response.

Method: A descriptive study of patients with refractory epilepsy and VNS was performed. The frequency of monthly seizures, number of ASDs, adverse effects and baseline quality of life at 6 and 12 months, measured by the QOLIE-10 scale, were recorded. The intensity and the stimulation cycle were analyzed in the last follow-up. These variables were compared between responder's (> 50% decrease in seizure frequency) and non-responder's patients.

Result: 41 patients (59% female, mean age 41±12.4 years-old) were included. The mean clinical follow-up time was 4.2 [3-10] years. The monthly frequency of seizures decreased at 6 and 12 months (baseline, 21 [4-60]; 6 months, 10 [1-30]; 12 months, 8 [0-15]; p <0.001). The percentage of responder's patients was 60%. The quality of life improved during follow up (baseline, 37.5 [18.5-57] at 6 months, 45.5 [22.5-75]; and 12 months, 54.5 [40-92]; p <0.001). Rapid cycling was associated with a higher proportion of responders (p=0.05). A longer duration of previous epilepsy or higher frequencies of baseline seizures were not related to a worse response.

Conclusions: VNS was an effective therapeutic tool in patients with drug-resistant epilepsy. Rapid stimulation cycles were associated with a good response.

Abstract Number: 536

Title: COVID-19 Infection in Patients Operated due to Intractable Epilepsy – Very Few Reasons for Serious Consternation

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Purpose: Despite US Centers for Disease Control and Prevention has included epilepsy on a list of conditions that may increase the risk of serious COVID-19 infection, upcoming information suggests there is a low risk of seizures getting worse for most people with epilepsy if they become infected. Data about the course of COVID-

19 infection and potential impact on seizure frequency in a specific group of patients operated due to intractable epilepsy are still missing.

Method: Our study with a cross-sectional design was conducted in March 2021, one year after the first case of COVID-19 infection was reported in the Republic of Serbia. One hundred fifty patients operated on epilepsy in the Clinical Center of Serbia were contacted by phone. Data of interest were collected during phone interview. Twenty-one patients (72%) fulfilled the criteria for confirmed COVID, while 8 patients (28%) were treated as probable COVID according to WHO COVID-19 Case Definition criteria. Sixteen patients (55%) were completely seizure-free since surgery (ILAE class 1a), while 13 patients had seizures despite surgery (45%).

Result: Most frequent complaints were loss of smell (55%), fever (41%), and tiredness (38%). Seven patients were diagnosed with bilateral pneumonia (24%). Only one patient reported habitual seizure during the course of illness (8% of patients having postoperative seizures). Patient suffered from bilateral pneumonia and a seizure occurred during fever. The patient was not treated with proconvulsive drugs (fluoroquinolones etc). No COVID-related deaths were reported. Four patients reported chronic complaints lasting several months following the COVID-19 infection (14%).

Conclusions: Operated patients do not represent a particularly vulnerable group of patients with chronic neurological disorders. COVID-19 infection was not associated with the increased frequency of seizures in the majority of patients who failed to achieve postoperative remission, neither coincidental seizures were reported in the group of postoperative seizure-free patients.

Abstract Number: 576

Title: Academic Attainment following Paediatric Epilepsy Surgery: A Systematic Review

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Purpose: Children with refractory epilepsy are at particularly high risk for cognitive impairment, recording poorer performance in word reading and arithmetic than their neuro-typically developing peers. Though paediatric neurosurgery has long-been associated with various cognitive changes, little is known of how epilepsy surgery during childhood impacts academic performance. The aim of the present systematic review is to identify the strength and direction of the relationship between neurosurgery and academic attainment, in order to determine the impact of paediatric epilepsy surgery on reading, writing and arithmetic.

Method: Embase, Medline, PubMed, and PsychInfo, were searched for studies investigating academic attainment after paediatric epilepsy surgery over the last three decades. 1987 articles were screened for relevance. Eleven of these studies met our inclusion criteria. Study reliability and quality was assessed independently by two reviewers, with disagreements resolved through discussion.

Result: Results indicate that paediatric epilepsy surgery is associated primarily with no significant change in academic attainment after neurosurgery, though some significant declines in reading accuracy and arithmetic were reported. Two studies found that more than half of children demonstrated academic underachievement before undergoing epilepsy surgery and continued to score at least one standard deviation below the test mean in at least one academic domain after surgery.

Conclusions: In line with previous findings, this review highlights that little change in academic attainment is discernible following paediatric epilepsy surgery, suggesting that neurosurgery does not have an adverse effect on attainment. Further research, with longer follow-up periods and non-surgical comparison groups, is necessary to fully understand the effect of epilepsy surgery on academic attainment. Still, the present review

provides valuable information for parents, practitioners and policy-makers regarding the potential academic benefits of surgical treatment for intractable epilepsy.

Abstract Number: 615

Title: Discontinuation of antiepileptic therapy after resective epilepsy surgery

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Purpose: Resective surgery as a treatment option for drug-resistant epilepsies is presently well accepted and performed worldwide, but the management of postoperative antiepileptic drug (AED) withdrawal is an unsolved therapeutic challenge. The overall aim was to determine the rate of successful AED discontinuation and to explore the potential prognostic factors that influence the outcome of withdrawal.

Method: We performed a retrospective analysis of the postoperative AED profile of 128 patients with epilepsy who underwent resective surgery performed between 2006 and 2017 in the National Institute of Clinical Neurosciences and were followed up for at least two years. We compared the possible risk factors in patients with successful AED discontinuation versus seizure recurrence during tapering.

Result: Pharmacotherapy was discontinued successfully in 20 patients (15.63%) and polytherapy was reduced to monotherapy in 28 patients (21.88%). Seizure recurrence occurred in 23 patients (17.97%) on attempted withdrawal. 35 patients (27.34%) did not achieve seizure freedom after surgery. After a successful resection tapering was started with topiramate in 83.33% and clobazam in 64.29% of patients receiving the medication in combined therapy. Carbamazepine (n=8, 28.57%), lamotrigine (n=7, 25.00%) and levetiracetam (n=8, 28.57%) were commonly used as monotherapy for patients with former polytherapy. The successfully discontinued group was more likely to have a shorter duration of epilepsy (11.67±8.55 vs. 20.50±16.75 years, p=0.0387), lower number of antiepileptic drugs prior to surgery (5.35±2.91 vs. 7.89±3.53, p=0.033) and younger age at surgery (29.13±11.30 vs. 36.74±12.86 years, p=0.0472) compared to the group who continued receiving medication.

Conclusions: The most difficult decision facing a clinician is when or how to stop antiepileptic treatment after resective surgery; a thoughtful weighing of the risks and benefits is required. Seizure recurrence risk could be minimized by considering the potential prognostic factors.

Abstract Number: 638

Title: Subsequent resection or disconnection surgery after corpus callosotomy in 30 pediatric patients with epileptic spasms.

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Purpose: The objective was to summarize seizure outcomes after subsequent resection/disconnection surgery following total corpus callosotomy (CC) for pediatric patients with epileptic spasms (ES).

Method: Thirty consecutive pediatric patients (12 male) who underwent subsequent surgery after CC for residual seizures with lateralized or focal epileptic abnormalities on EEG at Nagasaki Medical Center from January 2000 to December 2014 were included in this study. We considered drug-resistant patients with ES who have no exact localization on EEG or imaging to be candidates for CC. We examined the final seizure outcomes after subsequent surgery using Engel's Classification and analyzed the determinants for good seizure outcomes.

Result: The mean age at onset was 7.0 months, the mean age at CC was 42.6 months, and the mean age at subsequent surgery was 72.3 months. Subsequent surgeries included hemispherotomy (HS) in 5 patients (16.7%), sub-total hemispherotomy (ST-HS) in 7 patients (23.3%), posterior quadrantectomy (PQT) in 9 patients (30.0%), and lobectomy/ lobe disconnection (LB) in 9 patients (30.0%). Fifteen patients (50%) had Engel Class I, and there was a significant correlation between Class I with the findings of lateralization on pre-CC functional imaging such as SPECT or FDG-PET ($p<0.01$). Patients with Class I had a significantly higher DQ/IQ at pre-CC and last follow-up than other patients (<0.05). Besides, regarding the type of surgery, patients with Class I had significantly higher seizure-free rates in HS and ST-HS: 4/5 (80%) in HS, 6/7 (85.7%) in ST-HS, 3/9 (33.3%) in PQT, and 2/9 (22.2%) in LB ($p=0.03$).

Conclusions: Of the patients who underwent CC followed by subsequent focal resection/disconnection surgery, half had an excellent Engel Class I seizure outcome. Among patients with ES without clear focus identified by EEG or MRI, lateralization on functional imaging is a good indication for CC followed by additional surgery.

Abstract Number: 650

Title: Prognostic model for withdrawal of anti-seizure medications following epilepsy surgery in adults: a worldwide multicentre study.

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Purpose: More than half of adults with epilepsy undergoing resective surgery achieve long-term seizure freedom and might consider withdrawing anti-seizure medications (ASMs). We developed and externally validated a prognostic model to predict seizure outcomes after reducing ASMs postoperatively.

Method: We included 918 adults from nine centres from six continents who had resective epilepsy surgery and were free from seizures other than focal non-motor aware seizures (auras) before starting ASM withdrawal. We used Cox proportional hazards regression to develop a model predicting recurrent seizures other than auras after beginning of ASM withdrawal using data from the London (UK) cohort (n=231). We validated the model internally (London, n=119) and externally (all other cohorts, n=568).

Result: Independent predictors of seizure recurrence during and following the start of ASM withdrawal were auras after surgery and before withdrawal (adjusted hazards ratio [aHR] 5.5, 95% confidence interval [CI] 2.7-11.1), history of focal to bilateral tonic-clonic seizures before surgery (aHR 1.6, 95% CI 0.9-2.8), shorter time from surgery to the start of withdrawal (aHR 0.9, 95% CI 0.8-0.9), and number of ASMs at time of surgery (aHR 1.2, 95% CI 0.9-1.6). Model discrimination, i.e. the ability to correctly identify individuals with vs. without seizure recurrence after start of ASM withdrawal, showed concordance statistics of 0.68 in the internal validation subcohort and 0.67 in the external validation cohorts. Calibration plots indicated high agreement of predicted and observed outcomes.

Conclusions: A simple algorithm, available as graphical nomogram and online tool (predictepilepsy.github.io), can predict seizure outcome following postoperative withdrawal of ASMs. This multicentre validated model can assist in decisions on whether and when to consider ASM withdrawal after surgery.

Abstract Number: 654

Title: High frequency oscillations outperform interictal spikes in predicting seizure outcome following epilepsy surgery

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Purpose: The goal of epilepsy surgery is to resect the epileptogenic zone (EZ) to achieve seizure freedom. High frequency oscillations (HFO) are being established as biomarker for EZ. We compared predictive power of HFO, interictal spikes, and their combination for predicting seizure outcome.

Method: We re-analysed intracranial EEG data from 20 patients previously published (Fedele et al., Sci Rep 2017; 13836). Subsequent resective surgical outcomes were classified into seizure freedom (ILAE 1) or recurrence (ILAE > 1). HFO were defined prospectively by a fully automated detection algorithm. Interictal spikes were marked manually. We considered HFO, spikes, and spikes carrying HFO. For each biomarker we defined its area of maximal detection and its predictive power for seizure outcome. Further, we followed spike propagation.

Result: Specificity in predicting seizure outcome was 100% for HFO, 61% for spikes and 85% for spike+HFO. Sensitivity was 57% for HFO, 71% for spikes and 67% for spike+HFO. Positive predictive value was 100% for HFO, 50% for spikes and 67% for spike+HFO. Negative predictive value was 81% for HFO, 80% for spikes and 85% for spike+HFO. Accuracy was 85% for HFO, 65% for spikes and 79% for spike+HFO.

Compared to HFO, spike+HFO worsened outcome prediction in 4 cases, all with extratemporal lesional epilepsy. Spike+HFO improved on HFO prediction in two cases, both with hippocampal sclerosis. 2/4 patients showing propagating spike patterns were seizure free; in one the spike+HFO focus was the triggering zone for spike propagation, in the second spikes propagated from the resected HFO area. In one patient with recurrent seizures, spikes propagated from the non-resected HFO area, in the second patient, spike propagation was not associated with the HFO area.

Conclusions: HFO were more accurate than interictal spikes in prediction of postsurgical seizure freedom. Combining spikes with HFO increased sensitivity but decreased specificity.

Abstract Number: 688

Title: Intellectual trajectories in children before and after resective epilepsy surgery

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Purpose: Cognitive outcome after epilepsy surgery is evaluated typically against only a single assessment made shortly before surgery. Our aim was to gain a broader perspective on intellectual trajectories by analyzing multiple intelligence assessments both before and after surgery.

Method: We searched our epilepsy surgery database for children with unilobar resections and data on at least two preoperative and two postoperative assessments of verbal and performance intelligence quotients (VIQ and PIQ) excluding patients with any IQ < 50. This yielded 56 children operated between 1996-2018 with IQ assessments on average 4,3 (1,0-12,1) and 0,4 (0,0-1,4) years before and 0,5 (0,4-0,8) years and 2,0 (1,5-2,5) years after resection; mean age at surgery 11,6 (4,2-16,5) years; 43 % with left-sided resection; 40 % with frontal resection; 66 % with Engel I outcome two years postoperatively. VIQ and PIQ were combined as measures of general intelligence in multiple analyses of variance (MANOVAs) and then analyzed separately with univariate ANOVAs. Seizure outcome, side and site (frontal vs. other lobes) of resection were included as group factors in separate analyses. Additional IQ data available for 30 patients were used to evaluate the role of practice effects related to repeated assessments.

Result: Preoperative assessments revealed significant IQ decline which stopped after surgery ($p<0,001$). Postoperative catch-up of general intellectual functioning towards initial levels was seen in seizure-free patients ($p=0,049$); separately significant for VIQ ($p=0,017$), and after posterior resections ($p=0,007$); separately significant for PIQ ($p=0,004$).

Conclusions: Longitudinal trajectories show that intellectual deterioration is common in intractable pediatric epilepsy and should be accounted for when evaluating outcome. Deterioration may be stopped by resective surgery even without seizure freedom, but catch-up is most likely in seizure-free patients and less likely after frontal than more posterior resection.

Abstract Number: 714

Title: Insulo-opercular stereoelectroencephalography exploration in children: Indications, Techniques, and Safety

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Purpose: Sampling the insulo-opercular region with invasive recordings is crucial given the importance of this region in epileptic networks and a variety of electroclinical presentations. However, implantation of the insulo-opercular region via stereoelectroencephalography (sEEG) is considered technically challenging given complex vascular and grey matter relationships in this region. We investigated the safety of insulo-opercular sEEG exploration in children and young adults using standard sEEG approaches including: 1) orthogonal insulo-opercular approach, 2) pseudo-orthogonal insulo-opercular approach, and 3) medial-lateral insular oblique approach.

Method: We performed a retrospective cohort study of 30 consecutive patients who underwent 33 sEEG implantations. The patients all had drug-resistant focal epilepsy and were between the ages of 4 and 21 that were operated at UPMC Children's Hospital between January 2019 and March 2021. Medical records and neuroimaging were reviewed. Haemorrhage, infection, and other complications were considered as outcome variables for this study in order to evaluate the safety of insulo-opercular sEEG. We also evaluated the impact of sEEG on changing surgical planning, particularly in the insulo-opercular region.

Result: A total of 519 electrodes were placed. 81 have been placed orthogonally into the temporal lobe, 50 were placed orthogonally into the frontal lobe, and 15 were placed obliquely into the insula. sEEG electrodes localized seizure onset to the insulo-opercular region in 9 patients, leading to resection in 4 patients and ablation in 4 patients. Out of the 519 electrodes placed, none of them exhibited haemorrhage or serious complications. Out of the 15 electrodes placed into the insula, none had any serious complications and 1 had minor bleeding due to the electrode breaking.

Conclusions: These results demonstrate that both the orthogonal, pseudo-orthogonal, and oblique approaches to sampling the insula are safe.

Abstract Number: 717

Title: Anterior corpus callosotomy as resolution at super-refractory status epilepticus: first Latinoamerica experience

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Purpose: Super-refractory status epilepticus (SRSE) is defined as status epilepticus (SE) that continues 24 hours and persist beyond the withdrawal of anesthesia. In few reported cases Surgical treatment has shown to stop SRSE. A literature search found two case report of SRSE resolve by anterior corpus callosotomy (ACC) (Alexopoulos A et al. Neurology. 2005;64:567-570.) (Ma X et al. Epilepsy Research. 2001; 46:33–38)

Method: Herein we described a patient with SRSE that ended after the performance anterior corpus callosotomy and has remained seizure free during follow up.

Result: A 20-year-old Latin-American boy referred to the emergency room with generalized tonic seizures with lost of awareness, extension of the right arm and leg lasting for one hour, he had eight episodes with no recovery. He had a history of drug-resistant epilepsy of unknown etiology since seven-years of age. Intravenous (IV) midazolam was administered followed by IV phenytoin, which were ineffective. Elective intubation and a third line of treatment were initiated with Propofol at 2 mg/kg/hr and he was transferred to the ICU. Ictal EEG had generalized polyspikes. MRI showed nonspecific gliosis. In spite of propofol, patient continued with clinical and electrographical seizures. Midazolam and ketamine were added. All these showed poor results controlling his seizures. At 12th day of hospitalization, generalized tonic seizures, EEG findings and an unremarkable MRI a decision was made to perform an ACC, undertaken on the 14th day. After surgery, seizures stopped, he was extubated, his symptoms improved and was discharged. After three months follow-up, he remains seizure-free.

Conclusions: Only two cases have been reported of ACC during SE and SRSE
ACC showed resolution of SRSE and would be the two-case described in a literature search and the first one in LATAM. ACC can stop or improve seizures during SE and SRSE in selected cases.

Abstract Number: 722

Title: Automatic localization of the epileptogenic zone: network and machine learning analysis of interictal stereo-EEG

Giulia Varotto[1,2], Gianluca Susi[3,4], Ferruccio Panzica[5], Laura Tassi[6], Dunja Duran[1], Silvana Franceschetti[2], Francesca Gozzo[6], Roberto Spreafico[2]

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Purpose: The study was aimed at developing an automatic system to support the localization of the Epileptogenic Zone (EZ) and the identification of interictal network biomarkers in patients with drug-resistant focal epilepsy candidate to surgery. The system is based on interictal recordings of Stereo-EEG (SEEG) signals and makes use of network analysis and machine learning for imbalanced domain.

Method: The study enrolled 19 patients with drug-resistant epilepsy, with different EZ localization, negative MRI, divided into seizure free (SF) and non-seizure free (NSF) group, according to their post-surgical outcome. The whole automatic procedure was based on 3 min of interictal SEEG signals. Effective connectivity was estimated by means of a bivariate non-linear method, the non-linear regression index. Hubs were estimated trough 9 graph theory-based indexes of centrality were estimated to identify hubs and used as input of four machine learning techniques for imbalanced dataset. Classification was assessed using the leave-One-Patient-Out (LOPO) permutation and comparing the EZ as classified by our procedure to the EZ identified by expert clinicians and subsequently surgically resected.

Result: The proposed procedure was able to automatically localize the EZ with a sensitivity higher than 97% for seizure-free patients. Moreover, our results show a clear difference between SF and NSF patients, mainly in terms of false positive rate, (the percentage of non-EZ leads classified as EZ), significantly higher in NSF patients.

Conclusions: We implemented an automatic procedure, based on a combination of connectivity, graph theory and machine learning, able to identify the EZ on interictal recordings. Results pointed out that network centrality plays a key role in interictal epileptogenic network, even in case of absence of anatomical alteration. These findings also suggest that poorer post-surgical prognosis can be associated with larger connectivity alteration, with wider "hubs", and that this approach can be a promising biomarker for surgical outcome.

Abstract Number: 745

Title: Paediatric epilepsy surgery from 2000 to 2018: have we reached a plateau in seizure freedom rates?

Maria Eriksson[1,2,3], John Booth[2], Sophie Adler[1], Patricia Martin Sanfilippo[2], Kirstie Whitaker[3], Martin Tisdall[1,2], J Helen Cross[1,2,4], Konrad Wagstyl[5], Torsten Baldeweg[1,2]

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Purpose: Neurosurgery is a well-established treatment option for children with drug-resistant epilepsy. In this study, we provide a comprehensive characterisation of paediatric epilepsy surgery patients, describe how patient characteristics and surgery practices have changed over the past two decades in a nationwide cohort, and examine if outcomes have improved.

Method: Demographic information, epilepsy characteristics, surgical details, genetic results, histopathology diagnoses, and 1-year post-operative seizure outcome and anti-epileptic drug status for paediatric epilepsy surgery patients operated on at Great Ormond Street Hospital, UK from 2000 to 2018 (N = 1,235) were retrospectively collected and analysed.

Result: In total, 882 children (47% females, median age at surgery: 8.7 years) were identified as having undergone resective or disconnective surgery (neuromodulation/diagnostic procedures were excluded). The majority of patients underwent lesionectomy (44%), followed by hemispherotomy (25%). Temporal and frontal lobe represented the most frequently operated on lobes (30% and 17%, respectively), and low-grade epilepsy associated tumour (19%) and focal cortical dysplasia type II (14%) represented the most common aetiologies. On average, 63% of patients were seizure free at 1-year follow-up, and 14% of these were off anti-epileptic drugs. When separated into palliative and non-palliative procedures, the average seizure freedom rates were 10% and 67%, respectively. In spite of surgical cases almost doubling between 2000 and 2018 (average increase 1.8 cases per year, 95% CI=1.2-2.4, r=0.82, p<.001), there were no significant temporal trends in patient characteristics or seizure outcome. There were significant changes in type of surgery, aetiology, and post-surgical anti-epileptic drug status.

Conclusions: Paediatric epilepsy surgery has undergone a significant evolution over the past twenty years. We show a plateau in seizure freedom rates; however, this must be interpreted in the context of an increase in surgical cases, a trend toward more complex cases, and the introduction of a more aggressive anti-epileptic drug withdrawal policy.

Abstract Number: 755

Title: Serial changes in the functional brain network of children undergoing repeated epilepsy surgery

Giulia Iandolo[1,2], Nitish Chourasia[3], Georgios Ntolkeras[1,4], Joseph Madsen[4,5], Christos Papadelis[4,6,7], Ellen Grant[1,4], Phillip Pearl[3,4], Fabrizio Taffoni[2], Eleonora Tamilia[1,4]

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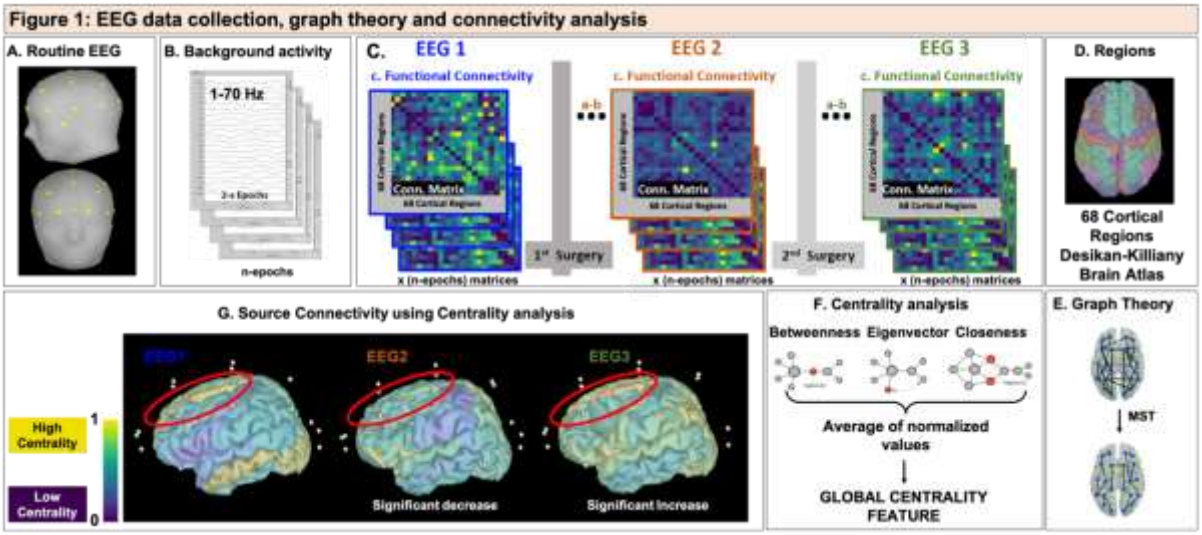
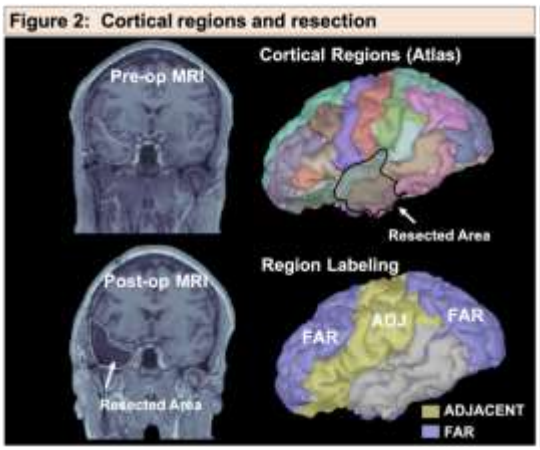
Purpose: About 30% of children with drug-resistant epilepsy (DRE) continue to have seizures post-surgery. Defining a re-operation plan for a second surgery is particularly challenging in these patients; thus, any novel noninvasive technique which can add to the test battery is highly valued. Since epilepsy is increasingly conceptualized as a network disorder, understanding how brain regions are connected may be crucial for planning treatment. Our purpose is to estimate brain source connectivity using scalp EEG in children that had repeated epilepsy surgery and assess how brain connectivity changes over time.

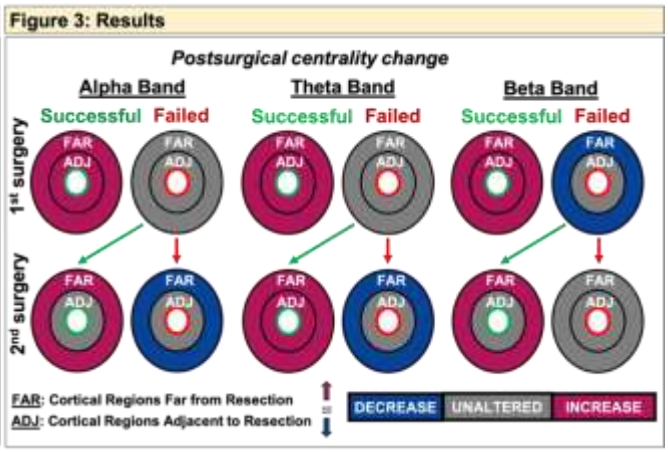
Method: We studied nine children with DRE who had repeated surgery (RS-group) and 13 patients who had one surgery followed by seizure-freedom (SF-group). We analyzed scalp-EEG epochs, without spikes, from three time-points (Figure1A-C): before first surgery, in-between two surgeries, and after reoperation. We estimated Functional Connectivity between cortical regions in different frequency bands (alpha, theta, delta, beta, gamma): graph-theory was applied to estimate *centrality* of each region within the network (Figure1C-G). We compared pre- and post-surgery connectivity of all brain regions (*far* or *adjacent* to resection, Figure2), for RS-group and SF-group (*Wilcoxon-signed-rank* test).

Result: In SF-group, cortical regions that were not resected increased their centrality post-surgery in alpha, theta and beta bands (Figure3). Contrarily, in RS-group, after each failed surgery, cortical regions (*far* or *adjacent*) showed decrease, or no change, in their centrality (Figure3). When re-operation was successful, post-surgical network centrality of *far* regions increased in the same frequency bands (Figure3).

Conclusions: Functional connectivity analysis at source level, using scalp EEG, can reveal brain networks changes that are associated with post-surgical outcome in children. We found that failed epilepsy surgery is associated with a decrease, or no changes, in the overall network centrality of the remaining brain regions. Successful surgeries, instead, are associated with an overall increase in network centrality.







Abstract Number: 789

Title: Comparative effectiveness of heart rate responsive vagus nerve stimulation in pediatric drug-resistant epilepsy patients

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Purpose: For patients with drug-resistant, unresectable epilepsy, vagus nerve stimulation (VNS) is a palliative surgical option. With VNS, 60% of patients will achieve ≥50% seizure reduction. Closed-loop VNS models have been developed that detect ictal tachycardia and deliver responsive stimulation. The efficacy of closed-loop compared to traditional VNS for pediatric epilepsy is unknown.

Method: We performed a single center retrospective review from January 1st, 2009 to January 1st, 2020. All VNS patients were included and divided into groups based on VNS model: 1) *traditional* VNS, 2) traditional VNS *transitioned* to closed-loop VNS, and 3) *closed-loop* VNS. The primary outcome was seizure frequency reduction. Chi-squared tests and independent sample t-tests were performed for group comparison.

Result: There were no differences in total seizure frequency reduction among the *traditional* (n=308), *transitioned* (n=53), and *closed-loop* (n=60) groups after years 1 (p=0.804), 2 (p=0.315), 4 (p=0.893), or latest follow-up (p=0.634). This finding held true for patients with preoperative focal seizures and preoperative generalized seizures. The mean change in AEDs from pre- to post-VNS was 0.03 ± 1.421 AEDs for the *traditional* VNS group, -0.09 ± 1.131 for the *transitioned* group, and 0.07 ± 0.841 for the *closed-loop* group, with no significant differences between groups (p>0.05 for all comparisons).

Conclusions: Among pediatric patients with drug-resistant, unresectable epilepsy, closed-loop VNS is not associated with increased patient achievement of ≥50% seizure frequency reduction compared to traditional models. This finding was also true among patients who transitioned from traditional to closed-loop VNS. Closed-loop VNS was not associated with reduction in AEDs compared to traditional VNS.

Abstract Number: 808

Title: Neurophysiological characterization of Focal Cortical Dysplasia subtypes using ictal phase-amplitude coupling in intracranial electroencephalography.

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Purpose: Focal cortical dysplasia (FCD) is a leading cause of drug-resistant epilepsy (DRE) in children and young adults. The identification of specific biomarkers of FCD subtypes is especially important in estimating the surgical prognosis in children with FCD undergoing presurgical investigations. The goal of this study is to evaluate whether ictal phase amplitude coupling (PAC) between high and low frequency activity could be used as a preoperative biomarker of FCD subtypes. We hypothesize that FCD seizures present unique PAC characteristics that may be linked to their specific histopathology.

Method: We retrospectively examined 12 children with FCD and refractory epilepsy who underwent successful epilepsy surgery (Engel class 1). We identified ictal onsets recorded with intracranial EEG. We estimated the strength of PAC between low-frequencies (3-4 Hz) and high-frequencies (80-250 Hz) for each seizure by means of modulation index. We determined the effect of neurophysiological variables (i.e. seizure-onset zone [SOZ] vs. non-SOZ electrodes, pre-ictal vs. ictal period) to characterize the role of PAC in identifying FCD subtypes (Fig. 1). Wilcoxon sign-rank tests and receiver operating characteristic curve analysis were used to test the association between ictal PAC and FCD subtypes.

Result: We provided evidence for the contribution of ictal PAC in differentiating FCD subtypes. Ictal PAC was significantly higher in patients with FCD type II compared to type I, only in SOZ-electrodes ($p<0.05$, Fig.2). No differences in ictal PAC were found in non-SOZ electrodes. Pre-ictal and ictal PAC predicted FCD type II histopathology with a sensitivity of 92%, specificity of 83.3% and accuracy of 87.5%.

Conclusions: The results of this study provide new insights on the neurophysiological origin of ictal activity in patients with FCD. The application of PAC on ictal recordings may provide new diagnostic biomarkers and improve the clinical management of children with FCD undergoing surgery

Figure 1.

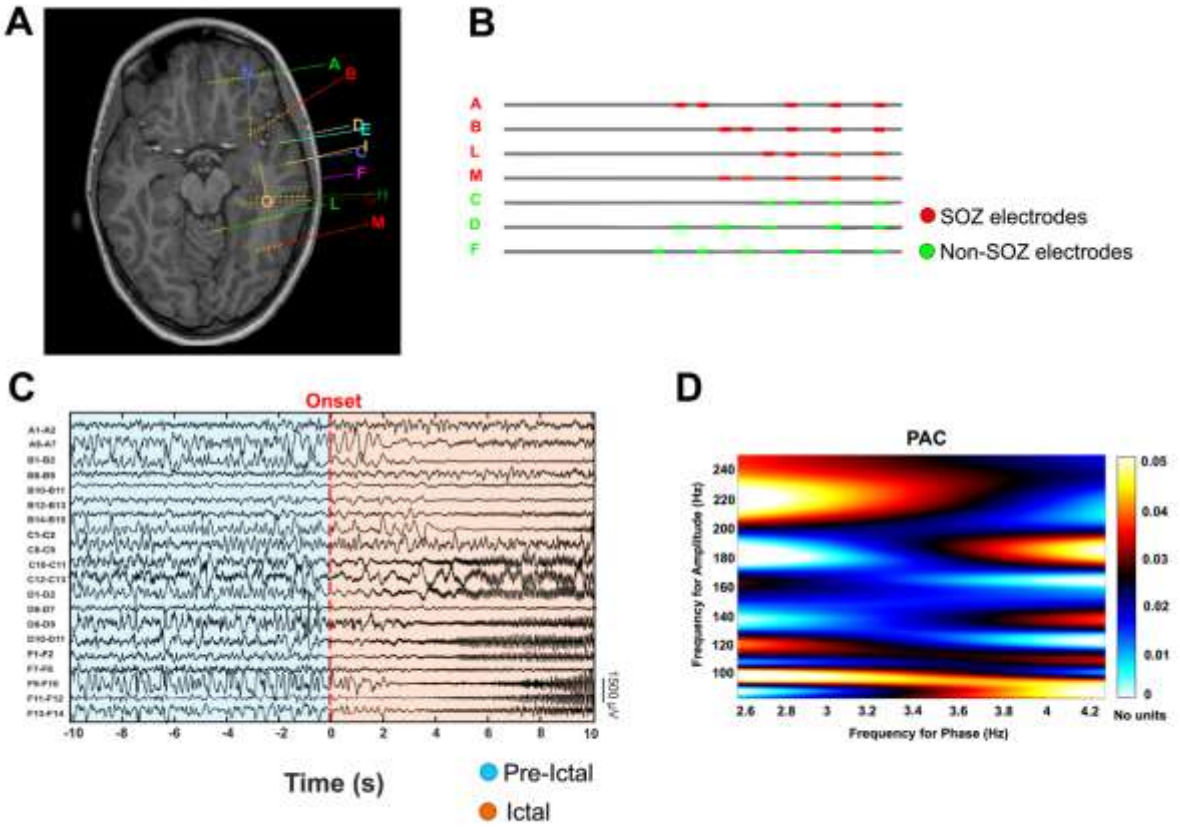
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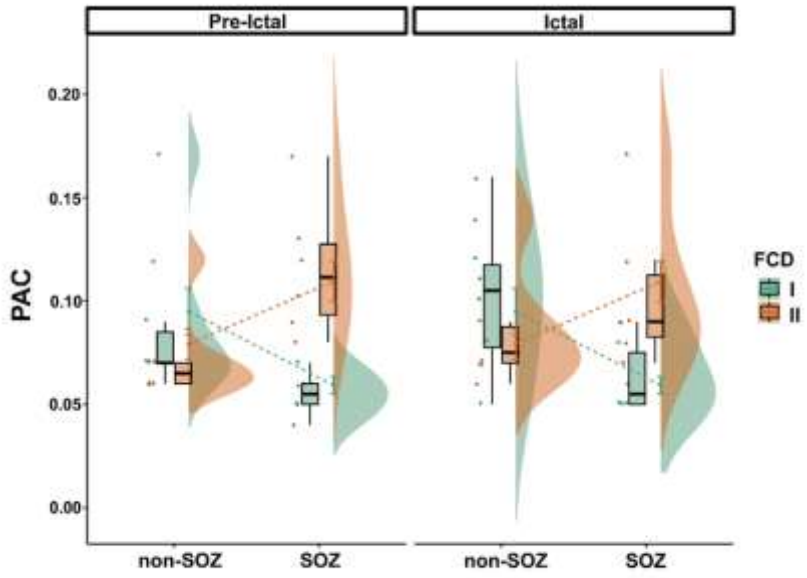
Figure 2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Abstract Number: 815

Title: Sensitivity of FDG-PET in non-lesional MRI in TLE and ETLE patients – a multi-center study

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Purpose: FDG-PET is a widely used diagnostic tool in presurgical assessment in epilepsy if standard diagnostics did not localize the epileptogenic lesion or results have been discordant.

Method: In this multicenter, retrospective study, we included consecutive patients with drug-resistant focal epilepsy, who had FDG-PET as part of their presurgical work-up. Data were collected at four tertiary epilepsy centers from three continents. We assessed the utility of FDG-PET, which was defined as contributing in the decision-making process to either referral to direct surgery or intracranial EEG (iEEG) or non-feasibility of surgery.

Result: Overall, 951 patients were included into this study. 479 patients (50%) were classified as having temporal lobe epilepsy (TLE), 219 (23%) as extratemporal lobe epilepsy (ETLE), and 253 (27%) as epilepsy of uncertain origin. In 275 patients (29%) MRI was lesional, in 578 (61%) non-lesional and in 98 (10%) equivocal. FDG-PET was concordant with ictal EEG in 74% in TLE and in 56% in ETLE. FDG-PET contributed to the decision to recommend direct surgery (n=78, 8%) or iEEG (n=187, 20%) or to state non-feasibility of surgery (n=131, 14%) in 222 (46%) TLE and 90 (41%) ETLE patients. In TLE, freedom of disabling seizures (ILAE 1+2) did not differ significantly between patients with *non-lesional MRI and EEG-PET concordance* (65%) and patients with *lesional MRI and EEG concordance* (68%). In ETLE, 50% of patients with *non-lesional MRI and EEG-PET concordance* and 75% with *lesional MRI and EEG-concordance* had no disabling seizures post-surgery.

Conclusions: In a large cohort of epilepsy patients, concordance between EEG and FDG-PET, in patients with non-lesional MRI, results in favorable surgical outcome. FDG-PET was a helpful diagnostic tool in 41-46% patients having epilepsy surgery assessment, in particular in patients with non-lesional MRI.

Abstract Number: 824

Title: High frequency oscillations rates and amplitudes across the brain regions in patients who underwent epilepsy surgery.

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Purpose: High frequency oscillations (HFO) are associated to epileptogenic tissue, but it is still controversial whether they can reliably predict seizure outcome (Jacobs J et al. 2018;9:e1040-e1052). To date, HFO vary in rates and amplitudes across brain regions (Guragin H et al. 2018;90:e639-e646). Here, we describe the features of HFO predictive of seizure outcome in different anatomical regions.

Method: We collected stereo-EEG recordings from 17 patients (11 Engel I). We detected HFO in 30 minutes NREM sleep and automatically, identified the HFO area in each individual patient and computed HFO predictive power of seizure outcome (as in Fedele T et al. 2017;7:13836). To study HFO variability across hippocampus (HP), parahippocampal gyrus (pHP), frontal lobe (FL), temporal lobe (TL), and parietal lobe (PL), we compared the HFO rates and amplitudes in the RA and non-RA. **Result:** We obtained PPV = 83% [36-100%], NPV = 100% [72-100%], sensitivity = 100% [48-100%], specificity = 92% [62-100%], which resulted in accuracy = 92% [71-100%]. The anatomically segregated analysis showed that HFO rates were significantly higher in the RA than non-RA in HP, pHP, and TL, while HFO amplitudes were significantly higher in the RA than non-RA in all anatomical regions. To distinguish the RA, non-RA in FL, PL, we applied Support Vector Machines (SVM) classifier with 5-fold cross validation, which additionally used HFO duration and entropy level. For FL, PL, the SVM classifier reached the mean accuracy = 75% [SD = 11%].
Conclusions: Our results support HFOs as reliable predictor of surgery outcome and indicate in HFO rates and amplitude key distinctive features, particularly for temporal areas. Besides the HFO rates and amplitude, duration and entropy level are able to improve the prediction in frontal, parietal areas. Our data contributes to map clinically relevant HFO features over different anatomical structures.

Abstract Number: 847

Title: Long-Term Longitudinal Follow-up in pediatric epilepsy surgery: a single center experience

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Purpose: To analyse the outcome of epilepsy surgery in our multidisciplinary unit in Bambino Gesù Children's Hospital.

Method: We reviewed patients who underwent epilepsy surgery between 2009 and 2019, under 18 years, with a minimum post-surgical follow-up of 2 years. We analysed clinical records, neuropsychological and presurgical evaluation (imaging, video-EEG, stereo-EEG), type of surgery and outcome (Engel class). We evaluated if there was any relationship between duration of epilepsy, age at surgery, age at onset of epilepsy and postoperative outcome.

Result: 174 patients met the inclusion criteria. The median age at seizure onset was 3,3 years (range 0,1-7 yy), median duration of epilepsy 2,3 years (range 0,1 -17,1 yy), the median age at surgery was 8,7 years (range 0,2 - 17,9 yy). 109 patients (63%) were drug-resistant. 168 patients (97%) had a positive MRI: 57 patients had malformations of cortical development (MCD), 59 Low-grade epilepsy-associated neuro-epithelial tumours (LEAT),11 Hippocampal Sclerosis (HS), 19 hypothalamic hamartoma (HH), 28 other pathologies.
All patients were in active follow-up at the time of analysis. The mean duration of follow up was 41 months (range 24-122 m). At last follow-up 146 patients (84%), were seizure free, and among them 84 (48%) were drug free.
There was a clear correlation between brief duration of epilepsy and favourable seizure outcome (p=0,001). Age at surgery and age of onset were not related to post-surgical seizure freedom.
Considering long term longitudinal follow up, HS and LEAT showed a good and stable outcome compared to FCD type I and type II (p=0,0004).

Conclusion: Surgery is a valuable option for children with drug-resistant focal epilepsies. Duration of epilepsy is a good prognostic factor for postoperative outcome, while age at onset of epilepsy and age at surgery, did not influence seizure outcome. Earlier surgery should be encouraged as it can improve surgical outcome.

Abstract Number: 876

Title: Can Presurgical interhemispheric connectivity predict seizure outcome in patients who underwent hemispheric surgery?

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Purpose: Hemispherotomy (HT) is a surgical option for treatment of intractable seizures due to hemispheric structural lesions. The reported seizure freedom rates in HT cohorts range from 50% to 90%. Factors affecting seizure outcome have not been fully clarified. The goal of this study is to evaluate interhemispheric connectivity in the presurgical EEG of patients who underwent HT. We hypothesized that surgical outcome can be predicted from EEG connectivity values in patients undergoing HT.

Method: We retrospectively reviewed all patients who underwent hemispherotomy in our center from 2009 to 2020. We examined 26 patients with available presurgical video-EEG. We dichotomized surgical outcome into seizure-free (SF) and non-seizure-free (NSF) after one year following HT. Pre-intervention EEG connectivity parameters (i.e. inter-hemispheric phase locking values) were compared between SF and NSF patients. Receiver Operating Characteristic (ROC) curves models were built to test whether EEG parameters predicted outcome.

Result: The age at surgery ranged from 0.2 to 31.7 years (median 6.7 years). Follow-up duration ranged from one to twelve years (median 6.1 years). 21 patients out of 26 (81%) were seizure free.

Conclusions: Concordant data on the role of EEG as a predictive factor for postsurgical outcome in patients who underwent HT are still lacking. We will discuss results of inter-hemispheric phase-locking EEG values, highlighting any possible differences in presurgical electrical connectivity between SF and NSF patients.

Abstract Number: 922

Title: Magnetic Resonance-guided Laser Interstitial Thermal Therapy for the treatment of hypothalamic hamartoma: report of 3 pediatric cases.

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Purpose: Hypothalamic hamartomas (HH) are benign lesions that cause medically refractory seizures, behavioral disturbances, and endocrine dysfunction.
Open surgical resection or disconnection of HHs carry a relatively high risk of morbidity and are associated with long hospitalization.
MRg-LiTT is a minimally invasive technique which reduces the high surgical complication profile of the open technique while guaranteeing a good seizure outcome.
Here we describe a series of 3 pediatric patients (<10 years of age) who underwent to HH laser ablation (MRg-LiTT) at Istituto GianninaGaslini. The purpose is to investigate seizure, behavioral and cognitive outcome and hospitalization length.

Method: Patients were evaluated before and after the procedure. Clinical evaluation, vEEG and validated questionnaires investigating behavior and development were administered. The median follow up was 6.5 months (3-10 months).

Result: None of the patients suffered post-surgical complications. All patients regained normal pre-surgical motility the second day after the procedure. Two patients (66%) were completely seizure free at the last follow-up. One patient experienced focal seizures in the first 30 days after surgery, currently he is seizure free on medication. All patients experienced an improvement in cognitive and social behavior; 100% has been discharged from hospital in less than five days.

Conclusions: Our data are consistent with data reported in literature in terms of seizure outcome. Future studies are needed to define behavior and adaptive abilities improvements.

Abstract Number: 998

Title: Seizure freedom in patients with Focal Cortical Dysplasia undergoing Epilepsy surgery: Experience of a tertiary care center from India.

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Purpose: Focal Cortical Dysplasia (FCD) is the leading cause of structurally related epilepsy in children and third most common cause in adults. There is dearth of studies on post-operative outcomes in FCD especially from India. Objectives are to study:

- seizure freedom after surgery for FCD.
- role of electrocorticography in epilepsy surgery for FCD.
- predictors of seizure recurrence.
-

Method: It is a retrospective observational study done at Comprehensive Epilepsy Care Centre at Seth GS Medical College and KEM Hospital, Mumbai and includes all histopathologically proven Focal Cortical Dysplasia cases operated between May 2006 and January 2020. We used individual duplicate archived files containing pre-operative workup and post-operative follow-up. Engel classification is used to classify the post-operative seizure outcome.

Result: Out of 159 FCD patients that got operated, 146 patients attended at least 1 year follow-up post-operatively. 15% (22/146) patients had primary focal cortical dysplasia, while 85% (124/146) patients had an accompanying lesion. 92.4% (135/146) had FCD in temporal lobe, 5.5% (8/146) in frontal lobe, 1.4% (2/146) in parietal lobe while only 0.7% (1/146) had in occipital lobe. At the end of 1 year post-operatively, Engel I seizure freedom was obtained in 88.4% (129/146) patients. It was 78.2% (111/142) at the end of 3 years and 68.3% (69/101) at the end of 5 years post-operatively. 46.5% (68/146) underwent non- ECoG surgery while 53.5% (78/146) underwent ECoG guided surgery. Seizure freedom rate at the end of 1st post-operative year in ECoG

guided surgery was 84.6% (66/78). Good prognostic factors for seizure freedom were temporal lobe involvement, unifocal lesion on MRI and complete resection.

Conclusions: FCD is amenable to excellent seizure outcomes with surgery. Complete resection of epileptogenic zone through meticulous pre-operative workup is imperative for good seizure freedom. Long term follow up is required for further prognostication.

Abstract Number: 1024

Title: Surgical outcome and Predictors in Posterior cortex epilepsy secondary to Gliosis with and without Ulegyria

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Purpose: To assess the surgical outcome and its predictors in patients with posterior cortex epilepsy secondary to gliosis and to compare the outcome between those with and without Ulegyria as an MRI substrate.

Method: Patients who underwent surgery for posterior head region epilepsy between 2001-2018 at a tertiary comprehensive epilepsy care center were identified from a prospectively maintained registry. From this cohort, patients with gliosis confirmed on pathology were identified and sub grouped into those with and without Ulegyria identified from MRI. The surgical outcome was assessed in terms of Engel score (1,2- good outcome; 3,4-bad outcome) and compared between the two groups. Overall predictors of seizure outcome in the entire cohort were analyzed with Mann Whitney U test, Chi square and Fischer exact test as indicated.

Result: A total of 138 patients were operated for posterior cortex epilepsy in the specified study period who had completed at least a 2-year follow-up.59 (42.7%) patients had gliosis confirmed on histopathology. 42 (71.2%) were males. Among these, 15% patients were found to have Ulegyria on MRI. Over all 35 (59%) patients had a favorable seizure outcome. A clearly localized ictal EEG *(p=0.026),* absence of spikes in postsurgical electrocorticography *(p=0.006*) and, completeness of resection in post –operative MRI *(p=0.000)* were predictors of good outcome. No significant difference in the surgical outcome between those patients with and without Ulegyria was identified (*p=0.803).*

Conclusions: More than half of the patients with PHR gliosis have had a favorable surgical outcome. Clearly localized ictal EEG, absence of spikes in postsurgical electrocorticography, and completeness of resection predicted surgical outcome in posterior head region epilepsy secondary to gliosis. Presence of Ulegyria does not portend a poor prognosis as is often considered, but probably can be considered as another MRI marker of gliosis.

Abstract Number: 1128

Title: Profile of surgically managed temporal lobe epilepsy; a case series from a limited resource setting

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Purpose: The highlight importance of epilepsy surgery in drug-refractory temporal lobe epilepsy (TLE) in achieving anti-epileptic drug (AED) withdrawal, reduction in the seizure frequency and improving quality of life in a resource limited setting.

Method: 17 patients evaluated and diagnosed to have drug refractory TLE and underwent epilepsy surgeries with median follow-up for twelve months were studied. History of antecedents, seizure semiology, clinico-radiological-electrophysiological concordance were studied, and all the patients underwent detailed neuropsychiatric assessment. Any red flags in diagnosis were noted. Histopathological analysis was performed for the resected region. Complications in the perioperative period were noted. For patients who underwent ATL+AH, the functional outcome was studied with the International league against epilepsy (ILAE) classification of outcomes with epilepsy. Descriptive statistics were expressed in percentages.

Result: Out of 17 cases, mean seizure duration was 15.3+9.6years, and antecedents were present in 8, the aura in 10, automatisms were seen in 11, arrest in 12, motor seizures in 14, abnormal neuro-psychiatric assessment in 12, extratemporal/ bitemporal epileptiform discharges were seen in 6, magnetic resonance imaging brain showing sclerosis in 12, dysplasia in 5, secondary MTS in 1, cavernoma in 1.Invasive monitoring was performed in 1, left temporal surgeries in 10, right temporal lobectomy in 7, Post-operative complications were seen in 4. The functionally better quality of life was seen in 88.2% of patients, AED withdrawal/ tapering in 76.4%.

Conclusions: Surgery remains a therapeutic option for patients with medically refractory epilepsy. The comprehensive presurgical evaluation includes electroencephalography (EEG) and video EEG in identifying patients who are likely to benefit from surgery, Majority of the patients who are not seizure-free experienced at least a substantial reduction in seizure frequency without or with very minimal cognitive or functional deficits.

Abstract Number: 1155

Title: The Virtual Epileptic Patient large scale brain modelling: relationship with seizure onset zone and surgical outcome

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Purpose: The virtual epileptic patient (VEP) is a novel brain modelling method based on the virtual brain technology, using electrophysiological (SEEG) data and large-scale brain modelling combining anatomical data (MRI and connectivity) and a computational neuronal model at an individual patient level. VEP has a potential interest in the pre-surgical assessment of pharmacoresistant epilepsy by identifying the regions most likely to generate seizures. We aimed to assess the performances of VEP approach in the detection of epileptogenic regions and to study whether VEP model can help to predict surgical outcome.

Method: VEP modelling was retrospectively applied in a cohort of 53 patients with pharmacoresistant epilepsy and available SEEG, MPRAGE- and diffusion-weighted MRI. Precision-recall was used to compare the regions identified as epileptogenic by VEP to the clinical analysis incorporating the Epileptogenicity Index (EI) method. In 28 operated patients, we compared the VEP results and clinical analysis with surgical outcome.

Result: VEP showed good precision (60%) but low sensitivity (33%) and tendency to underestimate the extent of the epileptogenic zone (EZ) defined according to the clinical standard. There was a better concordance with clinical results, with higher sensitivity (40%) and precision (68%), in seizure-free patients. ROI parcellation at lower spatial resolution improves VEP performances, while some region topographies are more difficult to detect. Regarding the surgical prognosis, there was a trend to a higher number of regions defined as epileptogenic by VEP that remained non-resected in not seizure-free patients, however, without reaching statistical significance.

Conclusions: The first VEP prototype is characterized by good precision in detecting the EZ defined by visual analysis combined with EI. Our data suggest the importance of the ongoing prospective multi-center trial to estimate the potential impact of VEP on improving surgical prognosis. The analysis of factors limiting actual model performances is crucial for its further development.

Abstract Number: 1176

Title: MR-guided laser ablation for hypothalamic hamartoma in children: case reports

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Purpose: Surgical treatment for Hypothalamic hamartoma (HH) has been moderately effective but with comorbidities. More recently, MR-guided laser interstitial thermal therapy (MRgLiTT) has shown to be effective treating epilepsy with better safety profile. We present two clinical cases that highlight the benefits of its use.
Result: 1. Full-term girl with Oro-facio-digital syndrome type and HH (24 mm wide). Precocious puberty at 13 months, treated. Gelastic seizures since 20 months, refractory to ASM. Psychomotor development started showing some delay at 23 months and agitation progressively increased. MRgLiTT was planned to be bi-staged due to the dimensions of the HH: first at 31 months and second one year later; both without endocrine or neurological complications. After the first treatment she was seizure free for 4 months and after the second, she had a progressive reduction of seizures (75%) and cognitive and behavioural improvement at 4 months follow-up.
2. 16 years old boy diagnosed with HH at 8 months old due to precocious puberty (treated) and refractory gelastic seizures (tonic-clonic seizures also since 2 years old). Progressive cognitive deterioration and behavioural problems. Radiosurgery at 11 years age without complications. Two months seizure free with relapse after, reaching 2-4 gelastic seizures/day and severe oppositional defiant disorder. MRgLiTT was performed at 15 years of age, without complications. Seizure free after 16 months follow-up. Improvement on learning abilities, but behavioural disorder non-controllable.

Conclusions: We report two cases of HH successfully treated with MRgLiTT, without complications. The patient operated at an earlier age, has shown a very favourable cognitive and behavioural evolution, despite not being seizure-free. The older patient, although seizure free, maintains a severe behavioural disorder. These cases highlight that MRgLiTT seems to be a safe and effective treatment for HH, even in small children and that treatment should be done as earlier as possible.

Abstract Number: 1179

Title: Organization of surgical care for patients with drug resistant epilepsy: first results

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Purpose: Epilepsy is a widespread neurological condition that requires surgical intervention in 20-40% of cases. Annually thousands of patients with epilepsy in Russia become drug resistant and require surgery to get back to the seizure free life, yet only a small fraction of them get the help they need. Our goal was to create a system of surgical care for such patients at our institution, and here we share the first results and outcomes.

Method: This study regards 62 adult patients (28 men and 34 women, average age 34±9 years) with verified drug resistant epilepsy who underwent epilepsy surgery in 2018-2021 at Research Center of Neurology, Moscow. Optimal medical therapy and primary outcomes were assessed by epileptologists. Every patient underwent a thorough pre-surgical and postoperative evaluation. The patients were treated according to the type of the verified lesion: 49 cases of anterior temporal lobectomy, 8 cases of extratemporal resections, 5 cases of functional hemispherotomy. The primary outcome was remission of seizures that impair awareness of self and surroundings. Secondary outcomes were the frequency and severity of seizures, verbal memory, the quality of life, disability, and death.

Result: In a relatively short period of time we managed to build a system of surgical care for patients with drug resistant epilepsy; 62 patients were treated so far, and 40 of them are evaluated in terms of 1-year follow-up. Among these patients the cumulative proportion of seizure-free cases is around 85%, vast majority of them experienced a significant improvement in the quality of life, there were no lethal cases.

Conclusions: Providing surgical care to patients with drug resistant epilepsy requires coordinated teamwork of highly qualified specialists, and building such a service is crucial for reducing the negative social impact of epilepsy. Surgical methods used in our study demonstrate high effectiveness and safety.

Abstract Number: 1249

Title: Contribution of FDG PET in the diagnosis of the epileptogenic zone in patients with refractory focal epilepsy of difficult characterization

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Purpose: In refractory focal epilepsy, surgical treatment is superior to medical treatment when the Epileptogenic Zone (EZ) can be identified. The 18F-FDG-PET (PET) is capable of detecting areas associated with EZ in selected patients.
OBJECTIVES:
Estimate the diagnostic accuracy of PET in the diagnosis of EZ in patients with refractory epilepsy candidates for surgery.
Identify subgroups of patients with greater benefit from the use of PET.

Method: Cross-sectional, retrospective, descriptive and analytical study.
Adults with epilepsy candidates for surgery studied with PET from two centers between January 2014 and May 2020 were included.

The sensitivity (S) and positive predictive value (PPV) of PET were calculated taking the group of operated patients with good evolution as the gold standard added to those not yet operated in which the EZ was determined by Stereoelectroencephalography (sEEG). The patients were divided into groups according to EZ location and MRI findings.

Result: 37 patients were identified with PET scan performed, they were divided into five groups: Lesional temporal lobe epilepsy (11p), lesional extratemporal epilepsy (7p), non lesional temporal lobe epilepsy, non lesional extratemporal lobe epilepsy (3p), unidentified EZ (11p).
We selected 21p for the assembly of the gold standard: 16 operated with Engel I-II and 5p not operated in which the EZ was defined by sEEG. PET showed a sensitivity of 55% (11 / 19p), and a PPV of 83% (2 false positive), in determining EZ. In patients with lesional temporal lobe epilepsy PET showed a sensitivity of 69%, and a PPV of 100%
In comparison, MRI had a sensitivity of 50%. In those patients in whom the MRI was not conclusive, the PET correctly identified 3 patients.

Conclusions: PET showed intermediate sensitivity and high PPV for a good postoperative prognosis in patients with refractory epilepsy, particularly in those patients with lesional temporal lobe epilepsy.

Abstract Number: 1297

Title: Results of the RCT HFO trial: intra-operative electrocorticography tailored epilepsy surgery based on high frequency oscillations versus spikes

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Purpose: Intra-operative electrocorticography (ioECoG) delineates the resection during epilepsy surgery. High-frequency oscillations (HFOs, 80-500Hz) are presumably more precise in identifying epileptogenic tissue than spikes. We prospectively tested the non-inferiority of HFOs to spikes for seizure outcome.

Method: We conducted a randomized controlled, single-blinded, non-inferiority trial and recruited children and adults scheduled for ioECoG-tailored epilepsy surgery (ClinicalTrials.gov: NCT02207673). We excluded patients with an occipital focus and chronic invasive EEG monitoring before surgery. Participants were assigned (1:1) to HFOs or spikes using a computer-generated randomization sequence (block size 2-4-6) stratified by temporal versus extra-temporal lobe epilepsy (eTLE). The primary outcome was seizure freedom one year after surgery (Engel 1A-1B). Secondary outcomes were surgical duration, resection volume, cognition, quality of life, neurological deficits and SAEs. The non-inferiority margin of 10% difference in seizure freedom was predefined. Analysis was by intention to treat.

Result: 78 (39/group) patients were enrolled (Oct'14-Jan'20). Seizure freedom occurred in 26 (66.7%) patients in the HFO and 35 (89.7%) patients in the spike group. The absolute difference was -23% (95% confidence interval (CI): -38 to -8, p=0.01). An unequal distribution of poor-outcome predictors (pathology, age at surgery, epilepsy duration, previous brain surgery) proved disadvantageous for the HFO-group; the adjusted difference was -5.4% (CI: -16.6-5.8; p=0.43). The difference in seizure freedom between HFOs and spikes was 6.5% (CI: -8.4-21.3;p=0.47;N=30) in eTLE versus -12.7% (CI -31.4-5.9;p=0.26;N=48) in TLE and 0.2% (CI: -13-13.4;p=0.98;N=39) in children versus -9.8% (CI: -28-8.4;p=0.37;N=39) in adults. Secondary outcome analyses revealed no significant differences. We registered eight SAEs requiring hospitalization.

Conclusions: After correcting for confounders, we could neither confirm nor reject non-inferiority of HFO to spike-based ioECoG-tailoring in general, and found non-inferiority only for the adjusted scores of the eTLE subgroup. A potential benefit of HFOs in children and eTLE needs further investigation.

Abstract Number: 1311

Title: Surgical outcome and Electro-Clinical profile of posterior cortex epilepsies

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Purpose: To assess the electrophysiological, clinical, imaging features and surgical outcomes in patients with refractory posterior cortex epilepsies.

Method: Retrospective analysis of clinical records of patients (n=103) undergoing surgery for refractory posterior cortex epilepsies with at least 2 years follow up after surgery was done. Clinical features, ictal and inter-ictal EEG findings were compared. Postoperative outcome was analysed as per ILAE grades.

Result: Mean age of onset of epilepsy was 8.3years(1month-37years) with 36(34.95%) females. Mean age at the time of surgery was 17.24years(1-46years). 14(13%) patients had history of perinatal insult. 32(31%) had below average intelligence quotient on neuropsychological assessment. 32 (31%) had daily seizures for atleast 6 months prior to surgery. 18(17%) had some visuo-motor neurodeficits at presentation. 57(55.5%) had concordant inter-ictal epileptiform discharges. 32(31%) had auras(visual, epigastric, somatosensory, psychic). Ictal semiology was lateralising in 55(53.3%) while ictal EEG onset was concordant to imaging in 60(58.2%). 59(57.2%) patients underwent lesionectomy, 27(26.2%) had posterior disconnection, while the rest had multi-lobar resection. On histopathological analysis 43 had cortical dysplasia, 27 had gliosis, 16 had tumoral lesions, 5 had tumor with surrounding dysplasia, 2 had gliosis with dysplasia, one had heterotopias and one oligodendroglial hyperplasia. Two years follow up was available for 97(94%) patients: 67(69%) were seizure free (ILAE class 1). Among patients who underwent resective surgeries 45(64%) were seizure free while 22(81.4%) of those with posterior disconnection remained seizure free at 2 years (p=0.19). Seizure duration of <10 years prior to surgery was associated with seizure freedom (ILAE 1 and 2a, p=0.0001) whereas semiology, EEG and imaging concordance, laterality of ictal EEG were not significantly associated with outcome.

Conclusions: Posterior cortex epilepsies pose significant morbidity. Although Electro-clinical features may not be concordant, surgical treatment after thorough clinical evaluation can lead to better outcomes.

Abstract Number: 1316

Title: Initiating an epilepsy surgery program with limited resources in Indonesia

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Purpose: To share the experiences of organizing the epilepsy surgery program in Indonesia with limited resource

Method: This study was divided into two periods based on the presurgical evaluation method: the first period (1999-2004), when interictal electroencephalogram (EEG) and magnetic resonance imaging (MRI) were used mainly for confirmation, and the second period (2005-2017), when long-term non-invasive and invasive video-EEG was involved in the evaluation. Long-term outcomes were recorded up to December 2019 based on the Engel scale.

Result: All 65 surgical recruits in the first period possessed temporal lobe epilepsy (TLE), while 524 patients were treated in the second period. In the first period, 76.8%, 16.1%, and 7.1% of patients with TLE achieved Classes I, II, and III, respectively, and in the second period, 89.4%, 5.5%, and 4.9% achieved Classes I, II, and III, respectively, alongside Class IV, at 0.3%. The overall median survival times for patients with focal impaired awareness seizures (FIAS), focal to bilateral tonic-clonic seizures and generalized tonic-clonic seizures were 9, 11 and 11 years (95% CI: 8.170-9.830, 10.170-11.830, and 7.265-14.735), respectively, with p = 0.04.

Conclusions: The utilization of stringent and selective criteria to reserve surgeries is important for a successful epilepsy program with limited resources.

Abstract Number: 1323

Title: Non-parametric Granger causality method for localization of epileptic seizure onsets based on a new matrix spectral factorization algorithm

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Purpose: Identification of the seizure onset zones (SOZ) and their propagations, which usually depends on the EEG recordings is crucial for successful epilepsy surgery. For this purpose, the analysis of high-frequency (>80 Hz) oscillations by non-parametric Granger causality (NPGC) method has been reported to be successful. NPGC method, which uses heavy mathematical computations, relies on matrix spectral factorization (MSF). So far, the Wilson algorithm for MSF dominated in neuroscience applications. However, an alternative Janashia-Lagvilava Matrix Spectral Factorization Algorithm (JLMSFA) also proved to be effective that is more reliable for unstable matrices than the former one.

Method: Two regions (X and Y) of interest and a time epoch were isolated by visual inspection of ictal EEG data of the patient. In order to apply NPGC estimation for these regions, cross power spectral density matrix $S(f)$ was constructed in frequency domain by the multitapers method. MSF, $S(f) = H(f)$å $H^*(f)$, where $H(f)$ is a transfer function and å is a noise covariances matrix, was performed by JLMSFA. The NPGC estimations $I_{Y\to X}(f)$ and $I_{X\to Y}(f)$ were computed for high frequency values ($f > 80\ Hz$) by the standard formula using $H(f)$ and å . These estimations were used to confirm the visually suspected SOZ and its propagation.

Result: The JLMSFA was used for the first time on specific real EEG data for localization of epileptic SOZ and its propagation by NPGC method. The algorithm was compared to the corresponding algorithm of Wilson. A thorough comparative analysis of these two methods should be the subject of the future work.

Conclusions: The recently developed JLMSFA has the potential to substitute the Wilson corresponding algorithm which is widely used in computational neuroscience at present.

Acknowledgements: The study was performed in a frame of the Internal Scientific Grant of Caucasus International University.

Abstract Number: 1326

Title: Non-parametric Granger causality method for localization of epileptic seizure onsets based on a new matrix spectral factorization algorithm

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Purpose: Identification of the seizure onset zones (SOZ) and their propagations, which usually depends on the EEG recordings is crucial for successful epilepsy surgery. For this purpose, the analysis of high-frequency (>80 Hz) oscillations by non-parametric Granger causality (NPGC) method has been reported to be successful. NPGC method, which uses heavy mathematical computations, relies on matrix spectral factorization (MSF). So far, the Wilson algorithm for MSF dominated in neuroscience applications. However, an alternative Janashia-Lagvilava Matrix Spectral Factorization Algorithm (JLMSFA) also proved to be effective that is more reliable for unstable matrices than the former one.
Methods: Two regions (X and Y) of interest and a time epoch were isolated by visual inspection of ictal EEG data of the patient. In order to apply NPGC estimation for these regions, cross power spectral density matrix $S(f)$ was constructed in frequency domain by the multitapers method. MSF, $S(f) = H(f)$å $H^*(f)$, where $H(f)$ is a transfer function and å is a noise covariances matrix, was performed by JLMSFA. The NPGC estimations $I_{Y\to X}(f)$ and $I_{X\to Y}(f)$ were computed for high frequency values ($f > 80\ Hz$) by the standard formula using $H(f)$ and å . These estimations were used to confirm the visually suspected SOZ and its propagation.

Results: The JLMSFA was used for the first time on specific real EEG data for localization of epileptic SOZ and its propagation by NPGC method. The algorithm was compared to the corresponding algorithm of Wilson. A thorough comparative analysis of these two methods should be the subject of the future work.

Conclusions: The recently developed JLMSFA has the potential to substitute the Wilson corresponding algorithm which is widely used in computational neuroscience at present.

Acknowledgements: The study was performed in a frame of the Internal Scientific Grant of Caucasus International University.

Abstract Number: 1334

Title: Epileptogenic network definition through game theory and connectivity dynamics

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Purpose: Presurgical workups for treating drug-resistant epilepsy (DRE) patients do not ensure favourable outcomes. Stereo-EEG (SEEG) is a valuable resource for defining the epileptogenic network (EN). However, SEEG quantification is non-standardized, largely due to the lack of consensus regarding the EN concept. Most computational approaches analyse local field potentials, while connectivity-based approaches compare EN

connectivity to non-epileptogenic networks (NN). No strategy so far provided consistent results of surgical outcome prediction. We propose a model for EN and NN connectivity dynamics through a game theory concept.

Method: We analyse the transition between states to assign nodes to either network. Connectivity measures between node pairs are features that determine states. Support vector machine classifies between default and ictal epochs, and random data splits are applied to simulate game scenarios. The probability of epileptogenic nodes winning is scored using the minimax algorithm. The highest-scoring nodes were selected as EN. The framework was validated on a chronological cohort of 21 DRE patients, with the only inclusion criterion of a 3-year follow-up.

Result: Surgical outcome prediction accuracy of 93% was achieved, which is the best to our knowledge. Several time intervals prior and during seizure were tested. The EN could not be inferred from the seizure event itself. Instead, an optimal time interval for EN definition was at the transition from pre-seizure to seizure.

Conclusions: In the proposed model, each SEEG channel is a network node that either plays against or for the EN, which pushes towards ictal states. The best time to distinguish the networks is the transition from non-seizure to seizure. This is the most interesting finding, beyond clinical applicability, since it suggests a push-pull dynamics not only in seizure propagation, as proposed by other works, but also during seizure start. Future works will elucidate these dynamics and potentially help understand cognitive processes.

Genetics

Abstract Number: 70

Title: Trio Exome Sequencing with In-depth Phenotyping in Epilepsy: A Prospective, Single-Centered Study with Return of Research Results to Patients

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Purpose:
We sought to demonstrate the yield of trio whole-exome sequencing(WES) in children with epilepsies, combining phenotypic and genomic expertise to analyze cases and deliver clinical results, as well as expand the phenotypes of known epilepsy-related genes and identify novel genes.

Method: Starting in 2018, we prospectively enrolled children with unexplained epilepsy at Boston Children's Hospital. WES were conducted and processed using a standardized alignment and variant calling pipeline. In-depth clinical history, including seizure semiology, epilepsy according to the ILAE classification, age of seizure onset, family history, EEG, MRI, presence of intellectual disability(ID) and autism, and treatment response were characterized by epileptologists. *De novo* and inherited variants were classified according to ACMG criteria, with special attention to a recursive and detailed phenotyping approach that allowed us to return to the patients and physician to obtain data relevant to a given gene.

Result: We evaluated sequencing data from 513 children: 311 trios and 202 proband-only, including 195(38%) developmental epileptic encephalopathy(DEE), 143(28%) generalized genetic epilepsy(GGE), 126(25%) non-lesional focal epilepsy(NLFE), and combined epilepsy. We identified clinically explanatory variants for 89(17%) cases and novel candidate genes in 104(20%) cases. The yield of clinically explanatory variants was highest in those with seizure onset earlier than preschool age(OR 2.49[95%CI 1.54-4.01], P=2.4X10^{-4}) and those with

ID(OR 3.16[1.89-5.28], *P*=9.1X10^{-6}). Probands with DEE had higher yield of clinically explanatory results vs. those with GGE or NLFE(OR 2.35[1.48-3.74], *P*=3.8X10^{-4}). Even so, we identified explanatory variants in the non-DEE groups.

Conclusions: We demonstrate a high yield of clinically explanatory results in children with unexplained epilepsy, especially in patients with early-onset epilepsy, ID, and/or DEE but also in other subgroups, phenotyped and sequenced with return of clinical results through an institutional platform. Research into candidate genes, including further case identification and functional studies, are predicted to increase this yield in the future.

Abstract Number: 77

Title: Diagnostic yield and cost-effectiveness of "dynamic exome-based approach" in epilepsy with neurodevelopmental disorders: a clinical experience

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Purpose: The advent of next generation sequencing (NGS) techniques in clinical practice led to a significant advance in gene discovery. We aimed to describe diagnostic yields of a "dynamic" exome-based approach in a cohort of patients with epilepsy associated with NDDs (Neuro Developmental Disorders).

Method: We conducted a retrospective, observational study on 72 probands. All patients underwent "dynamic exome-based approach" represented by a first diagnostic level of 135 gene panel, a second of 319 genes for inconclusive cases, and finally the analysis was extended to Whole Exome Sequencing for negative cases. Diagnostic yields at each step and cost-effectiveness were object of statistical analysis.

Result: Overall diagnostic yield in our cohort was 37.5%: 29% of diagnosis derived from the first level analysis, 5.5% from the second level and 3% form the third one. A significant difference emerged between the three diagnostic levels (p<.01), between the first and second (p=.001) and the first and third level (p.<<.001). The cost-effectiveness plane indicated that our exome based "dynamic" approach was dominant in terms of cost savings and higher diagnostic rate.

Conclusions: Our findings suggested that "dynamic" NGS techniques applied to well phenotyped individuals can save both time and resources. In patients with unexplained epilepsy comorbid with NDDs our approach might maximize the number of diagnosis achieved.

Abstract Number: 80

Title: Genotype-phenotype correlations in SCN8A-related disorders reveal prognostic and therapeutic implications

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Purpose: The spectrum of *SCN8A* ranges from benign familial infantile epilepsy (BFIE) with self-limiting seizures, over an intermediate phenotype to early onset developmental and epileptic encephalopathies (DEE). Here, we combined the largest cohort of individuals with *SCN8A*-related neurodevelopmental disorders investigated to date with functional studies and explored genotype-phenotype correlations in *SCN8A.*

Method: Phenotypic data was collected from clinicians worldwide in a standardized manner. Seizures were classified according to the ILAE classification. Variants were classified according to the ACMG guidelines. We performed functional studies expressing missense variants in ND7/23 neuroblastoma cells and primary neuronal cultures using recombinant tetrodotoxin insensitive human $Na_V1.6$ channels and whole-cell patch clamping

Result: Five different clinical subgroups could be identified: 1) BFIE 2) intermediate epilepsy 3) developmental and epileptic encephalopathy 4) generalized epilepsy and 5) affected individuals without epilepsy . Groups 1-3 presented with early-onset focal or multifocal seizures and epileptic discharges, whereas the onset of seizures in group 4 was later with generalized epileptic discharges. Two variants causing DEE showed a strong gain-of-function (GOF), and one variant causing BFIE or intermediate epilepsy showed a mild GOF. In contrast, all three variants causing generalized epilepsy induced a loss-of-function (LOF). Including previous studies, functional effects were known for 165 individuals. All 133 individuals carrying GOF variants had either focal or unclassifiable epilepsy, whereas 32 with LOF variants had either generalized, no or unclassifiable epilepsy; only two had DEE. Computational modeling in the GOF group revealed a significant correlation between the severity of the electrophysiological and clinical phenotypes. GOF variant carriers responded significantly better to sodium channel blockers (SCBs) than to other anti-seizure medications, and the same applied for all individuals of groups 1-3.

Conclusions: In conclusion, our data reveal clear genotype-phenotype correlations between age at seizure onset, type of epilepsy and gain- or loss-of-function effects of *SCN8A* variants.

Abstract Number: 166

Title: Preliminary Validation of a Novel WDR45 Mutation in a Male Patient with Lennox-Gastaut Syndrome

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Purpose: This study intends to validate the pathogenicity of novel WDR45 p.Ser247Ile mutation in a typical Lennox-Gastaut syndrome patient, thus establishing the relationship between autophagy and epileptic encephalopathies such as Lennox-Gastaut syndrome.

Method: Recombinant expression plasmids of WDR45 gene wild type and mutant type were constructed respectively using human WDR45 cDNA as a template. The expression vectors were then transfected into HEK293T cells and primary hippocampal neurons cultured in vitro separately. Western blotting technique was used to evaluate the expression of LC3-I and LC3-II, while double immunofluorescence labeling method (GFP-RFP-LC3) was used to observe the formation of autophagy structures in transfected HEK293T cells. The number of red fluorescent spots under microscope representing the formation of autophagosome was counted. Comparations between wild and mutant HEK293T cells were conducted to assess whether autophagy flux was blocked. Morphological changes in transfected neurons were also observed under confocal microscope to evaluate the effects of mutation on growth of neurons.

Result: The LC3 expression in mutant HEK293T cells was significantly higher than control, indicating the mutation caused the accumulation of LC3 positive vesicles. Similarly, the decrease of red fluorescent spots was observed in mutant carriers, representing reduced formation of autophagosome, which confirm that the WDR45 p.Ser247Ile mutation leads to obstruction of autophagy flux in non-neuronal cells. At the same time, reduced branching of neurons and aberrant dendrites were observed in mutant neurons, which may represent the mutation effects.

Conclusions: Patients with WDR45 gene mutations may present with Lennox-Gastaut syndrome. WDR45 p.Ser247Ile mutation can cause autophagy dysfunction in non-neuronal cells and disturb normal development of neurons.

Abstract Number: 181

Title: Biallelic pathogenic variants in RARS2 cause Progressive Myoclonus Epilepsy and variable epilepsy phenotype

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Purpose: Biallelic pathogenic variants of RARS2 are associated with pontocerebellar hypoplasia type 6 (PCH6) a rare mithocondrial encephalopathy typically manifesting with vermian hypoplasia and refractory seizures. We aim to characterize the epilepsy phenotype of individuals with *RARS2* mutations.

Method: All patients referred to our Institute and carrying pathogenic variants of *RARS2* were included. Variants were identified by WES and validated by Sanger sequencing. All patients underwent a comprehensive electro-clinical work-up.

Result: we selected 4 individuals (2 siblings, 2 isolated cases, mean age 29,5±1,29 years) all carrying compound heterozygous mutations of *RARS2* [NM_020320 *m1*:c.1A>T (p.Met1 Leu), *m2*:c.1544A>G (p.Asp515Gly); *m3*:c.1586+3A>T, *m4*:c.1366C>T (p.Arg456Cys); *m5*:c.1305+1G>A, *m6*:c.1026G>A (p.Met342Ile)]. One variant is novel.
The mean age at seizure onset was 12,08±16,19 months (40 days-3years). One patient presented with myoclonic and GTCS evolving in status epilepticus, 2 with spasms and one with tonic and GTCS. A transient response to vitamin B6 was documented in one individual. With disease progression, 2 patients developed polymorphic seizures (focal motor to bilateral T-C seizures, absences, tonic/atonic, eyelid myoclonia), 2 showed myoclonic and GTCS, respectively. Two unrelated individuals with earlier age at onset showed microcephaly, spastic tetraparesis, profound intellectual disability (ID) with absent language, and cortical blindness. Interictal EEG showed a severe slowing of background activity with multifocal epileptiform abnormalities. Brain MRI highlighted the typical pontocerebellar atrophy. The other 2 unrelated patients manifested a milder phenotype with moderate ID, cerebellar signs and action myoclonus, resembling Progressive myoclonus epilepsy (PME). Interictal EEG showed epileptiform discharges predominant posteriorly and a photoparoxysmal response. Brain MRI was normal.

Conclusions: Biallelic pathogenic variants of *RARS2* cause mitochondrial encephalopathy with variable inter and intra-family severity: from classic PCH6 to a milder clinical phenotype with myoclonic epilepsy, action myoclonus and photosensitivity. Pontocerebellar atrophy is not a mandatory feature. Our data widen the epilepsy phenotype of *RARS2*, to include PME.

Abstract Number: 315

Title: GABRB3 related epilepsy: novel variants, clinical features and therapeutic implications

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Purpose: *GABRB3* variants are associated with a broad phenotypic spectrum of epilepsy from febrile seizures to epileptic encephalopathy. We aimed for a comprehensive of genetic and phenotypic aspects of *GABRB3*-related epilepsy and explored potential prospects of personalized medicine.

Method: Through the collaboration of multicenter in China, we analyzed the genotype-phenotype correlation and antiepileptic therapy of 25 patients with *GABRB3*-related epilepsy.

Result: 25 pathogenic/likely pathogenic *GABRB3* variants were identified, among which 11 variants were novel and 24 were verified as de novo. Mosaicism occurred in one patient. Seizure onset age was ranged from 1 month to 21 months (median age: 4 months). Seizure types predominated including focal seizures (23/25, 92%), generalized tonic-clonic seizures (6/25, 24%), epileptic spasms (4/25, 16%), myoclonic seizures (3/25, 12%). Two patients manifested epilepsia partialis continua (EPC). Clinical features included cluster seizures (20/25, 80%), fever-sensitivity (14/25, 56%), and developmental delay (24/25, 96%). Neuroimaging was abnormal in 9 patients, including dysplasia of cerebral cortex, delayed myelination, and corpus callosum dysplasia. Ten patients were further diagnosed with epilepsy syndrome, including four with West syndrome, three with epilepsy of infancy with migrating focal seizures (EIMFS), one with epilepsy with myoclonic-atonic

seizures (EMAS), one with Dravet syndrome, one with febrile seizures plus (FS+). Seizures were controlled in 60% of patients (15/25).

Conclusions: The clinical features of *GABRB3*-related epilepsy included seizure onset in early infancy, cluster seizures and fever-sensitivity. Epilepsy phenotypes were severe in most of patients. However, seizures could be controlled by valproate, levetiracetam, topiramate, perampanel, or vigabatrin in the majority.

Abstract Number: 317

Title: From single-cell-based coexpression networks to overcoming drug resistance in epilepsy

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Purpose: Approximately half of the 65 million epilepsy cases worldwide can be traced to single genetic mutations. Genetics-driven therapeutic approaches delineate the onset of precision medicine treatments and could overcome the high drug resistance seen in many severe epilepsy cases. While treatments only exist for the very first few genes, their potential to overcome drug resistance can be multiplied through the inference of epilepsy-associated gene networks that are functionally related to these first druggable targets. In order to discover novel treatment modalities in an unbiased manner we have developed a bioinformatics pipeline that links previously unassociated genetic interactors with causative genes in epilepsy.

Method: Genetic interactors have in the past indicated new target leads in small compound inhibitor strategies (Srivastava P et al. *Nature Comm* 2019;9:3561). New analyses based on single-cell whole-brain transcriptomics allow us to determine potential gene networks among the over 100 epilepsy-associated genes and thus expand the group of pharmacological targets at an unprecedented resolution. The distinction of glial from excitatory/inhibitory neuron gene networks will further guide and improve specificity of the anti-seizure drug discovery and assist in targeting co-occurring symptoms such as Intellectual Disability.

Result: Based on whole-brain analysis, single-cell transcriptomics has identified highly co-expressed pathway members at the intersection of synaptic vesicle cycling and energy metabolism. Core machinery of vesicle fusion and fission is strongly coexpressed with a defined metabolic pathway across the brain. Dissecting excitatory and inhibitory pathways in the mouse brain revealed epilepsy-associated genes with different coexpressed partners in the GABAergic or Glutamatergic system.

Conclusions: Our genetic interaction map holds the potential to inform CRISPR-based stem cell screens in the future, and already validation of larger functional epilepsy gene networks has started based on an established *in vivo* pairwise deficiency paradigm in *Drosophila*, efficiently modeling seizure behavior and opening new therapeutic avenues.

Abstract Number: 337

Title: Expanding the knowledge spectrum of the genetic background in pediatric Argentinean patients with epileptic encephalopathy

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Purpose: The aim of this study was to extend our knowledge of the genetic background of Argentinean pediatric patients with epileptic encephalopathies (EEs) without known etiology, applying a Next Generation Sequencing (NGS) panel.

Method: We included 31 patients with EEs after ruling out structural abnormalities, metabolic disorders and large chromosomal abnormalities. They presented with the following clinical phenotypes: Dravet syndrome (DS)(n:10), West syndrome (WS)(n:6) West Syndrome/Lennox Gastaut (WS/LG)(n:4), unclassified epileptic encephalopathy (UEE)(n:6), epilepsy of infancy with migrating focal seizures (EIMFS)(n:2), myoclonic status in non-progressive encephalopathies (MSNE)(n:1), myoclonic atonic epilepsy (n:1), EE with multifocal spikes (n:1). Neurologic examinations, seizure semiology, brain magnetic resonance imaging, and standard/video electroencephalography studies were analyzed. We designed a custom capture NGS panel to study 53 genes most frequently associated with EEs.

Result: Pathogenic variants were detected in 12 cases (39%), including seven novel pathogenic variants and five previously reported as being pathogenic. Single nucleotide pathogenic variants were identified in *SCN1A (5)*(DS*), SCN2A (1)*(UEE*), SCN1B (1)*(DS*), GABRG2 (1)*(UEE*) and STXBP1 (2)*(WS and MSNE). Additionally, a deletion involving *SCN1A, SCN2A and SCN3A* genes was detected in one patient with EIMFS, and the most frequent triplet expansion in *ARX* gene was observed in a patient with WS. It should be noted that, while most of the variants were found in heterozygosity in agreement with the dominant inheritance pattern frequently associated with these syndromes, the patient with the variant in *SCN2A* gene was a mosaic with 20% of the variant in leukocytes and one patient with DS was homozygous for *SCN1B* gene variant.

Conclusions: Using NGS panel, a genetic diagnosis was achieved in 39 % of patients, being nearly 58% of them cases with non-previously reported variants. This study broadens the knowledge of the molecular basis associated with EE to strengthen current international databases with Latin American population information.

Abstract Number: 401

Title: The clinical features and genotype-phenotype correlation of CACNA1A variants in children with epilepsy

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Purpose: To explore genotypes and phenotypes of *CACNA1A* variants in children with epilepsy.

Method: Eighteen children with *CACNA1A* variants were identified by next-generation sequencing.

Result: There were 14 missense variants, 2 nonsense variants, 1 frameshift variant and 1 splicing-site variant. 16 variants were de novo. Seizure onset age ranged from 1 day to 8 years old, the median age was 8 months. Multiple seizure types were observed, including focal seizure, generalized tonic-clonic seizure, myoclonic seizure, absence seizure, epileptic spasms and tonic seizure. Focal convulsive status epilepticus(FCSE) occured in 10 patients and generalized convulsive status epilepticus occured in 2 patients. All 18 patients showed varied degree of development delay. FCSE results in unilateral cerebral atrophy in 5 patients. Interictal EEG showed focal discharges in 12 patients whereas 5 patients had generalized discharges. Three patients were seizure free whereas 15 patients still had seizures and 5 patients had recurrent status epilepticus in the last follow-up. Patients with *CACNA1A* variants located in the transmembrane region are at high risk of status epilepticus.

Conclusions: Most epilepsy children with *CACNA1A* variants had early seizure onset and developmental delay. Focal seizure was the most common seizure type. Most patients experienced status epilepticus. Unilateral brain atrophy could occur after FCSE.

Abstract Number: 403

Title: Developmental trajectories in STXBP1-DEE

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Purpose: Mutations in STXBP1 cause a severe neurodevelopmental disorder (STXBP1-DEE). The clinical manifestations are variable in severity and outcome, and are associated with a similarly diverse genotypic spectrum. The aim of the study is to analyze the factors contributing to the phenotypic variability in STXBP1-DEE and trace developmental trajectories.

Method: Retrospective clinical data were collected through international collaboration. A „score“ has been elaborated to compare the development between different patients.

Result: 46 patients with *de novo* STXBP1 variants were included (34 novel and 12 published). 33% of patients become seizure-free, 73% of these within the 1st year of life. Half of the patients present developmental delay before epilepsy onset; however, epilepsy onset co-occurs with developmental stagnation in most of patients. The age at seizures onset correlates with the severity of the developmental outcome and the developmental milestones achieved: later onset is associated with a better psychomotor outcome. On the contrary, age at seizure remission or epilepsy duration do not seem to have an impact on neurodevelopmental outcome. We could not establish clear genotype-phenotype correlations; however, monozygotic twins present an identical phenotype and disease course.

Conclusions: STXBP1-DEE natural history presents two main trajectories, with an early seizure remission or a pharmaco-resistant epilepsy, and diverse neurodevelopmental outcomes ranging from mild to profound psychomotor impairment. Epilepsy impact on neurodevelopment seems to be limited to the age at seizures onset. A standardized longitudinal study of the natural history of STXBP1-DEE is crucial in the view of clinical trials with targeted therapies.

Abstract Number: 415

Title: CONDSIAS: A rare Neurodegenerative disease - Case Report

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Purpose: CONDSIAS (Stress Induced Childhood Onset Neurodegeneration with Variable Ataxia and Seizures) is a rare autosomal recessive disease caused by defects in the ADPRHL2 (ADP RIBOSYLHYDROLASE LIKE2) gene involving 1p34.3. It is a very rare disorder with very few cases reported across the world. Here, we report the first case of CONDSIAS in the Indian population.

Method: A 9-year-old male child, born out of a second-degree consanguineous marriage, with normal developmental history until one and a half years of age, presented to us with complaints of right focal motor seizures occurring initially with a frequency of once per week, which increased gradually to 3-4 episodes per day. At the age of 3 years, his mother noticed stimulus sensitive myoclonic jerks involving only upper limbs along with flexion of neck. Habituation on repeated stimulus was present.

6 months later, swaying to both sides while walking along with intention tremors was seen. By the age of 6yrs, broad based gait, increased instability while walking and difficulty in passing through narrow passages and recurrent falls along with distal weakness in lower limbs were seen. Behavioural disturbances in the form of verbal and physical aggression were seen.
There was regression of developmental milestones.
Examination showed cerebellar signs with peripheral neuropathy. His metabolic workup and imaging were normal, screening for inborn errors of metabolism was negative and EEG was normal.
In view of inconclusive workup, a clinical exome sequencing was done.

Result: Exome sequencing revealed a mutation of ADPRHL2. Both the phenotypic and genotypic evidence were consistent with CONDSIAS cases reported across the world.

Conclusions: CONDSIAS is an ultra-rare neurodegenerative disorder that should be considered as a differential for diseases like Progressive Myoclonic Epilepsy, Progressive Myoclonic Ataxias.

Abstract Number: 478

Title: Genetic repair of POLG-related epilepsy

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Purpose:
Point mutations in the *POLG* gene cause one of the most severe forms of intractable epilepsy. Current anti-seizure medications are ineffective and many children die within months to years after seizure onset, usually due to status epilepticus and/or liver failure. Gene therapy holds promise to directly target the root of the disease. We aim to use the recently developed gene editing techniques prime editing and base editing to repair disease-causing mutations of patients with *POLG*-related epilepsy.

Method: We developed guide RNAs to guide base editing and prime editing machinery to the most common A467T POLG mutation, the most common pathogenic variant resulting in *POLG*-related epilepsy. These guide RNAs were designed based on established in-silico predictions of maximal gene editing efficiency. Fibroblasts were then transfected with prime or base editing plasmids along with these guide RNAs. Using Sanger sequencing, we assessed gene editing efficiency and unwanted bystander edits.

Result: We were able to establish repair of the A467T mutation in 25% of DNA in patient-derived fibroblasts using base editing and 46% using prime editing. We did not observe any unwanted bystander edits with either technique

Conclusions: Our study is the first to show that base editing and prime editing can be effective in repairing disease-causing mutations in the *POLG* gene. We expect that this approach will pave the way towards eventual causal treatment of patients suffering from *POLG*-related epilepsy as well as other forms of monogenic refractory epilepsy.

Abstract Number: 499

Title: Genetic diagnostic yield in a large cohort of patients with developmental and epileptic encephalopathy from Latin America: a preliminary report

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Purpose: The advances in the genetic diagnosis of developmental and epileptic encephalopathies (DEEs) have improved overall medical care for these patients. However, few genetic studies of patients with admixed genetic backgrounds have been performed. Therefore, we aim to study a large cohort of patients with DEE recruited in different epilepsy centers in Latin America as part of a collaborative multicentric project.

Method: We assessed a total of 244 patients and performed exome sequence (WES, *SureSelectXT Human All Exons V6* and *Illumina Hiseq 4000/NovaSeq 6000*) in 236 patients and chromosomal microarray (CMA, *Genome-Wide Human SNP Array 6.0*) in 241 patients. Variants identified in the WES were called using GATK, followed by applying a bioinformatics panel that prioritized variants present in epilepsy-related genes. CMA data were filtered based on size, the number of markers, coverage, and frequency of the structural variants found (CNVs). For both approaches, the variants were classified according to criteria proposed by the American College of Medical Genetics and Genomics (ACMG).

Result: In the WES data, we found 162 variants of interest in 81 genes. Overall, 70 patients have variants classified as pathogenic or likely pathogenic. Mutations in the *SCN1A* gene were the most frequently found. In the CMS data, we found 31 CNVs putatively associated with the phenotypes, and overall, 11 patients have pathogenic CNVs.

Conclusions: Applying the ACMG criteria, we confirmed a genetic etiology of the DEE for 33.2% of our patients, with a higher diagnostic yield provided by the WES (29.7%) compared to the CMA (4.6%). Thus, supporting the initial use of a sequence-based genetic test in these patients. However, there are patients in whom a genetic diagnosis is best achieved using CMA.

Abstract Number: 515

Title: Everolimus as a precision therapy for drug-resistant epilepsy caused by mutations in the GATOR1 complex genes DEPDC5 and NPLR3

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Purpose: GAP activity towards RAGs 1 complex (GATOR1) functions as a negative regulator of mechanistic target of rapamycin (mTOR) signalling. Heterozygous pathogenic variants of genes encoding GATOR1 (*DEPDC5*; *NPRL2*; *NPRL3*) are associated with drug-resistant epilepsy and a disproportionate risk of sudden unexplained

death in epilepsy. Similar to tuberous sclerosis complex (TSC), epileptogenesis in the 'GATORopathies' appears to be mediated by excessive mTOR activation. Everolimus, a mTOR inhibitor is an approved treatment for drug-resistant seizures in TSC. Here, we study everolimus as a treatment for drug-resistant seizures in GATOR1 epilepsies.

Method: An observational open-label study of everolimus as a treatment for drug-resistant seizures in GATOR1 epilepsies. People with epilepsy (PWE) caused by mutations in the *DEPDC5*, *NPRL2* or *NPLR3* genes were identified by research whole exome sequencing (WES) and confirmed at an accredited genetics laboratory.

Result: Four individuals with drug-resistant epilepsy and GATOR1 mutations (3 *DEPDC5*; 1 *NPLR3*) have started treatment with everolimus. Three have nocturnal frontal lobe epilepsy, and one has multifocal epilepsy with peri-ictal psychiatric symptoms. Two have co-morbid intellectual disability. All have normal MR imaging of brain. Prior to commencing everolimus, two had daily seizures and two had 2-3 seizures per week. The mean duration of treatment is 7.25 months (range 3-16 months). Two have experienced a greater than 50% improvement in seizure frequency since commencing everolimus. No adverse events have led to treatment discontinuation.

Conclusions: Non-TSC mTORopathies are emerging as an important cause of drug-resistant epilepsy. Diagnostic WES should be considered in cases of refractory non-lesional epilepsy or refractory epilepsy due to focal cortical dysplasia. Preliminary data suggests that everolimus may be an effective targeted therapy for drug-resistant epilepsy caused by mutations in GATOR1 genes.

Abstract Number: 532

Title: Identification of functional gene co-expression networks in drug-resistant epilepsy using Drosophila as a model

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Purpose: Severe epilepsy acutely affects 6 million EU citizens, about half with single underlying genetic mutations and a third leading to drug-resistant epilepsy (DRE). It has been found that some genetic epilepsies may be functionally related and share common mechanisms, indicating that they can be co-targeted in the same networks. A gene co-expression network (GCN) of 320 genes, enriched in epilepsy genes and protein-protein interactions, has previously been identified (Delahaye-Duriez et al. Genome Biology 2016;17:245). However, a pipeline for validation of functional relationships, mechanistic analyses and drug testing is still missing. Here we establish *Drosophila* as a powerful model to overcome current limitations in scaling up functional validation and investigation of epilepsy mechanisms in the context of an intact nervous system.

Method: Starting from previous analyses and own single-cell based gene co-expression network analysis (Long et al., poster #317), we selected a candidate module of 20 genes including 6 genes implicated in epilepsy, *ATP6V1A*/*CAMK2A*/*DNM1*/NAPB/*SYNJ1*/*YWHAG* as well as the most highly co-expressed gene partners for further characterization. Gene-specific knockdown was achieved with the UAS-Gal4 system, a pan-neuronal Gal4 promotor line and UAS-RNAi lines from genome-wide resources. For each gene, we tested whether individual genetic ablation specifically in neurons confers susceptibility to seizure-relevant behaviors in *Drosophila* (Lasko and Lüthy. Faculty opinions 2021;doi:10.12703/r/10-10), and causes other neurological phenotypes.

Result: About one third of our disease models showed seizure-relevant behaviors following either mechanically or heat-induced stimulation. These and the other identified phenotypes are currently used to reveal functional interaction between genes in our module by generating double knockdown flies and evaluate pair-wise genetic interactions.

Conclusions: Based on *in silico* predictions, animal models were established for 20 genes and multiple seizure-relevant behavior phenotypes were identified. Our further analysis will identify epilepsy genes that can be co-targeted and provide novel insights into mechanisms and therapeutic approaches.

Abstract Number: 653

Title: Functional assessment of KCNB1 loss- and gain-of-function variants and correlation with electro-clinical phenotypes

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Functional assessment of *KCNB1* loss- and gain-of-function variants and correlation with electro-clinical phenotypes

Purpose: Pathogenic variants in the *KCNB1* gene, encoding the voltage-gated K^+ channel (Kv) α-subunit, are associated with a spectrum of phenotypes ranging from severe developmental and epileptic encephalopathies (DEE) to mild intellectual disability without epilepsy [1]. Kv2.1 exerts an electrical role in neurons and KCNB1 variants may result in the loss of channel voltage-dependence or ion currents conductance [2]. We functionally characterized different pathogenic variants in *KCNB1* and correlated the results with the electro-clinical phenotypes of the patients.

Methods: *KCNB1* pathogenic variants were identified through NGS. Kv2.1 mutants were expressed in HEK293 cells and membrane currents evaluated using the *patch-clamp* technique. Cells were stimulated with constant pulse-potentials ranging from -80 to +120 mV, Δ=20 mV ($n \geq 4$ experiments for each variant). Patients were deeply phenotyped through clinical charts collected from referring clinicians.

Results: We identified 5 *KCNB1* pathogenic variants: p.T210M; p.T804A; p.V349F; p.F416L; P.R312H. Four were *de novo*, while the p.T804A was inherited from the affected mother. K_V2.1 p.T804A mutant stayed open at >+50 mV potentials (gain-of-function). This variant was associated with a mild phenotype (focal epilepsy without psychomotor delay). The other K_V2.1 mutants showed loss of the ion current conduction. These variants were found in 4 patients with severe phenotypes (DEE).

Conclusions: *KCNB1* variant may impact patients' phenotypes depending on the functional effect on the channel. Milder phenotypes are more often associated with gain-of-function variants whereas loss-of-function variants usually lead to severe phenotypes.

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Abstract Number: 669

Title: Exploring potential biomarkers for comorbidity of epilepsy and congenital heart disease using whole exome sequenced Europeans from UK Biobank

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Purpose: The congenital heart disease (CHD) has the highest prevalence in newborns comparing to other congenital malformations. Clinical studies have found that cardiac surgery can significantly increase the incidence of seizures among them. Moreover, whether the individual has experienced cardiac surgery or not, the incidence of epilepsy in CHD is significantly higher than that in normal people. A recent study has shown that some common genetic factors can be shared between CHD and neurodevelopmental diseases (NDD). To explore the potential genetic risk factors between CHD and epilepsy, we performed gene burden analyses using whole exome sequencing data from UKBiobank.

Method: We selected CHD and epilepsy cases by International Classification of Disease 10th version from diagnoses information of 200K WES samples in UKBiobank. The controls were rigorously selected from the samples without any congenital malformations, neurological diseases or vascular diseases. We separately conducted case versus controls tests on CHD and epilepsy using SKAT-O. The overlapped significant genes were analyzed by network analyst to establish differential gene protein interaction network.

R**esult:** 1,686 European patients with epilepsy , 362 European patients with CHD and 2,000 controls were selected. We found 67 disease associated genes in common from SKAT-O analyses. Alternative splicing and platelet-derived growth factor receptor signaling pathway were the most significantly enriched pathway, while RNA binding and Zinc-finger were enriched significantly. In the PPI network analysis, survival motor neuron 1 protein may be the critical module. 17 hub genes were extracted including PDGFRB, SMN1, PTPN11.

Conclusions: We found critical genes and signaling pathway in epilepsy and CHD. These are critical for metabolism, inflammation, pericyte function which has been treatment targets in some neurological diseases. This study further confirmed shared genetic factors between CHD and NDD, which provide potential targets that lead more precise approaches for the treatment.

Abstract Number: 786

Title: HLA-A*31:01 and HLA-B*15:02 are not associated with cutaneous adverse reactions induced by aromatic antiseizure medication in a Brazilian population

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Purpose: To investigate if HLA-A*31:01 or HLA-B*15:02 are associated with aromatic antiseizure medication-induced cutaneous adverse reactions (CAR) in a Southern Brazilian population.

Method: Patients with history of CAR induced by aromatic antiseizure medication (ASM-A) presenting up to 12 weeks after its initiation composed group CAR+. Epilepsy patients with regular ASM use for at least 12 weeks

without CAR were consecutively enrolled in group CAR-. For each case, at least two subjects tolerant to the same ASM-A were included (CAR- plus CAR+). HLA-A*31:01 and HLA-B*15:02 loci were investigated by Next Generation Sequencing. HLA-A*31 and HLA-B*15 allelic frequencies were compared between CAR+, CAR- and control group, composed by subjects from the same Brazilian state registered in the National Registry of Bone Marrow Donors.

Result: We included 106 CAR+, 98 CAR-, with no differences in sex or age, and 341.639 controls. Carbamazepine was the main drug triggering rash (49%), followed by lamotrigine (23%), phenytoin (19%), phenobarbital (13%), and oxcarbazepine (5%). Severe CARs cutaneous adverse reactions affected 37% of patients. HLA-A*31 allelic frequency was found to be higher in CAR+ (10.8%), but not CAR- (8.1%), than in control group (5%) (P<0.0001, OR=2.58, IC=1.6-3.9 and P=0.02, OR=1.85, IC=1.0-2.9, respectively). HLA-B*15 allelic frequency did not differ between CAR+ (8.6%), CAR- (8.6%) and controls (8.7%) (P=0.95). Among CAR+ and CAR-, HLA-A*31:01 was the only allele from HLA-A*31 found, no HLA-B*15:02 was observed. No association between HLA-A*31:01 and any type of CAR induced by any ASM-A was observed. Even after grouping all ASM-A and all CARs, HLA-A*31:01 frequencies were similar between CAR+ and CAR- (P=0.4, OR=1.34, IC=0.62-2.94).

Conclusions: HLA-A*31:01 and HLA-B*15:02 are not associated with CARs induced by ASM-A in this Brazilian population. HLA-A*31 allelic frequency was higher between CAR+, but not CAR-, than controls, suggesting there will be other factors associated with CARs in our population.

Abstract Number: 836

Title: The natural history of SCN8A epilepsy and realted diseases

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Purpose: The *SCN8A* clinical spectrum embraces a variety of phenotypes with different prognoses, ranging from benign familial infantile epilepsy (BFIE) to severe epileptic encephalopathies (DEE), including patients without epilepsy. We conducted a retrospective natural history study of children and adults with *SCN8A*-related diseases using investigator-observed and parent-reported outcome measures to obtain data that will be useful for targeted counseling and future clinical trials.

Method: From our database of 512 patients with pathogenic *SCN8A* mutations enrolled through a collaborative network worldwide, we selected those with available clinical information at different time-points. Primary outcome measures were (1) medical history, including seizure types/frequency, cognitive/motor development, medical interventions and comorbidities; (2) developmental history, evaluating all milestones domains; (3) EEG features; (4) genetic information (mutation / functional effect).

Result: we selected 291 patients with (1) DEE (n=198) presenting with early onset epilepsy, severe cognitive/motor regression from the second year-of-life, worsening over the following 3-6 years. Seizures were drug-resistant, partially responding to high doses of sodium channel blockers (SCBs) and to ketogenic diet. Premature death was reported in about 5% of cases. (2) Sporadic and familial patients with non-progressive mild-to-moderate intellectual disability and neurological signs and treatable focal epilepsy (n=43), or generalized epilepsy (n=28) better responding to non-SCBs. Behavioural disturbances or autism may become the prominet problem over time; (3) BFIE (n=17) with self-limiting epilepsy, responding to low doses of SCBs,

normal cognition, and no/minor neurological deficits; (4) Patients with isolated cognitive, behavioral or movement disorders (=5). These seem to be non-progressive disorders.

Conclusions: We identified different patterns of evolutions and prognostic factors in individuals with different *SCN8A* phenotypes. This is the first study describing the long-term natural history of *SCN8A* related diseases, obtaining specific outcome measures for future prospective observational studies and for clinical trials, ultimately improving the care of individuals with *SCN8A* diseases.

Abstract Number: 846

Title: Analysis of electronic medical records reveals the clinical phenotypic evolution of genetic epilepsies through time

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Purpose: A genetic diagnosis can inform prognostication and treatment in epilepsy. Comparison of a patient's clinical features, and their evolution, to reference cases is important for selecting which etiologies to test for, and for interpretating previously unreported results. We explored whether longitudinal comparison of electronic medical records (EMR) in a genetic epilepsy center might provide reference data to assist with genetic diagnosis.

Method: We analyzed our reference cohort of 658 individuals, whose clinical features were coded as Human Phenotype Ontology (HPO) terms. These were annotated to the ages between which they were recorded in the EMR. Using phenotypic similarity analysis, we calculated the phenotypic similarity (PhenSim) of individuals with each genetic etiology within 3-month age intervals. PhenSim quantifies the distinctiveness of the clinical constellations of individuals sharing a genetic etiology relative to a wider cohort. We calculated cumulative PhenSim to the ages of 1, 2½, 5, 10, 18, and 25 years for each recurrent etiology in our cohort. We compared these to empirical distributions expected by chance in this cohort and corrected for the testing of multiple hypotheses.

Result: Of 36 recurrent etiologies, individuals with one of 14 etiologies *(CACNA1A, DEPDC5, GRIN1, IQSEC2, KCNB1, KCNQ2, KCNT1, PCDH19, PRRT2, PURA, SCN1A, SCN2A, SCN8A,* and *STXBP1)* had significantly similar clinical histories by age 5 years. *ATP1A3* reached significance at 10 years. The clinical distinctiveness of each of these genetically defined epilepsies, together accounting for 18% of the cohort, was sustained into adulthood.

Conclusions: Despite genetic epilepsies having clinical constellations that vary with age and from one individual to another, analysis of real-world EMR data demonstrates that 40% of recurrent genetic etiologies have distinctive age-specific clinical features. Thus, analysis of the EMR of cohorts at large epilepsy centers might provide reference data that assist the genetic diagnostic process within a learning healthcare system.

Abstract Number: 857

Title: Heart rate variability alterations in Dravet Syndrome: the role of status epilepticus and a possible association with mortality risk

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Purpose: Preliminary data suggest that patients with Dravet Syndrome (DS) have a reduced heart rate variability (HRV). This seems particularly evident in patients who experienced Sudden Unexpected Death in Epilepsy (SUDEP). This study aims at confirming these finding in a large cohort and at defining clinical, genetic or electroencephalographic predictors of HRV impairment in DS patients.

Method: We screened all the patients with DS followed at our Institution to perform a 24h-ECG Holter and derive HRV parameters. We used as control population patients with epilepsy (PWEs) and healthy controls (HCs). In DS patients, we assessed the impact of different clinical, neurophysiological and genetic features on HRV alterations through multiple linear regression. After a mean follow-up of 7.4±3.2 years since the HRV assessment all DS patients were contacted to record death or life-threatening events.

Result: 56 DS patients had a significantly reduced HRV compared to both HCs and PWEs, irrespective of antiseizure medications intake. A recent history of status epilepticus (SE) was the only significant predictor of lower HRV in the multivariate analysis while the frequency of generalized tonic-clonic seizures and Stiripentol use were significant only when considered individually. Conversely, a complete DS phenotype, frequent EEG abnormalities and having a truncating mutation were not determinant. At follow up, only one patient died; her HRV was lower than that of all the controls and was in the low range for DS patients.

Conclusions: Having a lower HRV is predicted by a recent history of SE; a longitudinal investigation of HRV in patients with SE of different aetiology will help to better explain the mechanisms behind this association. Compared to the literature, our cohort showed better HRV and lower mortality, reinforcing the hypothesis that HRV may be a useful biomarker for mortality risk. Multicentre and longitudinal studies are needed to confirm these findings.

Abstract Number: 861

Title: Mild Case of Unverricht-Lundborg Disease Presenting as Juvenile Myoclonic Epilepsy

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Purpose: Juvenile myoclonic epilepsy (JME) and Unverricht-Lundborg disease (ULD) are distinct entities, but they share several clinical features. The gene for ULD is cystatin B (CSTB) gene on chromosome 21q22.3. The most common mutation is a dodecamer repeat. We reported a JME phenotype in an Italian family with ULD.

Method: A 27-year-old man had one generalized tonic-clonic seizure (GTC), myoclonic jerks on awakening at age of 13 years, consistent with JME. He is seizure free under valproate. His 37-year-old sister developed action myoclonus, GTCs, photosensitivity, ataxia, at age of 12 years, consistent with ULD. She is treated by clonazepam, valproate, levetiracetam and perampanel. There was no cognitive impairment. The parents were consanguineous. An extensive clinical and laboratory investigation was performed. Screening for mutations in CSTB gene was performed in the two patients and their parents.
Result: In the proband, EEG-polygraphic recording revealed generalized spike and waves (GSWs), photo-paroxysmal-response (PPR), with no myoclonus. In her sister, EEG-polygraphic study showed GSWs, PPR, involuntary, stimulus and action activated myoclonic jerks. Both patients exhibited giant SSEPs and C-reflex bilaterally and normal brain MRI at 3T. Clinical and EEG evaluations were unremarkable in their parents. Both siblings carried a similar (60 to 68) homozygous dodecamer expansions in CSTB gene**.**

Conclusions: We identified a CSTB dodecamer expansion in a patient with JME phenotype. Although ULD is often confused with JME in early stages of disease, it is exceptional to find patients with ULD around age 30 who are as well controlled and high functioning as this patient. It remains unclear the reason why similar size of CSTB dodecamer expansions are associated with extremely heterogenous phenotypes. Our findings emphasize mild end of phenotypic spectrum of CSTB mutations, confirming phenotypic heterogeneity of ULD. Screening of CSTB gene should be considered in JME patients with evidence of recessive transmission.

Abstract Number: 883

Title: The phenotypic spectrum of KCNT1: a new family with variable epilepsy syndromes and severity

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Purpose: To show that pathogenic variants in *KCNT1* can be associated with milder extra-frontal epilepsies, we report a *KCNT1* family with a wide spectrum of phenotypes ranging from developmental and epileptic encephalopathy (DEE) to milder focal epilepsies not consistent with sleep-related hypermotor epilepsy.

Method: A large Canadian family of Caucasian descent including 10 affected family members was recruited and phenotyped by direct interview and review of medical records. Clinical gene panel analysis was performed in two family members, and research exome was used to investigate the most severely affected family member. Segregation analysis was done by Sanger sequencing in two other affected and one unaffected relative.

Result: Phenotypic information was available for five family members. Two individuals had DEE (epilepsy of infancy with migrating focal seizures and Lennox-Gastaut syndrome) and three had normal development and focal epilepsy with extra-frontal onset. The three family members with focal epilepsy had predominantly nocturnal seizures without hyperkinetic features. All three reported clusters of seizures at night with feeling of being unable to breathe associated with gasping for air, choking and/or repetitive swallowing, possibly suggesting insular or opercular involvement. Presurgical workup including ictal subtraction SPECT and PET in

one individual with focal epilepsy was most consistent with a left temporal onset. Genetic analysis identified a rare heterozygous *KCNT1* c.2882G>A, p.(Arg961His) variant that was predicted to be deleterious.

Conclusions: This family demonstrates that the phenotypic spectrum associated with *KCNT1* pathogenic variants is broader than previously assumed. Our findings indicate that variants in *KCNT1* can be associated with milder extra-frontal focal epilepsies and rare KCNT1 variants should not be excluded during variant interpretation in patients with milder presentations based solely on previously understood gene-disease validity. The significant variability in severity and epilepsy syndrome within our and other published families also suggests that additional factors influence the phenotype.

Abstract Number: 917

Title: The phenotypic spectrum of PCDH12 associated disorders - three new pediatric cases and review of the literature

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Purpose: PCDH12 is a member of the non-clustered protocadherin family of calcium-dependent cell adhesion proteins, which are involved in the regulation of brain development and endothelial adhesion. To date, only few families have been reported with *PCDH12* associated disease. The main clinical features previously associated with PCDH12 deficiency are developmental delay, movement disorder, epilepsy, microcephaly, visual impairment, brain malformations and intracranial calcifications.

Method: We report the clinical course, imaging data, and the genetic findings of three pediatric patients with homozygous truncating mutations in *PCDH12*, and review the literature. Genetic diagnoses were identified by next-generation sequencing methods and confirmed by Sanger sequencing.

Result: Three children are presented harboring two novel homozygous truncating *PCDH12* mutations. Novel *PCDH12* associated clinical features in our patients include late-onset epilepsy, episodes of transient developmental regression and dysplasia of the medulla oblongata. While two siblings showed dysplasia of the medulla oblongata and two patients showed intracranial calcifications, no signs of diencephalic-mesencephalic junction dysplasia or abnormal vasculature – such as previously described in patients with *PCDH12* mutations – were observed in our cohort. Patients with PCDH12 deficiency show a clinical overlap with interferonopathies. We report an elevated interferon score in one patient, possibly suggesting a role of interferon I mediated autoinflammation in the disease mechanism.

Conclusions: This case series expands the genetic and phenotypic spectrum of *PCDH12* associated diseases and highlights the broad clinical variability.

Abstract Number: 940

Title: Expanding the phenotypic and genetic CUX2 spectrum

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Purpose: Pathogenic variants at position p.(Glu590Lys) of the cut homeodomain transcription factor (*CUX2*) gene have recently been described as a genetic cause for infantile-onset developmental and epileptic encephalopathy (DEE). This study aims to provide an overview of *CUX2* related disorders and expand the phenotypic and genetic spectrum.

Method: Electro-clinical and genetic data from 16 patients with *CUX2* variants, including the 10 previously reported and six previously unpublished patients, were reviewed. Additional electro-clinical information were available in 8/10 previously reported cases.

Result: Patients were 11 males and 5 females, with a mean age of 15.3 years (range 1 – 47 years). 14/16 harbored the recurrent p.(Glu590Lys) variant, and the remaining two patients had novel de novo missense variants (c.3052C>T, p.(Arg1018Cys); c.1046T>C, p.(Ile349Thr)). All p.(Glu590Lys) patients had severe cognitive impairment and autistic features. Thirteen out of 14 patients suffered from epilepsy, with onset at a median age at 6.5 months, presenting with myoclonic seizures, atypical absence with myoclonic component, and focal seizures. Epilepsy was drug-resistant in most patients, though 4/13 (31%) achieved seizure control with valproate. EEG showed generalized and multifocal polyspike-and-waves (10/13, 77%). Cognitive regression was noticed for 6/9 (67%) patients and was related to epilepsy onset in 3/4 (75%). The novel variants display a clinical spectrum characterized with developmental delay, drug resistant epilepsy, speech impairment, and generalized polyspikes-and-waves and photo-paroxysmal response on EEG.

Conclusions: We broader the *CUX2* phenotypic and genetic spectrum, including patients with intellectual disability without epilepsy and patients with pathogenic variants different from the classical p.(Glu590Lys) variant. The majority of patients carrying the p.(Glu590Lys) *CUX2* variant display a relatively homogeneous phenotype comprising infantile-onset generalized epilepsy with myoclonic features, associated with severe cognitive impairment. A similar phenotype was observed in patients harboring the other variants, although not predicted to interfere with conserved domains or functional constraint.

Abstract Number: 972

Title: Genetic Landscape of Infantile Spasms with Focal Brain Malformations

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Purpose: Focal brain malformations are a common cause of infantile spasms (IS). We aimed to investigate the genetic landscape of IS in individuals that underwent epilepsy surgery.

Method: We performed histopathologic review and genomic testing in 52 individuals with IS who underwent resective epilepsy neurosurgery for seizure control at the Royal Children's Hospital, Melbourne. Individuals with acquired etiologies were excluded. Genomic testing was performed on blood or brain tissue using 200x (n=3) or 400x depth WES (n=25), or targeted sequencing with a brain malformation gene panel (n=24). Variants were filtered using GATK & MuTect variant caller pipelines to filter for germline and somatic candidate variants.

Result: Histopathologic analysis of brain tissue demonstrated tuberous sclerosis (TSC) (n= 22), focal cortical dysplasia (FCD) I (16) and II (9), dysembryoplastic neuroepithelial tumor (1), complex malformation of cortical development (1) and non-specific findings (3). The genetic basis of IS was identified in 35/52 (67%) individuals. Germline putative pathogenic variants were identified in 22/52 (42%) individuals, in *TSC2* (x16), *TSC1* (x1), *CDKL5* (x1), *DEPDC5* (x1), *PIK3CA* (x1), *COL4A1* (x1) and *NPRL3* (x1) genes. Putative pathogenic somatic variants in brain were identified in 13/52 (25%) cases, in *SLC35A2* (x7), *AKT3* (x2), *DEPDC5* (x1) *MTOR* (x1), *TSC1* (x1) and *TSC2* (x1) genes. Somatic variants identified in brain tissue ranged in variant allele frequency between 0.95-41.0%. mTOR pathway variants were identified in most individuals with TSC and FCD II. Brain somatic variants in *SLC35A2* were identified in individuals with FCD I and non-specific malformations.

Conclusions: The genetic landscape of IS with focal brain malformations comprises germline and brain somatic variants. Given the under-diagnosis of focal brain malformations, brain somatic variants are likely an under-recognized cause of IS. Our data highlights somatic variants in *SLC35A2* as a major cause of IS with focal malformations.

Abstract Number: 1043

Title: Diagnostic yield of exome sequencing in patients with ultra-refractory epilepsy without intellectual disability

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Purpose: The diagnostic yield of whole exome sequencing can be as high as 40% in people with intellectual disability (ID) and seizures. However, the utility of exome sequencing is currently unclear for people with epilepsy without ID. The aim of this study was to evaluate the yield (percentage) of genomic testing, following American College of Medical Genetics (ACMG) guidelines, for pathogenicity in people with epilepsy without learning disability, stratified by response to anti-epileptic drug treatment.

Method: Cases, identified via the Beaumont Hospital Electronic Patient Record (EPR) system, were clinically phenotyped and sub-divided into 4 groups: super-refractory focal epilepsy (who have failed five or more medications), super-refractory generalized epilepsy (who have failed three or more medications), ILAE-defined refractory epilepsy (despite trials of two medications) and responders (who have achieved seizure freedom with medication). Exome data was analyzed using a genomic analysis toolkit (GATK/in house pipeline and Congenica) and were discussed at an epilepsy-genetics multidisciplinary team meeting.

Result: A total of 327 individuals were included in the study, of whom 3.06% had an identifiable genetic cause for their epilepsy. Of 140 patients with super-refractory epilepsy (combined focal and generalized), the

diagnostic yield was 5.71%, elevated beyond the level observed in responsive patients (1%) although the difference was not significant (p = 0.08).

Conclusions: We have suggestive evidence that super-refractory epilepsy may be enriched for cases with an identifiable ACMG-satisfying mutation. We are currently extending the study to a larger patient group and analysis is ongoing.

Abstract Number: 1071

Title: Cortical and subcortical networks dysfunction in NEXMIF encephalopathy

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Purpose: to describe the structural and functional MRI findings in a patient with *NEXMIF* encephalopathy and an EEG pattern of eye closure sensitivity.

Method: NGS exome sequencing and segregation analysis were performed. For structural MRI studies (cortical thickness and subcortical volume analyses) the patient's data were compared with those of 20 female controls (HC) and 20 female patients with generalized genetic epilepsy (GGE); functional MRI studies (EEG-fMRI during eye-closure and eye-opening conditions) were also obtained, and the patient's fMRI maps were compared with those of 13 healthy controls and 14 patients with GGE.

Result: Subcortical structures comparison between the patient and HC group showed volume reduction in right thalamus (p=0,02), right amygdala (p=0,04), and left caudate (p=0,04); in comparison with the GGE group a volume reduction in right thalamus (p=0,05) was observed. Cortical thickness analyses in the patient compared with HC showed reduced cortical thickness in left (p=0,005) and right caudal middle frontal gyrus (p<0,001), left fusiform (p=0,03), left inferior parietal gyrus (p=0,004), left (p=0,01) and right (p=0,03) lateral occipital gyrus, left lingual gyrus (p=0,03); in comparison with GGE group the case displayed reduced cortical thickness in left (p=0,02) and right caudal middle frontal gyrus (p=0,01), left lingual gyrus (p=0,05).
The functional MRI studies showed that, when closing the eyes, the case showed higher BOLD changes in the left cuneus compared to controls. When compared with GGE, the eye-closure in the case was accompanied by a higher metabolic demand of the left precentral gyrus, the left basal ganglia, the bilateral superior temporal gyrus, the right inferior frontal gyrus, and the pons.

Conclusions: Even if limited to a single patient, this is, to our knowledge, the first study to describe advanced neuroimaging results in *NEXMIF* encephalopathy; the data obtained from our patient show a significant disruption in cortical and subcortical networks.

Abstract Number: 1074

Title: Genotype-phenotype correlations in patients with de novo KCNQ2 pathogenic variants

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Genotype-phenotype correlations in patients with de novo *KCNQ2* pathogenic variants

Purpose: Early identification of de novo *KCNQ2* variants in patients with epilepsy raises prognostic issues toward optimal management. We analyzed the clinical and genetic information from a cohort of patients with de novo *KCNQ2* pathogenic variants to dissect genotype-phenotype correlations.

Methods: Patients with de novo *KCNQ2* pathogenic variants were identified from Italy, Denmark, and Belgium. Atomic resolution Kv7.2 structures were also generated using homology modeling to map the variants.

Results: We included 34 patients with a mean age of 4.7 years. Median seizure onset was 2 days, mainly with focal seizures with autonomic signs. Twenty-two patients (65%) were seizure free at the mean age of 1.2 years. More than half of the patients (17/32) displayed severe/profound intellectual disability; however, 4 (13%) of them had a normal cognitive outcome.
A total of 28 de novo pathogenic variants were identified,mostmissense (25/28), and clustered in conserved regions of the protein; 6 variants recurred, and 7 were novel.We did not identify a relationship between variant position and seizure offset or cognitive outcome in patients harboring missense variants. Besides, recurrent variants were associated with overlapping epilepsy features but also variable evolution regarding the intellectual outcome.

Conclusions: We highlight the complexity of variant interpretation to assess the impact of a class of de novo KCNQ2 mutations. Genetic modifiers could be implicated, but the study paradigms to successfully address the impact of each single mutation need to be developed.

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Abstract Number: 1080

Title: The genetic basis of Focal Cortical Dysplasia

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Purpose: FCD is characterized by alterations in the cytoarchitecture also observed in other Malformations of cortical development, such as tuberous sclerosis (TS) and hemimegaloencephaly (HME). Recently, mosaic mutations were identified in TS, HME and FCD. We aim to investigate the genetic basis of FCD in a large cohort of patients.

Method: Genomic DNA was extracted from brain tissue and blood from 12 patients with FCD. These samples were submitted to deep sequencing of mTOR/GATOR pathway genes. Capturing and enrichment were performed with the SeqCapEZ Choice Library (NimbleGen, Roche). Samples were sequenced in a Miseq (Illumina), to achieve at least 600X of coverage. Mosaicism was evaluated using the software Mutect2, VarScan, and Strelka. Variants were classified as mosaic mutations when less than 10% of reads were not aligned to the reference human genome and are present only in BTRS. Variants were filtered prioritizing frameshift, missense, nonsense and splicing site mutations.

Result: A total of 11 mosaic mutations, localized in 10 genes, were identified in 67% of patients (n=8/12). Five mutations (*MTOR* n=2*, DEPDC5* n=1*, TSC2* n=1 and *RPTOR* n=1) had already been described in the literature; however, we identified additional six novel mutations (*RPS6KA1* n=1*, ULK1* n=1*, MAPK3* n=1*, PIK3CD* n=1*, WDR59* n=1 and *WDR24* n=1). These mutations were not found in the GnomAD and a BipMed (www.BIPMed.org).

Conclusions: We identified somatic mutations in genes of the mTOR and GATOR pathways. Furthermore, somatic mutations in mTOR genes seem to be relatively common in patients with FCD since they are present in 67% subjects of our cohort. However, these preliminary data should be confirmed by Digital PCR. Currently, our cohort of patients was submitted to very deep whole-exome sequencing (>1000x coverage). We believe that data from this experiment will allow more accurate identification of somatic mutations and CNVs in patients with FCD.

Abstract Number: 1082

Title: Improving early diagnosis of rare diseases using Natural Language Processing in unstructured medical records: an illustration from Dravet syndrome

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Purpose: The growing use of Electronic Health Records is promoting the application of data mining in health-care and encouraging the development of analytic models for early diagnosis. Dravet Syndrome (DS) is a rare Developmental and Epileptic Encephalopathy that commonly initiates in the first year of life with febrile seizures (FS). Age at diagnosis is often delayed, as it is difficult to differentiate DS at onset from FS. We aimed to explore if some clinical terms (concepts) are significantly more used in the narrative medical reports of individuals with DS before the age of two years compared to those of individuals with only FS. These concepts would allow an earlier detection of patients with DS.

Method: Data were collected using a document-based data warehouse, Dr Warehouse, which employs Natural Language Processing (NLP), a computer technology consisting in processing written information. Using Unified Medical Language System Metathesaurus, phenotype concepts can be recognized in medical reports. We selected individuals with DS and individuals with only FS, with confirmed diagnosis after the age of four years. A phenome-wide analysis was performed evaluating the statistical associations between the phenotypes of DS and FS, based on concepts found in the reports produced before two years.

Result: We found significative higher representation of concepts related to seizures' phenotype distinguishing DS from FS in the first phases, namely the major recurrence of complex febrile convulsions and other seizure-types. Some typical early onset non-seizure concepts also emerged, in relation to neurodevelopment and gait disorders.

Conclusions: Narrative medical reports of individuals younger than two years with FS contain specific concepts linked to DS diagnosis, which can be automatically detected by software exploiting NLP. This approach could represent an innovative methodology to decrease time of diagnosis of DS and could be transposed to other rare diseases.

Abstract Number: 1083

Title: Sleep problems in patients with SCN8A epilepsy

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Purpose: Children with developmental and epileptic encephalopathies frequently experience sleep disturbances, negatively impairing family's quality of life. We aimed to determine frequency and nature of sleep problems in *SCN8A*-related epilepsies.

Method: Patients have been enrolled through a collaborative network in Europe and USA. Collected data included demographic and genetic information, seizure types, frequency, and timing (daytime vs nocturnal predominance), cognitive/motor development, antiepileptic drugs and relevant comorbidities. The Sleep Disturbance Scale for Children (SDSC), the Children's Sleep Habits Questionnaire (22-item version) and the pediatric daytime sleepiness scale were distributed to parents/guardians of 21 patients with *SCN8A* –related epilepsies. Completed questionnaires were evaluated by factor scores and Composite Sleep Index.

Result: Questionnaires were completed for 16 patients, age 2-21 years. Sleep problems were reported in 12/16 (75%). Eleven out of 15 (73%) scored with SDSC had an abnormal total sleep score, with difficulty initiating and

maintaining sleep (11/15= 73%) sleep breathing disorders (7/15= 47%), and sleep–wake transition disorders (6/15= 40%) with moderate daytime sleepiness (6/15= 40%). Six out of 16 (37.5%) took medication to assist sleep. Eight out of 15 (53%) recently had nocturnal seizures and 2/16 (12.5%) were seizure free. Symptoms severity was not associated with gender/age, motor impairment, respiratory/gastro-intestinal problems.

Conclusions: In this preliminary study, 75% of patients with *SCN8A*-related epilepsies had a parental-reported bad sleep quality, mainly consisting of sleep instability and night waking, with moderate daytime sleepiness. Symptoms severity was apparently not related to seizure frequency or nighttime seizure predominance, highlighting the importance of sleep assessment also in seizure-free *SCN8A* patients. Animal studies showed sleep disturbances in *SCN8A* as well as in *SCN1A*- Dravet Syndrome mice models, suggesting a sodium channels role in the regulation of sleep. Understanding the effects of *SCN8A* dysfunction on sleep stability may guide future therapeutic efforts to alleviate this often distressing symptom.

Abstract Number: 1097

Title: Whole genome sequence data implicate RBFOX1 in epilepsy risk in baboons

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Purpose: Baboons exhibit a genetic generalized epilepsy (GGE) that resembles juvenile myoclonic epilepsy and may represent a suitable genetic model for human epilepsy. The genetic underpinnings of epilepsy were investigated in a captive baboon colony through the analysis of whole-genome sequence (WGS) data.

Method: Baboons housed at the Southwest National Primate Research Center (San Antonio, TX) were diagnosed for epilepsy from available veterinary records and scalp EEG recordings. WGS data were obtained for 38 cases and 19 healthy controls from the NCBI Sequence Read Archive (SRA) repository and were processed and aligned to the reference assembly Panu_3.0. After standard QC filtering, two subsets of variants were examined: (1) 20,881 SNPs from baboon homologs of 19 candidate GGE genes; and (2) 36,169 genome-wide SNPs predicted to be protein-altering by snpEff. Association tests were conducted in SOLAR, and gene set enrichment analyses (GSEA) and protein-protein interaction (PPI) network construction were performed on genome-wide significant association results (P<0.01; n= 441 genes).

Result: Heritability for epileptic seizure in the pedigreed baboon sample was estimated at 0.76 (SE=0.77; P=0.07). A significant association was detected for an intronic SNP in *RBFOX1* (P=5.92 × 10^{-6}; adjusted P=0.016). For protein-altering variants, GSEA revealed significant positive enrichment for genes involved in the extracellular matrix structure (ECM; FDR=0.0072) and collagen formation (FDR=0.017), which was reflected in a major PPI cluster.

Conclusions: SNP association results implicate *RBFOX1* in baboon epilepsy, a gene that plays a key role in neuronal excitation and transcriptomic regulation, and has been previously linked to human epilepsy, both focal and generalized. Moreover, protein-damaging variants from across the baboon genome exhibit a wider pattern of association that links collagen-containing ECM to epilepsy risk. These findings suggest a shared genetic etiology between baboon and human forms of GGE and provide the foundation for potential follow-up research.

Abstract Number: 1100

Title: The KCNB1 phenotypic and genetic spectrum

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Purpose: Pathogenic variants in *KCNB1* have been recently associated with neurodevelopmental disorder with or without epilepsy. In this study, we aimed to provide a deep electro-clinical characterization of a large cohort of *KCNB1* patients.

Method: Through an international collaboration, we collected the clinical, video-EEG and MRI data of 31 unpublished *KCNB1* probands and additional electro-clinical data of 65 previously published patients.

Result: All patients presented some neurological disturbances, mainly consisting of speech impairment (100%; expressive in 66%), oro-facial (76%) and fine/gross motor impairment (88%), gait disorder (72%; 22% of non-ambulatory patients), hypotonia (68%), and apraxia (47%). All the *KCNB1*-probands, in infancy, manifested mild/moderate to severe intellectual disability, associated with behavioral disorders (66%) and epilepsy (83%). The mean age at epilepsy onset was 16 months and the most common seizure types were myoclonic/ hemi-clonic seizures (82%). Thirty-three (92%) patients had interictal epileptiform discharges, with main foci Rolandic and frontal. Activation of the IEDs during NREM-sleep occurred in the majority of the patients, sometimes resembling ESES/CSWS pattern. MRI showed focal frontal and/or uncal cortical dysplasia in three patients. A brain biopsy, performed in one patient with unremarkable MRI, revealed a frontal cortical dysplasia. The genetic defect comprised mainly missense variants, mainly located in the S4-S6 region and with slightly different phenotypes depending on variants localization.

Conclusions: *KCNB1*-related manifestations encompass a neurodevelopmental disorder of various severity with or without epilepsy, and often associated with behavioral disturbances or autism. A prominent motor system involvement and an EEG sleep activation seem to be cardinal features.

Appendix:
***KCNB1* Working group** Zaid Afawi, Siddharth Banka, Bernardo Dalla Bernardina, William Campbell, Anna Chassevent, Mahgenn Cosico, Barbara Fiedler, Elena Fontana, Francesca Furia, Pia M Gellert, Ara S Hall, Katherine Helbig, Maja Hempel, Christina E. Hoei-Hansen, Bobby P C Koeleman, Karl Martin Klein, Mary D King , Bryan Lynch, Johannes Lemke , Adriana Magaudda, Marina Nikanorova, Manuela Pendziwiat, Nils Rahner, Rosa Reveles, Carlotta Spagnoli

Abstract Number: 1132

Title: GABRA1-related disorders: from genetic pathways to a broader spectrum of clinical phenotypes

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Purpose: Pathogenic variants in *GABRA1*, encoding 1 of $GABA_A$ receptor subunit, have been associated with a broader spectrum of epileptic syndromes like juvenile myoclonic epilepsy (JME) as well as epileptic encephalopathies. However, the clinical phenotype and the functional impact of *GABRA1* variants remain to be fully defined. The aim of this study is to explore the spectrum of epilepsy syndromes related to *GABRA1* mutations and to establish genotype-phenotype correlations.
Method: We collected genetic, clinical and EEG data of 19 new patients, with 10 novel missense variants, and 2 follow-up patients and reviewed published data of 72 cases with *GABRA1* pathogenic variants. To estimate the pathogenicity of the variants, we used established and newly developed in silico prediction tools.

Result: We discerned 4 different phenotypic groups across the newly identified and previously published patients: (1) 20 affected individuals with neonatal onset of encephalopathy, early-onset epilepsy (spasms), permanent neurologic deficits with movement disorder, intractable seizures and neuroimaging abnormalities; (2) 42 patients with infantile onset of febrile and/or afebrile seizures, usually hemiclonic, with developmental regression after seizure onset, sometimes resembling Dravet Syndrome, despite generally monotherapy response and later appearance of unusual types of seizures (atonic seizures); (3) 25 patients or families with late-onset generalised seizures (i.e. JME) and benign course on monotherapy with no cognitive or neurological impairment; (4) 6 patients with autism spectrum disorder or cognitive impairment and with adolescence onset of sporadic seizures. We added 10 new disease-related variants to the 43 *GABRA1* pathogenic variants previously described. A strong genotype-phenotype correlation was observed for neonatal encephalopathy.

Conclusions: These data expand the genetic and phenotypic spectrum of *GABRA1*-related disorders to a diverse range of epilepsies. Further understanding of pathomechanism will help in predicting phenotype severity as well as eligibility for potential precision medicine approaches.

Abstract Number: 1162

Title: LOF or GOF – to which extend functional studies may be helpful in understanding SCN1A mutations.

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Purpose: The *SCN1A* mutations are linked to a spectrum of epileptic phenotypes ranging from GEFS+ to DRVT. GEFS+ is mainly due to missense mutations causing gain- or lost– of function (GOF or LOF) defects. In DRTV truncating and missense mutations lead to non-functional Nav1.1.
In some families the variability of phenotypes due to particular mutations is observed, suggesting the involvement of additional factors, modifying the "*basic phenotype*". In such cases, the question arises about the *"basic"* Nav1.1 dysfunction. Functional studies are considered to be fundamental for explaining mutations' mechanism – but in some cases, the results are contradictory.
Here we discuss problem of such inconsistent functional study results of *SCN1A* substitution p.Arg1596Cys, identified in family showing evolution of epilepsy phenotypes.

Method: The family with heterogenous epilepsy phenotype due to *SCN1A* mutation - p.Arg1596Cys was investigated. The Nav1.1 dysfunction was investigated in *vitro* by voltage-clamp methodology.

Result: The cosegregation of missense mutations in the *SCN1A* and milder/severe epilepsy syndromes has been demonstrated in three-generations family. The patch-clamp study showed, that substitution p.Arg1596Cys changes in channel's steady-state inactivation properties and in the current amplitude. The overall impact of the mutation was negative; however, the mutated channel was capable of conducting a sodium current which is in contradiction to results of Kluckova D et al. [2020]* who presented complete LOF of Nav1.1 due to this mutation.
Conclusions: Now, when personalized therapy is around the corner the goal of diagnostic should be not only identification of the causative mutation, but establish its functional consequences. However, if the results of functional studies are to be useful, we need standardization of such analysis.
Financed by funds of Polish NSC; grant 2015/17/B/NZ4/0266
*Kluckova D et al. Study among the Genotype, Functional Alternations, and Phenotype of 9 SCN1A Mutations in Epilepsy Patients. *Sci Rep* 10 (2020)

Abstract Number: 1232

Title: Genotypic correlates of progressive myoclonus epilepsy syndromes in South India- what is the yield?

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Purpose: Progressive myoclonus epilepsy (PME) are disorders presenting as a syndrome complex characterized by progressive myoclonus, cognitive impairment, ataxia, and other deficits. There is a paucity of studies which ascertain the yield of genetic testing in these disorders in the subcontinent.

Method: From the prospectively maintained database of patients who met the clinical criteria for various electroclinical phenotypes of PME between 2012-2020 and who were subsequently investigated by targeted next generation sequencing (NGS), the yield of pathogenic/likely pathogenic variants (ACMG criteria) was determined.

Result: Thirty two patients who met the elctroclinical criteria for various PME syndromes subsequently underwent genetic testing (18 males and 14 females). Median age at admission was 6.4yrs (interquartile range IQR=6.4) and median age at symptom onset was 2.5 yrs (IQR=3.52). Twelve patients (37.5%) had a positive family history of either epilepsy or global developmental delay. Consanguineous parentage was noted in 13 (40.6%). Phenotypes suspected after evaluation, MRI and video-EEG included neuronal ceroid lipofuscinosis (NCL) in 12 (37.5%), Lafora body disease in 1 (LBD; 3.1%), Unverricht Lundborg Disease (ULD) in 1(3.1%),

mitochondrial disorders in 9 (28.1%) and unclassified or possible PME in 9 (28.1%). Genetic variants were identified in 25 (78.1%), of which pathogenic variants were noted in 5 (15.6%), likely pathogenic in 8 (25%), variants of unknown significance in 12 (37.5). A heterogeneous profile was apparent among unclassified PME and NCL (CLN3, CLN5, CLN6, CLN8, CLN2, KCTD7, MFSD8, CDKL5). Other variants included EPM2A in LBD, metabolic variants (GBA, DLD, PEX1, DOLK, GLDC) and mitochondrial disorders (POLR3B, MT-ATP6, TPP1, RRM2B). The yield was determined to be 13/32 (40.6%) with no variants identified in 12 patients (37.5%).

Conclusions: Our study confirms a heterogeneous profile and high yield of genetic testing among PME syndromes. Trios-based multicentre sequencing studies are likely to throw further light with counselling and therapeutic implications.

Abstract Number: 1259

Title: Infantile spasms associated with the variant in the KCNQ3 gene with response to the use of carbamazepine: a case report.

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Purpose: Describe the association between the KCNQ3 gene mutation and the development of infantile spasms that responds to the use of carbamazepine.

Method: Case report: A female infant who debuts at two months with seizures type infantile spasms, an electroencephalogram study shows a pattern with hypsiarrhythmia. Neurological examination: hyporeactive, inadequate visual contact, axial and peripheral hypotonia, inadequate head support, decreased strength and tendon reflexes. She presents an inadequate response to treatment with levetiracetam, prednisone, valproic acid and vigabatrin; initial response to ACTH, but relapse with similar clinical manifestations when medication was discontinued; ketogenic diet is started and a vagus nerve stimulator is placed. Exome sequencing is performed that reports a variant in the KCNQ3 gene, so it was decided to start treatment with carbamazepine, achieving a significant reduction in spasms frequency of over 90%.

Result: Exome sequencing: nucleotide variants in the KCNQ3 Gene, position c.2505 G> C, Amino Acid Position p.Glu 835Asp. Brain MRI and electroencephalogram in figures 1 and 2.

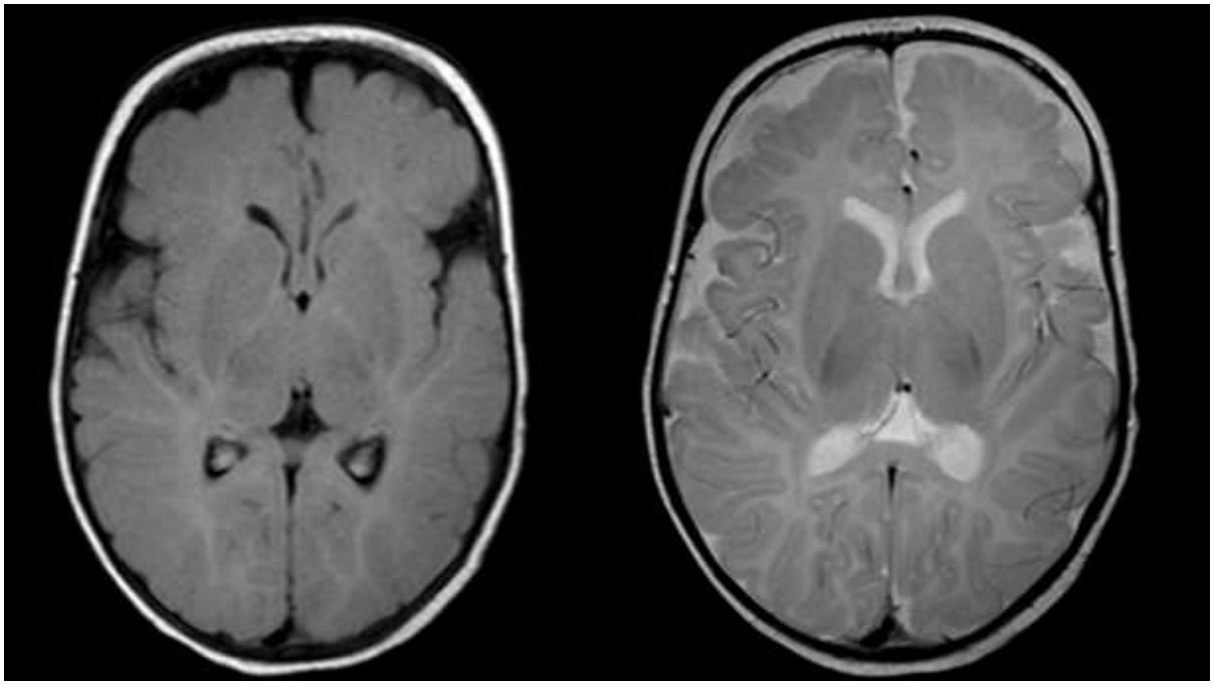
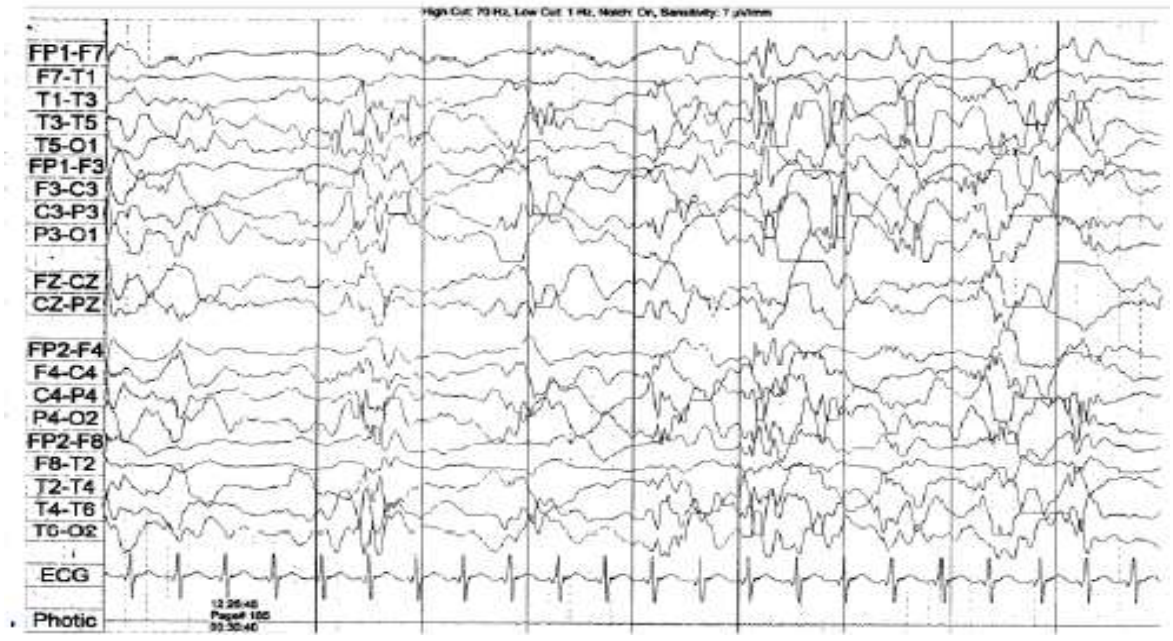


Figure 1: Brain MRI: prominent front temporal cortical grooves.



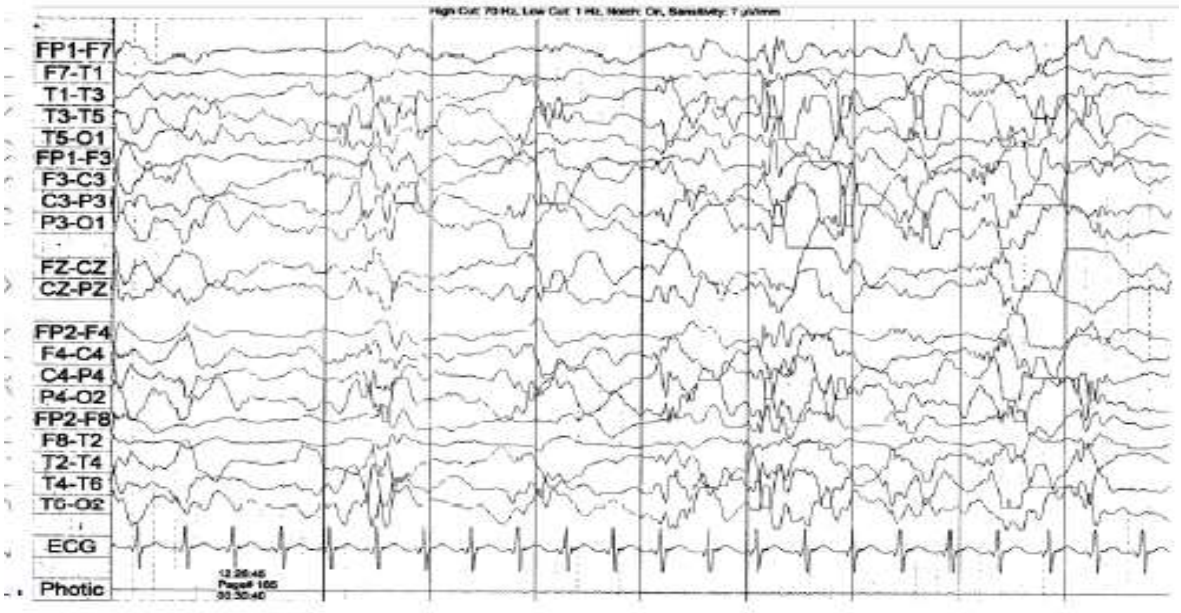


Figure 2: Interictal EEG: slow activity of great amplitude, with periods of voltage suppression, compatible with hypsiarrhythmia pattern.

Conclusions: The variants found in the KCNQ3 gene have been associated with early-onset epileptic encephalopathy, of which there are few publications between the association of this gene and West syndrome and additionally, little literature that reports clinical improvement with the use of carbamazepine, such as it was in our case. The variant in the KCNQ3 gene and its response to carbamazepine use suggest a connection between KCNQ3 gene mutations, infantile spasms, and response to CBZ. This leads us to generate a greater focus on the early recognition of the electroclinical genotype through genetic studies in order to determine a correlation between the different pathogenic variants and the development of genotype-directed therapeutic approaches.

Abstract Number: 1347

Title: Functional analysis of patient-derived cells harboring a homoygous likely-pathogenic KATNAL2 variant

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Purpose: KATNAL2 (KATNA-like2) is an enzyme that resembles the A-subunit (p60subunit) of katanin protein family and carries microtubule severing activity. KATNAL2 is associated with autistic spectrum disorder however, it is not fully understood how the KATNAL2 gene product is responsible for this phenotype. The aim of this study is to understand how a homozygous missense variant in the KATNAL2 gene (p.Ser392Pro) affects fibroblasts and neural cells, and thereby causes a severe neurodevelopmental phenotype including epilepsy and autistic behaviour.

Method: The variant was identified by our group in a large cohort of pediatric patients born to consanguineous marriages with the help of whole exome sequencing. To perform functional studies, we first generated a primary fibroblast cell line from a skin biopsy of the patient. After one passage, these cells were nucleofected with episomal vectors to generate induced pluripotent stem cells (iPSCs). After confirming the pluripotency, normal karyotype and non-integration into genome, İPSCs were transferred to our laboratory for differentiation to neural progenitor cells (NPCs). In parallel to the iPSC generation studies, we performed Western Blotting and Immunofluorescence analyses of various cytoskeleton- and microtubule-related proteins.

Result: Western blot analysis revealed that protein levels of KATNAL2 and the cytoskeleton-related proteins (e.g. KATNA1, Tubulin-alfa, Dynein, NDEL1 ve NUBP2) are similar between the patient and control fibroblasts. However, microtubule organization during anaphase are disorganized in KATNAL2 patient cells. Also, timing of cleavage furrow formation during telophase seemed different.

Conclusions: In this study, we generated the first iPSC cell line from a patient with a likely-pathogenic KATNAL2 variant. Upon conversion into NPCs, we will be able to study the effects of this variant on neural cells and shed light into mechanisms leading to the severe neurodevelopmental phenotype observed in our patient. iPSC-based disease models provide several opportunities ranging from basic science research to developing treatments.

Neuroimaging

Abstract Number: 178

Title: Focal hypertrophy in mesial temporal lobe epilepsy

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Purpose: Mesial temporal lobe epilepsy (mTLE) is associated with focal brain atrophy but little knowledge exists on hypertrophy. We assessed areas of brain hypertrophy in mTLE and their clinical correlates.

Method: We analysed T1-weighted MRI data of 135 patients with unilateral mTLE with pathology-confirmed hippocampal sclerosis (77 left, 58 right) and 47 matched healthy volunteers (HV) using whole-brain voxel-based morphometry (VBM), subcortical volumetry, and shape analysis. We validated our findings in an external cohort (18 patients with mTLE, 18 matched HV). We evaluated the functional implications of the findings on memory encoding using fMRI.

Results: VBM detected increased grey matter volume of the contralateral amygdala in both left ($t=8.7$, $p<0.001$) and right ($t=7.9$, $p<0.001$) mTLE. We confirmed the larger volume of the contralateral amygdala using volumetry (left mTLE 1.74±0.16 ml vs. HV 1.64±0.11, $p<0.001$; right mTLE 1.79±0.18 ml vs. HV 1.70±0.11, $p=0.002$) and surface shape analysis (left mTLE $p\leq0.005$; right mTLE $p=0.006$). We validated the hypertrophy of the contralateral amygdala in an external cohort (mTLE 1.91±0.20 ml vs. HV 1.75±0.13, $p=0.009$). Contralateral amygdala hypertrophy was associated with poor verbal memory in left mTLE and with more frequent secondarily generalized seizures in right mTLE. Larger volume of the contralateral amygdala correlated with increased functional activation of the parietal memory network on fMRI.

Conclusions: Unilateral mTLE due to hippocampal sclerosis is associated with hypertrophy of the contralateral amygdala. This hypertrophy may represent plasticity to compensate for verbal memory deficits or may be the consequence of seizure spread to the contralateral hemisphere. Our findings highlight the impact of unilateral epilepsy on the contralateral hemisphere and reinforce the concept of epilepsy as a network disorder.

Abstract Number: 225

Title: Characteristic hippocampus malfunction predicts drug responsiveness in Chinese temporal lobe epilepsy patients

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Purpose: To study the functional connectivity differences between treatment failure and drug responsive temporal lobe epilepsy (TLE) patients and identify imaging predictors of treatment failure TLE.

Method: 52 TLE patients and 55 healthy controls participated in the cohort. The patients underwent a follow-up until the outcome could be classified as treatment failure or seizure freedom. We identified 29 treatment failure patients and 20 seizure freedom patients in the final analysis. fMRI data were acquired during a Chinese version of verbal fluency task. Subject groups were compared in terms of activation, task-residual functional connectivity (trFC), and generalized psychophysiological interaction (gPPI) analysis. Imaging characters were extracted for logistic regression and ROC evaluation.

Result: Chinese character verbal fluency task successfully activated the language network and cognitive control network (CNN), as well as deactivated the default mode network (DMN). In the treatment failure group, trFC seeding from left hippocampus to posterior cingulate cortex, middle cingulum, inferior parietal lobule, superior frontal gyrus, and middle temporal gyrus was attenuate (threshold free cluster enhancement, $p<0.05$, family-wise error corrected). For gPPI analysis, group differences were located at precuneus, middle frontal gyrus, and inferior parietal lobule ($p < 0.001$, uncorrected, voxel > 30). The regression model presented high accuracy of discriminating treatment failure patients (AUC = 0.803, 95% CI = 0.683~0.924).

Conclusions: In treatment failure TLE patients, connectivity between left hippocampus and central nodes of DMN, CNN, as well as language network was disrupted. Independent to hippocampus sclerosis, the abnormality observed is an imaging biomarker for drug responsiveness in Chinese TLE patients

Abstract Number: 232

Title: Atypical microstructural gradient organization in temporal lobe epilepsy

Jessica Royer[1], Sara Larivière[1], Raul Rodriguez-Cruces[1], Shahin Tavakol[1], Andrea Bernasconi[1], Neda Ladbon-Bernasconi[1], Birgit Frauscher[2], Boris Bernhardt[1]

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Purpose: Although temporal lobe epilepsy (TLE) is increasingly recognized to perturb the structure and function of the whole brain, its epicenter lies in temporo-limbic networks. Prior work in healthy individuals has shown that the neocortex can be characterized along a gradient of microstructural organization, differentiating sensory regions with clear lamination patterns from more agranular or dysgranular paralimbic cortices. Here, we studied whether and how these gradients are altered in TLE.

Method: A cohort of 20 mesial TLE patients (9 women; mean±S.D. 37.65±12.28 years) and 26 healthy controls (11 women; 34.65±7.99 years) underwent high-resolution T1-weighted and microstructural imaging at 3T. In each subject, we sampled intracortical quantitative T1 (qT1) intensities along 14 equivolumetric surfaces between pial and white matter boundaries, yielding cortex-wide microstructural intensity profiles. Profiles were cross-correlated while controlling for the cortex-wide average, resulting in microstructural similarity matrices between all vertex pairs. We derived the principal eigenvector of microstructural similarity from each

microstructure similarity matrix using diffusion map embedding and examined group differences in the resulting microstructural gradient. Gradient scores were compared using surface-based models controlling for effects of sex and age. Findings were corrected for multiple comparisons using random field theory.
Result: Both controls and TLEs showed a robust sensory-fugal gradient of cortical microstructure. Comparing groups, differentiation between sensorimotor and paralimbic anchors was reduced in TLE relative to controls. Reductions in TLE primarily targeted agranular and dysgranular paralimbic regions, and peak effects were observed in ipsilateral anterior and mesial temporal cortices (pFWE<0.05).

Conclusions: Our findings suggest shifts in cortical microstructural organization in TLE. Given the role of microstructure in shaping cortical connectivity, future work will explore connectome-level association of atypical microstructural gradients in TLE.

Abstract Number: 236

Title: Functional MRI based effective connectivity in surgical remediable epilepsies.

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Purpose. Simultaneous EEG-fMRI can contribute to identify the epileptogenic zone (EZ) in surgical epilepsies. However, fMRI maps related to Interictal Epileptiform Discharges (IED) show often multiple regions of signal changes rather than focal ones. Dynamic causal modeling (DCM) applied to fMRI data estimates the effective connectivity, i.e. the causal effects exerted by one brain region. Herein we tested if this approach can help the localization process of EZ in cases with complex IED-related fMRI maps.

Method. 35 patients with focal epilepsies underwent a presurgical evaluation protocol including a simultaneous EEG-fMRI study. After performing an IED-related fMRI analysis, 10 patients shown multiple IED-related fMRI regions of signal changes with at least one cluster concordant with the presumed EZ. In this group, DCM was applied to test if this approach can help to localize the EZ. For each subject, a family of deterministic plausible DCM bilinear models were constructed using IED as autonomous input on each node one at time. DCM findings were classified based on the presurgical evaluation findings as either "Concordant" if the node identified by DCM matches the presumed focus, "Discordant" if the node is distant from the presumed focus, or "Inconclusive" (no statistically significant result). Additionally, patients having intracranial EEG recordings or surgery were considered as having an independent validation of DCM results.

Results. The effective connectivity focus identified using DCM was Concordant in 7 patients (70%) Discordant in two cases (20%) and Inconclusive in one (10%). Independent validation of DCM findings was obtained in 6 patients (60%): in 4 out of 6 patients (66%), DCM findings were valid, invalid in two.

Conclusion. DCM applied on fMRI maps might contribute to reveal the EZ in patients with widespread IED-related hemodynamic changes thus adding value to the significance of the EEG-fMRI within the epilepsy presurgical protocol.

Abstract Number: 237

Title: Extent of resection and optimal postsurgical memory and seizure outcome in temporal lobe epilepsy: Voxel-wise and numerical analysis

Daichi Sone[1,2], Maria Ahmad[1], Pamela Thompson[1], Sallie Baxendale[1], Sjoerd Vos[1], Jane de Tisi[1], Andrew McEvoy[1], Anna Miserocchi[1], John Duncan[1], Matthias Koepp[1], Marian Galovic[1,3]

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Purpose: This study aims to define optimal resection margins that are a safe compromise regarding cognitive outcome while maintaining a high rate of postoperative seizure freedom.

Method: This cohort study evaluated the resection extent on postoperative structural MRI in 142 consecutive patients with unilateral drug refractory temporal lobe epilepsy (TLE) who underwent comprehensive presurgical evaluation followed by standard anterior temporal lobe resection (ATLR) and received standardized pre- and post-surgical neuropsychological evaluation. Postoperative memory decline and seizure freedom were assessed at one-year after ATLR.

Result: In total, 74 patients with left TLE and 68 with right TLE were included. Voxel-wise analyses revealed that postsurgical verbal memory decline correlated with resections of the posterior hippocampus and inferior temporal gyrus, whereas larger resections of the fusiform gyrus were associated with worsening of visual memory in left TLE. Limiting the posterior extent of left hippocampal resection to a maximum of 55% reduced the odds of significant postoperative verbal memory decline by a factor of 8.1 (95% CI 1.5-44.4, p=0.02). Limiting the posterior extent of left temporal lobe resection to a maximum of 75% reduced the odds of postoperative verbal memory decline by a factor of 6.1 (95% CI 1.2-31.6, p=0.03). Seizure freedom was not related to posterior resection extent, but to the extent of piriform cortex removal after left ATLR. In right TLE, variability of the posterior extent of resection was not associated with verbal and visual memory decline or seizures after surgery.

Conclusions: The extent of surgical resection is an independent and modifiable risk factor for cognitive decline and seizures after left ATLR. Adapting the posterior extent of left ATLR might optimize postoperative outcome, with reduced risk of memory impairment while maintaining comparable seizure-freedom rates. The current, more lenient, approach might be appropriate for right ATLR.

Abstract Number: 258

Title: Digging deep in 7T MRI: potential epileptogenic and surgical lesions in epilepsy patients with nonlesional 3T MRI

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Purpose: To explore the role of 7T MRI among patients with nonlesional 3T MRI, correlating imaging findings with phase one and two monitoring followed by surgical intervention.

Method: This is a single institution retrospective study of patients who underwent 7T with seizure protocol between March 2018-April 2020 with initial nonlesional 3T structural MRI. Electronic medical records were abstracted for history and imaging.

Result: Fifty patients were included: male 46%; median seizure onset 14 years IQR 8.8-25; median epilepsy duration prior to 7T 8.5 years IQR 3.4 - 15. Potentially epileptogenic abnormality was reported in 18/50 (36%) cases on initial 7T review. Among 36 patients with available ictal scalp EEG, 36% had temporal lobe epilepsy, and 67% showed concordance with the 7T MRI epileptogenic lesion. Thirteen patients underwent phase 2 monitoring, of which five had 7T lesions (hippocampal changes, encephalocele and vascular malformation). Among those who underwent surgical intervention, excellent Engel class 1a/1b outcomes were seen in 5 of 6 patients who had resection or ablation intervention. Greater than 50% seizure reduction was present in 1 of 3 patients with neuromodulation.

Conclusions: Patients with medically refractory focal epilepsy and nonlesional 3T MRI may benefit from further imaging with 7T MRI which can provide additional potentially epileptogenic abnormalities. Tailored phase 2 monitoring including these lesional targets can identify surgical candidates who benefit from resective surgery or neuromodulation therapy.

Abstract Number: 262

Title: Structural network alterations in neocortical temporal lobe epilepsy

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Purpose: Temporal lobe epilepsy (TLE) is the most common drug-refractory seizure syndrome in adults. While generally associated with hippocampal sclerosis (HS), in about 30% of patients seizures originate from neocortical pathology (TLE-NC; Bluemcke et al., NEJM 2017). Animal models indicate detrimental effects of neocortical seizures on the hippocampus (Otte et.al. Epilepsia 2012). Additionally, *ex vivo* studies revealed extensive cortical atrophy in TLE-NC (Blanc et.al. Epilepsia 2011). Yet, contrary to the wealth of imaging data in TLE-HS showing widespread cortical atrophy and network disruptions, evidence is limited for TLE-NC. Here, we evaluated brain morphology and network topology of TLE-Neo.

Method: We studied 30 patients with TLE-NC (mean±SD age 31±9.9 years; epilepsy duration 7±3 years; 15 left), 30 with TLE-HS (age 35±11 yrs; duration 17±10 years, 11 left) and 30 matched controls. All subjects underwent high-resolution 3D-T1-weighted 3T MRI. Surface-based image processing included analysis of cortical thickness (Kim et.al., Neuroimage 2005) and hippocampal subfield volumetry (Caldairou et al., MICAI 2016). Graph-theoretical metrics (*path length* and *clustering coefficient*) assessed structural covariance networks. Patient cohorts were compared to healthy controls and each other, correcting for disease duration and age. Results were corrected for multiple comparisons (FDR<0.05).

Result: Compared to healthy controls, both patient groups exhibited similar degrees of neocortical atrophy involving bilateral frontocentral, temporo-occipital and ipsilateral temporal regions, as well as ipsilateral hippocampal atrophy. Graph-theoretical analysis revealed shorter path length and reduced clustering in TLE-Neo, indicative of a more random network topology, while TLE-HS displayed the opposite patterns, representing a more regularized configuration.
Conclusions: Our findings contrast with previous work suggesting minimal damage in TLE-NC. Indeed, TLE-NC and TLE-HS displayed similar damage across the neocortex and hippocampus. Conversely, they showed a remarkable dichotomy in network topology, which may differentiate both entities when structural MRI is unrevealing.

Abstract Number: 268

Title: Automated ICA-based denoising appropriate for data derived from naturalistic fMRI: Movie-driven inter-subject correlation in drug-resistant epilepsy

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Purpose: For individuals with drug-resistant epilepsy, surgical resection of epileptogenic brain tissue is a viable option for controlling seizures. Successful post-surgical outcomes rely upon the precise localization of the epileptic focus through rigorous multimodal evaluations. Conceptualizations of epilepsy as a "network disorder" point toward the potential for naturalistic functional magnetic resonance imaging (fMRI) paradigms to complement standard surgical planning tools, by improving the identification of functionally disturbed networks. To establish clinical utility, research is needed to evaluate such paradigms in conjunction with commonly used strategies for removing motion-induced signal variation from fMRI data (aka denoising). We aimed to identify global alterations in neural synchronization in epilepsy across resting and movie-driven fMRI scans using inter-subject correlation (ISC) analysis. Moreover, this is the first ever investigation of the effects of an automated Independent Components Analysis-based denoising strategy (ICA-AROMA, Pruim RHR et al. Neuroimage 2015; 112:278-287) on the temporal characteristics of movie-driven fMRI data derived in a clinical sample.

Method: Presurgical epilepsy patients and demographically matched healthy controls were recruited as part of a large province-wide initiative (Eplink). Participants underwent resting and movie-driven 3T fMRI scans. ISC analysis was performed to investigate the influence of participant group, scan type, and denoising procedure (with or without ICA-AROMA) on neural synchronization at a global level.

Result: Results revealed significantly higher global ISCs during movie-driven compared to resting-state condition in healthy controls, regardless of denoising procedure. In contrast, people with epilepsy exhibited consistently low global ISCs during rest and movie-driven conditions. Further, data denoised with ICA-AROMA revealed higher ISC values than data denoised without ICA-AROMA, in the movie condition.

Conclusions: To conclude, alterations in neural synchronization exist in people with epilepsy, even at the whole-brain level. This investigation supports denoising with ICA-AROMA: it may be appropriate, or even ideal, for data derived from naturalistic fMRI paradigms.

Abstract Number: 296

Title: Comparison the Brain-MRI Scan between Tuberous Sclerosis Complex patients with and without epilepsy

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Purpose: Tuberous Sclerosis Complex (TSC), an autosomal dominant disorder resulted from mutations in *TSC1* or *TSC2,* is a multisystem disorder [Peron,Northrup. American Journal of Medical Genetics 2018;178C:274-277] and epilepsy is the most frequent symptom (90%)[Cavenini et al. Am J Med Genet 2018;1–10]. Cortical Tubers are observed in 90% of TSC individuals [Northurp,Krueger. Pediatr Neurol 2013;49(4):243–254], and may be classified as type A, B and C [Gallagher et al,2010. J Neurol 2010;257:1373-1381]. The tuber count and its relationship with the severity of epilepsy is still a discussed and controversial subject of interest.

Method: In an outpatient service with follow-up of 127 patients diagnosed according to the diagnosis based on the International Diagnostic Criteria for TSC in 2012 , we selected 45 patients: 30 with epilepsy and 15 without epilepsy. In these patients,the tubers found in the MRI were counted and categorized by an experienced neuroradiologist.

Result: In the epilepsy group the median of the total number of tubers was 14.5(varying from 2-71):4 type A; 6.5 type B, 0 type C. In the non epileptic group the total median number of tubers was 9(varying from 0-38): 3 type A; 5 type B; and 0 type C. The median number of calcified tubers was 0 in both groups, however the concentrations of zero calcified tubers, were higher in the group without epilepsy compared with the group with epilepsy (p=0.070).

Conclusions: In our patients, is observed that the pattern of the median number of tubers is higher in the group with epilepsy compared to the non epileptic group. One mechanism responsible for epileptogenesis, is the volume the tubers occupy in the brain. We can speculate about considering the tuber count role contributing to the origin of epilepsy, besides other biomarkers. Further studies with diverse imaging methods are necessary.

Abstract Number: 297

Title: Magnetic Resonance Imaging Findings in Childhood Epilepsy at a Tertiary Hospital in Kenya

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Purpose: Access to appropriate imaging in sub-Saharan Africa is modest, consequently, etiological descriptions of childhood epilepsy in the region are limited. We sought to describe MRI findings in children with epilepsy presenting to a tertiary hospital in Kenya.

Method: A retrospective review of MRI findings of children aged between 0 and 18 years with a diagnosis of epilepsy presenting to the pediatric neurology department of Aga Khan University Hospital in Nairobi, Kenya, between January 2014 and July 2020 was undertaken. Over this period, the hospital had a 3T MRI machine (Philips 3T Ingenia). MRI images were independently reviewed by two study radiologists, and the findings were summarized and categorized into a study database. Related clinical and electroencephalographic (EEG) details were extracted from patient records. Categorical data analysis methods were applied to investigate for relationships between clinically relevant neuroimaging findings and key clinical and EEG observations.

Result: Over the study period, 288 children with a confirmed diagnosis of epilepsy had an MRI. They were of median age of 6 [interquartile range (IQR) 2-11] years. Ninety-five (33%) children had abnormal findings on imaging. The most common findings were encephalomalacia related to chronic infarcts (n = 18: 6.3%), cerebral atrophy (n = 11: 3.8%), disorders of neuronal migration (n = 11: 3.8%), periventricular leukomalacia (n = 9: 3.1%), and hippocampal sclerosis (n = 8: 2.8%). Findings related to infectious etiology were only observed in four children. Clinical comorbidity and inter-ictal epileptiform activity on EEG were independently associated with abnormal findings on imaging.

Conclusions: Up to a third of the children who underwent an MRI had a positive yield for abnormal findings. Comorbidity and inter-ictal epileptiform activity on EEG were associated with abnormal findings on imaging and should be considered in informing prioritization for imaging in childhood epilepsy in this setting.

Abstract Number: 361

Title: Significance of 2-[18F]FDG PET abnormalities beyond the seizure onset zone in mesiotemporal lobe epilepsy

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Purpose: To identify the value of presurgical 2-[^{18}F]FDG patterns in patients with drug resistant mesial temporal lobe epilepsy (MTLE) due to hippocampal sclerosis (HS) who underwent a selective amygdalohippocampectomy (SAHE) based on post-surgical long-term seizure outcome.

Methods: This retrospective study included 172 patients with drug resistant MTLE due to HS who underwent presurgical evaluation and SAHE between July 1994 and December 2019 at the Epilepsy Surgery Service of the Medical University of Vienna. Follow-up was conducted for at least one year, evaluating surgical outcome in accordance with the ILAE Outcome Scale (class 1 and 1a meaning seizure freedom, SZF, and class 2-6 meaning seizure recurrence, SZR). Only patients with a preoperative brain 2-[^{18}F]FDG PET scan were included, allowing a categorization into two groups based on visual analysis: 1) abnormal tracer uptake in the temporal lobe defined for surgery and 2) affectation beyond this area (extratemporal involvement) or no significant hypoperfusion area.

Results: 97 patients (47 female) with a mean age of 39 years (range 16 ± 62 years) were included in the final analyses. At the latest postoperative follow-up visit 69.1% of patients were seizure-free. Patients without significant hypoperfusion area or with involvement of extratemporal regions revealed a trend towards lower successful surgical outcome rates (58.3% achieved SZF) as opposed to patients with concordant temporal lobe tracer uptake abnormalities (72.6%), results were not significant (p =.189).

Discussion: Our results stand in accordance with studies showing that the extent of temporal lobe hypometabolism is not predictive for surgical outcome, but the presence of extratemporal metabolic abnormalities is. A limiting factor is our small number of cases and the implementation of a very specific surgical approach. These results instigate into viewing focal epilepsy (especially MTLE due to HS) as a brain network disease in which connectivity seems to play a big role.

Abstract Number: 387

Title: Temporal subcortical T2 hypointensity on MRI in epilepsia partialis continua, a non ketotic hyperglycemia rather than herpes encephalitis

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Purpose: Hyperglycemia can present as many neurological problems, one of them is seizure. Different brain MRI features can be seen in focal seizures associated with nonketotic hyperglycemia, cortical T2 hyperintensity, diffusion restriction and subcortical T2 hypointensity that subcortical T2 hypointensity is the only characteristic one. Finding this MRI feature is highly valuable in early diagnosis and treatment.

Method: Our patient was a 60-year-old female, a case of type 2 diabetes mellitus. She was brought to Emergency Room (ER) with focal colonic status epilepticus of right face and arm associated with confusion and drowsiness progressed over 2 weeks prior to admission. At first, acyclovir was started alongside anti-seizure medication with doubt of herpes encephalitis but antiviral was discontinued after normal LP result and characteristic MRI features.

Result: Subcortical T2 hypointensity in left temporal and insular lobe was seen on first MRI that was resolved on follow up MRI after she was treated. Accumulation of iron and free radicals or petechial hemorrhage may play a role.

Conclusions: Epilepsia partialis continua in the setting of non ketotic hyperglycemia should be differentiated from that in herpes encephalitis in a diabetic patient presenting with subacute confusional state and focal status epilepticus considering characteristic MRI finding of subcortical T2 hypointensity.

Abstract Number: 396

Title: cognitive deficits in temporal lobe epilepsy reflect atypical functional connectome hierarchy

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Purpose: Drug-resistant temporal lobe epilepsy (TLE) is typically associated with hippocampal pathology. Widespread network alterations are increasingly recognized and suggested to perturb cognitive function in multiple domains. Here we tested whether TLE shows atypical cortical hierarchical organization, differentiating sensory and higher-order systems, and whether atypical hierarchy predicts cognitive impairment.

Method: We studied 72 well-characterized drug-resistant TLE patients and 41 healthy controls with similar age and sex using multimodal MRI analysis and cognitive testing. To model cortical hierarchical organization *in vivo*, we used a bidirectional stepwise functional connectivity analysis tapping into the differentiation between sensory/unimodal and paralimbic/transmodal cortices. In details, after generating the connectivity matric, we calculated the number of connections (*degrees*) linking seed regions (sensory areas and hippocampus) to the rest of the brain at connection lengths or steps, ranging from 0 (*i.e.*, the seed) to 100 steps away (Sepulcre J et al. J. Neurosci 2012; 32*)*. Linear models compared patients to controls. Finally, we assessed associations to TLE-related cortical atrophy, microstructural anomalies, as well as clinical and cognitive parameters.

Result: Compared to controls, TLE presented with bidirectional disruptions of sensory-paralimbic functional organization. Stepwise connectivity remained segregated within paralimbic and salience networks at the top of the hierarchy, and sensorimotor and dorsal attention at the bottom. While paralimbic segregation was associated with atypical cortical myeloarchitecture and hippocampal atrophy (P<0.0005), connectional derangements of sensorimotor cortices reflected diffuse cortical thinning (P<0.0005). The degree of abnormal hierarchical organization covaried with broad cognitive impairments spanning sensorimotor, attention, fluency, visuo-constructional ability and memory, and was more marked in patients with longer disease duration.

Conclusions: Our findings show atypical functional integration between paralimbic/transmodal and sensory/unimodal systems in TLE. Differential associations to paralimbic microstructure and sensorimotor atrophy suggest that system level imbalance likely reflects complementary structural processes, but ultimately accounts for a broad spectrum of cognitive impairments.

Abstract Number: 404

Title: Sensitivity of Segmentation Methods for the Detection of Hippocampal Sclerosis

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Purpose: Hippocampus volumetry is an important biomarker to quantify atrophy in patients with temporal lobe epilepsy. We investigate the sensitivity of automated segmentation methods to detect hippocampal sclerosis (HS). Results from the established tools FreeSurfer and FSL FIRST are contrasted to a deep learning-based segmentation method.

Method: We have used T1-weighted MRI scans from 105 patients with epilepsy (among them 31 diagnosed with HS), and 354 healthy controls. FreeSurfer, FSL FIRST, and a deep learning-based method were used for brain anatomy segmentation. We have calculated effect sizes (Cohen's d) between left/right HS and healthy controls using asymmetry of hippocampal volumes. Additionally, we derived 14 shape features from the segmentations and used them as input for a support vector machine (SVM) to identify patients with hippocampal sclerosis.

Result: Deep learning-based segmentation of the hippocampus is the most sensitive to detect HS. The effect sizes of the asymmetries are larger with the deep learning-based segmentations (left=3.6, right=4.1) than with FreeSurfer (left=2.9, right=3.6) and FSL (left=2.1, right=2.5). For the classification using the shape features, the area under the curve (AUC) was higher for the deep learning-based segmentation (AUC=0.74) than for FreeSurfer (0.65) and FSL (0.66). The surface-to-volume ratio had the highest feature importance.

Conclusions: Our findings suggest that deep learning-based segmentation methods yield a higher sensitivity to quantify hippocampal sclerosis than atlas-based methods. The surface-to-volume ratio of the hippocampus might be an easy-to-interpret quantitative imaging biomarker for HS.

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Abstract Number: 424

Title: Decomposing the complex imaging signature of temporal lobe epilepsy using latent phenotypes

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Purpose: Common epilepsy syndromes such as temporal lobe epilepsy (TLE) are increasingly recognized to be highly heterogenous, which motivates subtyping and more personalized approaches for the prediction of clinically relevant outcomes. Here, we utilized unsupervised machine learning to estimate multivariate *latent relations* from MRI features representing whole-brain patterns of structural pathology, or *disease factors*, and quantified their co-expression within each patient. We assessed their diagnostic validity for predicting drug response, surgical outcome and cognitive scores.

Method: We studied 82 TLE patients and 41 age- and sex-matched healthy controls using multimodal 3T MRI features.

Result: We identified four latent disease factors variably expressed across patients. Factor-1 was defined by ipsilateral hippocampal microstructural damage, loss of myelin and atrophy; Factor-2 by gliosis in bilateral paralimbic neocortex and hippocampus; Factor-3 by bilateral neocortical thinning; and Factor-4 by bilateral white matter microstructural anomalies. Bootstrap analysis showed within sample robustness of the four factors, supporting their generalizability. Classifiers trained on latent disease factors out-performed those operating on group-level findings of individual MRI features, predicting drug-response in 76±3% (vs. 60-68% across features) and postsurgical seizure outcome in 88±2% (vs. 57-80%). Similarly, correlations between predicted and true cognitive scores were consistently higher for factor-derived regressions (verbal IQ: r=0.40±0.03 vs. 0.08-0.3, memory: r=0.35±0.03 vs. 0.02-0.1, sequential motor tapping: r=0.36±0.04 vs. 0.02-0.28).

Conclusions: By quantifying the co-expression of latent patterns of gray and white matter structural pathology across the hippocampus and the whole brain, this study provides a novel description of the continuum of interindividual variability in TLE. Superior performance compared to conventional group-based analysis stresses the ability of dimensional modeling to mine salient disease characteristics that would otherwise be missed, ultimately refining the prediction of relevant clinical outcomes.

Abstract Number: 542

Title: Gray matter changes in Juvenile Myoclonic Epilepsy. A Voxel-Wise Meta-Analysis

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Purpose: In the present study we did a Voxel-Wise meta-analysis on the volumetric differences of the gray matter in juvenile myoclonic epilepsy (JME).

Method: Our meta-analysis included 12 studies that compared the gray matter changes in patients with JME to healthy controls, with the use of voxel-based morphometry (WBM). All the studies reported the results in Montreal Neurological Institute (MNI) of Talairach space. The total number of JME patients was 325, and of healthy controls 357.

Result: Our study showed statistically significant increase of the gray matter in the left median cingulate/paracingulate gyri (Brodmann area 23, SMD-Z: 1.404, p=0.0002, Voxels: 820, MNI Coordinates: -4, -6, 42), the right superior frontal gyrus (Brodmann area 10, SMD-Z: 1.446, p=0.0002, Voxels: 530, MNI coordinates: 20, 60, 18), the left precentral gyrus (Brodmann area 6, SMD-Z: 1.093, p=0.0017, Voxels: 186, MNI coordinates: -20, -20, 66), the right supplementary motor area (Brodmann area 6, SDM-Z: 1.135, p=0.0013, Voxels: 152, MNI Coordinates: 8, 10, 60) and left supplementary motor area (Brodmann area 6, SDM-Z: 1.139, p=0.0013, Voxels: 72, MNI Coordinates: -8, 12, 68). It also showed a decrease in the gray matter volume in the left thalamus (SDM-Z: -1.1875, p=0.00001, Voxels: 970, MNI Coordinates: -12, -6, 8), and in the right insula (Brodmann area 48, SDM-Z: -1.372, p=0.0008, Voxels: 553, MNI Coordinates: 42, 2, 6).

Conclusions: The volumetric changes found in the present study could be related to the impaired frontal lobe functions, the emotional dysfunction and impaired pain empathy, and to disrupted functional connectivity of supplementary motor areas described in JME. It additionally shows changes in the volume of left thalamus, supporting the theory of thalamocortical pathways being involved in the pathogenesis of juvenile myoclonic epilepsy.

Abstract Number: 571

Title: Imaging the atypical language connectome – lessons learned from preoperative functional MRI

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Purpose:
The structural and functional neuronal networks underlying atypical language-lateralization (ALL) in epilepsy patients are largely unknown. ALL can be described as right-lateralized, bi-lateralized and crossed-lateralized language representations. The aim of this study was to explore functional and structural connectivity differences in right and left temporal lobe epilepsy (TLE) patients with ALL.

Method: The lateralization indices of 26 TLE patients, who underwent fMRI for preoperative language evaluation, were calculated for the frontal and temporal lobes separately using the bootstrap method, implemented in the LI-toolbox. A total of 19 TLE patients (rTLE: n=10, 6 lesional; lTLE: n=9, 6 lesional) with ALL were identified and included in this study. The fMRI pattern analysis was performed using SPM12. The CONN-toolbox was used for the functional connectome analysis (FCA). The structural connectome analysis (SCA) was performed using MRtrix3.

Result: Atypical language representations in lTLE were found in the right angular gyrus [$p_{uncorr.} \leq 0.001$, z=4.60], right pole of superior temporal gyrus [$p_{uncorr.} \leq 0.001$, z=4.54], right posterior middle temporal gyrus [$p_{uncorr.} \leq 0.001$, z=4.29], right precentral gyrus [$p_{uncorr.} \leq 0.001$, z=4.20] and left angular gyrus [$p_{uncorr.} \leq 0.001$, z=4.08]. In rTLE significant activations were observed in the left superior frontal gyrus [$p_{uncorr.} \leq 0.001$, z=4.15], right precentral gyrus [$p_{uncorr.} \leq 0.001$, z=4.11] and right posterior middle temporal gyrus [$p_{uncorr.} \leq 0.001$, z=4.10]. The FCA showed more extensive intra- and interhemispheric connectivity in atypically lateralized patients with rTLE. The SCA showed more extensive intrahemispheric connectivity from the right banks of the superior temporal sulcus in subjects with lTLE and no differences from the right pars opercularis of the inferior frontal gyrus.

Conclusions: ALL networks share a range of commonalities amongst right and left TLE patients. A more extensive atypical language connectome in rTLE patients points towards different modes of neuroplasticity between right and left TLE. Preoperative clinical FCA and SCA opens new diagnostic possibilities ultimately aiming to improve individual patient outcomes.

Abstract Number: 577

Title: Structural covariance network changes in the common epilepsies: a worldwide ENIGMA study

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Purpose: Structural covariance analysis captures across-subject correlations of morphological measures derived from magnetic resonance imaging (MRI) data. These have described topological alterations in structural network organization in individuals with epilepsy relative to controls. Analyses, however, have been restricted to individual sites and/or to specific syndromes. Moreover, neurobiological substrates of these macroscale changes remain unclear. In this multisite ENIGMA study, we assessed structural organization in the common epilepsies using graph theoretical analysis of covariance networks. To explore potential neurobiological underpinnings, macroscale network findings were spatially correlated with *postmortem* gene expression data.

Method: We included two patient cohorts with site-matched controls: temporal lobe epilepsy with neuroradiological evidence of hippocampal sclerosis (TLE; 15 sites, $n_{HC/TLE}$=1,311/717) and idiopathic/genetic generalized epilepsy (IGE; 10 sites, $n_{HC/IGE}$=973/309). Cortical thickness and subcortical volume measures were harmonized across sites and corrected for age, sex, mean thickness, and intracranial volume. Site- and cohort-specific covariance networks were computed from cortical thickness and subcortical volume correlations. We computed clustering coefficient (quantifying local network efficiency) and path length (quantifying global efficiency), and compared patients to controls across sites via Cohens' *d* effect sizes and multivariate linear models. Spatial patterns of topological alterations were then correlated with expression maps of epilepsy-related risk genes.

Result: Comparing TLE patients to controls, we observed increased clustering and path length in mesiotemporal regions, indicating network regularization. Conversely, IGE patients showed decreases in clustering coefficient and path length in bilateral fronto-central cortices, suggesting network randomization. Topological alterations in TLE followed gene expression patterns of hippocampal sclerosis, whereas topological changes in IGE correlated gene expression patterns of generalized epilepsy. Network associations did not correlate with other disease-related transcriptomic maps, indicating specificity

Conclusions: As the largest structural network study in epilepsy to date, our work highlights syndrome-specific brain network organization that follows the spatial expression of epilepsy risk genes.

Abstract Number: 602

Title: Use of Computerized Tomography Perfusion in emergency department to identify seizures. Retrospective study

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Purpose: Our aim is to study the diagnostic value of Computerized Tomography Perfusion (CTP) to detect seizures in patients who come to emergency department with stroke suspicion and finally result to be a Stroke Mimics.

Method: We enrolled, retrospectively, patients who came to emergency department with focal neurologic deficit, that mimic symptoms of stroke, and received an emergency CTP between January of 2019 and December of 2020. We collected demographic data, presentation on admission, seizure history, semiology and other variables.
We included patients who underwent CTP who did not show large vessel occlusion or acute lesions on Simple Computerized Tomography and whose final diagnosis was seizure or status epilepticus

Result: A total of 822 patients underwent a CTP, of which, 118 did not present acute cerebrovascular disease. Finally, we included 38 patients whose final diagnosis was seizure or status epilepticus.

In our cohort, the mean age was 66.1 (SD: 17.22), 60.5% were women, the most common symptom was aphasia (50%), 31.6% of patients had previous history of seizures or epilepsy.
From all of 38 patients, 36.8% (14) had CTP alterations, showing 92.8% (13) hyperperfusion and 1.2% (1) hypoperfusion. 42.9% showed epileptiform activity on electroencephalography.
We compared patients who presented hyperperfusion on CTP and their diagnosis was seizure or Status Epilepticus with patients who had focal neurological deficit that mimic symptoms of stroke and presented hyperperfusion on CTP, we observe statistically significant differences ($p<0.05$).

Conclusions: In our cohort CTP is a useful tool for the diagnosis of seizures in the emergency department.

Abstract Number: 620

Title: AI-assisted quantitative analysis of FDG-PET in medial temporal lobe epilepsy

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Purpose: Fluorodeoxyglucose-positron emission tomography (18F-FDG-PET) was widely used in epilepsy surgery. In patients with medial temporal lobe epilepsy (MTLE), the lateralization value of FDG-PET varied by visual analysis. We conducted this study to establish a robust quantitative method for lateralization epileptogenic foci and examine the value of machine-assisted analysis of PET in MTLE.

Method: We retrospectively reviewed patients who underwent epilepsy surgery for MTLE with high resolution brain MRI and 18F-FDG-PET. Three clinicians who were blind to the side of surgery identified the side of MTLE by visual inspection. The side of surgery was set as a standard in this study. Two segmentation methods and corresponding atlases (AAL atlas for DARTEL, aparc+aseg atlas for freesurfer) were used to extract the normalized PET uptake of the interested regions. The two atlases were applied to automatically delineate MTLE associated regions in either hemisphere, respectively. The lateralization index of each MTLE associated regions were submitted for machine learning to establish MTLE side classification model.

Result: A total of 95 patients were enrolled in this study (47 left, 48 right). The hit rate of lateralization by visual analysis was 74.7%. In DARTEL segmentation method, the accuracy of lateralization according to 11 ROIs achieved 95.8% with Cosine KNN model, and the area under the ROC curve (AUC) is 0.99. When we limited the ROI to amygdala and hippocampus only, the accuracy decreased to 92.6%. When compared the freesurfer and the DARTEL method, there is no significant differences (accuracy 96.8%, AUC 0.99).

Conclusions: Visual analysis of FDG-PET to lateralize MTLE showed inter-rater difference and a lower hit rate compared to the results of machine-assisted interpretation. While reviewing the PET in MTLE, taking the information of the regions of MTLE associates into consideration showed a better performance than analyzing the regions limited to amygdale and hippocampus.

Abstract Number: 639

Title: Progressive hippocampal changes before and after surgery in refractory temporal lobe epilepsy

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Progressive hippocampal changes before and after surgery in refractory temporal lobe epilepsy

Purpose: Temporal lobe epilepsy (TLE) is associated with progressive thinning of the cortex that may be prevented by successful resective surgery. There is little knowledge on accelerated morphological changes of the hippocampus before and after epilepsy surgery.

Method: In this longitudinal case-control neuroimaging study, we included patients with unilateral refractory TLE before (n=24) or after (n=54) anterior temporal lobe resection and healthy volunteers (n=120) matched for age and sex. We evaluated hippocampal volumes and surface shape morphology on paired structural magnetic resonance imaging scans in all participants and compared progressive changes between groups using linear mixed effects models.

Result: In left TLE, there was progressive preoperative hypertrophy of the contralateral hippocampus, particularly affecting areas in the superior hippocampal head ($p<0.001$) and the inferior hippocampal body ($p=0.01$). This accelerated hypertrophy of the contralateral hippocampus persisted after left anterior temporal lobe resection (head, $p=0.009$; tail, $p<0.001$). In right TLE, there was a trend towards focal progressive hypertrophy of the contralateral hippocampal tail before surgery ($p=0.07$). After right temporal lobe resection, there was focal accelerated hypertrophy of the contralateral hippocampal head ($p=0.003$). We did not detect accelerated volume changes before surgery in the ipsilateral hippocampi of patients with left or right TLE.

Conclusions: Refractory left TLE, and to a lesser extent right TLE, are associated with progressive focal hypertrophy of the contralateral hippocampus before and after resective surgery. These contralateral changes may represent use-dependent plasticity due to ipsilateral epilepsy-related neuronal network disturbances or resection of the ipsilateral anterior temporal lobe. In contrast to progressive cortical thinning, the ipsilateral hippocampus does not show accelerated atrophy shortly before TLE surgery.

Abstract Number: 685

Title: Differential alterations of thalamic subregion volumes in patients with temporal lobe epilepsy

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Purpose: Thalamus is thought as the part of temporal lobe epilepsy (TLE) network. Functional alterations in anterior nucleus and pulvinar had been reported in functional MRI studies. However, how these structures change in TLE patients has not been well studied. Therefore, we aimed to identify whether the differential changes of the thalamic subregion volume occur in left and right TLE.

Method: We enrolled 23 left-TLE, 32 right-TLE patients, and 28 controls. All subjects received high-resolution three-dimensional T1-weighted MRI. Volumes of the 25 thalamic subregions were calculated by FREESURFER (version 7.1.1). The normalized values of the thalamic subregion volume were compared among three groups by multivariate analysis of covariance analysis, and their relationship with the epilepsy duration, spike burden, and seizure frequency were calculated using partial correlation analysis.

Result: Both TLE patients had significant volume reduction in the ipsilateral anterior, lateral, medial subregions, and the contralateral lateral area; while the total thalamic volume did not significantly change. Left-TLE had

more extensive subregion volume reduction. Intralaminar nuclei volume only decreased ipsilaterally in left-TLE, and the left anteroventral nucleus had most significant volume reduction. Volume of ventral and posterior subregions only decreased ipsilaterally in right-TLE, and the right limitans demonstrated most significant volume reduction. Epilepsy duration was primarily negatively related to left subregion volumes in both TLE. Seizure frequency was positively related to right subregion volumes in L-TLE, and was negatively related to left subregions in R-TLE. Qualitative spike burden was only negatively associated with the ipsilateral subregions in L-TLE.

Conclusions: Thalamus is involved in TLE, but presents differential subregions involvement in left- and right-TLE patients. The subregion volume reduction is most extensive in left-TLE, and primarily restricted in ipsilateral side in right-TLE. Anterior nucleus seems to be an important structure in both TLE networks, and is susceptible to the ipsilateral seizures.

Abstract Number: 701

Title: Multimodal Voxel-based Analysis of MRI for Covert Lesion Detection in Focal Epilepsy

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Purpose: One third of patients with medically refractory focal epilepsy have normal-appearing MRI scans. This poses a problem, as identification of the epileptogenic region is required for surgical treatment. This study performs a multimodal voxel-based analysis (VBA) to identify brain abnormalities in MRI-negative focal epilepsy.

Method: Data was collected from 58 focal epilepsy patients (42 with discrete lesions on MRI scans, 16 with no visible findings on scans), and 61 healthy controls. MR images comprised T1-weighted, fluid-attenuated inversion recovery (FLAIR), fractional anisotropy (FA) and mean diffusivity (MD) from diffusion tensor imaging, and neurite density index (NDI) from neurite orientation dispersion and density imaging. These multimodal images were coregistered to T1-weighted scans, normalized to MNI space, and smoothed with 8mm FWHM. Initial analysis performed voxel-wise one-tailed t-tests separately on FLAIR, FA, MD, and NDI, comparing each subject with epilepsy to controls. A multimodal non-parametric combination (NPC) analysis was also performed simultaneously on these same modalities. Resulting p-maps were family-wise error rate corrected, threshold-free cluster enhanced, and thresholded at $p<0.05$. Sensitivity was established through visual comparison of results to manually drawn lesion masks or seizure onset zone from intracranial EEG. A leave-one-out cross-validation with the same analysis protocols was performed on controls to determine specificity.

Result: NDI was the best performing individual modality, detecting focal abnormalities in 37.5% of patients with normal MRI. FA demonstrated the lowest sensitivity at 25.0%. NPC provided superior performance to univariate analyses with 56.3% sensitivity. Specificity in controls ranged between 96-100% for all analyses.

Conclusions: This study demonstrated the potential utility of multimodal VBA utilizing NPC for detecting epileptogenic lesions in MRI-negative focal epilepsy. Future work will apply this approach to datasets from other centres and will experiment with different combinations of MR sequences.

Abstract Number: 732

Title: Abnormal cortical and subcortical structure in juvenile myoclonic epilepsy demonstrated with advanced MRI analysis

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Purpose: Juvenile myoclonic epilepsy (JME) is the most frequent genetic generalized epilepsy syndrome (1). It typically occurs during adolescence with predominant myoclonic seizures, which can be intermixed with generalized tonic-clonic and absences. Neurophysiological, neuropsychological and imaging studies in JME have consistently shown focal abnormalities in the medial and dorsolateral prefrontal lobe. The aim of our study was to explore for additional evidence of focal cortical abnormalities in JME using advanced neuroimaging techniques.

Method: We enrolled 16 consecutive patients (9 women, mean age: 30.2+10.4 years) with JME, and 16 age and sex-matched controls. All subjects underwent 3T MR study using standard protocol that included T1-3D TFE (Turbo Field Echo) images with 1 mm thickness, to measure surface and thickness of several cortical Regions of Interest (ROIs), as also volumes of several subcortical ROIs. The volumes of deep subcortical GM structures were extracted, and vertex-wise shape analysis was performed using standard Freesurfer analysis. Our study analysed 158 quantitative parameters.

Result: Thirteen/158 variables presented significative differences between the two groups. In patients with JME, there was a bilateral volumetric reduction of thalami, putamina, nuclei caudati and nuclei accumbentes, associated with bilateral increase of volume in globi pallidi. Moreover, it was found an increased surface of left frontal pole, a decreased surface of right pars opercularis and a reduced thickness of left medial orbitofrontal cortex.

Conclusions: Our findings further illustrate a structural cortical and subcortical abnormality in JME with main involvement of mesio-frontal structures, which likely play a pathogenetic role in this syndrome. Indeed, a dysregulation of fronto-talamic network is considered a causative mechanism underlying seizures in JME, due to the absence of thalamic inhibitory inputs towards cortical structures (2). We also found significative volumetric differences in basal ganglia, whose modulatory role on cortical excitability has been recently advocated (3).

Abstract Number: 734

Title: Automated method to map cortical brain regions to the nearest scalp electroencephalography electrode.

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Purpose: The mapping of cortical structures to scalp electroencephalography (EEG) electrodes remains unclear. The gold standard 10/20 system only accommodates the derivation of underlying lobes. This study sought to create a fully automated method to map each 10/20 electrode to the nearest cortical region.

Method: T1w MRI images from ten healthy participants and four participants with epilepsy (non-lesional) were analysed. A nonlinear registration was used to warp 19 electrodes from the MNI template space to the participant's T1 MRI image. Cortical regions were labelled according to the Desikan Killiany atlas (using FreeSurfer). Two approaches were applied to calculate the distance from each electrode to each cortical region: (1) the minimum ("min") method and (2) the inverse square (IS) method. Only surface cortical regions were kept; for all 70 regions, the closest electrode was identified using both approaches.

Result: Using the IS approach, 18/19 electrodes were consistently mapped between subjects. Conversely, using the min approach, only 15/19 electrodes were consistently mapped between subjects. For both methods, between-subject variation was predominantly in the frontal lobe regions (i.e. some participants showed that electrode Fp1 was closest to the lateral orbital frontal cortex, while others showed that F7 was the closest electrode). Both methods displayed a between-subject variation for the following electrode pairs C3/F3, C4/F4, P3/C3, T3/F7, O2/PZ.

Conclusions: The Desikan Killiany atlas was used with nonlinear registration to obtain subject-specific distance measurements between cortical regions and electrode positions. It demonstrated that between-subject variability needs to be accounted for when positioning electrodes, particularly in the frontal lobe. The techniques described may offer greater cortical region specificity than the 10/20 montage alone. It could be used to improve the accuracy of electrode placement and subsequently improve automated seizure detection.

Abstract Number: 737

Title: Accurate detection of typical absence seizures using a two-channel wearable behind the ears

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Purpose: Patients with absence epilepsy recall less than 10% of their absence seizures. The clinical gold standard to assess absence epilepsy is a 24-hour EEG recording, which is expensive, obtrusive and time-consuming to review. Our aim was to investigate the performance of a discrete two-channel behind-the-ear

EEG-based wearable, the Sensor Dot (SD), to detect typical absences and develop a sensitive automated absence seizure detection algorithm to reduce the review time.

Method: We recruited 12 patients (median age: 21 y; range: 8 – 50 y; seven female) who were admitted to the epilepsy monitoring unit of University Hospitals Leuven for a 24-hour 25-channel video-EEG recording to assess their refractory typical absences. For concomitant recording with the SD, two additional electrodes were attached behind each ear and ipsilateral electrodes were connected. Typical absence seizures were defined as 3 Hz spike-and-wave discharges on EEG, lasting three seconds or longer. Seizures on SD were blindly annotated on the full recording and on the file containing the automated seizure detections. The SD annotations were compared to gold standard 25-channel EEG annotations. Patients or caregivers were asked to keep a seizure diary. Performance of the SD and seizure diary were measured using the F1-score.

Result: Blind reading of SD data gave a sensitivity of 0.81, a precision of 0.89 and F1-score of 0.73, whereas a score of 0.83, 0.89 and 0.87, respectively, was obtained for review of the automated detection files. Patient self-reporting gave a sensitivity of 0.08, a precision of 1.00 and F1-score of 0.15

Conclusions: The wearable SD reliably detected typical absence seizures. Our automated absence detection algorithm reduced the review time of a 24-hours recording from 1-2 hours to around 5-10 minutes.

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Abstract Number: 740

Title: Automated subcortical volume estimation from 2D MRI in epilepsy, comparison with 3D MRI and implications for clinical trials

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Purpose: Most techniques used for automatic segmentation of subcortical brain regions are developed for three-dimensional (3D) MR images. MRIs obtained in non-specialist hospitals may be non-isotropic and two-dimensional (2D). Automatic segmentation of 2D images may be challenging and represents a lost opportunity to perform quantitative image analysis. We determine the performance of a modified subcortical segmentation technique applied to 2D images in patients with idiopathic generalised epilepsy (IGE).

Methods: Volume estimates were derived from 2D (0.4x0.4x3mm) and 3D (1x1x1mm) T1-weighted acquisitions in 31 patients with IGE and 39 healthy controls. 2D image segmentation was performed using a modified FSL FIRST (FMRIB Integrated Registration and Segmentation Tool) pipeline requiring additional image reorientation, cropping, interpolation and brain extraction prior to conventional FIRST segmentation. Consistency between segmentations was assessed using Dice coefficients and volumes across both approaches were compared between patients and controls.

Results: All average Dice coefficients showed excellent agreement between 2D and 3D scans across subcortical structures (0.86-0.96). Most 2D volumes were consistently slightly lower compared to 3D volumes. Significant volume reduction of the left and right thalamus and putamen was observed in patients relative to controls across 2D and 3D images.

Conclusions: Automated subcortical volume estimation of 2D images using a modified segmentation pipeline is consistent with volumes from 3D images. Thalamic and putamen atrophy has previously been reported in

patients with IGE. Automated subcortical volume estimation from 2D images is feasible and reliable and provides an opportunity to perform quantitative image analysis studies in clinical trials.

Abstract Number: 749

Title: An advanced multi-modal imaging approach in non lesional frontal lobe epilepsy

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Purpose: Frontal Lobe Epilepsy (FLE) is a common form of epilepsy in which seizure onset is usually caused by structural lesions on frontal areas. Some patients with FLE can be defined as non-lesional (nlFLE) if seizures start in the frontal lobe, but there are no clearly identifiable abnormalities on brain Magnetic Resonance Imaging (MRI). Using advanced neuroimaging, we aimed to investigate whether nlFLE patients show undetected microstructural white matter and/or grey matter abnormalities compared to healthy controls (HC).

Method: MRI data were acquired from 127 nlFLE patients and 127 age- and sex-matched HC. Diagnosis of nfFLE was based on typical ictal semeiology and interictal frontal EEG discharges. We performed group comparisons using multimodal MRI analysis: voxel-based morphometry (VBM), cortical thickness (CT), Diffusion tensor imaging (DTI) and Tract-based spatial statistics (TBSS). Subsequently, we focused on the corpus callosum (CC), since abnormalities within this region have been frequently reported in epilepsy patients. In particular, values of thickness, fractional anisotropy (FA) and mean diffusivity (MD) were extracted from 50 regions of interest (ROIs) along the callosal midsagittal profile. At each ROI, analysis of variance was performed to assess differences between patients and controls, with age and sex as covariates.

Result: VBM analysis in nlFLE patients revealed regional atrophy in rolandic operculum compared to HC (p-value<0.05, TFCE-corrected). TBSS analysis in our nlFLE patients also showed significantly increased FA, increased MD in NAWM of CC (p-value<0.05, TFCE-corrected), especially in sections I (rostrum, genu and rostral body) and III (posterior midbody).

Conclusions: although nlFLE are supposedly “MRI-negative”, our study confirms and reinforces that subtle MRI functional and morphological anomalies are found. Our findings at level of CC suggest a possible role of white matter abnormalities in the network abnormalities sustaining frontal lobe seizures, questioning the traditional concept of epilepsy as a “cortical–only disease”.

Abstract Number: 758

Title: Alterations in functional connectome hierarchy in newly diagnosed focal epilepsy reveals brain expression of genes implicated in epilepsy.

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Purpose: Neuroimaging research has provided insights into epilepsy as a disorder of brain connectivity which may have an identifiable underlying genetic component. Impairments have been observed in varied domains ranging from sensory and motor functioning to higher-order cognitive processing often from early stages of the

disorder. We used gradient mapping of resting-sate fMRI to examine whether this impairment pattern can be accounted for by imbalance in a large-scale connectome gradient spanning from unimodal to transmodal associative networks and the potential genetic basis of such an alteration.

Method: We compared cortical maps of gradient scores in patients with newly diagnosed focal epilepsy (NDfE, n=27) with minimal exposure to anti-seizure medication (ASM) to a group of age and sex-matched controls (HC, n=36). Differences between persistent seizure (PS, n=10) and seizure free (SF, n=17) patients at 12-months follow-up were also investigated.

Result: We found increased functional separation between unimodal and transmodal networks in NDfE which was particularly pronounced in the PS group. Differences corresponded to gradient score reductions in the visual network and increases in limbic and default mode systems associated with higher-level cognition. The cortical map of NDfE–control differences was spatially correlated with patterns of prior brain-wide gene expression. A disease enrichment and pathway analysis revealed that genes most strongly associated with NDfE–control (but not PS-SF) differences along the cortex were part of a network of genes previously implicated in seizure-related disorders including focal epilepsy.

Conclusions: In conclusion, we propose that large-scale functional hierarchy has the potential to contribute to a more parsimonious account of wide-ranging impairments associated with focal epilepsy. Combining functional neuroimaging and transcriptional data analysis particularly in patients with minimal exposure to ASM can provide mechanistic insight into how gene processes may drive alterations in large-scale features of brain dynamics mediating the genetic risk of epilepsy.

Abstract Number: 772

Title: Alterations of midbrain structure volume, estimated myelin and functional connectivity in idiopathic generalised epilepsy

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Purpose: Neuroimaging studies have reported abnormalities of the striatal basal ganglia in idiopathic generalised epilepsy (IGE). Midbrain basal ganglia structures have received less attention given the insufficient resolution of individual structures on routinely acquired T1-weighted scans. In this study we have acquired isotropic T1-weighted and T2-weighted images, and resting state fMRI to investigate volumetric, estimated myelin and functional connectivity of the substantia nigra, subthalamic nuclei and red nuclei in patients with IGE.

Method: 34 patients with IGE (23 refractory, 11 non-refractory) and 18 age and sex matched healthy controls were recruited. Volume estimation of the midbrain structures was performed on T2-weighted images using an automated segmentation technique. Myelin content of the above structures was estimated using T1-weighted/T2-weighted ratios. Functional connectivity analysis of the structures was performed using seed-to-voxel resting state fMRI analysis.

Results: All patients had significantly increased volumes of the left (p=0.03) and right substantia nigra (p=0.02) and increased estimated myelin in the right substantia nigra (p=0.05) relative to controls. No substantia nigra functional connectivity differences was observed. Although no difference in volume or estimated myelin was

found in the subthalamic nucleus between patients relative to controls, significantly decreased functional connectivity was found between the left subthalamic nucleus ($p<0.05$) and the right occipital cortex in patients with non-refractory IGE compared to controls and patients with refractory IGE. Functional connectivity increases between the left red nucleus and the right supramarginal gyrus was observed in patients relative to controls; no differences in volume or estimated myelin of the left or right red nucleus was observed.

Conclusions: Morphometric alterations of the substantia nigra and functional connectivity alterations of the subthalamic and red nuclei exist in IGE. This supports previous experiential work demonstrating pathophysiological abnormalities of the lower basal ganglia in animal models of generalised epilepsy.

Abstract Number: 828

Title: MELD Project: Predictors of lesion location and postsurgical seizure freedom in focal cortical dysplasia (FCD)

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Purpose: Focal cortical dysplasias (FCDs) are an important cause of drug-resistant epilepsy. The impact of FCD location on clinical presentation and surgical outcome is largely unknown. We created a large neuroimaging cohort of patients with FCD to determine predictors of lesion location and postsurgical seizure freedom.

Method: The MELD project collated a retrospective cohort of 580 FCD patients from 20 epilepsy centres. MRI-based maps of individual FCD lesions with accompanying clinical information was collected for each patient. We mapped the distribution of FCD lesions across the cerebral cortex and examined for associations between clinical factors and lesion location using logistic regression models. Post-hoc analyses of significant factors included correlational analyses (r_{rank}) which were compared with those from 1000 spherically rotated maps to determine statistical significance (p_{spin}).

Result: FCDs were non-uniformly distributed, concentrating in the superior frontal sulcus, frontal pole and temporal pole. Age of epilepsy onset was typically before age 10. Earlier epilepsy onset was associated with lesions in primary areas while later epilepsy onset was associated with lesions in association cortices ($r_{rank}=0.40$, $p_{spin}<0.01$). Lesions associated with shorter durations of epilepsy were more likely to be located in temporal and occipital lobes and tended to be larger ($r_{rank}=-0.44$, $p_{spin}<0.05$). Seizure freedom rates varied with FCD location, around 30% in visual, motor and premotor areas compared to 75% in superior temporal and frontal gyri.

Conclusions: The MELD project has gathered the largest neuroimaging cohort of patients with FCD to date. The location of an FCD is an important determinant of its size, the age of epilepsy onset and the likelihood of seizure freedom post-surgery. Using an open-science collaboration, we have characterised the spatial distribution of a focal pathology to identify data-driven, patient-specific predictors of lesion location and postsurgical seizure freedom to inform clinical decision-making.

Abstract Number: 829

Title: MELD Project: Automated surface-based detection of focal cortical dysplasias

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Purpose: Drug-resistant focal epilepsy is often caused by focal cortical dysplasias (FCDs) which are notoriously difficult to visually identify on structural MRI but are amenable to surgical resection. We aimed to develop an open-source, surface-based machine-learning algorithm to automatically identify FCDs on heterogeneous structural MRI data from epilepsy surgery centres worldwide.

Method: A retrospective cohort of 555 patients with epilepsy due to FCD and 390 controls from 21 epilepsy centres worldwide was collated. Multiple surface-based features, containing morphological and image intensity information, were extracted from T1w and FLAIR MRI contrasts. Manual lesion masks were created for each FCD and registered to the surfaces. Features were smoothed, harmonized across sites using ComBat, and normalized for intersubject and interregional morphological differences. The dataset was split 50:50 into a train cohort and a withheld test cohort, and a neural network was trained to classify lesional cortex. All hyperparameter optimisation was performed on the train cohort.

Result: After including a border zone around the lesion masks to account for uncertainty around manual delineations, the developed MELD surface-based algorithm had a sensitivity (prediction overlapping lesion mask) of 72.3% and specificity (any false positive clusters on controls) of 29.0% on the train/validation cohort and a sensitivity of 68.0% and a specificity of 33.3% on the withheld test cohort. In the gold-standard cohort of histopathologically confirmed FCD type II patients who were seizure free post-operatively, the sensitivity was 79.2%.

Conclusions: Through open infrastructure, freely accessible pipelines and protocols for parallel post-processing of clinical MRI scans and collaborative working practices we have developed a clinically meaningful machine-learning tool for FCD detection that could be used in the presurgical evaluation of patients with epilepsy.

Abstract Number: 834

Title: MELD project: Quantitative analysis of associations between MRI features and FCD histopathology

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Purpose: Focal cortical dysplasias (FCDs) are classified into different subtypes based on post-surgical histopathological specimens. Previous studies have shown that FCD lesions can be identified based on MRI features. This study aims to leverage a large multi-centre cohort of patients, the MELD cohort, to offer the largest analysis of MRI features in FCD subtypes.

Method: This study was performed on 355 patients with a histologically confirmed FCD subtype (12% FCD1, 33% FCD2A, 55% FCD2B) from the MELD cohort. Multiple surface-based features were extracted from T1w and FLAIR images. Features were harmonized across sites using ComBat and normalized for intersubject and interregional differences. Lesion distributions were mapped onto the cortex for each group. ANOVA and Levene statistical tests tested for feature differences in means and variances between FCD subtypes, with a significance level set at 5% level.

Result: FCD2A/2B (FCD2) differed from FCD1 in cortical thickness (ANOVA p_A=0.095, Levene p_L=0.007), intrinsic curvature (p_A=0.003, p_L=0.001) and grey-white matter contrast (p_A=0.004, p_L=0.002). FCD2B differ in variance from FCD2A in FLAIR intensity in the white matter (p_A=0.08, p_L=0.05). FCD2 lesions were mainly located in the frontal and temporal lobes, whereas FCD1 occur predominantly in the temporal lobe. In

addition, FCD1 lesions were larger than FCD2 (p_A=0.001, p_L=0.16). There were no differences in age of epilepsy onset or duration.

Conclusions: The spatial distribution of lesions across the cerebral cortex as well as the MRI features differ between FCD subtypes. FCD2 differed from FCD1 in cortical thickness, intrinsic curvature, grey-white matter contrast and in lesion size and location. FCD2B was characterised by an increase in FLAIR intensity in the white matter, not seen in FCD2A, which is likely reflective of the transmantle sign. This study highlighted measures that can differentiate subtly differing histological abnormalities on presurgical MRI.

Abstract Number: 871

Title: Correlation between depressive and anxious symptoms and white matter changes in relatives of TLE patients

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Purpose: Investigate associations between microstructural white matter changes and depressive and anxious symptoms in relatives of TLE patients.

Method: We analyzed brain MRI with DTI parameters from 40 TLE relatives (median age: 48 years), and applied the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). We extracted 6 white matter tracts (fornix, cingulum, uncinate fasciculus (UF), inferior fronto-occipital fasciculus (IFO), corpus callosum (CC), corticospinal tract (CST)) and analyzed fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD) and radial diffusivity (RD). We investigated correlations between scores (BDI and BAI) and the DTI measures. Symptoms of depression were positive with BDI scores above 10, while symptoms of anxiety were positive with BAI scores above 11. We used SPSS26 for statistical analysis.

Result: We observed a prevalence of 37.5% of depressive symptoms and 27.5% of anxious symptoms in our sample of TLE relatives. BDI negatively correlated with FA in the left cingulum (p=0.0003; r=-0.547); positive correlations were observed between MD and BDI in the right cingulum (p=0.015; r=0.401), in the right and left UF (p=0.023; r=0.374 and p=0.021; r=0.363, respectively). Positive correlations were also observed between RD and BDI in the left and right cingulum (p=0.0003; r=0.583 and p=0.015; r=0.401, respectively). The BAI negatively correlated with FA in the fornix (p=0.026; r=-0.352), and positively correlated with MD in the left cingulum (p=0.01; r=0.415) and left UF (p=0.003; r=0.374). Additionally, BAI correlated with RD in the left cingulum (p=0.022; r=0.371) and left UF (p=0.01; r=0.440).

Conclusions: The regions correlated with psychiatric symptoms in the present study overlap with the regions affected in previous studies OF TLE. However, these regions differ from areas mainly affected in patients with isolated depression. Thus, we hypothesize a possible genetic substrate involved in comorbidity between epilepsy and depression, distinct from psychiatric disease in people without epilepsy**.**

Abstract Number: 884

Title: The Influence of Wakefulness on The Brain Networks Involved in Centrotemporal Spike Generation in CETCS

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Purpose: The frequency of centrotemporal spikes (CTS) in Childhood epilepsy with centrotemporal spikes (CECTS) is modulated by the sleep-wake cycle, with a documented increase in NREM sleep. The aim of this study is to explore how spontaneous fluctuations in wakefulness affect effective connectivity (coupling) of the brain networks involved in CTS generation.

Method: We simultaneously acquired functional MRI (fMRI) and electroencephalography (EEG) in 25 patients at rest. We estimated the instantaneous CTS frequency (Vaudano et al. Front.Neurol. 2019;10:1316) and the EEG Wakefulness Index (EWI) - a high temporal resolution characterization of wakefulness versus drowsiness - based on the combination of different EEG power values from different channels (Knaut et al. Clin.Neurophysiol. 2019;130:1375-1386). We then identified the brain regions in which BOLD signal changes are significantly correlated with instantaneous CTS frequency, resulting in 6 regions of interest (ROIs): bilateral motor cortex, thalamus and insula. Finally, a psychophysiological interaction (PPI) analysis was conducted, treating wakefulness-dependent brain states (indexed by EWI) as the psychological context and using the BOLD signal of the 6 ROIs as the physiological signal.

Result: The group PPI analysis showed enhanced connectivity between four of the six CTS-related ROIs and the left frontal operculum (FO).

Conclusions: The PPI results suggest that either the influence of the CTS-related network on brain activity in the left FO is modulated by different wakefulness-dependent brain states, or the response of the left FO to fluctuations in wakefulness are modulated by activity in the CTS network. Therefore, the left FO may be an important element in the relationship between CTS and wakefulness-dependent brain states.

Abstract Number: 894

Title: Evaluating the disease-modifying effects of anti-seizure medication using longitudinal structural MRI

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Purpose: Widespread accelerated cortical atrophy is a feature of focal epilepsy. Progressive cortical thinning measured using serial MRI may represent a morphological biomarker of disease progression in epilepsy. We investigated whether anti-seizure medications (ASMs) modulate progressive cortical thinning.

Method: We performed a series of nested propensity score-matched case-control studies in a large focal epilepsy cohort (n=171) and matched healthy controls (n=141) with longitudinal structural MRI. For each evaluated ASM (clobazam [CLB], carmabazepine [CBZ], lamotrigine [LTG], levetiracetam [LEV], oxcarbazepine [OXC], phenytoin [PHT], topiramate [TPM], sodium valproate [VPA]) we assessed (i) the contribution of the ASM to cortical thickness cross-sectionally and (ii) its effect on the change of cortical thickness over time (i.e. longitudinally) compared to patients not taking the ASM and (iii) to aging-related thinning in healthy controls.

Result: Patients treated with OXC had less cortical atrophy measured cross-sectionally (12.6 resels, $p<0.001$) and less cortical thinning over time measured longitudinally (5.4 resels, $p<0.001$) compared to a matched group of patients not treated with OXC. Patients treated with OXC also had reduced aging-related cortical thinning measured longitudinally compared to healthy controls (3.6 resels, $p<0.001$). Case-control comparisons of other

ASMs (CLB, CBZ, LTG, LEV, PHT, TPM, VPA) did not reveal similar effects that would be compatible with signs of neuroprotection/disease-modification. These comparisons mainly showed more atrophy cross-sectionally (VPA, CBZ, CLB, and to a lesser extent LTG) or accelerated age-related cortical thinning (LTG, LEV, CBZ, TPM).

Conclusions: Our findings provide proof-of-concept for the use of longitudinal MRI as a sensitive biomarker of morphological disease progression in epilepsy. Oxcarbazepine, but not other ASMs that were evaluated, showed effects that may point towards disease-modification and warrant further prospective analysis.

Abstract Number: 902

Title: Novel User-Friendly Application for Accurate Definition of the Surgical Brain Resection following Epilepsy Surgery

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Purpose: Studying associations between resected brain volume and patients' post-surgical outcome constitutes a well-established approach for the identification of epilepsy biomarkers or outcome predictors in epilepsy surgery. Accurate determination of the resected brain volume in neuroimaging data therefore represents a crucial step. To date, slice-by-slice tracing by experts remains the gold standard, which is yet extremely time-consuming: no segmentation algorithm has been specifically designed to investigate neurosurgical resections. Our study aims to develop a user-friendly application to define an accurate 3D model of the surgical brain resection and its anatomical labelling in patients who had epilepsy surgery.

Method: We retrieved pre-operative and post-operative MRIs from 36 patients who had resective epilepsy surgery at Boston Children's Hospital. We developed 12 different automatic pipelines (Figure1A) for pre-processing input MRIs based on two main methods (*single-seed region-growing* and *whole-brain binarization*). Each pipeline was tested for seven different sets of parameters (inclusion/binarization tolerance). Performance was evaluated computing similarity between each pipeline's output and the gold standard (defined by hand-drawn resection) through the *Dice coefficient* (range: 0-1). The best performing pipeline was validated using cross-validation.

Result: Among the 12 implemented pipelines, we identified the best performing one, which consisted of a region-growing algorithm applied to the post-operative MRI with local contrast adjustment (Figure1B). This method was trained and tested through cross-validation and presented a *Dice coefficient* of 0.84 ± 0.03. We also developed a Graphic-Use-Interface (GUI) to perform the segmentation, visualize it in the MRI space and provide a "*sublobar classification report*" of the resected tissue (Figure2).

Conclusions: We proposed and validated a user-friendly method to define neurosurgical resections in the 3D MRI space, which presented 84% similarity (*Dice*=0.84) with a hand-drawn gold standard. We also developed a graphic interface that allows non-expert users to run the proposed pipeline and visualize 3D resection results.

Figure 1

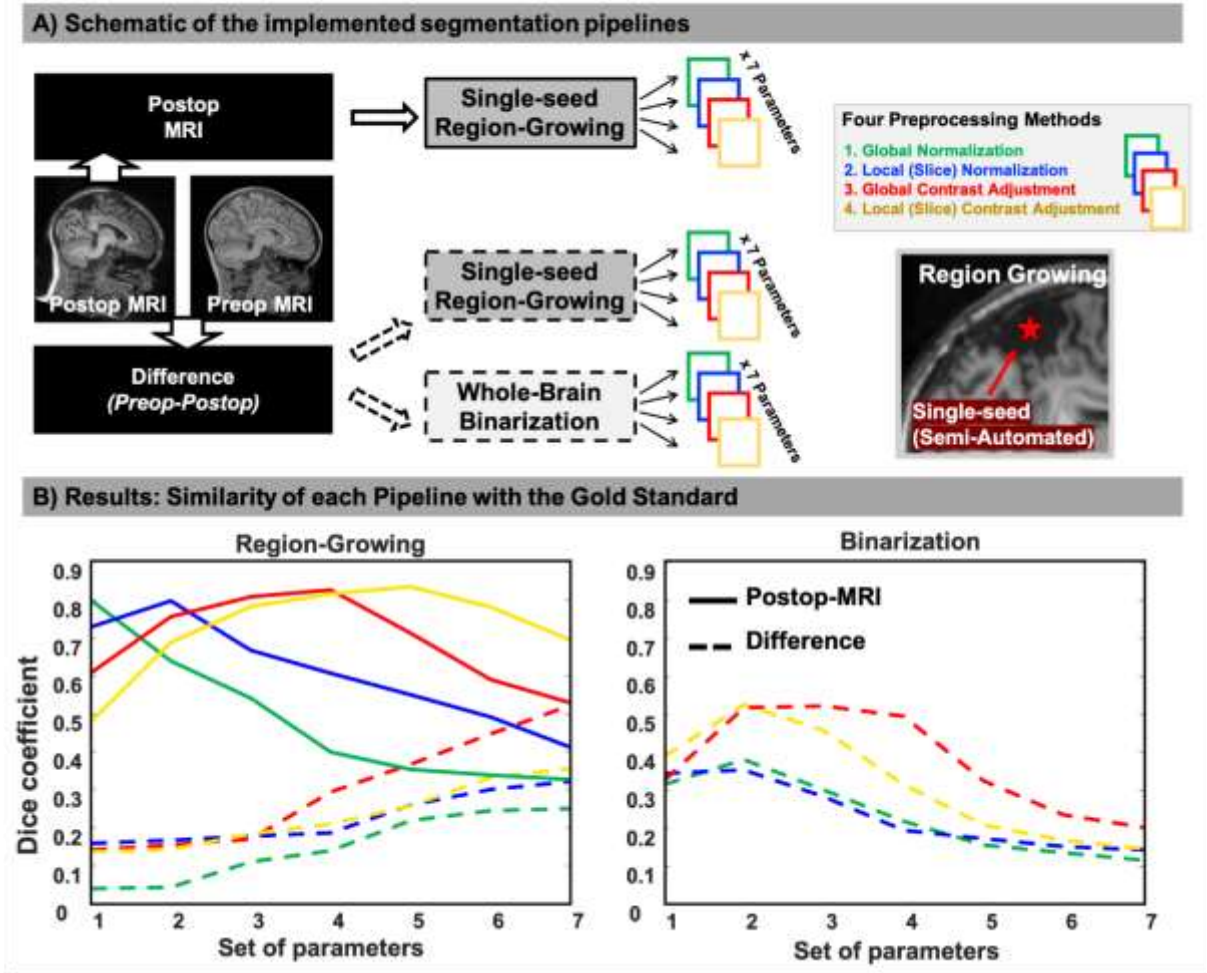
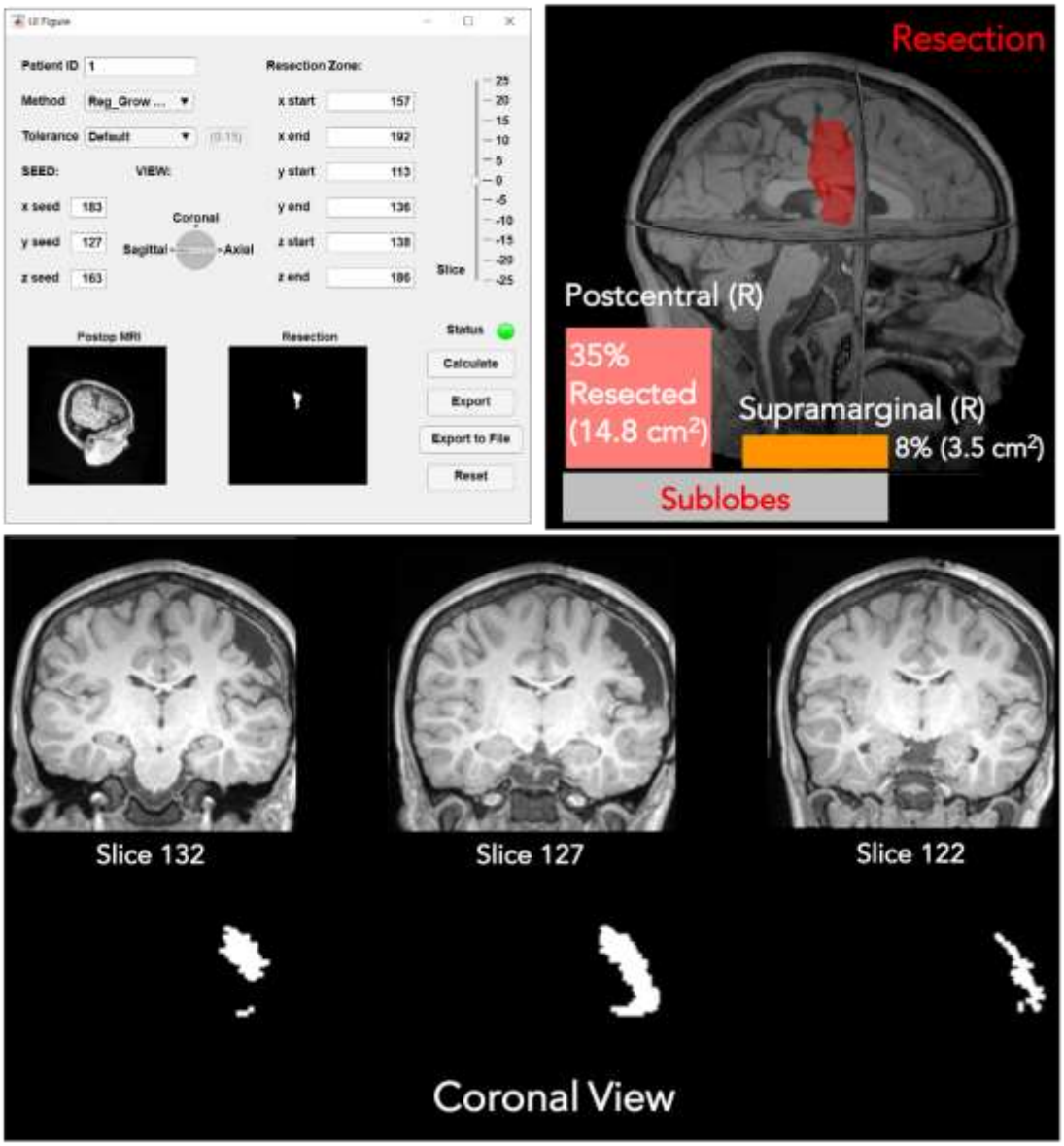

A) Schematic of the implemented segmentation pipelines
Postop MRI
Postop MRI
Preop MRI
Difference (Preop-Postop)
Single-seed Region-Growing
Single-seed Region-Growing
Whole-Brain Binarization
x 7 Parameters
x 7 Parameters
x 7 Parameters
Four Preprocessing Methods
1. Global Normalization
2. Local (Slice) Normalization
3. Global Contrast Adjustment
4. Local (Slice) Contrast Adjustment
Region Growing
Single-seed (Semi-Automated)
B) Results: Similarity of each Pipeline with the Gold Standard
Region-Growing
Binarization
Dice coefficient
Set of parameters
Set of parameters
Postop-MRI
Difference

Figure 2. Graphic User Interface and Output



Abstract Number: 946

Title: Temporal dynamic connectivity (Chronnectome) profile of hippocampal sclerosis patients with epilepsy

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Purpose: To explore temporal properties of dynamic functional networks connectivity in epilepsy patients with hippocampal sclerosis (HS) compared with a group of normal subjects using resting fMRI.

Method: We analysed temporal characteristics of dynamic functional networks connectivity using resting state fMR images (3Tesla, 204 timepoints, TR:3s) of 33 patients with confirmed diagnosis of temporal lobe epilepsy and HS (19 Left) compared with 30 healthy age and sex matched controls. Independent component analysis was performed to identify 28 functional networks using a template-based approach including (6) Sensori-Motor, (1) Basal Ganglia, (1) Auditory, (6) Visual, (6) Attentional, (4) Default Mode and (4) Frontal independent components with GIFT Toolbox v3.0c (20 times, ICASSO and Infomax Algorithm). Temporal time-courses and spectral properties were extracted at 30s windows interval for each component, then 5 functional clustered states of mean correlations were recognised using PCA in patients and controls adjusted for age, sex and head movement covariates. Temporal properties of functional networks correlations including Mean dwell time and Meta-states transitions were compared (2 sample T-test, FDR corrected at p 0.05) between controls and patients and also between Left and Right HS subgroups.

Result: Mean dwell time was significantly reduced in patients for component 3 (p.0008) and more extended in component 5 (p.0198) than in controls. The same dwell time difference remained also comparing individual left and right HS groups with controls. There was no difference comparing patients with left and right HS.
The number of transited states was higher in controls (p.0278) and controls also showed greater state span (p.0201) than patients.

Conclusions: Dynamic temporal properties of functional networks connectivity in patients with epilepsy and HS displays a distinctive pattern. The observed interaction differences between networks domains may serve as a promising biomarker for diagnosis, cognitive assessment and clinical prognosis.

Abstract Number: 947

Title: Differences in thickness, cortical surface and volume in patients with refractory epilepsy with and without depression.

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Purpose: Depressive symptoms are more frequent in patients with epilepsy than in the general population. The prevalence of major depression disorder (MDD) has been estimated at 30-50% for patients with refractory epilepsy (Mayor, 2006). Our purpose was to describe differences in cortical thickness, surface and volume in patients with refractory epilepsy with depression and without depression using MATLAB.

Method: Cross-sectional, analytical and descriptive study in patients with temporal and extratemporal focal epilepsy. Analyzing cortical thickening, surface and volume in MRI studies using MATLAB. Shapiro Wilks normality test was used, for analytical analysis we used fisher exact test, chi-square for dichotomous data and U Mann-Whitney U test for continuous data.

Result: Ten patients were included, mean age 34 years (18-54 years); five with frontal lobe epilepsy semiology with a mean of 13.8 (± 9.07) years of evolution and 5 temporal lobe semiology with a mean of 30.60 (± 6.5) years of evolution (p = 0.012). Seven patient had diagnosis of MDD. Less volume and cortical surface were found among patients with MDD (p=<0.0001) in most of the sulci analyzed in the prefrontal, orbitofrontal, insular, cingulum, temporal, parietal and occipital lobe analysis (p=<0.005)

Conclusions: In our study, the presence of MDD in patients with epilepsy was associated with smaller volume and cortical surface in sulci involved in the prefrontal, orbitofrontal and cingulate cortex, which are already known areas in MDD pathology.

Abstract Number: 955

Title: Altered dynamic functional connectivity of striatal-cortical circuit in Juvenile Myoclonic Epilepsy

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Purpose: Juvenile myoclonic epilepsy (JME) involves a widespread brain network. But the dynamic functional connectivity (dFC) of the striatal-cortical circuits in JME remains unknown.

Method: We adopted the resting-state EEG-fMRI and dFC approach to explore the dynamic striato-cortical circuitry in thirty JME patients compared with 30 well-matched health controls (HCs). The sliding-window approach was adopted to assess dFC for six pairs of striatum seeds and the standard deviation of dFC variability was quantified. We also performed the correlation analysis between the dFC variability and clinical variables in JME patients.

Result:JME patients exhibited increased dFC variability in striato-executive control network (ECN); while decreased dFC variability between striatal-default mode network (DMN) compared with HCs ($p<0.05$, GRF corrected). In addition, the hypervariability between left ventral-rostral putamen (VRP) and left superior medial frontal gyrus was positively ($r= 0.493$, $p=0.008$) correlated with the frequency score of myoclonic jerks and the hypovariability between the left ventral striatum inferior and the right supramarginal gyrus was positively related with ($r=0.378$, $p=0.047$) the age at seizure onset of JME.

Conclusions:JME is associated with impaired dFC variability of striato–cortical circuits mainly with the pattern of increased dFC in the striatal-ECN and concomitantly decreased striatal coupling with DMN regions. The dFC alteration in VRP-medial prefrontal cortex circuitry may account for the severity of JME. These results provide novel information about the dynamic neural striato–cortical circuitry of JME and this abnormal dynamic striatal-cortical circuitry may be a core pathophysiological mechanism of JME.

Abstract Number: 1078

Title: using a clinical paradigm to lateralize verbal memory with functional magnetic resonance imaging

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Purpose: Functional MRI (fMRI) was introduced as a promising non-invasive tool for predicting postsurgical deficits in the presurgical evaluation of patients with pharmacoresistant temporal lobe epilepsy (TLE), but its predictive outcome power is very heterogeneous among centers. We aimed to assess fMRI validity predicting verbal memory lateralization with a clinical paradigm and compare results to neuropsychological scores.

Methods: fMRI protocol based on both encoding and retrieval phases aiming to achieve a sensitive laterality index of hippocampal involvement by using bootstrapping and an anterior-posterior index along the hippocampus. The verbal memory task was intended to be simple and reliable for assessing hippocampal function, therefore we used an adapted version of the Rey Auditory Verbal Learning Test. Depending on the task, a hippocampal or language ROI was included to focus on the area of interest.

Results: Fifty patients, 32 females, median age 31 years (IQR: 43-27), 40 of them with left TLE, and 22 healthy controls (HC) with no significant sex and age differences. In left TLE, verbal memory lateralization was rightward in 11 (32.35%) patients, 14 (41.18%) showed a leftward activation and 9 (26.47%) activation in both hippocampi while in right TLE only 1 (10%) patient activated bilaterally and in HC only 3 (13.6%). Verbal memory activation in right hippocampus was significantly higher in patients 272 (IQR 622) compared to HC 62.5 (IQR 376) [p=0.035]. Verbal memory activation in left hippocampus was not significantly different among HC, left TLE and right TLE [x2(2)=5.38, p=0.07]. These are preliminary results and validation to neuropsychology by ROC analysis is pending by the time of submission.

Conclusions: fMRI may be clinically relevant if we find a proper method for hippocampal activation. Left TLE show a higher tendency to bilateral activation, potentially secondary to reorganization in memory encoding processes.

Abstract Number: 1111

Title: Can DTI help in predicting the white matter changes in MTLE-HS syndrome?

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Purpose: It has been shown earlier in small series that TLE is associated with white matter (WM) abnormalities that are extensive and bilateral, even in patients with unilateral mesial temporal sclerosis (MTS) Patients with TLE without any lesion in MRI have also demonstrated to have diffusion tensor imaging (DTI) abnormalities .
1. We studied the extent of WM abnormalities through diffusion imaging tractography (DTIT) in a large cohort of patients with TLE with unilateral MTS /hippocampal sclerosis (MTLE-HS).
2. If such WM abnormalities are seen widespread outside the temporal lobe, we analysed the significance of these abnormalities clinically in terms of patients studied as compared to controls.

Method: DTI measurements were obtained from tractography for arcuate fasciculus, cingulum, corticospinal tract, inferior longitudinal fasciculus; inferior frono-occipito fasciculus, optic radiation, superior longitudinal fasciculus and uncinate fasciculus in 50 patients with MTLE-HS and were compared to 50 age and sex-matched controls. Diffusion parameter values (FA and ADC) of RMTS , LMTS and controls were compared using multivariate analyses (MANCOVA).

Result: Compared to controls, significant differences in FA values of arcuate fasciculus, inferior fronto-occipital fasciculus, and optic radiation and ADC value of optic radiation 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, inferior frono-occipito fasciculus tracks and FA value alone in optic radiation of left hemisphere.

Conclusions: Our finding indicates widespread WM degeneration in areas away from temporal lobe in other parts of limbic system in chronic temporal lobe epilepsy. The existence of such a diffuse epileptic network is probably one of the reasons for a less than optimal expected 100% outcome in patients even when a very focal abnormality like hippocampal sclerosis is resected for drug-resistant epilepsy.

Neuropsychology

Abstract Number: 60

Title: Analysis of patients with psychogenic non-epileptic seizures and other functional neurologic disorders in a Japanese emergency hospital

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Purpose: Psychogenic non-epileptic seizures (PNES) are a subtype of functional neurologic disorder (FND) and often diagnostically difficult to differentiate from genuine epilepsy. In an emergency hospital setting, the aim of the present study was to find characteristics of PNES that differ from other types of FND.

Method: We searched the medical records of patients with FND who had been referred to the department of neurology of our hospital between January 1st and December 31st 2019. FND was diagnosed on the basis of DSM5. Dissociative disorders were excluded from this study. We checked the age, gender, subtypes of FND, medical history, presence of psychological stressors, and the duration, severity, treatment, and outcome of the illness.

Result: Twelve patients were diagnosed as having FND (3 male, 9 females). The phenotypes of FND included PNES (n=4, 33%), FND combined with weakness and sensory loss (n=4, 33%), sensory loss (n=1), weakness and visual disturbance (n=1, 8%), tremor (n=1, 8%) and dystonic movement (n=1, 8%). Of the 12 patients with PNES, all were female. The patients with PNES were younger on average than those with other FND subtypes (30 vs 40 years old). One patient with PNES had coexisting genuine epilepsy and was treated on the basis of status epilepticus with respirator support. Patients with PNES had more severe illness and a poorer prognosis than those with other subtypes of FND. For diagnosis, it had been necessary to rule out organic neurological diseases such as encephalitis, stroke, epilepsy, peripheral nervous disease and metabolic disease on the basis of various examinations such as MRI, EEG, blood tests, CSF test and nerve conduction studies.

Conclusions: PNES is the most common clinical phenotype of FND even in non-epilepsy centers. General neurologists maybe able to play a major role in the diagnosis of PNES and other subtypes of FND.

Abstract Number: 115

Title: Impact of Cognitive Rehabilitation in Juvenile Myoclonic Epilepsy: A Novel Study

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Purpose: This study aimed to evaluate cognitive rehabilitation's impact on cognitive deficits of persons with Juvenile Myoclonic Epilepsy (JME).

Method: 80 patients with JME were evaluated for this study, and 54 were invited for the present study after neurological and psychiatric evaluation. 42 patients agreed with the cognitive rehabilitation protocol that consisted of 12 individual sessions (6 months), divided into planning/organization, attention, and impulsivity. 27 patients finished the protocol, and all patients had pre- e post neuropsychological evaluations and self-rating questionnaires. Generalized Estimating Equations (GEE) inferential statistics were used to verify the protocol's effect, and a 95% confidence interval was adopted.

Result: We found significant improvement in selective attention (TMT A [p < 0,01] and Stroop test 2 [p = 0,03]), inhibitory control (Stroop test 3 [p = 0,02], FAS [p < 0,01], CPT commissions [p < 0,01]), mental flexibility [WCST categories p < 0,01] and implicit decision making (IGT blocks A [p < 0,01], B [p = 0,02], C [p < 0,01] and D [p < 0,01]. All components of the Behavioral Rating Index of Executive Functions (BRIEF-A) metacognition index, and the general quotient (G.E.C) had significant improvement (initiative [p ≤ 0,01], working memory [p ≤ 0,01], planning and organization [p ≤ 0,01], task monitor [p = 0,02] and organization of materials [p = 0,02]). Regarding the Behavioral Regulation Index (B.R.I), the "Emotional Control" was improved [p = 0,03] . The attentional component and general scores of the Adult Self-Report Scale (ASRS-A) for ADHD symptoms in adults also changed significantly [p ≤ 0,01].

Conclusions: Impulsiveness improved in instruments based on self-perception, but not in the neuropsychological evaluation. Executive function and attention had an improvement in objective and subjective tests. Our findings provide support that cognitive rehabilitation may be a valuable resource to alleviate cognitive deficits in patients with JME.

Abstract Number: 194

Title: Impoverished future thinking in TLE: a novel cognitive deficit in epilepsy and its implications for surgical counselling

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Purpose:
"*What will my life look like if I proceed with surgery and become seizure-free?... What will it look like if I decline?*"
Discussing treatment options with epilepsy patients assumes they can mentally project themselves into an imagined future, envisaging the pros and cons of various outcomes. This study evaluated this assumption in unilateral temporal lobe epilepsy (TLE) by evaluating the integrity of their future thinking ability, including laterality effects.

Method: Sixty-eight participants comprising 37 adults with TLE (18 Left TLE; 19 Right TLE) and 31 controls matched for age, sex, and educational attainment. Future thinking was measured using an imagined experiences task separating prospection (i.e., future thinking) from atemporal scene construction. Tools well-established in epilepsy measured potential cognitive correlates of prospection.

Result: ANOVA revealed impoverished future thinking in both Left and Right TLE relative to controls (P=.001, η_p^2=.206), with no difference between patient groups (P>.05). Hierarchical multiple regression assessed whether laterality of seizure focus predicted worse future thinking, after adjusting for cognitive functions thought to underpin this domain. The final model accounted for 70% of the variance in future thinking scores; after controlling for verbal function, autobiographic memory and scene construction, Right TLE patients had significantly worse future thinking than both Left TLE patients and controls (P=.026 and P=.022, respectively); moreover, future thinking in Left TLE patients no longer differed significantly from controls (P>.05).

Conclusions: Both Left and Right TLE patients show significant impairments in their future thinking, suggesting that patient counselling must be reengineered to tailor for this novel cognitive deficit. While impoverished future thinking is linked to verbal cognitive dysfunction across all groups, the presence of right temporal lobe disease appears to exacerbate future thinking impairments. These findings highlight that future thinking is a multi-determined cognitive operation in which the right temporal lobe plays a key role.

Abstract Number: 212

Title: Childhood Trauma Profiles in Epilepsy and Psychogenic Nonepileptic Seizures

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Purpose: Psychogenic nonepileptic seizures (PNES) and epileptic seizures (ES) are similar in clinical presentations, leading to the risk of misdiagnosis. Given that childhood trauma is thought to be part of the PNES aetiology in some cases, this study aimed to determine whether patients with PNES and ES possess different childhood trauma profiles and whether childhood trauma history could be used for screening to help distinguish PNES in clinical settings.

Method: Data were collected from two sources: a retrospective discovery cohort comprising patients who were admitted to a video-EEG monitoring (VEM) unit between 2014 and 2017 (n_{ES} = 144, n_{PNES} = 59), and a prospective validation cohort comprising patients admitted for VEM between 2018 and 2019 (n_{ES} = 172, n_{PNES} = 37). All participants completed the Childhood Trauma Questionnaire (CTQ).

Result: Confirmatory factor analyses evaluated and supported the purported five-domain measurement model of the CTQ in both cohorts. CTQ profile differences between the two patient groups were investigated using general linear mixed-effects models. A diagnostic group by CTQ domain interaction effect was founded in the retrospective discovery cohort (p = .02) and verified in the prospective validation cohort (p = .005). The two cohorts demonstrated consistent CTQ profile differences between patients, with PNES having higher scores on emotional abuse, emotional neglect, and sexual abuse than the ES group. Logistic regression models showed that patients who endorse a more severe childhood trauma history of any type show a higher risk for PNES diagnosis than ES.

Conclusions: These findings support incorporating a childhood trauma screening tool into routine clinical workflow to aid early identification of PNES from ES, to facilitate early treatment and better prognosis for people with PNES. The different childhood trauma profiles suggest the relevance of trauma type being pertinent, adding to the literature reinforcing association between childhood trauma and PNES.

Abstract Number: 316

Title: Do patients with PNES fail on cognitive measures of malingering?

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Purpose: The Rey Visual Memory Test (Rey 15-item test) is widely used to detect malingering.The aim of this study was to compare Rey 15-item test in patients with psychogenic non-epileptic seizures (PNES) and an age-matched group of patients with temporal lobe epilepsy (TLE) during admission to a video electroencephalography monitoring unit (VEMU).

Method: Patients diagnosed with PNES or TLE at a VEMU were prospectively recruited. Neuropsychological, demographic, clinical, and treatment variables were collected. The number of correct items, number of items in their correct placements and intrusions in the Rey 15-item test were compared between both groups using a t-Test. The relationship between the scores of the Rey 15-item test with a global cognitive impairment index, executive and attention functions was evaluated.

Result: We studied 24 patients with PNES and 24 patients with TLE. There were no differences between PNES and TLE patients in number of correct items (p=0.26), number of items in their correct placements (p=0.14) and number of intrusions (p=0.19). In PNES patients a higher number of intrusions was related to poorer cognitive performance (p = 0.013), executive (p=0.05) and attention (p=0.018) functions which was not observed in TLE patients. In both groups, patients with a higher number of correct items had better cognitive performance.

Conclusions: PNES and TLE patients perform similarly in a malingering detection test, confirming that PNES do not generally occur because of a conscious effort to deceit but due to a dissociative mechanism.

Abstract Number: 349

Title: The Internalized Stigma of Persons with Epilepsy in the Canadian Province of Manitoba

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Purpose: This study aims to illustrate the extent and burden of internalized stigma among people with epilepsy. Internalized stigma occurs when the stigmatized individual internalizes society's biased views and inflicts a negative stereotype onto themselves, greatly impacting their quality of life and sense of wellbeing.

Method: A 40-question online survey was distributed to patients with an established epilepsy diagnosis attending the only adult epilepsy clinic in the Canadian province of Manitoba, located at a tertiary care hospital. The survey included a demographic questionnaire, the Internalized Stigma of Epilepsy Inventory (ISEI, adapted from the Internalized Stigma of Mental Illness Inventory) and the Stigma Scale of Epilepsy (SSE). Both tools use a 5-point Likert scale, which allowed for a composite stigma score from the results of the two surveys. Correlational analysis compared stigma scores to demographic variables. Individual participant ISEI and SSE scores were analyzed for consistency across measures.
Result: The mean composite stigma score of 34 participants (12 men, 22 women) was 0.29±0.11 (29%). Higher level of education negatively correlated with composite stigma score ($p<0.05$). A significant difference was found between the composite stigma scores of the two measures (ISEI and SSE) themselves, with 100% of participants scoring higher on the SSE compared to the ISEI ($p<0.01$).

Conclusions: Internalized stigma is prevalent among people with epilepsy, with some groups experiencing greater stigma than others; the most notable difference being in level of education. Furthermore, the significant and consistent difference in stigma scores between the two measures (SSE>ISEI) provides an opportunity for further research. Though the tools aim to measure the same phenomenon, they differ in narrative point of view from third person (SSE) to first person (ISEI). Better understanding of why this discrepancy exists will ultimately lead to a better understanding of the experience of internalized stigma of epilepsy.

Abstract Number: 427

Title: How does "locus of control" affect persons with epilepsy?

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Purpose: Locus of control (LOC) is the degree to which people believe that they have control over the outcome of events in their lives. A person with internal, external or chance LOC believes that his life can be controlled by himself, external factors or chance respectively. We aimed to determine the health LOC, anxiety, and depression levels in patients with epilepsy and assess whether LOC is related to anxiety, depression and seizure control.

Method: Patients aged ≥18years with history of epilepsy for at least 1 year were recruited from SCTIMST, Trivandrum from January 2019-May 2020. Patients filled the questionnaire consisting of demographic data, present seizure control, etc. The Hospital Anxiety and Depression (HAD) scale and Form-C of Multidimensional Health Locus of Control (MHLC) scale were used to estimate the level of anxiety and depression and health LOC respectively. Healthy controls aged ≥18years were also studied. The mean scores of anxiety, depression and locus of control were compared between the two groups.

Result: 100 patients with epilepsy and 70 healthy controls were studied. The mean anxiety and depression scores were 8.13(SD=4.23) and 5.85(SD=3.66) in the patient group and 6.75(SD=3.39) and 4.14(SD=2.96) in the control group respectively. The internal, external, and chance LOC scores were 24.95(SD=10.92), 26.94(SD=4.96) and 24.41(SD=6.46) in patients and 29.44(SD=5.62), 26.53(SD=5.79) and 19.9(SD=7.13) in controls respectively.
Patients with epilepsy had higher chance LOC scores and lower internal LOC scores than controls. ($p=0.00003$, $p<0.00001$ respectively). There was no significant difference in the External LOC scores between the two groups ($p=0.620$). Patients with epilepsy with some level of anxiety had lower internal LOC scores than patients with no anxiety ($p=0.04$).

Conclusions: Patients with epilepsy have low perceptions of internal and strong perceptions of chance health LOC. This means they feel that chance plays an important role in their disease control.

Abstract Number: 494

Title: Visual and acoustic perception disturbances in pediatric patients with pharmaco-resistant temporal lobe epilepsy

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Purpose: to compare performance in visual and acoustic perception tasks in children with refractory temporal lobe epilepsy (TLE) and children with non-epileptogenic focal brain lesion.

Method: Neuropsychological evaluation in 40 children (7-16 years old) with MR-positive refractory TLE and in 12 children of same age with focal brain lesions that had never suffered from seizures, as a control group, was administrated. All patients in control group had lesions in temporal, parietal or occipital lobe. Types and frequency of errors in visual and acoustic perception tasks are reported.

Result: Errors in perception tasks were divided into two groups: 1) related to planning and control of perception activity or motor component (in case of acoustic task) and 2) paragnosia (misunderstanding of picture or perceptionally close answers with attempts to find the right word) or error in estimation in short and long sequence (in case of acoustic task). It was revealed that, compared to controls, children with TLE made significantly more errors in visual perception tasks due to impulsivity, lack of control and inhibition. This finding corresponds to executive function deficit found in neuropsychological evaluation of children with TLE. In acoustic perception tasks, compared to controls, children with TLE made significantly more errors due to perseverations.

Conclusions: The analysis of perception task performance suggests that obtained impairments in children with refractory TLE mix up deficit of perception that can be related to focal brain lesion (especially in a case of acoustic perception) and executive functions deficit that significantly affects performance of perception tasks and are related to frontal lobe dysfunction. Our results are in line with researches that showed aberrant functional connectivity that involves both anatomically intact and damaged structures in pathologically working networks.

Abstract Number: 502

Title: Randomized Controlled Trial on Neuropsychological Rehabilitation for Patients with Drug Refractory Epilepsy: Challenges, Adaptations & Findings

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Purpose: Reviews of neuropsychological rehabilitation literature in epilepsy outnumber the original studies with one Randomized Controlled Trial (RCT) reported till date. A home-based neuropsychological rehabilitation program was developed for patients with Drug Refractory Epilepsy (DRE) [Post-Operative (PO) & Not Cleared for Surgery (NCS)]. The COVID-19 pandemic posed challenges of follow-up and tele- assessment. Adaptations were made to the ongoing study and solutions were found based on available literature and focus group discussions with experts in the field of neuropsychology and epileptology. The efficacy was studied.

Method: 27 consenting adults with DRE were recruited in a single blind RCT (CTRI/2019/10/021777) with 14 patients in the Intervention (IG) (PO=13, NCS=1), and 13 in the Treatment As Usual (TAU) (PO=11, NCS=2) groups. They were of any gender, aged 18-45 years diagnosed with DRE atleast 1 year back, with minimum primary level of education, IQ > 80, having an available primary caregiver. At 3 months, reasons for non-compliance to rehabilitation due to COVID-19 were noted and a booster session was given. Pre-post neuropsychological assessment included Auditory Verbal Learning Test and Everyday Memory Questionnaire (EMQ). All follow-ups were done through tele-assessment at 6 months and coded for validity on a 3-point scale. The 6-week neuropsychological rehabilitation program included psychoeducation, compensatory training and cognitive retraining aimed at improving memory. The booster session focused on internal and external aids.

Result: Themes of non-compliance included 1) Non-availability of time due to shift to virtual work/study 2) Increased household work. Mann-Whitney test of the absolute differences of the test scores (follow-up score-baseline score) between two groups revealed significant differences in immediate recall ($p=0.002$), delayed recall ($p <0.001$), long term retention ($p=0.024$), patient reported EMQ ($p <0.001$) and caregiver reported EMQ ($p <0.001$) with IG showing improvement.

Conclusions: Despite challenges of the pandemic, efficacy of the rehabilitation was observed.

Abstract Number: 505

Title: Visual surround suppression in people with epilepsy correlates with attentional-executive functioning, but not with epilepsy or seizure types

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Purpose: Following reports that an index of visual surround suppression (SI) may serve as a biomarker for an imbalance of cortical excitation and inhibition in different psychiatric and neurological disorders including

epilepsy, we evaluated whether SI is associated with seizure susceptibility, seizure spread, and inhibitory effects of antiseizure medication (ASM).

Method: In this prospective controlled study, we examined SI with a motion discrimination task in people with genetic generalized epilepsy (GGE) and focal epilepsy with and without focal to bilateral tonic-clonic seizures. Cofactors such as GABAergic ASM, attentional-executive functioning, and depression were taken into account.

Result: Data of 45 patients were included in the final analysis. SI was not related to epilepsy or seizure type, GABAergic ASM treatment or mood. However, SI correlated with attentional-executive functioning (r = .32), which in turn was associated with ASM load (r = -.38). Repeated task administration (N = 7) proved a high stability over a one-week interval (r_{tt} = .89).

Conclusions: Our results do not support the hypothesis that SI is a reliable biomarker for mechanisms related to inhibition of seizure spread or seizure frequency, i.e., it does not seem to reflect inhibitory capacities in epilepsy. Likewise, SI did not differentiate GGE from focal epilepsy, nor was it influenced by ASM load or mode of action. Thus, in epilepsy, no added value of including SI to routine diagnostics can be concluded.

Abstract Number: 516

Title: Impaired Embodied Cognition in Patients with Mesial Temporal Lobe Epilepsy and Hippocampal Sclerosis

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Purpose: Sensorimotor systems, involved in experiences, are recruited in attributing meaning to words, configuring the so-called embodied cognition. We aim to assess whether the processing of graspable objects and their nouns is impaired in patients with mesial temporal lobe epilepsy (MTLE).

Method: Fourteen patients (8 women; mean age: 31.4±9.66 years) with MTLE and 15 matched controls were enrolled. Five out of 14 patients had hippocampal sclerosis (HS). None had language deficits history. Forty Italian nouns of natural objects and 40 pseudowords, as well as 40 digital color photos depicting natural objects and 40 distorted images, were used as stimuli. Twenty nouns and 20 photos were referred to natural graspable objects, while the remaining to non-graspable ones. Subjects had to respond whether the stimulus concerned a real object and to abstain if meaningless. The mean value of reaction times (RTs) and error numbers were calculated for each Object Graspability and Stimulus Type combination.

Result: RTs below 130ms or above 1000ms were excluded from the analysis. In the control group, the slower RTs were recorded for stimuli related to graspable objects (nouns: 597±109ms; photos: 616±98ms) compared to non-graspable ones (nouns: 574±108ms; photos: 557±111ms). The MTLE group showed two types of results. MRI-negative patients had RTs like controls for nouns (graspable: 504±79ms; non-graspable: 476±72ms) and photos (graspable: 569±93ms; non-graspable: 491±68ms). Instead, HS-MTLE patients showed faster RTs for nouns referred to graspable objects (470±53ms) compared to those non-graspable (500±54ms) and photos' stimuli (graspable: 546±46ms; non-graspable: 510±99ms). The mean error number was greater in the MTLE-HS group (8.6±10.3) compared to MTLE-negative one (2.4±1.6).

Conclusions: HS-MTLE patients did not show the slower RTs related to graspable objects expressed by nouns, appearing less accurate to perform the task. Our results indicate that embodied cognition is impaired in these patients, which indicates dysfunction in frontoparietal sensorimotor systems.

Abstract Number: 698

Title: "The role of amygdala subnuclei in cognitive performances of patients with temporal lobe epilepsy"

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Purpose: The aim of the present study is to correlate the cognitive performances of temporal lobe epilepsy (TLE) patients with the volumes of subcortical amygdala structures.

Method: 42 TLE patients were recruited: 22 affected by cryptogenic TLE (cTLE) and 20 with TLE symptomatic of mesial temporal sclerosis (sTLE). All participants underwent a high-resolution structural MRI volumetric T1(T13D) on 3T scanner and the same neurophysiological battery tests. Phonemic (PF), category fluency (CF) and verbal memory (VM) raw scores were extrapolated for subsequent statistical analysis. T13D were analysed using the FreeSurfer pipeline[1], including a segmentation of amygdala nuclei according to Saygin & Kliemann's atlas[2]. Two statistical analysis (SPSS[4]) were performed: 1. an independent samples t-test and effect size estimation (Cohen's D) to highlight the anatomical differences between cTLE and sTLE, and 2. a linear regression analysis to investigate the relationships between cognitive performance and the subcortical amygdala volumes.

Result: The comparison between cTLE and sTLE groups showed an increased volume of the left (p=0,025) and right (p=0,004) medial nucleus of the amygdala, and left (p=0,016) and right (p=0,019) cortical nucleus of the amygdala in cTLE compared to sTLE. Considering the whole TLE sample, PF correlates negatively with the bilateral central nucleus volumes [left (p=0,022), right (p=0,025)], and the right medial nucleus (p=0,022) volume. CF performances correlates negatively with the volumes of the bilateral central nucleus [left (p=0,026), right (p=0,030)], and the bilateral medial nucleus of the amygdala [left (p=0,046) and right (p=0,005)]. We did not disclose any relationship between the volume of the amygdala nuclei and the VM scores. When considering the cTLE and sTLE separately, CF correlates with the cTLE only.

Conclusions: Our findings suggest that the amygdala and its nuclei might interfere with both the linguistic performances and the executive aspects of the cognitive tests in TLE patients.

Abstract Number: 738

Title: Adaptive behavior profile of 35 adolescents and adults with Dravet Syndrome

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Adaptive behavior profile of 25 adolescents and adults with Dravet Syndrome

Purpose: Diagnosis achievement has a positive impact on long-term outcome of subjects with Dravet Syndrome (DS), which can benefit from adequate antiseizure treatment and appropriate rehabilitation intervention. Rehabilitation treatment is tailored to the individual, reflecting the peculiar cognitive, neuropsychological, motor and adaptive characteristics of DS. These features are largely reported in the literature for the pediatric age, but poorly acknowledged for adolescents and adults. This is a relevant point, since DS has been described for the first time quite recently (1978) and many subjects obtain diagnosis in their adult age, also thanks to the increasing awareness and diffusion of genetic diagnosis techniques.

Method: In order to assess the adaptive profile of adolescents and adults with DS, we administered to 25 subjects the Vineland Adaptive Behavioral Scale in its first and second versions.

Result: Almost all patients obtained the minimum scores in all subscales of Vineland-II interview ("floor effect"); conversely, with Vineland-I intra-individual and inter-individual variability in different domains emerge. Raw scores analysis allows to identify a common generic profile: socialization, writing, and personal and community daily-living skills are the most afflicted domains, while personal daily-living skills and verbal communication are more preserved.

Conclusions: The study of adaptive behavior allows to outline the functional impairment in daily life of adolescents and adults with DS. The awareness of a common profile helps to address the rehabilitation intervention, tailored according to personal skills and difficulties. Further studies comparing DS with other severe developmental and epileptic encephalopathies are needed to evaluate the specificity of this adaptive behavior profile.

Abstract Number: 792

Title: Inhibitory control and cognitive flexibility in adults with drug-resistant focal epilepsy

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Purpose: We investigated the maintenance of inhibitory control and cognitive flexibility in adults with drug-resistant focal epilepsy (DRE) by examining two oculomotor saccade tasks of unequal difficulty that were either interleaved or repeated.

Method: Fifty-five patients with DRE and 31 healthy age-matched controls completed two oculomotor paradigms: (1)cognitive flexibility switching task: interleaved simple prosaccades (PS: look at target) and cognitively more difficult antisaccades (AS: look away from target) producing four trial types – two consecutive difficult trials (AS–AS), two consecutive simple trials (PS–PS), switching from difficult to simple trial (AS–PS), switching from simple to difficult trial (PS–AS); (2)Block AS task: 48 consecutive AS trials. Performance was measured as latency (ms, response time) and error (%). Switching task performance was further examined as: (1)PS switch cost: switching from difficult to simple trial (AS–PS) relative to performing two simple trials (PS–PS); (2)AS switch cost: switching from simple to difficult trial (PS–AS) relative to performing two difficult trials (AS-AS). AS switch was compared to AS block to examine inhibitory control under different cognitive load.

Result: DRE patients were similarly capable to controls when switching from difficult to simple trial (DRE PS latency switch cost = control PS latency switch cost: Δmean=7.7ms,p=0.201). However, DRE patients alone found it easier to switch from a simple PS to a difficult AS compared to completing two difficult AS trials consecutively (AS error switch benefit: Δmean=-8.4%,p<0.001). This difficulty in sustaining inhibitory control

over consecutive AS trials was worse in the AS block which required 48 consecutive AS (AS switch task mean error=26.2% vs. AS block task mean error=33.6%,p=0.003).

Conclusions: DRE patients have more difficulty in sustaining inhibitory control compared to switching from reflexive to inhibitory task. Our findings suggest prominent top-down inhibitory dysfunction in DRE patients, rather than cognitive inflexibility per se.

Abstract Number: 820

Title: Follow-Up and Outcome of Psychogenic Non-Epileptic Seizure Patients Diagnosed via Video-EEG Monitoring

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Purpose: The aim of this study was to examine the factors affecting the prognosis and the quality of life in psychogenic nonepileptic seizures (PNES).

Methods: We investigated patients with PNES admitted to video-EEG monitoring unit at Süleyman Demirel University Neurology Clinic from 2013 through 2020.Sociodemographic characteristics,clinical findings,psychiatric characteristics and seizure remission after diagnosis were examined.Psychiatric scales (Beck Depression Inventory,Symptom Check List-90-Revised,Short Form-36) were used to evaluate the severity of depressive symptoms, the level of organic and psychiatric symptoms and quality of life.
Results: Fifty-four patients (40 females and 14 males) met the inclusion criteria.The mean delay in diagnosis was 5.57±7.49 years.The history of multiple AED use was statistically significantly higher in patients with concurrent epilepsy (p:0.0007).Twenty participants (37%) were seizure-free at follow-up.Age at onset (p:0.047),marital status (p:0.001),education (p:0.001),better adaptation to treatment process (p:0.035),absence of epilepsy at the time of diagnosis (p:0.045) were associated with this outcome.There were more somatic complaints,pain,worsening of general health perception,loss of physical functionality,fatigue symptoms,depressive symptoms,phobia and anxiety in patients resistant to treatment. These findings were statistically significant.When the seizures were investigated,it was found that 38.9% were akinetic PNES,46.3% were generalized motor PNES,9.3% were subjective PNES and 5.6% were focal motor PNES.No association found between the duration or semiology of PNESs and seizure remission.

Conclusions: The outcome of patients with PNES was generally poor.Earlier age onset,marital status,higher education level,better adaptation to the treatment,absence of concurrent epilepsy,less psychosomatic symptoms,less physical/social restriction may affect the seizure outcome in patients with PNES. Multi-center studies with larger cases are needed for more consistent results.

Abstract Number: 821

Title: Left Temporal Lobe Epilepsy in High Functioning Mathematics Prodigy: Neuropsychological Outcome, Looking Beyond Numbers

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Purpose: Temporal Lobe Epilepsy (TLE) and Anterior Temporal Lobectomy (ATL) with amygdalohippocampectomy have been found to be associated with cognitive deficits. The circuit for mathematical ability is widespread with involvement of temporal, frontal and parietal lobes.

Neuropsychological outcomes of a 23 year old mathematical prodigy with left mesial temporal sclerosis who underwent successful ATL are discussed. His unique mathematical ability involved being able to calculate the exact day of the week of any given date in history within 1-2 seconds.

Method: Cognitive assessment at baseline and 2 year follow-up included Verbal Adult Intelligence Scale, Arithmetic Ability, Colour Trails Test, Auditory Verbal Learning Test, Complex Figure Test and Verbal Fluency. Subjective assessment and mood screening were done using Everyday Memory Questionnaire, Hamilton Depression Inventory, Hamilton Anxiety Inventory and Quality of Life in Epilepsy-31. The unique ability was assessed using 5 dates picked at random.

Result: Arithmetic and unique ability along with Verbal IQ showed preservation of ability at 2 years. Attention improvement with the total time reducing from 48 seconds (60^{th} PR) to 36 seconds (84^{th} PR). Though an increase in total time from 85 seconds to 97 seconds was noted for executive function, the performance was maintained in the 70^{th}-73^{rd}PR. Working memory and visuospatial abilities were also maintained at follow-up. Slight improvement was noted in language with a change from 27^{th} PR to 40^{th} PR. However, performance on verbal and visual memory was consistently impaired (PR>15). Improvement was also noted in subjective cognitive complaints, depression and quality of life.

Conclusions: Despite impaired memory, his unique ability remained stable at 2 years with subjective improvement in mood and quality of life. This emphasizes the need for multidisciplinary management and importance of looking beyond test scores and understanding the patient's performance within the larger context of their background and surgery expectations.

Abstract Number: 1013

Title: Cognitive impairment and Facial Emotion Recognition in Sleep-Related Hypermotor Epilepsy:a case control study of brain connectivity.

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Purpose: To evaluate cognitive impairment (CI) and Facial Emotion Recognition (FER) in the Sleep-Related Hypermotor Epilepsy (SHE) and describe the power spectrum findings (PS) and brain connectivity (BN) changes between SHE patients and controls.

Method: We enrolled SHE patients aged 18-80yo and controls matched by sex, age and education. Each subject underwent a neuropsychological battery. A 64-channel HD-EEG recording per subject was acquired in resting state (open and close eyes; 10 minutes before/after task) and during cognitive tasks: Verbal Phonemic Fluency, Rey Auditory Verbal Learning Test and FER task. The FER task included two phases: the Recognition and the Memory task. The PS and BN, including Default Mode (DMN), Fronto-Parietal (FPN) and Affective Network (AN) were performed using sLoreta/eLoreta

Result: We enrolled 15 patients and 15 controls. The patients failed from 1 to 4 tests and in particular: REY, Stroop, Corsi, Phonemic Fluency. The tests were failed more frequently by older patients, especially in presence of epileptiform discharges in EEG.

Regarding FER, patients disclosed impairment in the recognition of the "Fear" (p-value<0.05) which was misunderstood with "Disgust". A subgroup analysis revealed that FER impairment was prevalent in patient with drug resistant epilepsy and extra-frontal epileptogenic zone.
The study of DMN during the “Rey task” showed an increase in connectivity in the beta 3 band between the middle right temporal gyrus and the right angular gyrus in patient respect to controls (threshold 4.2 t(0.05)= 4.097). The Intra-groups PS analysis (FERvsResting state) showed an activation in beta bands of limbic areas in patients, while in frontal lobe in the controls.

Conclusions: Our work confirmed the presence of CI in SHE and reports for the first time the presence of FER impairment in these patients. The brain connectivity analysis showed a different pattern between the two group, probably secondary to a compensation mechanism in patients’ group.

Abstract Number: 1026

Title: No indication of different depression phenotypes in epilepsy dependent on potential risk factors

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Purpose: We examined whether the presumed complex biopsychosocial etiology of depression in epilepsy is reflected in different distinguishable phenotypes of depression when using Beck Depression Inventory (BDI) for screening.

Method: In a retrospective study design, confirmatory and exploratory factor analyses on BDI data from 352 adult patients with epilepsy from a tertiary centre were performed. Using the resulting factors, a cluster analysis was calculated to identify possible phenotypes of depression within the group classified as depressed (N =156 with BDI ≥10). Finally, factors were related to aspects of the epilepsy and psychosocial factors.

Result: Confirmatory factor analysis could not confirm the three-factor solution of the BDI that was repeatedly obtained in non-epileptic samples by other groups. Exploratory factor analysis revealed two but highly correlated factors, named “Negative Affect” (NA) and “Personal Impairment” (PI) according to the constituting items. Cluster analysis identified three groups with depression with quantitatively rather than qualitatively different patterns. Notably, no connections to most of the considered etiological factors (e.g. clinical factors such as side/site of epileptic focus) were found. However, the factor NA was significantly connected to unemployment ($p = .03$), and the factor PI was negatively correlated with attentional-executive functioning ($p < .001$) and verbal memory performance ($p = .014$).

Conclusions: Using BDI data from a huge patient sample, no differential phenotypes of depression in epilepsy were found. Rather, the BDI captures one single construct of depression in this population. Depression was related to the socioeconomic situation and cognitive dysfunctions but no other clinical factors. Future research should further examine the relationship between depressive mood, cognition and life conditions in epilepsy.

Abstract Number: 1318

Title: Attention and executive deficits differentiate autoimmune TLE caused by limbic encephalitis from TLE of non-autoimmune etiologies

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Purpose: Patients with temporal lobe epilepsy caused by autoimmune limbic encephalitis (AI-TLE) are clinically similar to patients with temporal lobe epilepsy of non-autoimmune etiologies (NAI-TLE) but have a different prognosis and require other specific therapies. The objective of this study was to investigate if patients with these forms of TLE can be discerned by means of neuropsychological assessments.

Method: Data from 103 TLE patients (*n* = 39 with AI-TLE and *n* = 64 with NAI-TLE, including *n* = 39 with hippocampal sclerosis (HS), and *n* = 25 with low-grade epilepsy-associated tumors (LEAT)), and 25 healthy controls who underwent comprehensive neuropsychological assessments were analyzed retrospectively. The neuropsychological characteristics (mean *z*-scores) were compared between groups using one-way ANOVA, independent-samples *t*-tests, and discriminant function analysis (DFA).

Result: Significantly lower performances of the patients' subgroups compared to healthy controls were obtained for all but one cognitive domain (attentional, visuospatial, verbal memory, and nonverbal memory functions). Solely for executive functions, a significantly lower performance of AI-TLE vs. NAI-TLE patients was found regarding cognitive flexibility ($p = 0.025$) and verbal fluency ($p = 0.018$). DFA identified semantic verbal fluency ($p = 0.001$) and reaction time ($p = 0.027$) to be most appropriate to discern AI-TLE from NAI-TLE patients with HS. Group membership was correctly predicted for 74.4% of patients using cross-validation.

Conclusions: Deficits in attention and executive functions, beyond the expected TLE-typical memory impairments were identified in AI-TLE patients that differed significantly from cognitive profiles of NAI-TLE patients. This finding allows to define which cognitive domains to focus on in the neuropsychological evaluation of AI-TLE patients and facilitates the choice of suitable psychometric tests in clinical routine.

Neurostimulation

Abstract Number: 59

Title: Characterization of the cardiac regulatory function of the human insula

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Purpose: The link between brain function and cardiovascular dynamics is an important issue yet to be completely elucidated. The insula is a cortical brain area that is thought to have a cardiac chronotropic regulatory function, but its role in cardiac contractility is unknown. This study aims to analyze the heart rate and cardiac contractility changes after functional activation of different insular regions through direct electrical stimulation (E-stim) in humans.

Method: We performed an observational, prospective study, including patients admitted for stereo-electroencephalographic recording because of refractory epilepsy in whom the insular cortex was implanted. Patients with anatomical or electrophysiological insular abnormalities and those in whom E-stim produced subjective symptoms were excluded from the analyses. Heart rate (HR), stroke volume (SV), and cardiac output (CO) were recorded beat-to-beat and their variations after insular E-stim were analyzed and compared with control E-stim of cortical non-eloquent brain regions and sham stimulations.

Result: Ten patients were included, 5 implanted in the right insula and 5 in the left. Demographic and clinical characteristics of both groups were similar. 52 E-stim were performed in the right insula and 37 in the left. E-stim of both insulas induced a significant decrease of the CO and HR, and an increase of the SV that followed a predictable pattern, with increasing responses due to increasing E-stim intensities. No functional differences between hemispheres or between the anterior and posterior insular regions were observed. E-stim of the control electrodes and sham stimulations were not associated with variations in cardiac function. No changes were observed in blood pressure or respiratory rate.

Conclusions: Our results suggest a direct chronotropic and inotropic cardiac depressor function of the right and left insulas. The evidence of an insular direct cardiac regulatory function may open a path in the prevention or treatment of heart failure, arrhythmias, and SUDEP.

Abstract Number: 94

Title: Precise Determination of Seizure Onset Is Critical for Good Seizure Treatment Outcome in RNS Implantation Patients

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Purpose: Responsive neurostimulation (RNS) has been proved to be an effective treatment for drug-resistant epilepsy if less than 2 seizure foci being identified. However clinical outcomes vary significantly. It remains contentious if precise localization of the seizure onset is required before device implantation. We have noted that precisely defining the seizure onset regions is critical for good seizure treatment outcome and likely may prevent ineffective intervention.

Method: We retrospectively analyzed data from a small cohort of patients with RNS implantation. Seizure treatment outcome was determined by seizure frequency after the RNS implantation during the follow-up. Preimplantation data, ictal scalp video-EEG, interictal FDG-PET, brain MRI, and intracranial invasive intracranial EEG (iEEG) monitoring were compared between responder vs non-responder to the RNS treatment.

Result: Total 7 patients (5 males and 2 females with average age 32±9) were included for analysis. And the average followup after RNS implantation was 4 years. Five patients were with median reduction of seizures of 72%. Among these patients, three had over 6-months seizure-free interval. Among these patients, four underwent iEEG monitoring and confirmed the seizure onset foci to guide the RNS implantation.
Two patients did not respond to the RNS treatment. Repeat scalp EEG recording with magnet triggered timestamp on RNS were analyzed when these two patients experienced clinical seizures. The timestamp data showed latency between the seizure clinical onset and the RNS iEEG. Such data guided the decision for a second RNS implantation in one patient. After the second RNS implantation, this patient reported close to ~50% reduction of the seizure frequency and sustained 5 months seizure-free interval during the follow up.

Conclusions: We have noted that precisely defining the seizure onset regions before implantation is critical for good seizure treatment outcome and may prevent ineffective intervention.

Abstract Number: 294

Title: Brain-derived neurotrophic factor Val66Met polymorphism in vagal nerve stimulation patients affected by drug-resistant epilepsy.

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Purpose: VNS is safe and effective in adults and children with epilepsy according to FDA. BDNF is implicated in many neurophysiological processes and exerts effects on hippocampal serotonergic pathways during both acute and chronic VNS stimulation. BDNF gene encodes a precursor peptide (proBDNF) and non-conservative single nucleotide polymorphism (SNP) has been identified in humans producing an aminoacid substitution (Val66Met). This SNP affects intracellular processing and secretion of BDNF, leading to impaired hippocampal function in humans. (Egan MF, et al., Cell. 2003; 112:257–69.)
Thus, assuming that Val66Met polymorphism underlies an ineffective processing mechanism in DRE, we structured a pilot study to identify whether this SNP is present and correlates with low responder implanted epileptic patients.

Method: After approval by the ethics committee, 25 patients (17 M, 8 F) aged between 14 and 58 yo (median age 44), with DRE, not eligible for surgical treatment, were selected.
Genomic DNA was extracted from blood samples and then amplified by PCR+RFLP to detect BDNF Val66Met. Mann-Whitney test was used to verify different presence of polymorphism in responders versus non-responders.

Result: Clinical response to VNS was assessed with McHugh classification (McHugh JC, et al., Epilepsia. 2007; 48(2):375–8.) before and 1 year after VNS: 11 patients (class I and II) were considered responders, 14 patients (class III or more) non-responders.
There is a correlation between the presence of Val66Met Polymorphism and worse clinical response (p-value 0.0015**; Mean±SEM of Class I-II: 0,1818±0,122, n=11; Mean±SEM of Class III-V: 0,7857±0,1138, n=14).

Conclusions: The correlation between the presence of Val66Met polymorphism and reduced response to VNS, if confirmed on a larger number of individuals, could be a useful marker in clinical practice to better tailor therapies proposed to individual patients. Moreover, this finding would also confirm in humans a reduced neuronal plasticity when the polymorphism is present.

Abstract Number: 398

Title: Rationale, Design, and Hypotheses of the CORE-VNS Study: A Comprehensive Outcomes Registry in Subjects Treated With Vagus Nerve Stimulation Therapy

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Purpose: VNS Therapy® is the most studied neuromodulation therapy for people with drug-resistant epilepsy (DRE), with 25 years of innovation and more than 125,000 patients implanted globally. Much remains to be elucidated about regionally distinct patterns of care impacting seizure and non-seizure outcomes of the

therapy. CORE-VNS (NCT 03529045) is a worldwide post-market outcomes study examining the long-term benefits and safety profile of VNS Therapy.

Method: Subjects who are implanted with VNS Therapy are followed from between 36 to 60 months. The study protocol allows for a maximum of 2,000 subjects at up to 80 centers internationally. Seizure-associated outcomes include traditional measures of clinical benefit such as changes in seizure frequency and severity, while non-seizure outcomes include measures of sleep quality (PSQI or CSHQ), quality of life, anti-seizure medication use, healthcare resource utilization data and adverse events.

Result: Samples of hypotheses that we will test with the CORE-VNS registry include an examination of regional differences in access to care and variation in clinical outcomes associated with novel features of VNS Therapy (for example scheduled programming, responsive VNS, day/night programming). The CORE-VNS database is expected to offer ample opportunity to explore demographic and phenotypic characteristics of individuals undergoing treatment with VNS Therapy. As of March 2021, 812 subjects have been enrolled at 61 sites in 16 countries.

Conclusions: CORE-VNS will likely be the largest and longest investigation of a neuromodulatory therapy in patients with DRE. The volume of data collected will allow for robust analyses of VNS Therapy dosing, titration, concomitant drug use, and general safety outcomes.

Abstract Number: 633

Title: Prediction of VNS efficacy based on EEG analysis

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Prediction of VNS efficacy based on EEG analysis

Purpose: Vagal nerve stimulation (VNS) is well-established treatment option in patient with drug-resistant epilepsy. Despite high numbers of implanted patients, our ability to predict VNS efficacy based on pre-implantation data is limited. In our previous work, we developed a statistic model for VNS prediction analysing pre-implantation routine EEG. Our previously-published work was based on changes in power spectra within defined EEG time-intervals (Brazdil M, Front Neurol 2,10:392). In our next work, we focused on a more-detailed analysis by use of a floating window.

Method: We identified the total number of 56 patients with VNS: 22 non-responders (seizure reduction < 50%), and 34 responders (seizure reduction ≥ 50%) with standardized EEG with a photic stimulation, a hyperventilation, and a eyes opening. EEG was segmented into 10 time-intervals, and filtered into frequency bands (theta, alpha, beta, and gamma). The differences in power spectra between responders and non-responders were analysed by a 26-seconds-long floating window.

Result: The significant differences between responders and non-responders were predominantly present in alpha and gamma frequency bands. In these two frequency bands, the differences started to appear during a photic stimulation and continued for most of the EEG.

Conclusions: There are significant differences in pre-implantation EEG between responders and non-responders. These differences can be highlight by use of a floating window. We plan to apply this approach in our statistic model.

Abstract Number: 765

Title: Vagus Nerve Stimulation elicits sleep EEG desynchronization and network changes in responder patients in epilepsy

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Purpose: Neural desynchronization is a key mechanism of Vagus Nerve Stimulation (VNS) action in epilepsy, and EEG synchronization measures may be explored as possible response biomarkers. During sleep, brain connectivity is characterized by higher synchronization than in wakefulness, and sleep neural networks show resemblances with epileptic circuitry organization (e.g. between sleep spindles and spike-wave discharges). We aimed to explore the differences of VNS acute effects on EEG connectivity and networks in wakefulness and sleep, and to study whether these measures can distinguish responders from non-responders to the therapy.

Method: EEG epochs from calm wakefulness and stage 2 NREM sleep were analyzed in VNS-treated epileptic patients. Weighted Phase Lag Index (wPLI) was computed as connectivity measure of synchronization, for VNS OFF and VNS ON conditions. We also computed directed connectivity and extracted subsequent Global Efficiency (GE), a graph measure of network integration. Ratios OFF/ON were obtained as desynchronization/de-integration index. Values were compared between responders and non-responders (> or <50% seizure frequency reduction) and between EEG states of vigilance. ROC curve and area-under-the-curve (AUC) analysis was performed for response classification.

Result: Twenty-four patients (11 responders, 13 non-responders; 6 generalized, 18 focal epilepsy) were included. Compared to non-responders, stronger VNS-induced theta desynchronization ($p<0.05$) and decreased GE ($p<0.05$) were found in responders in sleep, but not in wakefulness. Theta sleep wPLI Ratio OFF/ON yielded an AUC of 0.825. With a cut-off of 1.05, 73% sensitivity, 85% specificity and 79% overall accuracy were obtained for response classification. Considering all patients, the VNS-induced GE decrease was significantly more important in sleep compared to awake EEG ($p<0.01$).

Conclusions: Stronger sleep EEG desynchronization in theta band distinguishes responders to VNS therapy from non-responders. wPLI Ratio OFF/ON was identified as response biomarker. VNS induces a decrease in network integration in sleep significantly more than in wakefulness.

Abstract Number: 805

Title: Deep brain stimulation of the anterior nucleus of the thalamus for drug resistant epilepsy in a real-world setting: MORE registry 2-year results

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Purpose: The efficacy of deep brain stimulation of the anterior nucleus of the thalamus (ANT-DBS) in drug resistant epilepsy (DRE) patients was demonstrated in the double-blind Stimulation of the Anterior Nucleus of the Thalamus for Epilepsy (SANTE) randomized controlled trial. The Medtronic Registry for Epilepsy (MORE) aims to understand the safety and longer-term effectiveness of ANT-DBS therapy in routine clinical practice.

Method: MORE is an observational registry collecting prospective and retrospective clinical data. Participants were at least 18 years old, with focal DRE recruited across 25 sites from 13 countries. They were followed for at least 2 years in terms of seizure frequency (SF), health-related quality of life (Quality of Life in Epilepsy Inventory 31, QOLIE-31), depression, and safety outcomes.

Result: Of the 191 patients recruited, 170 (mean (SD) age of 35.6 (10.7) years, 43% female) were analysed. At baseline, 38% of patients reported cognitive impairment. Over 2 years the median monthly SF decreased progressively by 33,1% ($P<0.0001$) compared to baseline and QOLIE-31 improved by a median 2.3-point ($P<0.05$). No change in depression severity was seen. In the subgroup of patients that completed 5 years of follow-up, SF was reduced by 55.1%. Factors influencing SF reduction included seizure type, absence of cognitive impairment and number of implants per site. The most reported adverse events were new or worsening seizures (16% of patients), memory impairment (15%) and depression (13%). One definite SUDEP case was reported.

Conclusions: The MORE registry supports the benefit and safety of ANT-DBS therapy in a real-world setting in the 2-years following implantation. Patients without cognitive impairment may benefit more from this type of neuromodulation therapy than those with such impairment.

Acknowledgement: This study was sponsored by Medtronic plc.

Abstract Number: 826

Title: Personalized multichannel transcranial direct current electrical stimulation guided by SEEG in epilepsy: clinical and neurophysiological effects

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Purpose: Transcranial direct electrical stimulation (tDCS) was introduced several years ago as a new treatment for patients suffering from refractory epilepsy. This non-invasive technique is applied to decrease cortical activity with two (conventional tDCS) or several electrodes (multifocal tDCS). We investigated effects of personalized multisession, SEEG-targeted multifocal tDCS on seizure frequency (SF) and scalp functional connectivity (Fc) as measured by EEG in patients with drug-resistant epilepsy.

Method: Ten patients suffering from focal refractory epilepsy were recruited to study therapeutic and neurophysiological effects of long-term multifocal tDCS treatment (Starstim, Neuroelectrics). Therapy consisted of three cycles (six months) where each stimulation cycle corresponded to five consecutive days where each patient received two daily multifocal personalized tDCS sessions of 20 minutes (2x20 min tDCS at 2 mA

separated by 20 min off). The montages were personalized to target epileptogenic area of each patient as defined by SEEG recordings. SF after the treatment was compared with baseline. Fc changes were analysed using EEG recordings performed before and after each stimulation cycle.

Result: After the last tDCS session, 50% of patients (responders) had a SF decrease of 50% or more (mean 75% of decrease) compared with baseline. We estimated Fc changes between cycles and across responder (R) and non-responder (NR) patients. We found that R presented a decrease in Fc ($p<0.05$) at the third session in alpha and beta frequency bands compared to NR.

Conclusions: We validated the clinical usefulness of personalized multifocal tDCS targeting epileptic areas identified by SEEG. Moreover, we demonstrated that a decrease in SF is associated to a significant decrease of Fc after three stimulation cycles. Such results suggest that tDCS-induced functional plasticity changes may underlie the clinical outcome differences between R and NR. Further investigations regarding the precise effects of tDCS on Fc at brain source level should be analysed.

Abstract Number: 928

Title: Cerebral Blood Flow Differences Between High- vs Low-Frequency VNS Therapy in the Epileptic Baboon

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Purpose: Cerebral blood flow (CBF) tracks physiological effects of ictal or interictal epileptic discharges (IEDs) and neurostimulation. This study compared CBF changes between high-frequency (HF; 300 Hz) microburst, and standard, low-frequency (LF; 30 Hz) vagal nerve stimulation (VNS) Therapy in 2 baboons with genetic generalized epilepsy (GGE), one photosensitive with active epilepsy (B1), the other asymptomatic (B2), but with generalized IEDs.

Method: The baboons were selected on the basis of video recordings and scalp EEG studies. They were both implanted with Sentiva™ 1000 devices capable of stimulating at standard and microburst frequencies. Nine $H_2{}^{15}O$ (10-20 mCi) positron emission tomographic (PET) scans were performed each session (two PET sessions acquired for each animal). The baboons were sedated with ketamine and paralyzed, and monitored with scalp EEG. CBF changes were compared between the two modes of stimulation and resting scans in the first study, while in the second, VNS Therapy trials were combined with intermittent light stimulation (ILS) at 25 Hz and compared to CBF changes induced by ILS alone.

Result: ILS-associated IED rates were slightly reduced by HF- and LF-VNS Therapies in B1, while spontaneous IEDs were completely suppressed by HF-VNS Therapy in B2. Regional CBF changes were consistent between the two modes of therapy, in particular the activation of the superior colliculus. Neither VNS mode suppressed the photoepileptic response in B1, but demonstrated activations of the right substantia nigra (SN) and globus pallidum (GP) with both modes. In B2, IED suppression was associated with bilateral deactivations of the frontal, parieto-occipital and temporal cortices and bilateral cerebellar activations.

Conclusions: This pilot study reveals similar activation/deactivation patterns between LF- and HF-VNS Therapies. Their therapeutic targets appear to be subcortical, most consistently the superior colliculus, SN/GP, and cerebellum, all of which modulate corticothalamic networks, with HF-VNS Therapy associated with more diffuse CBF changes.

Abstract Number: 950

Title: Extra-operative Cortical Stimulation in Patients Implanted with Depth Electrodes: Patterns and Impact on the Surgical Treatment of Epilepsy

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Purpose: To describe how cortical stimulation (CS) impacts surgical decision-making in medically resistant epilepsy (MRE) patients implanted with depth electrodes (DE).

Methods: We included patients with MRE who underwent DE implantation and CS for surgical planning from October 2018 to March 2021. Patients were admitted to the epilepsy monitoring unit and underwent CS for surgical planning. Demographic clinical and presurgical data was collected, including DE recording evaluation, CS (time, frequency, mapping of data, duration, morphology, presence of after-discharges(AD)), surgical decision, and outcomes after surgery treatment.

Results: A total of 61 patients were implanted with DE and signed the consent to complete this study. 19 patients were analyzed and 12 met inclusion criteria. Mean age at implantation was 35 years (20-64 years; SD 11), 66% were female (n=8). The most frequent indication for SEEG was lesion-related epilepsy (n=4, 33%), followed by suspicion of mesial vs. neocortical temporal epilepsy (n= 4, 33%). Initial hypothesis of epileptogenic zone was mesial temporal in 58.3% (n=7), followed by neocortical temporal and mesial frontal (n=2, 16.7% each). All patients were implanted bilaterally. The mean length of stay was 14 days (6-25 days), CS duration had a mean of 98 minutes (33-180). Mapping of eloquent cortical areas was completed in 58.3% (n=7) of patients. ADs were present in 83.3% of cases (n=10); seizures were triggered during CS in 58.3% (n=7). In 58.3% of patients (n=7), resective surgery was recommended. Hypothesis of epileptogenic network was estimated in 58.3% (n=7) of cases using CS findings. The results of CS altered the proposed area for resection in 50% (n=6) of patients.

Conclusion: Our data suggests that CS has an impact on epilepsy surgery. CS may improve surgical decisions and outcomes for patients evaluated using DE. CS should be encouraged as a part of presurgical planning in all cases.

Abstract Number: 995

Title: Deep brain stimulation of the anterior nucleus of the thalamus for treatment of focal drug-resistant epilepsy using a continuous stimulation setting.

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Purpose: Deep brain stimulation of the anterior nucleus of the thalamus (ANT-DBS) has emerged as an effective treatment for drug-resistant epilepsy. Optimal stimulation parameters are currently in debate, with cyclic stimulation (as opposed to continuous) has been the predominant type of stimulation used across the

studies. The purpose of this study is to report the outcomes of our cohort of patients receiving ANT-DBS using a continuous stimulation setting.

Method: We describe clinical characteristics, stimulation parameters and outcomes in 6 patients with focal drug-resistant epilepsy in whom ANT-DBS was implanted. All patients were set to continuous unipolar stimulation, with amplitudes between 4 to 5 V.

Result: Five patients, average age 39 (range 22-57) years old and with a mean duration of epilepsy of 21 years (range 4-39), were ANT-DBS implanted between 2011 and 2020. All of them suffered drug-resistant epilepsy with more than one type of seizure. Resective surgery was contra-indicated after presurgical evaluation due to multifocal onset of seizures and/or overlap of the epileptogenic zone with eloquent cortex. Stimulation parameters were those of the SANTE trial except in that continuous stimulation was used. Along follow-up (mean 46 months, range 6-115 months), 80% of the patients experienced a significant (>50%) reduction in seizure frequency and a mean 66% seizure frequency reduction, with the most severe seizure type being the type more responsive to stimulation (81% reduction). None became seizure free. There were no major adverse events; however, three patients experienced transient depressive symptoms at therapy onset.

Conclusions: DBS of the ANT is an effective and safe neuromodulatory palliative treatment for patients with drug-resistant epilepsy, being its most beneficial effect on severe seizure types. The rate of responder observed in our cohort suggests that continuous stimulation may increase its efficacy.

Abstract Number: 1076

Title: Circadian and infradian rhythms and deep brain stimulation in status epilepticus – a canine case study

Sebastian Meller[1], Mayela Zamora[2], Robert Toth[2,3], Karen Wendt[2], Filip Kajin[1], Gregory Worrell[4], Antonio Valentin[5], Holger Volk[1], Timothy Denison[2]

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Purpose: Deep brain stimulation (DBS) is established for the management of different neurological diseases like Parkinson's disease and epilepsy. Responsive implantable devices however often run fixed algorithms, ignoring chronobiological aspects, which constitute important properties in disease processes of epilepsy. In order to investigate the efficacious exploitation of biological rhythms, a highly adaptive DBS device with multiple sensing options was implanted in a canine with severe drug-resistant generalized epilepsy and recurrent status epilepticus (SE). The DBS paradigm was tuned to optimally treat seizures and develop the concept of 'digital zeitgebers'.

Method: Electrodes were implanted bilaterally into the centromedian nucleus (CM) of the thalamus of a canine with drug-resistant epilepsy. After initial trials of high frequency (HF) stimulation (130 Hz, 90 µs pulse duration), a low frequency (LF)-entrainment protocol was adjusted to a normal canine dominant rhythm during restful and alert activity (13 Hz/350 µs), with the possibility of HF-emergency stimulation in case of breakthrough seizures. Furthermore, slow diurnal and infradian adaptations of stimulation parameters were used.

Result: DBS resulted in prevention of SE and severe cluster seizure evolution, especially after LF-entrainment. Since epilepsy onset, the number of seizures during periods of seizure occurrence was 5.84±6.73 [mean±SD, range 1–26] vs. 1.71±1.5 [mean±SD, range 1–5] after LF-entrainment started [P=0.0429]. The time between the first and last seizure during a seizure occurrence period (isolated seizures = 0 h, cluster seizures >0 h) was

20.57±23.42 h [mean±SD, range 0–74.5] vs. 5.36±9.16 h [mean±SD, range 0–19.5] before and after LF-entrainment, respectively [P=0.0475].

Conclusions: This proof-of-concept study showed favorable outcomes in seizure semiology and SE control in a dog with severe drug-resistant epilepsy. The high adaptability of this approach allows for individualized therapies with devices with physiological sensing capability. The synchronization of DBS to latent rhythms is an emerging concept for therapy optimization.

Abstract Number: 1089

Title: Effectiveness of low frequency repetitive transcranial magnetic stimulation in drug resistant epilepsy.

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Purpose: To investigate the efficacy of low frequency (<1Hz) rTMS as an alternative treatment for patients with drug-resistant focal epilepsy.

Method: Five patients underwent low frequency rTMS, using either, a round figure or a figure of 8 coil. Up to 1,000 pulses with a stimulation intensity above resting motor threshold in more than 2 different sessions were applied over the seizure onset zone. Three patients had motor focal seizures and 2 patients had epilepsia partialis continua (EPC). Seizure frequency, seizure duration and clinical notes of these patients were retrospectively reviewed. Clinical improvement was determined on a 12-24-hour period before rTMS and compared to a 12-24-hour period after rTMS. This was determined by either seizure frequency or seizure severity. Due to the small sample size of our cohort, a percentage change ≥50% was chosen as the level of a substantial change.

Result: All patients had motor focal seizures but varied in clinical onset of the seizure and the area of the seizure focus. All patients that showed a clinical improvement had motor focal seizure arising from the hand. In 3 out of the 4 patients who had seizures arising from the hand/arm area showed a clinical improvement after rTMS. One of the patients that showed no clinical improvement had focal motor seizures arising from the leg.

Conclusions: The three patients that showed a clinical improvement after the rTMS had seizure onset close to the primary motor cortex of the hand, a superficial brain area accessible using standard rTMS coils. As a result, rTMS is likely to be more successful in patients with a superficial region of epileptogenic foci. However, further investigation with a larger cohort and new types of TMS coils capable of reaching deeper areas is necessary.

Abstract Number: 1098

Title: The impact of Transcranial Magnetic Stimulation (TMS) on EEG and seizure course in people with or without epilepsy

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Purpose: To elucidate the effects of single and paired-pulse TMS on seizure activity at electrographic and clinical levels in people with and without epilepsy.

Method: A consecutive cohort of 35 people with epilepsy, two people with alternating hemiplegia of childhood (AHC) with no epilepsy, and 16 healthy individuals underwent single or paired-pulse TMS combined with EEG. Changes in resting-state EEG immediately after TMS exposure were analysed in a subset of 14 individuals. Clinical records and subject interviews were used to examine seizure frequency four weeks before and after TMS.

Result: EEG and clinical data analyses showed no significant differences in epileptiform discharges; spikes, spikes and waves, polyspike waves complex, sharp and wave, hypsarrhythmia or seizure frequency in any subject after TMS. There was no occurrence of seizures or EEG abnormalities in healthy individuals, and no worsening of hemiplegic attacks in people with AHC. Changes in antiseizure medication were reported in 14/35 people with epilepsy due to uncontrolled seizures (n=13) or side effects (n=1) in the four weeks preceding TMS.

Conclusions: No significant changes in interictal or ictal activity were found during or after TMS. This study adds evidence on the safety of TMS in people with and without epilepsy with follow-up of four weeks after TMS.

Abstract Number: 1149

Title: Sleep microstructure and seizure control of patients with deep brain stimulation of anterior nucleus thalami

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Purpose: The deep brain stimulation of the thalamic anterior nucleus (ANT DBS) is a neuromodulation technique used in pharmacoresistant epilepsies. Considering the key role of the thalamus in the regulation of sleep we aimed to evaluate the sleep fragmentation of our ANT DBS patients and to check its correlation with the therapeutic response.

Method: We performed polysomnography at 15 of our ANT DBS implanted patients, 6 of them underwent a follow up, extended overnight polysomnography. The implantation and the settings of the device corresponded with those used in the SANTE Trial. We analyzed the recordings for sleep stages and sleep fragmentation described by the ratio of AASM defined arousals and awakenings. Two measures were calculated. 1) DBS %: the percentage of DBS ON epoch leading to arousal, 2) DBS index: the ratio of DBS-related / non-DBS-related arousals.

Result: In responders we found DBS index and DBS % - respectively - 1.52 and 24% at stimulus onset night, and 2.38 and 43% at the PSG recording. In the non-responders the same numbers were 1.32 and 18% at stimulus onset night, that changed to 1.33 and 43% at the PSG recording.

Conclusions: We saw a tendency of more frequent arousals/higher arousal ratio at the responder patients, this could be consequently observed during The follow-up. The arousal-inducing effect of the DBS increased during the follow-up, however we did not verify any significant difference between the two groups.

Abstract Number: 1166

Title: Acut psychiatric symptoms after ANT DBS therapy initiation

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Purpose: The efficacy of anterior thalamic deep brain stimulation therapy in the treatment of therapy-resistant epilepsy has been demonstrated. However, research in recent years has highlighted that treatment may result in both acute and chronic psychopathological side effects, primarily affecting mood, as explained by the identified role of the target region in emotional functioning. The present study is based on the evaluation of psychopathological abnormalities occurring after DBS implantation in our institute, and aims to map the thalamic regions associated with their development.

Method: In six of the twenty implanted patients, psychopathological abnormalities were observed immediately upon programming or switching. These symptoms were recorded during a clinical interview. The effect of treatment on seizure status was evaluated by a statistical method compared to matched controls. Electrode localizations were analyzed on imaging data and plotted schematically.

Result: Acute symptoms were observed mainly on the right side of the anterior thalamus: cry attack, dysthimia, anxiety. Additional symptoms occurred during pacing outside the thalamus. The presence of a psychiatric symptom is a poor predictor of a decrease in seizure count.

Conclusions: Knowledge of symptom-related electrode localizations may contribute to the future avoidance of side effects, to the expansion of our neuroanatomical knowledge related to certain symptoms.

Abstract Number: 1190

Title: Local neuronal network and single unit changes evoked by single and paired pulse cortical stimulation in humans.

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Purpose: Cortical electrical stimulation is a tool to study the pathological and physiological connections in the brain. Intracortical processes after single shock electrical stimulation are poorly understood in humans. We aimed to record local field potentials and single unit activity after single (SCS) and paired pulsed cortical stimulation (PPCS).

Method: Cortico-cortical evoked potentials (CCEP) were recorded using a laminar-multi-microelectrode (IME) inserted in the gyral crown under subdural grid electrodes in therapy resistant focal epilepsy patients. We applied SCS (n=7, 10mA, 0.5Hz) and PPCS (n=10, ISI 6.6, 10, 20, 30, 40, 50, 100, 200, 500, 1000ms), and recorded CCEPS on both the surface grid and local field potentials (LFP) on intracortical IME. We calculated the laminar distribution of current source density (CSD), spectral power (TFR) and population and single unit (MUA and SUA) activity.

Result: We distinguished early (P1, N1) middle (P2, N2) and late (P3) components with 10, 20, 600, 140 and 340ms peak latencies in average respectively. Under P1 we saw surface source and middle layer sink, and during N1 surface sink and middle layer source, accompanied by MUA increase. In P2 surface source middle layer sink, followed by N2 with wide middle layer source both accompanied by MUA decreace, and succeded by the P3 with middle layer sink and MUA increase. With PPCS the N1-P2 varied according to the ISI according to the above mentioned MUA changes.

Conclusions: We concluded that early P1, N1 and late P3 are excitatory and P2 and N2 waves are inhibitory, also reflected in the effect of late waves on early ones during PPCS. Our results indicated that a characteristic sequence of different intracortical excitatory and inhibitory volleys are activated even by one single shock stimulation.

Abstract Number: 1205

Title: What if epilepsy required an error detector – the cerebellum?

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Purpose: The role of the cerebellum as an error detector and corrector of cortical activity suggests a potential role in keeping the balance between inhibition and excitation in epileptic foyers. This review posits that the cerebellum is a coordinator of inhibition and excitation of cortical cerebral activity, and the occurrence of a seizure is evidence of a surpassing of its capacity or an impairment of its function.

Method: A review of the literature on the cerebellum in epilepsy was conducted in medical databases (e.g., Medline and Embase). Several studies were reviewed and their findings synthesized.

Result: The discovery of the ictogenicity of cerebellar lesions displaces the cerebral cortex as the only site of epileptogenesis. Subcortical neurons act as modulators of cortical activity. However, the observation of changes in structural and functional connectivity of the cerebellum, Purkinje cell loss, volume changes, as well as modifications in cerebellar blood flow suggest an implication of the cerebellum in epilepsy, if not the impact of epilepsy on the cerebellum.
Several studies investigating the seizure-suppressive role of the cerebellum in animal models have produced mixed results. Important points for variable findings have to do with target choice, stimulation protocol, and the model being used. In humans, cerebellar targeting, though still in its infancy, is generally promising.
It is possible that activation of Purkinje cells reduces the excitatory output of cerebellar nuclei to the thalamus, thus reducing cortical excitability.

Conclusions: The cerebellum is a potential target of antiepileptic action, and might constitute an important target in new approaches to seizure control in the near future.

Abstract Number: 1207

Title: Using Transcranial Magnetic Stimulation (TMS) to Map Language Reorganization Prior to Brain Surgery

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Purpose: TMS is an evolving pre-surgical language mapping technique that can be used to create non-invasive "virtual lesions" in the language cortex. In healthy individuals, language generally lateralizes to the left hemisphere at an early age; however, in patients with epilepsy or brain tumours, language reorganization is frequent. In this study, we examined how speech is affected in individuals after brain surgery in TMS-identified language regions.

Method: We performed a retrospective chart search for 75 epilepsy and brain tumour patients whose language areas were mapped with TMS prior to surgery at Le Bonheur Children's Hospital between January 2014 and September 2020. 27 incomplete (in which frontal and temporal lobes in both hemispheres were not mapped)

and 5 inconclusive mappings were excluded, leaving a final analysis of N=43. TMS-mapped language regions and hemispheric dominance (as analysed using the Laterality Index) were assessed against the areas surgically resected.

Result: Of the 43 patients, 67% were left-hemisphere dominant, with the additional 33% split equally in between right and bilateral dominance, and 72% had activation in all four tested language areas. 49% of surgeries were in the TMS-identified dominant hemisphere, 39% were in the non-dominant hemisphere, and 14% were in a non-language area. One surgery was in both hemispheres. However, only 7 patients had transient speech deficits noted after surgery, 5 in the dominant hemisphere and 2 in the non-dominant hemisphere.

Conclusions: Although most patients were left hemisphere dominant, the majority of them had language activation bilaterally. Additionally, even when crucial brain areas in the dominant hemisphere were resected, only a small percentage of patients had speech deficits. Multi-centre research needs to be performed with a larger data set, but TMS shows promise as a means of exploring language reorganization in individuals with brain tumours or epilepsy.

Abstract Number: 1223

Title: Triad stimulation with VNS, RNS, DBS

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Purpose: Neurostimulation can be used for the treatment of epilepsy when antiseizure medications fail and surgery is not an option. Vagal nerve stimulation (VNS), deep brain stimulation (DBS) and responsive neurostimulation (RNS) can be used alone or in combination. Here we report the case of a woman with drug resistant epilepsy who, with a combination of VNS, RNS and DBS and antiseizure medications, has experienced >1 year seizure freedom.

Method/Result: 34 year-old left handed woman with drug resistant epilepsy with seizures consisting of behavioral arrest and oral/manual automatisms frequently progressing to bilateral tonic-clonic. This patient underwent VNS initially, but due to continued seizures, pursued presurgical work up which included normal MRI, PET scan showing right temporal lobe hypometabolism, LTVM with right temporal onset seizures and neuropsychology testing showed verbal > perceptual reasoning abilities. She underwent intracranial monitoring which revealed onset over the right medial temporal structures. Due to the patient's concerns regarding memory decline, no destructive procedure was performed, rather RNS was placed in the right medial temporal structures. After two years of RNS therapy, the patient continued to have convulsions 3-5 times per month. She underwent DBS of the anterior nucleus of the thalamus (ANT). After 3-4 months of DBS with titration to 5V (along with concomitant clobazam titration), she had no further clinical seizures at last follow up (>1 year) and RNS electrocorticograms have shown no ictal findings. All devices remain on. She has had no adverse effects of stimulation.

Conclusions: To our knowledge, this is the first report demonstrating that triad stimulation with DBS, RNS and VNS can be both efficacious and safe, though the degree to which medication contributes to seizure freedom in this case in unknown. Additionally, we demonstrate the ability of RNS electrocorticography to detect chronic changes in seizure occurrence related to DBS stimulation.

Paediatric Epileptology

Abstract Number: 46

Title: Paediatric EEG requests evaluation in a district general hospital: an audit

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Purpose: To investigate the electroencephalogram (EEG) requests at a district general hospital in the UK. The collected data were compared with NICE guidelines.

Method: A retrospective audit of EEG requests at the paediatric department of Peterborough city hospital in the UK. We identified the EEGs which were performed between March 2020 and December 2020. A total of 100 EEG requests were randomly selected. Patients with an established diagnosis of epilepsy before having the EEG were excluded.

Result: The final identified number was 66 EEGs. 10.6% (7) were requested by epilepsy specialists. Syncope and "funny turns" represented 15.1% (10) of the events for requesting an EEG; all were requested by non-epilepsy specialists. Patients with a first awake EEG represented 72.7% (48), while repeat EEG represented 22.7% (18). Repeat EEG was done during wakefulness in 50% (9/18) of these patients while the remaining 50% (9/18) were done during sleep. Abnormal activity on the EEGs was described in 54.5% (36/66) of the reports, while epileptogenic EEG activity was evident in 30.3% (20/66) of them. EEG contributed to the diagnosis of epilepsy in 19.6% (13/66) of the patients.

Conclusions: EEG is still being used to exclude the diagnosis of epilepsy in patients with “funny turns”. Awareness about the importance of sleep or sleep-deprived EEG is lacking. More strategies to maximize the use of EEG are needed.

Abstract Number: 81

Title: Analysis of spatio temporal propagation of occipito-frontal spikes in childhood epilepsies by 3D sequential voltage mapping and dipole localisation

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Purpose:
1.To study the spatio temporal propagation of occipito-frontal spikes in childhood epilepsies by sequential voltage mapping and dipole localisation
2.Identify types of occipito fronto spikes based on onset,propagation and stability of the dipoles.

Method: EEG of 10 children with Occipito-frontal spikes selected - 5 idiopathic Panayiotopaulos Syndrome and 5 Symptomatic epilepsies.Using a source localisation software(Besa Research 6.1), the spikes averaged in Average referentia montage by automated pattern matching and sequential 3D voltage maps analysed following the rules of mapping.Dipole localisation at onset and peaks done by Principal component analysis(PCA) using age appropriate template head model.

Results: 3 types of occipito-frontal spikes identified:
1. Seemingly**"**bilateral" occipito-frontopolar spikes(Fp-o) is seen in 4/ 5 idiopathic cases.These spikes were clone like and their dipoles ultra stable.They were seen to have a lateralised onset from lateral inferior parietal region which imparts initial occipital negativity and rapidly propagates through two ways.One goes to the ipsilateral superior surface of temporal pole (perisylvian spread) which imparts the virtual frontopolar negativity and another goes to the anterior wall of ipsilateral rolandic sulcus which imparts a contralateral frontal positivity.
2.Occipito –frontal spikes with stable dipoles:They were seen in one child with idiopathic and 1/5 of symptomatic epilepsies.Idiopathic case had propagation from a deep medial parietal foci to ipsilateral perirolandic region.
Symptomatic case had propagaton from a midline parietal focus(leads to false lateralisation) to the contralateral deep parietal region (interhemispheric synchrony).
3.Occipito –frontal spikes with unstable dipoles:seen in 4/5 of symptomatic epilepsies and has propagation from occipito parietal region to rolandic region with unstable dipoles with intraspike and interspike variabitlity with constantly rotating dipolar orientations.

Conclusions: There is no actual occipital to frontal propagation seen in occipito –frontal spikes. Intrahemispheric and interhemispheric synchrony both can result in occipito-frontal spikes.It is possible to predict their etiology by the stability of dipoles.

Abstract Number: 83

Title: Efficacy/Safety of Perampanel in Patients Aged 4–<12 Years with Focal-Onset or Generalised Tonic-Clonic Seizures who Converted to Monotherapy

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Purpose: Perampanel is a once-daily oral anti-seizure medication (ASM) for focal-onset seizures (FOS) and generalised tonic-clonic seizures (GTCS). Study 311 (NCT02849626) was a multicentre, open-label study of adjunctive perampanel oral suspension in paediatric patients with FOS (with/without focal to bilateral tonic-clonic seizures [FBTCS]) or GTCS. We report efficacy and safety data from patients who converted to perampanel monotherapy during Study 311 (Core/Extension A Phases).

Method: Baseline demographic information were recorded and efficacy assessments included median percent change in seizure frequency/28 days from baseline and seizure-freedom rates. Safety assessments included reporting treatment-emergent adverse events (TEAEs).

Result: Overall, 4/180 patients converted to perampanel monotherapy. Baseline demographics were (gender/seizure type/concomitant ASM[s]): Patient 1 (aged 7): female/GTCS/phenytoin; Patient 2 (aged 4): female/FOS/rufinamide, lacosamide; Patient 3 (aged 10): male/FOS/oxcarbazepine; Patient 4 (aged 9): male/FOS/oxcarbazepine. Median total perampanel treatment duration in these 4 patients was 363 days (range, 337–367 days), of which patients were receiving perampanel adjunctive therapy for a median duration of 203.5 days (range, 186–244 days) before converting to perampanel monotherapy (median duration, 152 days; range, 118–171 days). Perampanel doses received by these 4 patients during adjunctive and monotherapy perampanel periods were: Patient 1, 6 and 4 mg/day, respectively; Patient 2, 8 mg/day for both; Patient 3, 14 mg/day for both; Patient 4, 6 and 4 mg/day, respectively. At Weeks 40–52, median percent reduction in seizure frequency/28 days from baseline was 100.0% for Patients 1–3 and 75.0% for Patient 4. Patient 2 achieved seizure freedom at Weeks 40–52. During adjunctive/monotherapy, 29 TEAEs occurred in these 4 patients; 22 occurred prior to monotherapy conversion and 7 occurred during monotherapy.

Conclusions: In this case series analysis, conversion to perampanel monotherapy provided efficacy and was generally well tolerated. Further investigation is warranted due to the small sample size.

Funding: Eisai Inc.

Abstract Number: 99

Title: Pharmacokinetics, safety, and tolerability of intravenous brivaracetam in neonates with seizures: interim analysis of a phase 2/3, open-label trial

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Purpose: Evaluate pharmacokinetics, safety, and tolerability of brivaracetam in neonates with repeated electroencephalographic seizures not controlled with previous antiepileptic drug (AED) treatment (Exploratory Cohort), and identify optimal dose to subsequently evaluate efficacy.

Method: We present data for the completed Exploratory Cohort from N01349 (the PETITE trial)/NCT03325439, an ongoing phase 2/3, open-label trial of brivaracetam in neonates (postmenstrual age [PMA] ≥34 weeks; term neonates and preterm neonates [PMA <44 weeks]) with repeated electroencephalographic seizures. During the 48-hour Evaluation Period (from first brivaracetam infusion), study participants could receive 1–4 doses of intravenous brivaracetam 0.5mg/kg. Study participants benefiting from brivaracetam could enter the Extension Period (up to 28days of chronological age), during which they could switch to oral brivaracetam and enter into a long-term follow-up trial; the remaining proceeded to Safety Follow-Up Period for 30days. Brivaracetam plasma concentrations following first dose on Day 1 (primary variable), area under the curve (AUC), volume of distribution, clearance, and elimination half-life were assessed during the Evaluation Period; treatment-emergent adverse events (TEAEs) were assessed throughout BRV treatment.

Result: Exploratory Cohort comprised six study participants (mean PMA: 38.7weeks; mean chronological age: 2.5days; 66.7% female). Median brivaracetam treatment duration was 30hours. Geometric mean brivaracetam plasma concentration after first dose on Day 1 was 0.5342mg/L (0.5–1hours; n=5), 0.5001mg/L (2–4hours; n=6), and 0.3427mg/L (8–12hours; n=5). Geometric mean pharmacokinetic parameters of brivaracetam (n=6) were: AUC 4.4h•mg/L, volume of distribution 2.6L, clearance 0.23L/h, elimination half-life 7.6hours. 3/6(50.0%) study participants experienced TEAEs (anemia, hyperglycemia, apnea; 1/6[16.7%] each); 1/6(16.7%) experienced a serious TEAE (apnea). No drug-related TEAEs, brivaracetam discontinuations due to TEAEs, or deaths were reported.

Conclusions: In this first brivaracetam trial in neonatal study participants, observed brivaracetam plasma concentrations were consistent with data from adults receiving an intravenous dose of 25mg bid. Brivaracetam was well tolerated.

Funding: UCB Pharma-sponsored

Abstract Number: 116

Title: Long-Term Seizure Freedom with Adjunctive Perampanel in Patients Aged 4–<12 Years with Focal-Onset Seizures or Generalised Tonic-Clonic Seizures

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Purpose: Perampanel is a once-daily oral anti-seizure medication (ASM) for focal-onset seizures (FOS) and generalised tonic-clonic seizures (GTCS). Long-term seizure-freedom rates with adjunctive perampanel are maintained in adolescents/adults (aged ≥12 years) with focal to bilateral tonic-clonic seizures (FBTCS) or GTCS. Here, we assessed if seizure-freedom rates achieved with adjunctive perampanel during the 311 Core Study (NCT02849626) are maintained during long-term treatment in paediatric patients with FOS (with/without FBTCS) or GTCS.

Method: Seizure-freedom rates (FOS/FBTCS/GTCS) were assessed in patients who achieved seizure freedom during the Core Study Maintenance Period and then remained seizure free for 6 and/or 12 months (calculated from the start of their seizure-free period). Data were stratified by concomitant enzyme-inducing ASMs (EIASMs) (with/without) and age (4–<7/7–<12 years).

Results: For FOS, 13/17 (76.5%) patients remained seizure free for 6 months (with EIASMs, n=3/5 [60.0%]; without EIASMs, n=10/12 [83.3%]; 4–<7 years, n=1/3 [33.3%]; 7–<12 years, n=12/14 [85.7%]) and 6/11 (54.5%) remained seizure free for 12 months (with EIASMs, n=2/5 [40.0%]; without EIASMs, n=4/6 [66.7%]; 4–<7 years, n=0/1; 7–<12 years, n=6/10 [60.0%]). For FBTCS, 3/8 (37.5%) patients remained seizure free for 6 months (with EIASMs, n=0/1; without EIASMs, n=3/7 [42.9%]; 4–<7 years, n=0/3; 7–<12 years, n=3/5 [60.0%]) and 1/5 (20.0%) patient remained seizure free for 12 months (with EIASMs, n=0/1; without EIASMs, n=1/4 [25.0%]; 4–<7 years, n=0/2; 7–<12 years, n=1/3 [33.3%]). For GTCS, 6/10 (60.0%) patients remained seizure free for 6 months (no GTCS seizure-free patients received EIASMs; 4–<7 years, n=1/2 [50.0%]; 7–<12 years, n=5/8 [62.5%]) and 3/7 (42.9%) patients remained seizure free for 12 months (all 7–<12 years, n=3/6 [50.0%]).

Conclusion: Despite small patient numbers, seizure-freedom rates are maintained during long-term (1 year) perampanel treatment in paediatric patients, consistent with analyses in adolescents/adults.

Funding: Eisai Inc.

Abstract Number: 119

Title: Efficacy and Safety of Adjunctive Perampanel 4 mg/day in Patients Aged 4–<12 Years with Focal-Onset Seizures or Generalised Tonic-Clonic Seizures

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Purpose: Perampanel is a once-daily oral anti-seizure medication (ASM) for focal-onset seizures (FOS) and generalised tonic-clonic seizures (GTCS). Study 311 (NCT02849626) was a multicentre, open-label, single-arm study of perampanel oral suspension in paediatric patients (aged 4–<12 years) with FOS (with/without focal to bilateral tonic-clonic seizures [FBTCS]) or GTCS. Here, we report efficacy/safety of adjunctive perampanel 4 mg/day in paediatric patients (aged 4–<12 years) with FOS (with/without FBTCS) or GTCS in Study 311.
Method: The Core Study comprised 4-week Pretreatment, 23-week Treatment (11-week Titration; 12-week Maintenance) and 4-week Follow-up Periods. Efficacy assessments included median percent reductions in seizure frequency/28 days from baseline during the Treatment Period, and 50% responder and seizure-freedom rates during Maintenance in patients receiving a modal (most frequent) perampanel dose of 4 mg/day. Treatment-emergent adverse events (TEAEs) were assessed in patients receiving perampanel 4 mg/day at onset of their TEAE(s).

Results: Overall, 30 patients received perampanel 4 mg/day (modal dose; FOS: n=24; FBTCS: n=10; GTCS: n=6). Median percent reductions in seizure frequency/28 days for FOS, FBTCS and GTCS were 34.2%, 36.6% and 100.0%, respectively. Fifty-percent responder rates for FOS, FBTCS and GTCS were 10/24 (41.7%), 5/10 (50.0%) and 3/4 (75.0%), respectively. Seizure-freedom rates for FOS, FBTCS and GTCS were 3/24 (12.5%), 2/10 (20.0%) and 3/4 (75.0%), respectively. TEAEs occurred in 60/145 (41.4%), 26/52 (50.0%) and 14/31 (45.2%) patients with FOS, FBTCS and GTCS, respectively, who were receiving perampanel 4 mg/day at onset of their TEAE(s). The most common TEAE in patients with FOS and FBTCS was nasopharyngitis (6.2% and 11.5%); dizziness, irritability and pyrexia were the most common in patients with GTCS (9.7% each).

Conclusion: These data suggest adjunctive perampanel 4 mg/day is an effective and well tolerated ASM for paediatric patients (aged 4–<12 years) with FOS (with/without FBTCS) or GTCS.

Funding: Eisai Inc.

Abstract Number: 137

Title: Cannabidiol (CBD) in Patients With Lennox-Gastaut Syndrome (LGS) and Dravet Syndrome (DS) on a Ketogenic Diet Therapy (KDT) in Four Phase 3 Trials

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Purpose: KDTs are high-fat, low-carbohydrate diets used to treat medication-resistant epilepsy. CBD demonstrated efficacy and was well tolerated in patients with LGS or DS in 4 clinical trials. To evaluate safety of CBD in patients on KDT, we conducted a post hoc analysis of pooled data from these trials.

Method: Data were from trials GWPCARE3, 4 (NCT02224560, NCT02224690) in LGS and GWPCARE1, 2 (NCT02091375, NCT02224703) in DS. Patients received a plant-derived pharmaceutical formulation of purified CBD (Epidyolex®; 100 mg/mL oral solution) at 10 mg/kg/d (CBD10) or 20 mg/kg/d (CBD20) or placebo with a KDT.

Result: Of 714 patients, 25 (9%) taking placebo and 33 (8%) taking CBD were on KDT. Median (range) age was 7.2 (2.6–20.5) years, and the number of baseline antiseizure medications was 3 (1–4). In the KDT group only, 3 patients, all taking CBD20, discontinued treatment, 2 because of adverse events (AEs) and 1 met the withdrawal criteria. Median (range) treatment time was 100 (11–113) days for CBD and 99 (96–108) days for placebo groups on KDT. AEs were reported in 79% of patients on KDT (CBD, 91%; placebo, 64%) and 84% off KDT (CBD, 89%; placebo, 77%). The most frequent AE was somnolence in patients on and off KDT (22%, 18%). Serious AEs occurred in 14% of patients on KDT (CBD, 18%; placebo, 8%) and 16% off KDT (CBD, 20%; placebo, 9%). Elevated ALT >3×ULN occurred in 5 patients (24%) on KDT taking CBD20 (n=21); 4 were on valproate. No patient met Hy's law criteria for severe liver injury. There were no deaths on KDT. Case studies describing the practicality of managing CBD treatment and KDT will be presented.

Conclusions: Add-on CBD was well tolerated with no new safety concerns in patients with LGS or DS on KDT.
Funding: GW Research Ltd.

Abstract Number: 139

Title: Long-Term (>1 year) Safety of Adjunctive Perampanel in Paediatric Patients with Epilepsy in Phase III Study 311

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Purpose: The safety/efficacy of adjunctive perampanel in patients aged 4–<12 years with focal-onset seizures (FOS) or generalised tonic-clonic seizures (GTCS) following up to 1 year of treatment in Study 311 (NCT02849626) has previously been reported. Here, we report results from Study 311 Extension B to assess long-term (>1 year) safety and tolerability of perampanel in Japan/countries where an extended access programme was unavailable. Only patients with FOS were enrolled in Japan.

Method: Study 311 was an open-label study that consisted of the Core Study (4-week Pretreatment, 11-week Titration and 12-week Maintenance Periods), Extension A (29 weeks) and Extension B. Patients continued in Extension B as long as clinically appropriate until they reached 12 years of age, when they could switch to perampanel oral tablets, or when perampanel oral suspension became commercially available.

Result: A total of 43 (FOS, n=42, of whom 22 had focal to bilateral tonic-clonic seizures [FBTCS]; GTCS, n=1) entered Extension B. Of these, 42 patients (Japan, n=40 [all with FOS with/without FBTCS]; France, n=2 [FOS, n=1; GTCS, n=1]) were included in the Safety Analysis Set (SAS), since 1 patient turned 12 years old before receiving perampanel in Extension B. Overall, 36/42 (85.7%) patients completed Extension B; 5/42 (11.9%; inadequate therapeutic effect, n=3; patient choice, n=1; other, n=1) discontinued; and 1 was ongoing as of data cut-off. Based on cumulative data throughout Study 311, mean (standard deviation [SD]) exposure duration was 108.4 (24.6) weeks in the SAS and mean (SD) daily perampanel dose was 7.5 (2.3) mg/day. In Extension B, treatment-emergent adverse events (TEAEs) were reported in 35/42 (83.3%) patients; most common was nasopharyngitis (33.3%). Serious TEAEs occurred in 8/42 (19.0%) patients; no patients discontinued due to a TEAE.

Conclusions: Long-term (>1 year) adjunctive perampanel was generally safe and well tolerated in paediatric patients.

Funding: Eisai Inc.

Abstract Number: 146

Title: Children with Dravet syndrome in Sweden- a population-based study

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Purpose: The aim was to investigate the age at diagnosis, cumulative incidence (CI), proportion of individuals with a SCN1A mutation and mortality in Dravet Syndrome (DS) in Sweden.

Method: This was a population-based study. A register from a previous study and contact with pediatric neurologists and the Dravet Syndrome Association Sweden was used for identification of Swedish children with DS. Inclusion criteria of Nabbout R et al. Orphanet J Rare Dis. 2013;8:176. were applied. Fifty-five children born between January 1, 2000 and December 31, 2018 were identified. Data was collected from parents and medical records. Age at diagnosis and CI were calculated for children born in four different time periods: 2000-2004, 2005-2009, 2010-2014 and 2015-2018.

Result: CI for the whole period was 1/39,000 children born alive. There was a statistically significant difference in age at DS diagnosis (p=0.04) and CI (p<0.05) depending on when the children were born; median age at diagnosis and CI was 4.2 years and 1/68,000 for children born 2000-2004, 4.0 years and 1/36,000 for children born 2005-2009, 1.5 years and 1/26,000 for children born 2010-2014 and 1.9 years and 1/52,000 for children born 2015-2018. SCN1A analysis was performed on 53 children and in 51 of 53 a mutation was detected. Seven children had died, two of sudden unexpected death in epilepsy, three of pneumonia and two of pneumonitis. Median age at death was 4.7 years.

Conclusions: We observed a significant difference in CI and age at diagnosis of DS depending on when the children were born. A SCN1A mutation was detected in all patients except two.

Abstract Number: 170

Title: A Phase IV, Prospective, Post-Approval Study of Adjunctive Perampanel in Indian Patients Aged ≥12 to <18 Years with Focal-Onset Seizures: Study 508

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Purpose: In the US, EU and India, perampanel is approved for focal-onset seizures (FOS) and generalised tonic-clonic seizures (GTCS) in patients aged ≥12 years (FOS: ≥4 years, US/EU and GTCS: ≥7 years, EU). This post hoc analysis evaluated the tolerability and efficacy of real-world adjunctive perampanel in patients aged ≥12–<18 years with FOS in India.

Methods: Study 508 (NCT03836924) was a prospective, multicentre, post-approval observational study comprising a Screening/Enrolment Visit, a 6-month Treatment Period (monthly clinical visits) and a 30-day Follow-up Period. Assessments included: incidence of treatment-emergent adverse events (TEAEs; primary endpoint), median reduction in seizure frequency/28 days and 50% responder and seizure-freedom rates. Patients aged ≥12–<18 years were included.
Results: Overall, 200 patients were enrolled; 199 patients were included in the Safety Analysis Set. Of these, 30 (15.0%) patients were aged ≥12–<18 years; mean (standard deviation) age: 15.0 (1.5) years. Six TEAEs of mild-to-moderate severity were reported (ataxia, cough, fever, irritability, needle prick-like sensation and vertigo, n=1 each); irritability was the only TEAE considered related to perampanel treatment. No deaths/serious TEAEs occurred. Six (20.0%) patients discontinued treatment (most common: lost to follow-up, n=3); none were due to TEAEs.
Overall, 26 patients were included in the efficacy assessments. Median percent reduction in seizure frequency across the entire Treatment Period was 100.0%; 25/26 (96.2%) patients reported a ≥50% reduction in seizure frequency. Seizure freedom was achieved by 10 (38.5%), 16 (61.5%) and 13 (50.0%) patients during the first 3 months, the last 3 months and the entire 6-month Treatment Period, respectively.

Conclusion: Real-world adjunctive perampanel was well-tolerated and efficacious in Indian patients aged ≥12–<18 years. No unexpected safety signals emerged; >61% of patients achieved seizure freedom during the last 3 months of treatment.

Funding: Eisai Pharmaceuticals India Pvt. Ltd.

Abstract Number: 179

Title: Proteomic characterization of a novel mouse model of Dravet syndrome

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Purpose: Dravet syndrome is a rare, severe pediatric epileptic encephalopathy accompanied with intellectual and motor disabilities. Proteomic characterization of a novel mouse model can reveal alterations in protein expression involved in epileptogenesis and indicate potential new targets for Dravet syndrome treatment.

Method: Seizure, behavioral and proteomic profiling were performed in a novel commercially available knock-in mouse model of Dravet syndrome, carrying the mutation A1783V in the *Scn1a* gene. Hippocampal tissue was dissected from the left hemisphere of two- (prior to spontaneous seizures onset) and four- (following the spontaneous seizures onset) week-old male mice, fresh frozen and later analyzed using LC-MS/MS with label-free quantification. The right brain hemisphere was collected for immunohistochemical staining. Pathway enrichment analysis was performed using ConsensusPathDB pathway tool.

Result: Dravet mice exhibited spontaneous seizures, a high incidence of SUDEP, an increased susceptibility to hyperthermia-induced seizures and hyperactivity. Proteomic analysis of hippocampal tissue demonstrated more prominent changes in four-week-old Dravet mice. Specifically, a pronounced alteration of proteins involved in neurotransmitter dynamics, synaptic plasticity, receptor and ion channel function, neoangiogenesis, astrogliosis, and nitric oxide became evident. Pathway enrichment analysis identified 16 regulated pathways at the earlier and 127 regulated pathways at the later time point. Interestingly, several downregulated pathways in four-week old Dravet mice involved glutamatergic signaling and synaptic transmission. Differential expression of selected proteins was confirmed by immunohistochemical staining.

Conclusions: This study demonstrated molecular changes in Dravet mice that may either impact neuronal excitability or serve as a compensatory mechanism. The functional relevance requires further confirmation in follow-up studies. Additionally, molecular consequences of the *Scn1a* genetic deficiency can result in more complex pathophysiological mechanisms during the course of epilepsy, which may need to be considered for the management of Dravet syndrome.

Abstract Number: 202

Title: A computational approach to using routine MRI and EEG to identify developmental impairment in pre-school children with epilepsy

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Purpose: To apply a computational approach to identify children with early-onset epilepsy (CWEOE, onset <5 yrs.) with higher risk for cognitive and/or behavioural problems using routine MRI and EEG available from initial clinical presentation.

Method: MRI, EEG and psychometric data on 32 CWEOE from a regional population-based study (Hunter et al. Developmental Medicine & Child Neurology 2015;57:56-57.) were available for this cross-sectional study. Subcortical volumes, normalised by intracranial volume, were calculated from T1 MRI sequences. Twenty channels resting-state EEG were processed into a frequency spectrum between 0.5 and 45 Hz. Cognitive and behavioural scores were normalised to the same standard space. CWEOE were split into average (S+) and those with deficits (S-, <-2.0 standard deviation below the mean). MRIs, EEGs, and scores were jointly analysed by performing tensor-matrix-matrix decomposition simultaneously, a method to reveal underlying correlations among diverse datasets.

Result: The decomposition revealed four underlying components; one referring to S+, and another to S-. S+ and S- components were in the same EEG frequency range <10 Hz, with S- in the lower amplitude. The decomposition revealed asymmetry differences in the thalamus and hippocampus between S+ and S-. Asymmetry Index (AI) (Sarica *et al*. Frontiers in neuroscience 2018;12:576) was adopted to evaluate the result. ANOVA showed significant differences in thalamus-AI and behavioural scores (p=0.035), and hippocampus-AI and cognition/behaviour scores (p=0.039).
The decomposition showed volume difference in several regions. At α=0.05, Kruskal-Wallis test confirmed that the left thalamus was significantly different in behavioural scores (p=0.025). Other regions showed a trend at α=0.1, which will be further explored by integrating DTI data into the decomposition in future.

Conclusions: Our novel computational approach using decomposition identified characteristic differences between S+ and S- using routine MRI and EEG data, can potentially help prioritise CWEOE who would benefit from developmental interventions.

Abstract Number: 205

Title: Late-onset Lennox-Gastaut syndrome

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Title: Late-onset Lennox-Gastaut syndrome

Purpose: Lennox–Gastaut syndrome (LGS) is a severe epileptic encephalopathy accounting for 1%–10% of childhood epilepsies. It is characterized by multiple seizure types, abnormal electroencephalographic features and intellectual disability. An underlying cause is identified in approximately 75% of patients, which may include malformations of cortical development or hypoxic ischemic injuries. Chromosomopathies are not usually associated with this syndrome. Late-onset LGS is rare and its variable presentation and progression can make it more difficult to recognize.

Method: Case report

Result: A 35-year-old woman was followed in the neurology department due to refractory epilepsy. She had a past history of developmental delay, where is karyotype was found to have an 10p14 chromosome deletion. Her epilepsy history started at age 24 with different types of seizures: generalized tonic-clonic seizures, drop attacks (tonic and atonic seizures), atypical absences and focal seizures. The patient did an extensive work-up and she was not eligible for resective epilepsy surgery, having undergone the placement of a vagus nerve stimulator. Since the beginning of seizures there was also a cognitive regression. EEG showed generalized slow spike-and-wave complexes (2-3Hz) during wakefulness and bursts of fast activity/ rapid rhythmic discharge

occurring in sleep, classically described in the LGS. Despite multiple efforts of antiepileptic optimization, her epilepsy worsened. Therapeutic adjustment was made taking into account the LGS diagnosis and there was an improvement in the frequency and intensity of the seizures

Conclusions: We present an unusual case of LGS due to its late onset. Syndromic diagnosis is important for the therapeutic guidance of these patients. There are associations between LGS and some chromosomal disorders, usually with late onset, however the relationship with the 10q14 deletion has not yet been described.

Abstract Number: 226

Title: DRAVET ENGAGE. Parent Caregivers of Children with Dravet Syndrome: Perspectives, Needs, and Opportunities for Clinical Research

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Purpose: Dravet syndrome (DS) is an intractable developmental and epileptic encephalopathy significantly impacting affected children and their families. A novel, one-time AAV-mediated gene regulation therapy was designed to treat the underlying cause of DS, potentially improving the full spectrum of DS manifestations. To ensure the first-in-human clinical trial addresses meaningful outcomes for patients and families, we examined their perspectives, priorities, goals, and desired outcomes in the design phase through a mixed methods approach (quantitative and qualitative).

Method: We conducted a non-identifiable parent caregiver survey, shared through a patient advocacy organization (n=36 parents; children age ≤6 years [y]). Parents were also engaged via three group discussions (n=10; children age 2–20y) and optional follow-up in-depth individual interviews (n=6). Qualitative data analysis followed an inductive interpretive process, and qualitative researchers conducted a thematic analysis with a narrative approach.

Result: Survey results revealed most children (94%) were diagnosed by age 1, with onset of seizures at mean age 6.2 months and other DS manifestations before 2y. The most desired aspects to address with potential new disease-modifying therapies were severe seizures (ranked by 92% of caregivers) and communication issues (development, expressive, receptive; 72–83%). Qualitative results emphasized the need for trial outcomes that recognize the impact of DS on the whole family. Parents eventually hope for trials including children of all ages, and were both excited about the potential positive impact of a one-time disease-modifying therapy and mindful of potential long-term implications. Their main aspirations were (1) to stop neurodevelopmental stagnation and (2) to reduce seizures and they agreed with the potential trial design presented.

Conclusions: To our knowledge, this is the first study within a patient-oriented research framework that specifically explored parents' needs and perceptions regarding clinical trials of a potentially disease-modifying therapy for children with a severe, developmental disease, such as DS.

Abstract Number: 245

Title: Diarrhoea in Patients With Lennox-Gastaut Syndrome (LGS) or Dravet Syndrome (DS) Enrolled in Four Phase 3 Clinical Trials of Cannabidiol (CBD)

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Purpose: CBD significantly reduced seizures with an acceptable safety profile in patients with LGS or DS in 4 clinical trials. Diarrhoea was one of the most common adverse events (AEs) and was more common in patients taking CBD than placebo. We used pooled data from LGS (GWPCARE3, 4: NCT02224560, NCT02224690) and DS (GWPCARE1, 2; NCT02091375, NCT02224703) trials to evaluate the incidence and resolution of diarrhoea in patients taking CBD at 10 mg/kg/day (CBD10) or 20 mg/kg/day (CBD20), or matched-placebo solution.

Method: Patients received a pharmaceutical formulation of purified CBD (Epidyolex®; 100 mg/mL oral solution) or matched placebo for 14 weeks. Incidence, time-to-onset, and resolution of diarrhoea were evaluated.

Result: Safety data included 714 patients (placebo, 285; CBD10, 131; CBD20, 298). Median (range) age was 11.0 years (2.2–48.0); the number of baseline antiepileptic medications was 3 (0–5). AEs were reported in 76% of patients taking placebo, 85% taking CBD10, and 91% taking CBD20. Diarrhoea occurred in 9% of patients on placebo, 14% on CBD10, and 22% on CBD20; most cases (placebo, 93%; CBD10, 89%; CBD20, 80%) were mild in severity. Most first occurrences of diarrhoea were reported within 6 weeks of starting treatment (placebo, 78%; CBD10, 78%; CBD20, 88%). Cases resolved within 4 weeks of onset in 93% of patients taking placebo, 94% taking CBD10, and 60% taking CBD20. An additional 6% of patients on CBD10 and 18% on CBD20 experienced resolution before trial end. Case studies describing management of diarrhoea in patients taking CBD in clinical practice are presented.

Conclusions: In clinical trials of CBD in patients with LGS or DS, diarrhoea occurred in all treatment groups but was most frequent in the CBD20 group. First onset occurred early during treatment in most patients. The majority of cases resolved within 4 weeks of onset.

Funding: GW Research Ltd.

Abstract Number: 264

Title: Benefit from the families' perspective and safety of long-term video EEG monitoring in pediatric patients

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Purpose: Long-term video-EEG monitoring (LVEM) is a useful tool, both for diagnostic and presurgical evaluation in children with epilepsy. Activation methods like sleep deprivation, and discontinuation of medication are frequently used, but carry the risk of repetitive seizures, seizure induced injuries, and status epilepticus. However, data regarding the safety of children in LVEM are still scarce. The objective of this study was to investigate safety and benefit from parents' perspective of in-hospital LVEM for pediatric patients.

Method: A monocentric retrospective cohort study was conducted. All LVEMs performed in children (aged 0-18 years) from January 2016 to December 2019, were evaluated retrospectively regarding paroxysmal event rate, and patients' benefits using a standardized evaluation protocol. Rate of status epilepticus, injuries and other adverse events occurring during LVEM was investigated.

Result: A total of 163 (88 boys and 75 girls, mean age 10.9 years) pediatric patients underwent 178 LVEM sessions, with a mean duration of 5.4 days. In 142/178 (79.8%) cases, LVEM activation methods were used, such as drug tapering or withdrawal (in 65.7%), sleep deprivation (44.9%), hyperventilation (27.0%), and intermittent photic stimulation (20.2%).The rate of habitual event detection was 69.1%. Patients or their families found LVEM helpful in 75% of cases. Significant improvements in the disease course were reported by 45% of epilepsy patients. Three episodes of non-convulsive status epilepticus occurred, representing 1.7% of admissions and 1.9% of patients diagnosed with epilepsy, while no injuries were observed. One infant was transferred to a pediatric ward due to a febrile infection. One case of thrombophlebitis due to infection of the intravenous line was also noted.

Conclusions: LVEM is well-tolerated with a low risk of status epilepticus and injuries. LVEM is beneficial for pediatric patients from the perspective of patients and their families, even if patients are ineligible for epilepsy surgery.

Abstract Number: 270

Title: Neurophysiological and imaging results in children with drug-resistant epilepsy.

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Purpose: assessment of neurophysiological and imaging changes in children with DRE for early determination of drug resistance and a correct therapeutic approach.

Method: In the years 2018-2020 in the Republic of Moldova was conducted a prospective study on 48 children with DRE who were subjected to the study by Video EEG monitoring, brain MRI 3.0T-epilepsy protocol and plasma assessment of antiepileptic drugs (AED).

Result: In 31.3% (CI 24.61-37.99; p = 0.07) of children, the EEG changes did not correspond to the type of crisis they developed and suggested the worsening of the evolution of EP; in 62.5% (CI 55.51-69.49; p = 0.01) of children a developmental abnormality of the central nervous system was detected; in 20.8% (CI 14.94-26.66; p = 0.05) of children the plasma level of AED was well below the norm, despite the fact that the dose was correct in kg / mass / body.

Conclusions: Evolutionarily aggravated neurophysiological changes, detected by Video EEG monitoring in children with uncontrolled drug EP are important for determining a correct conduct tactic. Imaging should be performed as early as possible in the DRE for early detection of developmental abnormality of the central nervous system, which can be considered a potential predictor of drug resistance. The plasma level of AED may suggest in favor of the type of resistance and the correctness of the selected preparation. Further studies of children with DRE are needed to improve their quality of life.

Abstract Number: 338

Title: Association of serum and radiological biomarkers with calcification and epileptogenesis in neurocysticercosis: a longitudinal observational study

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Purpose: Neurocysticercosis (NCC) is a common cause of epilepsy. The objectives of the current study were to estimate the association of

- serum matrix metalloproteinase-9 (MMP-9) and high mobility group of proteins box-1 (HMGB-1) with calcification and epilepsy in NCC, and
- perfusion MRI parameters with epileptogenicity in calcified NCC.

Method: Single live parenchymal NCC cases were recruited from May 2017 to November 2019 at a tertiary care teaching hospital in north India. Baseline serum MMP-9 and HMGB-1 were evaluated before initiation of cysticidal therapy. At 6 months follow up, cases were classified as calcified or resolved and in a subset of calcified cases perfusion MRI brain was done.

Result: Overall, 70 cases (median age of 120 months {IQR:84-132} with 57.1% {40} males) completed 6 months follow up (49 {70%} calcified and 21{30%} resolved). Breakthrough seizures were seen in 20 (28.6%). Breakthrough seizures were present in 19.1% of resolved and 32.7% calcified cases respectively (p=0.2). Amongst those with breakthrough seizures, 20 % and 80% cases were resolved and calcified respectively (p=0.0002).
Median serum MMP-9 and HMGB-1 levels were more in the calcified group compared to resolved and in those with seizures compared to those without, however the differences were statistically not significant.
In a subgroup of calcified cases (n= 31) perfusion MRI was done of which 12 had breakthrough seizures. The median perilesional rCBV (relative cerebral blood volume) was less for those with seizures (10.7 {3.2-23.6}) compared to those without (25.2 {0.61-244.5}) (p = 0.05) implying perilesional chronic ischemic changes in the former, probably consequent to increased inflammation during acute degeneration of the cyst.

Conclusions: Serum biomarkers may not be predictive of outcome in single parenchymal NCC, as it's a localized brain infection. Neuro-radiological evaluation of inflammation provides a suitable option for the same and should be further evaluated.

Abstract Number: 341

Title: Advanced neuroimaging and qEEG correlates of cognition and behaviour in childhood and adolescent onset pharmaco-responsive non-lesional epilepsy

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Purpose: Pharmaco-responsive non-lesional epilepsies (PRNLE) constitute 50-60% of epilepsies and are of presumed genetic origin. The purpose of the study was to determine advanced imaging and quantitative electroencephalogram (qEEG) correlates of cognition and behaviour in this population for better understanding of the underlying biology.

Method: Fifty PRNLE cases, aged 6-17 years, seizure free for atleast 12 months, presenting to a tertiary care teaching hospital from January 2019-December 2020 in north India were included. They underwent evaluation of cognition, executive function (EF) and behaviour using Wechsler Intelligence Scale for Children (WISC-IV), Stroop test and Childhood Behaviour Checklist (CBCL) respectively. The WISC-IV and CBCL parameters were compared with age-matched, 31 normal historical controls. All the cases underwent DTI (diffusion tensor imaging), fMRI (functional magnetic resonance imaging) and qEEG evaluation.

Result: Mean age of the subjects was 146.2±34.1 months (66% males and 60% focal epilepsy). Compared to controls, in cases, mean full scale intelligence quotient, verbal comprehension index and perceptual reasoning index scores were significantly less and proportion of subjects having abnormal total and domain (social, attention and aggression) CBCL scores were significantly more.
Fractional anisotropy (FA) of uncinate fasciculus had significant positive correlation with cognition and EF scores. In cingulate fibres, right and left inferior fronto-occipital fasciculus and corticospinal tracts, FA had significant negative correlation with CBCL scores. Task related fMRI analysis showed significantly differential activation of insula, lingual gyrus, calcarine and cingulate cortex between impaired and unimpaired EF. Spectral powers of faster (γ) and slower (θ, δ) frequencies on qEEG showed significant positive and negative correlation respectively with cognition and EF scores.
Conclusions: The impairments in cognition, EF and behaviour in PRNLE is associated with abnormalities in axonal integrity of white matter association fibres, composition of background brain frequencies and functional integrity of inhibition pathways.

Abstract Number: 352

Title: The Clinical, Economic, and Humanistic Burden of Dravet Syndrome – A Systematic Literature Review

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Purpose: Dravet syndrome (DS) – a rare, treatment-resistant developmental and epileptic encephalopathy associated with *SCN1A* mutations – is a lifelong disorder characterized by early seizure onset, and severe neurodevelopmental and behavioral challenges. While published data on the burden of DS are increasing, a comprehensive review is lacking. This study aimed to synthesize estimates of the clinical, economic, and humanistic burden of DS.

Methods: A systematic review using Medline/EMBASE was conducted following Preferred Reporting Items for Systematic Review (PRISMA) guidelines. Data on the frequency and severity of clinical impacts by age, and the economic and humanistic (health-related quality-of-life [HRQoL]) burden of DS were synthesized.

Result: One hundred and thirty-two studies of DS patients were included, which included several recent large prospective studies; most older studies were small with short follow-up. Data on age-specific rates for clinical outcomes were limited; SUDEP remains the most common cause of death across age groups. First seizures occur during infancy and are frequently prolonged; the frequency of nighttime and convulsive seizures increase throughout childhood. Behavioral problems, neurologic impairments, and delayed motor development are often detected by age two years, and become more frequent with age. Costs data, available from the USA and Europe, were challenging to compare due to variability in samples, designs, and healthcare systems. The impact of DS on patient and caregiver HRQoL is dramatic, with many patients requiring 24-hour care. Key drivers for patient burden were disease progression, behavioral changes, and disability; for caregivers, drivers included patient severity, the extent of caregiving, and impact on activities of daily living.

Conclusions: While robust data on the clinical burden of DS are emerging, data characterizing the economic and humanistic burden, and the age-specific frequency of seizures and neurodevelopmental manifestations are lacking. More rigorous longitudinal studies using standardized measures to sufficiently characterize the burden of DS are needed.

Abstract Number: 376

Title: Efficacy of Levetiracetam VS Phenytoin in neonatal seizure in rural area of Thailand

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Purpose: Neonatal seizure is the emergency condition that effected to neurodevelopment and mortality. The prompt treatment and seizure termination is very crucial. Previous studies determined the efficacy of different type of antiepileptic drugs (AEDs), there is no concensus toward second-line AEDs in neonatal seizure. This study, we aimed to compared the efficacy of second-line AEDs in neonatal seizure, compared between Levetiracetam and Phenytoin.

Method: This is the retrospective cross sectional study. We recruited patients with diagnosis of neonatal seizure who admitted at Maharat Nakhon Ratchasima Hospital, Thailand, during 1st January 2018- 31th December 2020. Patients who had clinical seizure refractory to first-line AED (Intravenous Phenobarbital) and recieved second-line AEDs as Intravenous Levetiracetam or Intravenous Phenytoin were included. Etiologies of seizure, seizure types and other demographic data were recorded. The efficiacy of Levetiracetam and Phenytoin were determined compared the duration of seizure, the need for third-line AEDs and morbidity as developmental outcome, diagnosis of cerebral palsy and mortality rate.

Result: Total 25 patients (68% male) were recruited. 64% was diagnosed of HIE. The most common seizure type was subtle seizure (56%). 56% recieved Levetiracetam and 44% recieved Phenytoin as second-line AEDs. The mean duration of seizure was significantly different as 28.12 min in Levetiracetam and 42.72 min in Phenytoin (p-value 0.01). The drug adherence was higher in Levetiracetam group. 16% of Levetiracetam groups needed third-line AEDs to controlled seizure while 64% of Phenytoin group needed third-line AEDs but had no statistical significant. Mortality was 20% and 48% were diagnosed of cerebral palsy. There was no significant different of mortality and morbidity in two groups.

Conclusions: Levetiracetam had better efficacy in seizure controlled than Phenytoin in neonatal seizure but had no different effected to mortality and morbidity.

Abstract Number: 377

Title: The coexistence of idiopathic focal and idiopathic generalized epilepsies in children. It is not by chance!

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Purpose: Analysis of case histories of patients observed in Svt. Luka's Institute of Child Neurology & Epilepsy with coexistence of Idiopathic (Genetic) Focal and Idiopathic Generalized Epilepsies in children.

Method: We observed 33 patients aged 6 - 16 years (14 males and 19 females) with coexistence of electroclinical signs of idiopathic focal and idiopathic generalized epilepsies. An analysis of case history data, characteristics of epileptic seizures, video EEG monitoring and MRI was made, efficacy of antiepileptic treatment, and specific features of the clinical course and outcome are presented.

Result: In our patients we revealed two variants of combination: (1) idiopathic focal (rolandic or occipital) epilepsies and idiopathic generalized epilepsies (childhood absence epilepsy or eyelid myoclonia with absences - Jeavons syndrome) or (2) idiopathic generalized epilepsies in combination of BFEDC (benign focal epileptiform discharge of childhood) on EEG. These cases have some characteristic features: epilepsy started with focal seizures ("rolandic" or "occipital" type) and then transformed to generalized seizures (absences, generalized tonic–clonic, myoclonic and eyelid myoclonus) with presence of BFEDC on EEG. All patients have epilepsy onset in the childhood. This cases unlike epileptic encephalopathies with pattern CSWS, has the favorable prognosis because of seizure freedom and normal cognitive functions. The combination of valproates with ethosuximide (in some cases sultiam or topiramate) was optimal to control seizures and epileptiform activity. Prolonged seizure free period was achieved in 88%, but full electroclinical remission - 57.5% of cases.

Conclusions: Coexistence of idiopathic focal and idiopathic generalized epilepsies in children is not by chance. It has as background the common etiological factor - probably genetically determined «hereditary impairment of brain maturation». We revealed two variants of combination of idiopathic focal and idiopathic generalized epilepsies. The main result of our investigation – that this combination has a benign course for both seizures and cognition.

Abstract Number: 394

Title: The Transition Needs of Adolescents with Epilepsy: Comparing the Needs of Patients with Varying Cognitive Abilities

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Purpose: Adolescents with epilepsy experience a significant disruption in care when they transition from their pediatric neurologist to their adult one. Research has consistently demonstrated the importance of transition clinics; helping to educate and prepare these youths for their transition. Despite this, little research has compared the potentially varying transition needs of adolescents with epilepsy with typical development, mild intellectual disability (ID), and moderate-to-severe ID.

Method: In order to examine the potential differences in these three groups, baseline transition scores of 162 adolescents with epilepsy (113 typically developing, 20 with mild ID, 29 with moderate-to-severe ID) between the ages of 14 and 18, were examined and compared. Caregivers scores were used for the third group.

Result: When looking at participants with typical development, analyses found that older adolescents scored significantly higher on transition readiness than younger adolescents ($F(4,108)=5.522$, $p=.000$). Further examination of these older adolescents showed that they had developed the skills needed to manage their condition independently but lacked the skills needed to advocate for themselves. When looking at participants with mild ID, analyses found that transition scores did not significantly differ between younger and older adolescents ($F(4,18)=1.048$, $p=.418$). Further examination showed that these older adolescents lacked both the ability to advocate for themselves and the ability to manage their conditions independently. When looking at participants with moderate-to-severe ID, caregivers scored high on all transition items; suggesting that they had acquired the skills needed for transition. However, further assessment revealed the need for financial and social support for caregivers.

Conclusions: Results of this study show that the transition needs of this population change depending on the patient's cognitive ability; suggesting that "one-size-fits-all" transition clinics may be ineffective. Instead, it is important to have separate streams within transition clinics to ensure that the unique needs of all patients are met.

Abstract Number: 408

Title: Long-term outcome in a novel rat model of birth asphyxia and neonatal seizures matches with clinical findings: Paving the way for prevention studies

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Purpose: Birth asphyxia is a major cause of neonatal death and brain damage. The initial hypoxic-ischemic encephalopathy (HIE) is often associated with seizures, and the later-life outcomes include epilepsy, and motor, cognitive and behavioral impairments. Preclinical studies are urgently needed for development of effective therapies that prevent HIE and its consequences. Thus far, the most popular rodent models have used either exposure of intact animals to hypoxia, or a combination of hypoxia and surgically induced ischemia for induction of neonatal seizures and adverse outcomes. However, such models lack systemic hypercapnia, which is a fundamental constituent of birth asphyxia with major effects on neuronal excitability. Here we used a novel noninvasive rat model of birth asphyxia and neonatal seizures to study later-life adverse outcomes.

Method: In male and female postnatal-day 11 rats, intermittent asphyxia was induced by exposure to gas mixtures containing 9% or 5% O_2 (three 7+3 min cycles) at constant 20% CO_2. All pups exhibited seizures after asphyxia. Behavioral tests were performed systematically for over 14 months. The development of epilepsy was determined by video-EEG monitoring. Furthermore, structural brain alterations were examined.

Result: The animals showed impaired spatial learning and memory and increased anxiety when tested at 3-14 months of age. Video-EEG carried out at >10 months showed an abundance of spontaneous seizures, which was paralleled by neurodegeneration in hippocampus and thalamus, and by aberrant mossy fiber sprouting.

Conclusions: The present model recapitulates both the physiological aspects of birth asphyxia, and several of the later-life consequences associated with human HIE. Interestingly, the anxiety-related behavior increased with age, which matches with results observed in the Dunedin Multidisciplinary Health and Development Study. This model thus allows evaluation of the efficacy of novel therapies designed to prevent HIE and seizures following birth asphyxia, and how such therapies might alleviate long-term adverse consequences.

Abstract Number: 409

Title: Epilepsy and its mimickers in children referred to a dedicated first seizure clinic

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Purpose: We evaluated the range of diagnoses in children referred to the first seizure clinic of a tertiary hospital.

Methods: We retrospectively reviewed medical records of all children referred to our first seizure clinic – that combines consultation and a routine EEG recording – between 2008 and 2018 after experiencing one or more paroxysmal events, possibly seizures. The initial diagnosis, made after the first consultation, was compared with the diagnosis obtained after additional examinations and clinical follow-up of at least one year.

Results: We included 938 children (56.8% boys) with a mean age at presentation of 6.7 ± 4.7 years. In total, 312 children (33.3%) eventually received a definite diagnosis of epilepsy. In 60.6% of those the diagnosis was made after the first consultation. Epileptic abnormalities were seen on first EEG recordings in 63.1% children with a final diagnosis of epilepsy. In only two children, an initial diagnosis of epilepsy was rejected after follow-up. Half of the children with epilepsy were diagnosed with an electroclinical epilepsy syndrome. Childhood epilepsy with centro-temporal spikes, childhood absence epilepsy, and juvenile myoclonic epilepsy were the most common syndromes. Epilepsy etiologies included, among others, structural lesions (21.5%) and presumed or established genetic abnormalities (37.5%). Children without epilepsy often had staring spells, reflex syncope, sleep related conditions, tics, migraine, and breath-holding spells. Epileptic EEG abnormalities were seen in 4.0% of those in whom the diagnosis of epilepsy was rejected.

Conclusions: One third of all children referred to our first seizure clinic were diagnosed with epilepsy. Fast and reliably diagnosing epilepsy in children who present after one or more seizure-like events remains challenging due to the variety of seizure mimickers and the moderate diagnostic yield of routine EEG recordings. This study highlights the value of dedicated first seizure clinics in the diagnostic process.

Abstract Number: 428

Title: Rescue Medication Administration And Its Clinical Implication In Pediatric Patients with Status Epilepticus

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Purpose: Since there is limited data available of using rescue medication (RM) in Middle East region, our aim of this study is to gain further understanding regarding the use of RM in pediatric patients diagnosed with status epilepticus (SE) at KFSHRC in Riyadh, KSA.
Also, to determine the characteristics of SE in our group of patients and to identify potential areas for intervention to reduce the complications of SE.

Method: Out of the 281 potentially eligible patients, 200 patients met the criteria.
This is a cross sectional retrospective study conducted at KFSHRC in Riyadh from 2008-2020.
In case of missing or incomplete data we prospectively corroborated data with families and if data still missing, we exclude them from the study.

Result: Out of 200 SE pediatric patients, (60%) were boys and (40%) were girls, with (68.4%) were pre-school age. SE was continues in (62.0%) and majority (81%) presented with generalized onset.
The most common etiology is genetic 25%. Furthermore, the main precipitating factors were co-infection (60%) and abrupt or withdrawal of AEDs in (10%).
Regarding outcome, 40% required ICU admission with refractory SE and mortality reported in (10%) cases.
Giving sub therapeutic dose of RM was associated with prolonged length of hospital stay (p0.018).
In our population we found out that the median time to reach the ER was more than 50 minutes and to receive RM in patients who presented with SE was 8 minutes.
Although 78% of patients already have previous history of SE, only 16 patients received RM at home

Conclusions: Our study shed light into the low usage of pre-hospital RM as well as unacceptably delay management initiation. With the identification of these barriers to timely SE management, our center has taken on initiatives to improve management and time to RM administration.

Abstract Number: 432

Title: The Role of Neuropeptides in Electrical Status Epilepticus During Slow Sleep

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Purpose: The relationship between sleep and epilepsy has been recognized for long time. Sleep not only triggers epileptic seizures but also interictal epileptiform discharges (IED). Electrical status epilepticus during slow sleep (ESES) is an epileptic encephalopathy of childhood, characterized by diffuse or generalized spike-wave activity in electroencephalography (EEG) during non-rapid eye movement (NREM) sleep. The pathophysiology of ESES is not completely understood yet. Neuropeptides, involved in many physiological functions in human body, have also been demonstrated in several studies to function in sleep-wake cycle and display convulsant and anticonvulsant feature. In this study, we aimed to investigate the relationship between ESES and neuropeptides such as dynorphin, galanin, ghrelin, leptin, melatonin, orexin.

Method: Fifty-nine children with self-limited focal epilepsies between 4-15 years-old were divided into two groups according to their EEG features in NREM sleep as those with discharges remaining focal-bilateral focal (n:24) and those with discharges spreading into ESES pattern (spike-wave index greater than %70) and cognitive and/or behavioral disturbance (n:14). Twenty-one children with no medical history were included as controls. Level of neuropeptides named dynorphin, galanin, ghrelin, leptin, melatonin, orexin were measured in the sera of these three goups including the control group.

Result: The patients whose discharges converted to ESES pattern in sleep, showed a significantly higher leptin level and a significantly lower melatonin level compared to the control group. On the other hand, the level of orexin was found to be low in patients whose discharges converted to ESES pattern in sleep, compared to both the control group and epilepsy patients with focal-bilateral focal discharges.

Conclusions: These data emphasize that elevated or deficient levels of neuropeptides such as leptin, orexin and melatonin may be involved in ESES physiopathology through their actions on sleep-wake cycle and epilepsy seizures and facilitation of interictal discharges.

Abstract Number: 439

Title: The Long-Term Effects of Fenfluramine on Patients With Dravet Syndrome and Their Families: A Qualitative Analysis

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Purpose: CLINICAL TRIAL DATA INDICATE THAT FENFLURAMINE (FFA) PROVIDES MEANINGFUL REDUCTIONS IN SEIZURE FREQUENCY FOR PATIENTS WITH DRAVET SYNDROME (DS), WITH SIGNIFICANTLY MORE CAREGIVERS RATING PATIENTS AS “MUCH IMPROVED” OR “VERY MUCH IMPROVED” VS PLACEBO. THIS STUDY SOUGHT TO QUALITATIVELY ASSESS HOW FFA TREATMENT AFFECTS QUALITY OF LIFE (QOL) OF DS PATIENTS AND THEIR FAMILIES.

Method: STUDY PARTICIPANTS WERE PARENTS CARING FOR A CHILD WITH DS WHO HAD PARTICIPATED IN THE FFA CLINICAL TRIAL and clinicians who treated those patients. PARTICIPANTS RESPONDED TO QUESTIONS ABOUT SPECIFIC TREATMENT BENEFITS AND PARTICIPATED IN ONE-ON-ONE SEMI-STRUCTURED INTERVIEWS.

Results: To date, 59 caregiver participants (M47.8 y/o, SD 9.5; 85% female) and 3 clinicians (2 epileptologists/1 epilepsy nurse; M18.7 years in practice, SD 3.9; seeing M18 patients/week, SD 10) have been interviewed. The participants' children (M14.6 y/o, SD 8.1; range 2-33 years) had been receiving FFA at least 4.8 months (up to 59.2 months; M21.5, SD 16.3).

Parents/caregivers reported both seizure-related (ie, reductions in seizure activity, seizure triggers, post-ictal recovery times) and non−seizure-related benefits (ie, cognition, alertness, problem-solving, education, mood, motor function, sleep quality, speech) with FFA treatment. Caregivers reported feeling less overwhelmed, improved mood, and less personal and family stress. Clinicians independently corroborated caregiver reports. 98% of parent caregivers would "very" or "quite" likely recommend FFA to other families with children with DS.

Conclusions: CAREGIVERS REPORT THAT FFA TREATMENT IS ASSOCIATED WITH MEANINGFUL IMPROVEMENT IN MANY QOL DOMAINS FOR PATIENTS WITH DS WHO RECEIVE FFA AND THEIR FAMILIES. MANY REPORTED FEELING HOPE FOR THE FIRST TIME SINCE THE CHILD WAS BORN OR WAS DIAGNOSED WITH DS.

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Abstract Number: 443

Title: Predictive factors for the epilepsy occurrence in patients with Rett syndrome: thirty years of experience of a tertiary center from Serbia

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Purpose: The purpose of this study is to evaluate the influence of demographic characteristics and parameters of regression on the epilepsy occurrence in patients with Rett syndrome (RS).

Method: This retrospective study includes children with clinical diagnosis of RS examined or hospitalized at our Institute, from January the 1st 1986 until December the 31st 2016. The influence of the following factors on the epilepsy occurrence was considered: demographic characteristics at the end of the observation period (body weight, body height, head circumference) and parameters of developmental regression (hand stereotypes, speech function, hand function, sitting and walking function, existence of involuntary movements).

Result: The study included 94 girls. The average age at the time of analysis was 177.46 months (min 20, max 376 months, SD 88.29, median 179). At the time of analysis 40.7% of children had a body mass index below p3, 63.2% of the children had body height below p3, and 64.2% of children had head circumference below p3. The average age of onset was 18.98 months (min 5, max 36 months, SD 6.63, median 20). Hand stereotypes were observed in almost all (98.1%) girls with RS, and involuntary movements in 54.7%. At the end of the follow-up period, no girls spoke, 88.0% had no arm function, 32% did not sit, 72.7% did not walk, 86.5% had a respiratory disorder, and 50.6% had scoliosis. Epilepsy occurred in 73 (77.7%) girls in our study, whereas 70% had epileptiform altered EEG.

Conclusions: Our research has shown that the occurrence of epilepsy in patients with Rett syndrome is more common in children with smaller head circumference, do not preserve arm functions, do not sit and walk, do not speak, as well as those with respiratory disorders, scoliosis and pathological EEG findings.

Abstract Number: 446

Title: Predictors of atypical course of childhood epilepsy with centrotemporal spikes

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Purpose: Identification of factors influencing the course of childhood epilepsy with centrotemporal spikes.

Method: The retrospective study included data from 70 patients treated in our Center. All patients met criteria for childhood epilepsy with centrotemporal spikes, atypical childhood epilepsy with centrotemporal spikes, Landau-Kleffner syndrome and ESES and had data of brain MRI and video-EEG monitoring with sleep recording. 68% were patients with childhood epilepsy with centrotemporal spikes, 19% with atypical childhood epilepsy with centrotemporal spikes, 3% with Landau-Kleffner syndrome, 10% with ESES. Patient analysis was carried out in 4 categories: the age of onset, first antiepileptic drug respones, the presence of nonspecific changes in white matter of the brain, presence of diffuse spread of epileptiform activity.

Result: The age of onset of epilepsy before 3 y.o. was in 2% of childhood epilepsy with centrotemporal spikes, in 31% of atypical childhood epilepsy with centrotemporal spikes and in 14% of ESES. The onset of Landau-Kleffner syndrome was from 4 to 6 y.o in all cases. A positive response to initial therapy in patients with childhood epilepsy with centrotemporal spikes was in 83% of cases, and only in 15% of atypical childhood epilepsy with centrotemporal spikes. Nonspecific brane white matter changes were in 11% of childhood epilepsy with centrotemporal spikes patients, in 46% of patients with atypical childhood epilepsy with centrotemporal spikes, in 29% of ESES and not found in patients with Landau-Kleffner syndrome. Diffuse spread of epileptiform activity was found in 62% of patients with atypical childhood epilepsy with centrotemporal spikes, in 50% of Landau-Kleffner syndrome and in 100% of ESES.

Conclusions: Early onset of seizures, nonresponse on the start treatment, diffuse spread of epileptiform activity and nonspecific changes of white matter of the brain can be predictors of atypical childhood epilepsy with centrotemporal spikes, ESES and Landau-Kleffner syndrome.

Abstract Number: 453

Title: How the characteristics of the doctors who care pediatric patients with epilepsy in Latin America influence the communication of SUDEP

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Purpose: Relate personal characteristics of Latin American pediatric neurologists (PNs) who treat pediatric patients with epilepsy to their attitude towards communication of the risk of SUDEP.

Method: Latin American PNs were invited to participate in an online survey during August 2020. The survey included information about personal characteristics, complexity of epileptic patients attended, reported frequency, motivations and people included in the communication of SUDEP. An open question requesting information about personal experience was included. Responses were anonymized. The quantitative and qualitative data were analyzed.

Results: 380 PNs from 20 countries responded, approximately 18% of Latin American PNs. 34% of the sample reported to have experienced SUDEP firsthand. 75% responded it is relevant or very relevant to communicate

this risk of SUDEP, nevertheless only 18% communicate the risk of SUDEP very frequently or always. 77% reported the patient should be included during the communication of SUDEP risk. No significant differences in reported communication of SUDEP were found related to physician's age, level of experience or country, however professional experience with SUDEP, was a reason to leave patients out. Answering patients or caregivers questions, educating and as a strategy to improve adherence to treatment were reported as the main motivations to communicate the risk of SUDEP. Avoiding fear, low frequency and personal difficulties to approach SUDEP were the main reasons reported to not talk about the risk of SUDEP.

Conclusions: Latin American PNs consider SUDEP a relevant topic, but they usually don`t talk about SUDEP with families and patients. Risk factors are a strong reason to talk about SUDEP. The majority of doctors think that adolescents should be included in this conversation. Prejudices regarding the understanding of families and the lack of tools to address this issue were identified as barriers in SUDEP communication

Abstract Number: 467

Title: Post-Operative Outcomes of Epilepsy Surgery in Drug Refractory Pediatric Epilepsy From Western India

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Purpose: Uncontrolled seizures in drug refractory epilepsy (DRE) during childhood are known to be associated with developmental delay and cognitive decline. Cessation of seizures by epilepsy surgery in carefully selected cases along with reduction or discontinuation of anti-seizure medications (ASMs) has a significant impact on their cognitive and developmental outcome.

Method: We conducted a retrospective observational study of 150 medically refractory pediatric epilepsy patients who underwent epilepsy surgery, either anterior temporal lobectomy (ATL), or lesionectomy,between 2001 and 2018 with a follow-up of at least one year.Presurgical evaluation with a non-invasive protocol was done in all the cases.They were followed up periodically at three months,one year, five years and ten years post-op.Detailed neuropsychological assessment was done pre and post-surgery in all patients.
Result: 106 of 117 patients who underwent ATL completed one-year follow up, of which 88(83.01%) were seizure-free (Engel Class-1).Forty out of 41 patients (97.5%) who followed up at five years and all the seven patients who followed up at 10 years were seizure free. Thirty out of 33 post-lesionectomy patients completed a one-year follow up, of which 27(90%) were seizure-free (Engel class-1).At five years,10 out of 18 post-lesionectomy patients followed up, all of whom were seizure-free.Multiple seizure semiologies and extra-temporal epilepsies were found to be poor predictors among those who underwent lesionectomy.Significant improvement on behavior scales and quality of life scores was noted post-operatively.Improvement in verbal memory post right ATL and visual memory post left ATL was also observed.

Conclusions: Our results reiterate the current concepts surrounding the need for an early surgical intervention in a large cohort of refractory pediatric epilepsy cases. In addition to an improvement in seizure-freedom, a positive shift was notable in the overall quality of life and neuropsychological outcomes as well.

Abstract Number: 492

Title: Atypical febrile seizures. Descriptive analysis and utility of the videoelectroencephalogram

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Purpose: The aim of this study was to describe the clinical characteristics of patients with atypical febrile seizures and to analyze the role of the electroencephalogram (EEG) in predicting the recurrence of febrile and afebrile seizures.

Method: Pediatric patients in whom an EEG was performed due to atypical febrile crisis during a 3 years period were retrospectively identified and included from our prospective registry. Demographic, clinical and electroencephalographic variables were analyzed.

Result: In total 89 patients with atypical febrile seizures were analyzed. 68.4% were male and the median age was 22 months. 47.2% had a family history of febrile seizures. 74.2% presented at least 2 seizures in 24 hours, 18% presented focal-onset seizures, and 15.7% had duration greater than 15 minutes. During follow-up, 31.5% (n = 28) of patients had a recurrence of at least one febrile seizure and 5.6% (n = 5) had a spontaneous seizure. The EEG was performed with a mean of 7 days (median of 2). Only 11 patients (12.35%) had a pathological EEG tracing, 2 of them a focal slow and the remaining 9 regional epileptiform discharges, the majority at the frontal level (n = 6). The pathological EEG was associated with the appearance of afebrile seizures in the follow-up (10.7% vs 40% P = 0.05), but not with the recurrence of febrile seizures. The younger age at onset was associated with the recurrence of febrile seizures.

Conclusions: The percentage of patients with pathological EEG after atypical febrile seizures is low (12.35%), but it is significantly associated with the appearance of afebrile seizures during follow-up.

Abstract Number: 526

Title: What Magnitude of Reduction Is a "Clinically Meaningful" Change in Seizure Frequency? Analysis of Long-Term Fenfluramine Phase 3 Dravet Syndrome Data

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Purpose: A ≥50% reduction in monthly convulsive seizure frequency (MCSF) is traditionally accepted as clinically meaningful, although this threshold is largely empirically derived. Here, we used a robust, anchor-based method in a long-term open-label extension (OLE) study of fenfluramine for the treatment of Dravet syndrome to quantify the degree of MCSF reduction associated with various caregiver and investigator Clinical Global Impression of Improvement (CGI-I) ratings.

Methods: MCSF and CGI-I data were derived from an OLE interim analysis (N=330; 19 October 2020). Correlations between MCSF and CGI-I were analyzed by Spearman's rho. Receiver operating characteristic (ROC) analysis compared change in MCSF with binary versions of investigator and caregiver CGI-I Likert scale ratings. The cut point for a clinically meaningful change, defined by ratings of "Much Improved" or "Very Much Improved" on CGI-I, equaled the change in MCSF where sensitivity≈specificity.

Results: Caregiver or investigator CGI data at last visit were available from 299 and 313 patients, respectively. Median treatment duration was 631 days (range, 7-1086), with a fenfluramine dose range of 0.2-0.7 mg/kg/day. MCSF reduction was positively correlated with improvement in caregiver/investigator CGI-I scores (Spearman's rho, 0.530-0.545; *P*<0.0001). ROC analysis identified a ≥60.5% reduction in MCSF as the clinically meaningful cutoff for subjects rated as "Much Improved" or "Very Much Improved." Additionally, a ≥72% reduction in MCSF was associated with caregiver/investigator CGI-I ratings of "Very Much Improved."

Conclusions: This analysis of the association between percent reduction in MCSF and CGI-I rated by parents/caregivers or investigators suggests that a sustained ≥60.5% reduction from baseline in convulsive seizure frequency can be considered a clinically meaningful response in patients with Dravet syndrome.

Sponsor: Zogenix.

Abstract Number: 527

Title: Impact of Fenfluramine on Convulsive Seizure Frequency in Young (<6 years old) Patients With Dravet Syndrome: A Long-Term Open-Label Study

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Purpose: Fenfluramine has been demonstrated to reduce convulsive seizures in patients with Dravet syndrome, but its effectiveness in younger patients has not been separately reported. This post-hoc analysis was performed to assess the efficacy and safety of fenfluramine in young patients with Dravet syndrome (DS) (<6 years old at the time of initiation of treatment).

Methods: Patients (2-18 years old) with DS entered an open-label extension (OLE) study after completing 1 of 3 phase 3 studies. In the OLE, all patients initiated treatment with fenfluramine at 0.2 mg/kg/day. After 1 month, fenfluramine dose was titrated to optimal efficacy and tolerability up to a maximum dose of 0.7 mg/kg/day (absolute maximum, 26 mg/day), or 0.4 mg/kg/day (absolute maximum, 17 mg/day) for patients also receiving stiripentol.

Results: As of October 2019, 330 patients had enrolled in the OLE study and had been treated with fenfluramine for a median 631 days (maximum, 1086 days). A total of 91 patients (28%) were <6 years old. Median baseline monthly convulsive seizure frequency (MCSF) determined before double-blind treatment in the core phase 3 study in the <6-years-old cohort was 11.7 (minimum/maximum, 2.7/2719). During treatment with fenfluramine, MCSF was reduced by a median 70.3% compared to baseline (range, -100% to +187%; *P*<0.0001) in the <6-years-old group and by a median 62.1% (range, -100% to +711%; *P*<0.0001) in the ≥6-years-old group. The most frequently reported adverse events included pyrexia, nasopharyngitis, decreased appetite, and diarrhea. No valvular heart disease or pulmonary arterial hypertension was observed.

Conclusions: Treatment with fenfluramine provided sustained, clinically meaningful reduction in MCSF in both young and older DS patients. It is important to note that effective long-term control of seizures might be

expected to mitigate the negative neurodevelopmental outcomes reported to be associated with treatment-refractory seizures, particularly in early-onset epilepsy.

Funding: Zogenix, Inc.

Abstract Number: 548

Title: Potential benefit of D9-tetrahydrocannabinol in severe pediatric drug-resistant epilepsy: a case report

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Purpose: Cannabis has recently emerged as a promising treatment for seizures in specific pediatric drug-resistant epileptic encephalopathies. D9-tetrahydrocannabinol (THC) and cannabidiol (CBD) are the most abundant active compounds in cannabis. Studies to date have focused on the titration of CBD dosing and minimizing amount of exposure to THC. Our group reports a case of severe drug resistant pediatric epilepsy which developed breakthrough seizures on CBD-focused treatment and then became seizure free following the addition of THC.

Method: Demographic and clinical information was retrospectively determined through review of the patient chart from an electronic database (Telus PS Suite EMR software) at the Neurology Centre of Toronto.

Result: This was a previously healthy 4-year-old female who suffered an explosive onset of seizures of unknown etiology and subsequently developed an epileptic encephalopathy with significant ataxia. She failed multiple anti-epileptic medications and then responded to a whole-plant, CBD-rich extract oil. The preparation was 1:25 THC:CBD and was titrated to 10 mg/kg/day of CBD (corresponding THC dose of 0.4mg/kg/day). Her seizures immediately responded and she remained free of seizures for one year and her EEG completely normalized. She then developed sudden, multiple, frequent breakthrough seizures and recurrence of her encephalopathic picture. Following titration of CBD to 15 mg/kg/day, parents abruptly discontinued cannabis and she was slowly re-titrated up to 5.3 mg/kg/day CBD (with a corresponding THC dose of 0.1 mg/kg/day) without significant effect on seizures. Instead of continuing to titrate CBD, THC was added at night (dose of 0.1 mg/kg), to reach a total THC dose of 0.2 mg/kg/day. Briefly following this adjustment, without any other interventions, the patient became seizure free once again and repeat EEG demonstrated complete normalization.

Conclusions: This case brings forward the need for rigorous, well designed trials investigating the role of THC in severe drug-resistant epileptic encephalopathies.

Abstract Number: 570

Title: Prevalence of the EEG abnormality in overnight polysomnography of children.

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Purpose: The overnight polysomnography (PSG) is used as one of the diagnoses of sleep disorders. In addition to the evaluation of sleep and respiratory physiology, it is possible to find abnormal findings such as epileptic discharges and asymmetry by electroencephalography (EEG). It is known that the detection rate of epileptiform discharges during sleep is high in children, but there is little information on the pathological significance and treatment. We examine EEG abnormalities detected by PSG.

Method: The subjects were children under the age of 15 who underwent PSG from April, 2015 to March, 2020. EEG wearing site in PSG; F3, F4, C3, C4, O1, O2. Clinical information was collected by retrospective examination of medical records.

Result: Of the 1300 patients who underwent PSG, 68 patients(5.2%) detected epileptic discharges. Of these, 12 patients who had already been diagnosed with epilepsy and 27 patients who had not undergone general EEG were excluded. EEG was performed in 29 of 68 patients, and abnormal waves were found in 19 patients.

Conclusions: EEG abnormalities in PSG were observed in 5.2% excluding the history of epilepsy, and the results were similar to those reported in the past. There are two purpose of the PSG: (1) classification and severity of sleep apnea, and (2) diagnosis and evaluation of sleep disorders. Therefore, detection of epileptic discharges are incidental findings. There is some report suggesting a relationship between EEG abnormalities and transient cognitive impairment, and it is necessary to examine the pathological significance.

Abstract Number: 583

Title: A study on clinical profile of drug resistant epilepsy in children

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Purpose: Study on clinico-aetiological features of drug resistant epilepsy (DRE) in a cohort of children in a tertiary neurology care facility.

Method: Descriptive cross-sectional study conducted at Lady Ridgeway Children's Hospital. Children aged 1 month to 16 years with DRE defined according to ILAE definition.

Result: Total number of children evaluated was 60 with mean age of 8.6 years (SD 4.4); majority were in the 6-12 year category. Mean age of epilepsy onset was 2.2 years (SD 2.7). However, by age categories, largest group (40.0%) had onset between 0-6 months. Aetiology according to ILAE framework, majority remained unknown (46.7%). Structural (38.3%), genetic (5%), infections (3.3%), immune (5.0%) and metabolic (1.7%) encompassed the balance.
Commonest epilepsy type across all age groups was focal epilepsy (56.7%). Epilepsy syndrome was diagnosed in 24 (48.0%); West syndrome the commonest. Majority were developing normally at seizure onset (62.0%). Out of them, 14 subsequently slowed or regressed in development. Among those presented in status (48.3%), 31.6% had delayed development.
All these children were trialed on multiple ASDs. Some received other modalities of treatment such as immune therapy (30.0%), ketogenic diet (8.3%) and surgery (15.0%). All, except those who underwent epilepsy surgery had ILAE class 4 or 5 epilepsy control.

Conclusions: Majority of DRE in childhood began in infancy and majority remained without identifiable aetiology based on investigations offered. Detailed genetic testing will aid establishing their aetiology.

Abstract Number: 597

Title: Efficacy of repetitive transcranial magnetic stimulation therapy in children with focal drug refractory epilepsy: Randomized Sham Controlled Trial

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Purpose: To analyse the therapeutic effect of low-frequency repetitive Transcranial Magnetic stimulation (rTMS) on seizure control, cognition and behaviour in children with drug refractory focal epilepsy.

Method: Forty-nine children (5-18 years) with drug-refractory focal epilepsy with ≥4 seizures/month were randomly assigned to active (n=25) and sham treatment arm (n=24). The patient and outcome accessors were blinded. The seizure focus was localized with interictal, ictal EEG, Brain MRI and PET scan, wherever required. Cognition was assessed through Malin's Intelligence scale for Indian Children (MISIC) and behavior by Childhood behavior checklist (CBCL). rTMS protocol used: 10 days daily 45min session of 0.5Hz, 1200 pulses (2 trains of 600 pulses) at 110% of resting motor threshold (RMT) over seizure focus using figure-of-8 coil. The primary outcome (proportion of children who achieved >50% seizure reduction) and other study outcomes were assessed at 8 week post-therapy follow up.

Result: Baseline characteristics were comparable in the two groups. In active arm 76%(19/25) children achieved >50% seizure reduction verses 12.5%(03/24) in sham arm (p<0.0001), effect size 63.5% (95% CI: 42.1%-84.8%); mean weekly seizure reduced by 74.8±30.2% in active compared to 12.8±23.1% in sham group(p<0.001). Active arm had median percentage reduction in Spike-wave-index of 33%(17.6, 55.5; p<0.0001) vs 0(-13.3, 6.7) in sham arm. Between active and sham group mean change in IQ was 3.5±0.5 vs -0.91±0.3(p<0.0001); CBCL scores reduced in behavioral domains of inattention(-5.7±3 vs 0.41±0.7; p<0.0001), hyperactivity (-4.3±2.2 vs -0.5±0.2; p<0.006) and aggression(-3.1±0.5 vs 0.37±0.1; p<0.0001). Interestingly, motor cortex became more excitable/disinhibited after active TMS therapy as RMT got reduced by 7.84±0.12 vs -1.05±0.26. No major adverse events observed.

Conclusions: Targeted low frequency rTMS therapy is effective in inducing short term seizure control, cognitive and behavioral improvement in children with drug refractory focal epilepsy. rTMS reduces the degree of refractory epilepsy induced motor cortex disinhibition. *(CTRI/2019/02/017440)*

Abstract Number: 611

Title: Severe complications of influenza infection in SCN1A-Dravet syndrome

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Purpose: To determine the frequency and spectrum of complications of influenza infection in individuals with *SCN1A* positive Dravet syndrome (*SCN1A*-DS).

Method: Direct questioning of families and medical record review of 33 individuals with *SCN1A*-DS managed at the Royal Children's Hospital, Melbourne or the Austin Hospital Dravet clinic. Data obtained on individuals with a documented influenza infection included *SCN1A* variant, age, clinical characteristics prior to the influenza infection (including seizure types and frequency, antiseizure treatments, development, comorbidities and vaccination status), and detail of the influenza infection (including influenza type, presenting symptoms, investigations, treatment and sequelae).

Result: Seven individuals had nine documented influenza infections (eight influenza A, one influenza B) at age 0.8-11 years. One individual died due to pneumonia, and six presented to hospital in status epilepticus (eight admissions). Three individuals (four admissions), two of whom had received the seasonal influenza vaccine, recovered to baseline. Recovery was prompt in three admissions and took six weeks (gait deterioration) in the fourth. Three individuals (four admissions) were poorly responsive following termination of status epilepticus; brain imaging showed extensive bilateral cortical T2 hyperintensity acutely, with or without T2 hyperintensity of deep grey matter or diffusion restriction in subcortical U fibres. These individuals had permanent neurologic deficits compared with their baseline level of function, one having profound global impairments.

Conclusions: We identified a range of neurologic complications, some severe, suggesting that patients with SCN1A-DS are highly susceptible to sequelae of influenza infection. Safe administration of the seasonal influenza vaccine should be prioritised for this population.

Abstract Number: 613

Title: High prevalence of low bone mineral density and fractures in institutionalized children with refractory epilepsy and intellectual disability

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Purpose: To evaluate the prevalence of low bone mineral density (BMD) and the history of fractures in institutionalized children with refractory epilepsy and intellectual disability (ID).

Method: In 2016, all children residing in a long-stay care facility in the Netherlands (n=33) were invited to undergo a dual-energy X-ray absorptiometry (DXA) measurement of lumbar spine (L1-L4) and hip. Of the 26 children who participated, two were excluded due to unreliable scan results.
Data on fractures were retrospectively extracted from the medical files. Additionally, serum concentrations of albumin, calcium, and 25-hydroxyvitamin D were determined.

Result: Ages of the children (14 boys, 10 girls) ranged from 5 to 17 years with a mean age of 13.0 (±3.2 years). Four children (16.7%) were on monotherapy, the rest was on polytherapy.
Based on the Z-scores, eight children (33.3%) had a normal BMD and sixteen children (66.7%) a low BMD (Z-score ≤-2.0). According to the criteria of the International Society for Clinical Densitometry (ISCD), three of the latter group were considered as osteoporotic. They were 8, 10 and 17 years old at the time of BMD measurements.
Ten children (41.7%) were reported to have at least one fracture in their medical history, with a maximum of one child (4.2%) who suffered from nine fractures. Five children (20.8%) had had a major osteoporotic fracture. On the whole, serum concentrations of albumin-corrected calcium (2.28-2.50 mmol/L) and (supplemented) vitamin D (16-137 nmol/L) were within the normal range. Except for one child (95.8%), all were on vitamin D supplementation at the time of the study. Ten children (41.7%) were prescribed calcium supplements.

Conclusions: This study demonstrated that 67% of institutionalized children with refractory epilepsy and ID had low BMD and 42% had a history of at least one fracture, despite adequate supplementation of calcium and vitamin D.

Abstract Number: 625

Title: SISCOM in pediatric temporal lobe epilepsy

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Purpose: This study evaluates the association between subtraction ictal SPECT co-registered to MRI (SISCOM) hyperperfusion patterns and postoperative outcomes in children with drug-resistant temporal lobe epilepsy (TLE).
Method: A retrospective review of medical records and preoperative SISCOM imaging was performed. SISCOM hyperperfusion was categorized into four groups as follows; (i) anteromesial and anterolateral temporal hyperperfusion pattern; (ii) anteromesial and anterolateral temporal hyperperfusion plus posterior extension pattern; (iii) bilateral anterolateral temporal lobes hyperperfusion pattern; and (iv) atypical perfusion pattern; defined as hyperperfusion not consistent with aforementioned patterns. The association between 2-year postoperative outcomes and SISCOM patterns was evaluated using Fisher's Exact Test.

Result: Forty patients (15 females, 37.5%) were included, and the mean (±SD) age of seizure onset was 5 (±4.4) years. The mean (±SD) radiotracer injection latency was 23.1 (±16.0) seconds. Ten (25%), 14 (35%), 0 (0%), and 16 (40%) patients had SISCOM pattern (i), (ii), (iii), and (iv), respectively. Thirty-five patients (87.5%) underwent anterior temporal lobectomy, 3 patients (7.5%) underwent lesionectomy, and 2 patients (5%) underwent temporal corticectomy. Twenty patients (50%) had a favorable surgical outcome (ILAE class 1 or 2). SISCOM patterns were significantly associated with types of focal cortical dysplasia (FCD), (p-value = 0.04). FCD IIIa was seen most commonly in patients with SISCOM pattern (i) & (ii), (66.7% and 44.4%, respectively), while FCD IIa was seen most commonly in patients with SISCOM pattern (iv) (41.7%). There was no statistically significant association between SISCOM patterns and postoperative outcome (p-value = 0.92).

Conclusions: This study shows three types of SISCOM hyperperfusion patterns seen in children with drug-resistant TLE. SISCOM patterns were statistically significantly associated with types of focal cortical dysplasia. However, they were not statistically significantly associated with postoperative outcomes.

Abstract Number: 641

Title: The features of initial seizures and a further epilepsy course in a cohort of 22 children with CLN2 – a single center experience

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Purpose: The evaluation of epilepsy and the features of initial seizures in children with CLN2.

Method: The study included children with CLN2 treated in period from 2000– 2020. Diagnosis was confirmed by: TPP1 deficiency and/or CLN2 mutation, or pathognomonic electron-microscopy findings. The seizure features were evaluated: the age of onset, provocation, semiology, EEG and response to the treatment. Statistical analysis included T test, chi-square test, Wilcoxon-Mann-Whitney test, using SPSS statistics 25

Result: The study included 22 children with CLN2. Seizure was initial presentation in all cases, preceded by language delay in 18, and behavior problems in 14 pts. The first seizure was provoked in 9/18 children (febrile seizures in 7) at mean age of 33.8±4.6) months, and unprovoked in 9/18 at mean age of 34.8±2.0 months. The

average period from initial seizures to diagnosis was longer (35.1 months), with lower HS in provoked then in unprovoked (23.8 months) first seizures (p<0.008). Initial seizure were GTC (8), atonic (8), focal onset (4), with recurrence of seizure within two months in all. Multiple seizure types were recorded with progression: focal onset and myoclonic in all, GTC in 77%, atypical absence and/or atonic and/or provoked by fever each in about 50%. More than 1/3 experienced at least one episode of status epilepticus. A PPR during low-frequency photic stimulation was noted in 17 patients.

Conclusions: CLN2 patients have provoked initial seizures in 50% leading to later diagnosis comparing to children with the first unprovoked seizure. Febrile seizure might present the onset of progressive disease, and we point the red flags: preceding language delay and behavior problems, later onset comparing to the age when the first febrile seizure is the most frequent, atonic or focal seizure type, and recurrence of seizures within two months.

Abstract Number: 648

Title: Pulse Methylprednisolone with Oral Prednisolone versus Adrenocorticotropic Hormone In Children with West Syndrome: A Randomized Controlled Trial

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Purpose: West syndrome is an epileptic encephalopathy of infancy. According to guidelines Adrenocorticotrophic hormone (ACTH) is probably effective for short term management of infantile spasm but there is little uniformity in treatment due to variable response. This study has been done to evaluate the efficacy of pulse methylprednisolone as compared to ACTH in children with West syndrome in Bangladesh.

Method: Children between 3 months to 24 months with the diagnosis of West syndrome were included and ACTH and pulse methylprednisolone followed by oral prednislone were given after randomization. Total duration of treatment was 6 weeks in both groups.

Result: Total 87 children were enrolled; 12 patients lost in follow up. Finally 43 received ACTH and 32 received pulse methylprednisolone. In pulse methylprednisolone group 25.58 % showed 50-80% response, 25% showed 80-99 % response and 6 (19%) patients showed 100% response. In ACTH group , 41.8% showed 50-80% response, 25.58% showed 80-99 % response and only 3(6.91%) patients showed 100% response. Methylprednisolone treatment regimen did not cause significant or persistent adverse effects in children.

Conclusions: Pulse methylprednisolone followed by oral prednisolone for 6 weeks is as effective as ACTH. Thus Methylprednisolone therapy can be an important alternative to Adrenocorticotrophic hormone (ACTH).

Abstract Number: 649

Title: Yield of brain imaging of healthy children with first unprovoked non-febrile seizure

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Purpose: The aim of brain imaging (BI) following a first seizure is to investigate for an underlying structural aetiology which may require intervention. Current National Institute for Health and Care Excellence guidelines recommend performing MRI brain after a first seizure in: 1) all children under the age of 2 years; and 2) those with evidence of a focal onset on history, examination, or electroencephalogram, other than in benign focal

epilepsy. The aim of this study was to determine the yield of BI in healthy individuals following a first unprovoked afebrile seizure.

Method: Between Jan 2015 – 2021, 197 patients under the age of 17 years with a first seizure were examined. Those with: seizure onset during first month of life; insufficient information; recent head injury; or previous diagnoses of coagulopathy, developmental delay, or specific learning difficulties were excluded. The remaining 71 eligible patients had MRI Brain (epilepsy protocol) arranged. Of these, 3 patients failed BI procedures or did not attend, and 68 received the scan. MRI reports were categorised into normal or abnormal, with the abnormality considered significant if prompt referral or urgent intervention was required.

Result: Out of the 71 eligible patients, 37% were male and 34% female, with age range between 3 months and 16.4 years; mean age of seizure onset 7.7 years. A family history of epilepsy was identified in 21% of patients. MRI Brain was found to be normal in 65 of the 68 patients (96%), with the remaining 3 (4%) scans reported as abnormal. However, none of these were considered to be significant abnormalities.

Conclusions: Based on our findings, BI should not be routinely arranged for healthy children following a first seizure. The most important modality in the evaluation of a first seizure is a detailed medical history and physical examination.

Abstract Number: 676

Title: Next generation sequencing in children with seizure onset after two years of age: update over 2 1/2-year program in Europe and Middle East

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Purpose: Neurologic and metabolic disorders that include epileptic seizures are among the most common genetic disorders presenting in childhood. A molecular diagnosis for patients with epilepsy may allow for etiologically based treatment and management therefore maximizing the diagnostic yield in this group of patients has important implications. Goals of the program are to determine, in pediatric epilepsy patients between 2-5 years of age, the overall molecular diagnostic yield and the impact on diagnosing neuronal ceroid-lipofuscinosis type 2 (CLN2), a severe, rapidly progressive neurodegenerative disease with seizure onset at/after 2 years of age.

Method: A next generation sequencing (NGS)-based epilepsy panel was used. Copy number variant (CNV) detection from NGS was included. Variant interpretation was performed according to ACMG guidelines. The program was sponsored by BioMarin Pharmaceutical Inc.

Result: The results from 541 patients with first seizure at or after 24 months, and one additional clinical finding are reported. The median age at testing was 39 months and at first seizure was 28 months. The average delay from first seizure to genetic testing was 8.6 months. A genetic diagnosis was established in 115 patients for a molecular diagnostic yield of 21.3%. CNVs were reported in 20% of diagnosed patients and 28% of the CNVs identified were intragenic. The frequent molecular diagnoses included *MECP2* (12 patients), *TPP1* (*CLN2*) (11 patients), *SCN1A* (10 patients) and *SCN2A* (9 patients). CLN2 cases received a molecular diagnosis at an average age of 3 years 11 months, 1-2 years earlier than natural history data. At least 72 (62.6%) patients who received a molecular diagnosis had a disorder with targeted treatment, treatment optimization options, or on-going clinical trials available.

Conclusions: Our findings further the importance of the early use of genetic testing in this age group to efficiently identify severe disorders with targeted management available such as CLN2.

Abstract Number: 687

Title: Clinical utility of a sponsored gene panel testing program for pediatric epilepsy and CLN2 disease diagnosis: Results from 10,853 tests

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Purpose: Neuronal ceroid lipofuscinosis type 2 (CLN2 disease) is a rare, inherited, neurodegenerative lysosomal storage disorder caused by deficient activity of tripeptidyl peptidase (TPP1), encoded by the *TPP1* gene. CLN2 disease often presents with epilepsy between 2 and 4 years of age, accompanied by a history of language delay. However, limited disease awareness and the nonspecific nature of initial symptoms mean that diagnostic delays are common. Behind the Seizure® (BTS) is a sponsored, genetic testing program for pediatric epilepsy. The genetic tests and services are performed by Invitae.

Method: The BTS program uses a panel of more than 180 genes associated with both syndromic and non-syndromic causes of epilepsy. Individuals were eligible for testing through BTS if they were aged 24–60 months with unprovoked seizure onset at/after 24 months (Dec 2016 to Feb 2019) or, following program expansion, aged 0–60 months (Feb 2019 to Jan 2020) or 0–108 months (Jan to Nov 2020) with unprovoked seizures onset at any age.

Result: Between December 2016 and November 2020, a total of 10,853 tests were conducted through the BTS program. The molecular diagnostic yield was 13.6 % overall (n=1471; 103 genes) and 0.18% for *TPP1* (n=20). In the subset of individuals tested through BTS who were aged 24-60 months with seizure onset at or after 24 months (n=3,335), the molecular diagnostic yield was 7.3% overall (n=242) and 0.6% for *TPP1* (n=20). The average age of CLN2 disease diagnosis through the BTS program was 1-2 years earlier than the natural history reported average of 5 years. *TPP1* was the highest positive yield gene for autosomal recessive disorders.
Conclusions: These findings demonstrate that the use of broad epilepsy gene panel tests can facilitate the earlier diagnosis of CLN2 disease, and simultaneously identify other genetic causes of epilepsy.

Funding: BioMarin Pharmaceutical Inc.

Abstract Number: 691

Title: Ganaxolone Significantly Reduces Major Motor Seizures in CDKL5 Deficiency Disorder: A Randomized, DB, Placebo-Controlled Phase 3 Study

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Purpose: CDKL5 deficiency disorder (CDD) is a rare, genetically determined developmental and epileptic encephalopathy. Clinical characteristics include early-onset refractory epilepsy, severe neurodevelopmental

impairment, and major motor delay. Seizures associated with CDD are often refractory to treatment with existing antiseizure medications (ASMs) and improvements may be short-lived.

Method: In this global, double-blind, placebo-controlled, phase 3 trial, patients aged 2-21 years with a pathogenic *CDKL5* variant and uncontrolled major motor seizures (MMS >16/month) were randomized to adjunctive ganaxolone (maximum 63 mg/kg/day or 1,800 mg/day, TID) or placebo for 17 weeks. MMS were defined as bilateral tonic, generalized tonic-clonic, atonic/drop, bilateral clonic or focal to bilateral tonic-clonic. The primary endpoint was percentage change from baseline in major motor seizure frequency (MMSF) during the treatment period. Key secondary endpoints included ≥50% responder rate and clinical global impression of improvement (CGI-I) at the end of the treatment period.

Result: A total of 101 patients (79% female, 21% male) were randomized, 50 to ganaxolone and 51 to placebo. Patients were a median age of 6 years and had tried a median of 7 prior ASMs. Baseline median 28-day MMSF was 50.0 in the ganaxolone group and 57.3 in the placebo group. Patients taking ganaxolone experienced a median 32.2% reduction in MMSF relative to baseline compared to a 4.0% reduction in the placebo group during the treatment period (p=0.002, Wilcoxon Rank-Sum Test). Ganaxolone demonstrated improving trends (not significant) in the key secondary endpoints. Subgroup analyses suggest ganaxolone demonstrated MMSF reductions across the broad CDD population studied. The most common adverse events, occurring in ≥ 10% of patients and more frequently in the ganaxolone group, were somnolence, pyrexia and upper respiratory tract infections.

Conclusions: These data provide strong evidence that ganaxolone is effective and generally well-tolerated in the treatment of refractory epilepsy in patients with CDD.

Abstract Number: 699

Title: Treatment options in a case of focal cortical dysplasia

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Purpose: *The present paper aims at describing the challenges encountered in the management of a focal cortical dysplasia case.*

Method: *We present the case of a 12 years old boy, with unremarkable pregnancy and birth history and normal development, that presented phamacoresistant epilepsy with focal onset seizures at the age of 7 years.* From onset the seizure frequency was high, with multiple seizures daily described as: he stopped moving, then had ample, alternative movements of the limbs, short duration, no postictal deficits. The parents described behavioral changes in the patient such as agitation and hetereoagresivity, simultaneous with seizure onset. Multiple antiseizure drugs were given, without a longterm efficacy. The seizure semiology, ictal videoEEG, brain MRI ant PET-CT were concordant for a FCD involving the left cyngulate gyrus. At the time of investigations, the patient was receiving VPA and LTG in correct dosage and underdosed Nitrazepam. A decision to adjust Nitrazepam was made and subsequently the patient stopped having seizures. The parents were informed on the available treatment options, including epilepsy surgery and it was also explained that the current seizure-free period was most likely transitory. The parents refused to go further with the presurgical evaluation and the patient was lost to follow-up.

Conclusions: *We consider our patient to be suitable for epilepsy surgery with a possible good outcome. There are many factors involved in a patient's decision to decline surgery and they represent barriers to ideal care.*

Abstract Number: 705

Title: Epidemiology of West syndrome in Lubumbashi, Democratic Republic of Congo

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Purpose: West syndrome is a severe epileptic encephalopathy of the infant that is most often manifested between the 3rd and the 7th month of life. No data on this pathology is available in Lubumbashi, Democratic Republic of Congo. The objective of this study was to describe clinical, electroencephalographic, therapeutic, and outcome features of West syndrome.

Method: It was a prospective study, carried out at the University Clinics of Lubumbashi in the Democratic Republic of Congo, from July 2020 to March 2021. For each patient examined, we collected sociodemographic characteristics, clinical and electroencephalographic data, therapeutic modalities, and outcomes.

Result: We examined 6 infants with a male predominance (59%), whose mean age of appearance of spasms was 5 months (range: 2 and 9 months). History of neonatal suffering were noted in five infants (83.3%). In an infant, a polymicrogyrous cerebral malformation has been found. The epileptic spasms were present in all infants. Four infants (66%) presented flexural spasms and two (33.3%) presented mixed spasms. Psychomotor development was altered in all infants. The EEG showed hypsaryrhythmia in all patients. The sodium valproate is the most administered antiepileptic. The evolution was marked by stopping seizures in 5 infants.

Conclusions: West syndrome is an epileptic encephalopathy of the infant with specific clinical and electroencephalographic features. Magnetic resonance imaging and genetic testing are not available in our environment. In the absence of first-line treatment (adrenocorticotrophin), we resorted to the sodium valproate.

Abstract Number: 706

Title: Are you tuned in? The challenges of seizure identification in children with intellectual disability – a potential for video-based care-pathway

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Purpose: Epilepsy is common in children with intellectual disability (ID) and recognising seizures can be challenging. We aim to explore the challenges parents/carers face in seizure identification within children with co-existing epilepsy and ID.

Method: Eligible participants attending a tertiary epilepsy clinic were enrolled to the study with written consent. Qualitative interviews were carried out by a single interviewer. Transcribed verbatim, these transcripts were analysed. Themes and subthemes were drawn to reflect the findings. Each transcript was read and discussed by two members of the research team. NVivo 12 was the software used to assist data analysis.

Result: A total of 10 hours data gathered from 8 participants. The importance of knowing the child's normal and recognising changes to this baseline was consistently mentioned. All participants reported that being 'in tune' with their child assisted in seizure recognition. Most felt that health care professionals were poor at recognising seizures within their children. Participants had mixed thoughts on the difficulty the presence of a

learning disability provides to seizure recognition. The severity of the learning disability and the seizure type were the two main variables discussed.

Conclusions: Knowing the child well and understanding the normal behaviour of the child as an individual is crucial to seizure recognition. A detailed description of 'normal' behaviour and seizure presentation stored within the child's medical notes may assist health care professionals in improving seizure recognition. Our study highlights the potential benefit of a video-based care pathway, where videos could be used to illustrate examples of normal behaviour and seizure activity. Children with ID are likely to be looked after in multiple settings by different staff in school, respite and residential care settings. A video care plan is likely to reduce the chance of misdiagnosis normal behavior as seizures or failure to correctly identify epileptic seizures.

Abstract Number: 764

Title: Epilepsies associated with benign epileptiform discharges of childhood on EEG

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Purpose: To study a group of patients with epilepsies associated with benign epileptiform discharges of childhood (BEDC) on EEG, taking into account nosological, anamnestic, clinical, electroencephalographic, neuroimaging aspects and assessment of the efficacy of antiepileptic therapy.

Method: We examined 368 patients with various epileptic syndromes associated with BEDC on EEG (213 boys - 58%, 155 girls - 42%). The follow-up was carried out from 2010 to 2020.

Result: The study revealed three groups of epilepsy, including 11 epileptic syndromes. Group 1: idiopathic (genetic) focal epilepsy (IFE) - 54.1% of cases. Group 2: epileptic encephalopathies (EE) - 13.6%. Group 3: structural focal epilepsy associated with BEDC (SFE-BEDC) - 32.3%. Bilateral tonic-clonic seizures (BTCS) and focal clonic seizures (FCS) prevailed in all these groups (group 1: BTCS - 23%, FCS - 25.5%; group 2: BTCS - 18%; FCS - 26%; group 3: BTCS - 28%, FCS - 21%). As a result of observations, it was shown that while taking antiepileptic drugs, complete remission was achieved in 83.7% of cases in the general group (group 1 (IFE): 92.9%; group 2 (EE) - 54%; group 3 (SFE-BEDC) - 80.7%). According to the MRI results, structural changes in the brain were revealed in all patients (100% of cases) with SFE-BEDC. Periventricular leukomalacia in combination with cerebral atrophy and ventriculomegaly were most common (67 patients).

Conclusions: Our study demonstrated a wide range of forms of epilepsy associated with BEDC (11 epileptic syndromes), which have completely different prognosis. BEDCs can occur in IFE, in which patient's cognitive functions are normal and full recovery is possible. Also, BEDCs are recorded on the EEG during Epileptic Encephalopathies With Continuous Spike and Wave During Sleep, in which there is a regression of cognitive functions. A group of patients with structural focal epilepsy associated with BEDC deserves a separate study.

Abstract Number: 768

Title: A prospective study of neurobehavioral profile, inflammatory markers and response to steroids in ESES syndrome

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Purpose: Encephalopathy with Status Epilepticus in Sleep (ESES) is an epileptic encephalopathy characterised by progressive cognitive decline and behavioural abnormalities rather than seizures. We have prospectively studied the neurobehavioral profile, etiology, electrographic findings and response to immunotherapy in children with ESES. Baseline serum IL-6 and IL-8 levels in ESES were compared with age-matched children with well controlled epilepsy (WCE).

Method: Children (2-12 years) with immunotherapy naïve ESES (spike-wave index (SWI) in sleep ≥ 50%) were enrolled. Presenting complaints, SQ/IQ, behavioral problems (VSMS/MISIC and CBCL), and neuroimaging findings were documented. EEG was evaluated for background localization, SWI and sleep potentiation. Immunotherapy with five-day intravenous methylprednisolone pulse followed by oral steroids 2mg/kg for 6 weeks and tapering over next 6 weeks was given. Outcome assessed at six-months post therapy in form of change in seizure frequency, SQ/IQ and behavioural scores. Baseline serumIL6 and IL8 levels were compared with WCE (n=20) group.

Result: Twenty-three children with ESES {18 boys; median age 93 (78 to 120) mo were enrolled; pre-existent developmental delay was in 73%. Presenting complaints were cognitive decline {82.6%; median age: 21 ± 31 mo, global 69.5%, isolated language 13%}, behavioral problems {91.3%; inattention(15), hyperactivity(12), aggression(07), Autism(04), withdrawn(04), PDD(03)} and active seizures (56.5%). Etiology was structural in 56.5%. EEG characteristics were – Focal ESES (56.5%), SWI mean 82, (60-100); 50-75: 05, 75-100: 18; localization: anterior-07/23 and posterior-06/23, generalized -10/23. No seizures reoccurred in 10/13; SQ/IQ improved > 10-point in six, >5 point in nine. Hyperactivity, aggression and inattention improved to non-clinical range in 09/12, 05/07, 10/15 respectively. Serum IL-8 was significantly raised in ESES compared to WCE [50.42(25.3-189.89) vs 21.945(16.54-45.685), p=0.047].

Conclusions: ESES presents with complex neurobehavioral complaints, not all will have active seizures. Raised serum IL-8 levels may suggest ongoing neuroinflammation. Treatment with steroids improve seizures, behaviour and cognition in majority.

Abstract Number: 774

Title: Volumetric Analysis in Rasmussen's Disease

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Purpose: Rasmussen's Encephalitis is a rare, chronic neurological disorder characterised by drug resistant focal epilepsy, progressive neurological deficits, cognitive decline and unilateral hemispheric atrophy.

Anatomic changes of atrophy may be subtle in earlier phases of the disease, and progressive changes on serial scans may be difficult to observe with visual inspection only. We applied automated volumetric magnetic resonance imaging analyses to patients diagnosed with Rasmussen encephalitis to asses the degree of cerebral atrophy.

Method: We analysed 5 patients diagnosed with Rasmussen's encephalitis in our clinic. They underwent a total of 14 MRI. The volumetric analysis was made using VolBrain, an online MRI brain volumetry system. It works in a fully automatic manner and is able to provide brain structure volumes without any human interaction

Result: In al the analysed patients there was a volume loss detected. In one patient, there were very small differences between volumes on studies done 9 months apart. The only notable change was the initiation on imunotherapy.

Conclusions: The volumetric measurement enables quantitative analysis of various brain structures, allowing comparison in serial MRI studies. It also may assist the diagnosis of patients with Rasmussen's Encephalitis by providing additional information on the degree of atrophy, especially when changes are discreet.

Abstract Number: 775

Title: Pitfalls in Ketogenic Diet Initiation in an Infant with GLUT1 Deficiency Syndrome

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Purpose: GLUT1 deficiency syndrome is a rare, treatable neurological disorder, caused by a mutation in the SLC2A1 gene for which ketogenic diet (KD) represents the gold standard treatment. *The present paper aims at describing the difficulties faced when trying to initiate the* ketogenic diet *in a breastfed infant.*

Method: We present the case of a 26 months old girl, with unremarkable pregnancy and birth history, that presented phamacoresistant epilepsy with focal onset seizures and myoclono-atonic seizures. Subsequently she associated movement disorder and delayed psychomotor development. A brain MRI was performed which revealed delayed mielination. Early on, a genetic cause was suspected and testing revealed a variant in the SLC2A1 gene. At the time of diagnosis (8 months old), she was exclusively breastfed and a decision to wean her and start KD was made, together with the mother. Her KD consisted of expressed breast milk and Ketocal, in a 4:1 ratio.

Result: The process of weaning was stressful for both child and mother, the child refused alimentation which led to dehydration and metabolic acidosis and required transfer to the Pediatric Ward for metabolic compensation. The mother became progressively distressed, which led to a decreased compliance. Later, with familial and psychological support, the KD was reintroduced with better results.

Conclusions: *In the past, at the initiation of ketogenic diet the breastfeeding was stopped, because of the concern that the carbohydrate content of breast milk would prevent adequate levels of ketosis from being attained. However, given the importance breast milk has in a child's development, the psychological impact abrupt weaning has on child and mother with consequently decreased compliance, the incorporation of breast milk can be preffered options. With proper monitoring and psychological support, it is possible for infants to receive the ketogenic diet treatment while also continuing to benfit from breastfeeding.*

Abstract Number: 777

Title: Fenfluramine Provides Clinical Benefit in Adults and Children With Dravet Syndrome: Real-World Experience From the European Early Access Program

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Purpose: In a recently completed phase 3 program, patients with Dravet syndrome (DS) treated with fenfluramine demonstrated sustained, profound reductions in seizure frequency, prolonged periods of seizure freedom, and improvement in executive functions. The European Early Access Program (EU-EAP) was initiated to allow pre-approval access to fenfluramine for DS patients.

Methods: Patients with a confirmed diagnosis of DS for whom seizures were not adequately controlled by their current anti-epilepsy treatment regimen and who had no alternative options (eg, other treatment, access to a clinical trial) were eligible to enroll in the EU-EAP. Fenfluramine dosing typically was started at ≤0.2 mg/kg/day and was titrated based on efficacy and tolerability. Maximum dose was 0.7 mg/kg/day (absolute maximum, 26 mg/day), or for patients receiving concomitant stiripentol, 0.4 mg/kg/day (absolute maximum, 17 mg/day).

Results: A total of 150 patients with DS from the EU-EAP at multiple centers in Germany, Italy, Spain, and UK were included in this pooled analysis. The median age at the start of fenfluramine treatment was 7.2 years (range, 0.8-46 years), 49% were female, 96% had an *SCN1A* variant, and median exposure was 338 days. After 3 months (n=139), reductions in seizure frequency ≥50%, ≥75%, or 100% were observed in 79%, 56%, and 27%, respectively, and after 12 months (n=80), these seizure reduction thresholds were demonstrated by 80%, 51%, and 16%. Sixty-two percent were rated by the investigator as "much" or "very much" improved. Thirteen percent of patients have discontinued fenfluramine, primarily due to lack of efficacy. The most common adverse events were somnolence or sleep disorder (n=31) and loss of appetite (n=30). No valvular heart disease or pulmonary artery hypertension was observed.

Conclusions: DS patients treated with fenfluramine in a "real-world" setting experienced similar benefits and tolerability as those observed in phase 3 clinical trials.

Sponsor: Zogenix.

Abstract Number: 778

Title: Ketogenic diet in pediatric population: is antiseizure medication withdrawal a realistic goal?

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Purpose: Ketogenic diet is a safe and effective treatment for children with pharmacoresistant epilepsy and could help reduce drug load. The aim of this study is to investigate the feasibility of weaning antiseizure medication(s) (ASM) after commencing ketogenic diet in children and adolescents and identify predictors of successful ASM withdrawal.

Method: This was a retrospective study collecting clinical data from hospital electronic database. Children started on ketogenic diet in our hospital between January 2013 and June 2018 were included. The primary outcome was the proportion of patients with a successful withdrawal of ≥ 1 ASM. A successful withdrawal of an ASM was defined as a time period of ≥ 3 months off that drug without restarting it or starting a new ASM.

Result: Of 104 children, 88 were included (38.6% female); median age of seizure onset was 5 months (IQR 2-18), median age at the diet initiation was 58.8 months (IQR 18-115). Sixteen children were excluded (Glut-1-transporter-deficiency-syndrome without seizures, n=3; discontinued the diet prior to 3 months, n=3; insufficient data, n=7). The median time to start weaning of the 1st ASM was 4 months (0-19 months) after commencing ketogenic diet and the median number of ASM at ketogenic diet commencement was 2 (IQR 2-3). Weaning of ≥ 1 ASM was attempted in 58 out of 88 patients (65.9%) and was successful in 36/58 (62%). 13 out of 58 (22.4%) children were off ASM at last follow-up. Regression analysis identified seizure outcome at 3 months and younger age at ketogenic diet commencement as predictors for successful withdrawal.

Conclusions: Reducing ASM load can be a realistic therapeutic goal in children and adolescents after ketogenic diet initiation. Weaning of ASM should be considered after the diet onset to reduce the ASM burden, risk of drug side effects and improve quality of life.

Abstract Number: 839

Title: Review of etiological spectrum of Drug Resistant Epilepsy among children attending a tertiary hospital in Saudi Arabia.

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Purpose: The International League Against Epilepsy (ILAE) has proposed in 2010 the term of Drug-resistant epilepsy which place a great toll on health practice. Identifying this entity early and resorting to non-pharmacological management can play a part in better prognosis and neurological outcome of patients. We aimed to focus on finding the etiological spectrum of drug-resistant epilepsy, identifying the clinical, electrophysiological and neuroimaging associated with those patients.

Method: The cases were collected through a retrospective cross-sectional chart review of patients attending our clinics from 2019 to present day. We included patients who met 2010 ILAE criteria of drug resistant epilepsy; failure of two or more tolerated and appropriately chosen antiepileptic drugs to achieve a period of seizure freedom. (whether as monotherapies or in combination).

Result: A total of 150 children were recruited in the study, Majority of patients developed their first seizure in the infantile period 74(49.33%).
The most encountered underlying etiology was Genetic/Metabolic 54(36%), followed by structural cause 49(32.67%), while 32(21.33%) had unknown cause, and lastly infectious cause was in 15(10%) of cases. There was a statistically significant difference between age at onset and the etiology of drug resistant epilepsy. Genetic/ metabolic disorder was more among patients with infantile onset (45.95%), structural cause was more among patients with neonatal onset (60.87%), while unknown causes were more prevalent in patients with childhood onset (33.96%) (p=0.0007).

Electroencephalography showed mostly Multifocal epileptiform discharges 53(35.33%), while neuroimaging showed that 59 (39.33%) of patients had potentially epileptogenic lesions.

Conclusions: The etiological spectrum in our population pointed toward Genetic/Metabolic predilection, that was different from other published studies of DRE patients which may be explained by our highly consanguineous population in Saudi Arabia.
We found statistical significance in age of onset distribution among different etiological groups, which might direct future prospective studies to confirm this relation.

Abstract Number: 844

Title: Epileptic syndromes associated with focal clonic seizures

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Purpose: to study clinical, electroencephalographic features, prognosis of the course of epilepsy in the group with focal clonic seizures (FCS), to assess the efficacy of antiepileptic therapy.

Method: We examined 1258 patients with various forms of epilepsy with the onset of seizures from the first day of life to 18 years. A group with FCS was singled out.

Result: FCS was identified in 263 patients (20.9%). There was a predominance of male (male - 59.7%; female - 40.3%). FCS were included in the structure of 13 different epileptic syndromes: Rolandic epilepsy (28.1%), structural focal epilepsy (27.5%), structural focal epilepsy associated with benign epileptiform discharges of childhood (SFE-BEDC) (20.6%), focal epilepsy of unknown etiology (7.5%), epilepsia partialis continua (4.6%), pseudo-Lennox syndrome (3.4%), ESES syndrome (2.7%), **Landau-Kleffner syndrome** (1.5%), Dravet syndrome (1.1%), benign occipital epilepsy (1.1%), benign focal epilepsy in infancy (0.8%), MISF syndrome (0.8%), cognitive epileptiform disintegration (0.8%). In 50% of cases, epilepsy associated with FCS debuts before 5 years (from 1 month to 18 years, average age 4.26 ± 3.9). Only FCS were observed in 25.5% of cases. Two or more types of seizures were observed in 74.5%, 3 or more types of seizures in 37.2%, 4 or more in 11%. There were bilateral tonic-clonic seizures (46.4%), febrile seizures (15.2%), focal sensory seizures (9.9%), atypical absences (9.1%), negative myoclonus (9.1 %), focal motor seizures (8.7%), epileptic spasms (6.8%), occipitallobe seizures (6.8%), tonic seizures (6.5%), focal motor seizures with **automatisms** (5.7%), focal myoclonus (5.3%). There is a high percentage of complete remission while taking antiepileptic drugs (63.5%). In 23.6% of cases, the frequency of seizures decreased >50%. Only 12.9% had no effect on seizures.

Conclusions: The groups of syndromes associated with FCS have different prognosis for remission of seizures. Prognostic predictors of remission are BEDC on EEG, periventricular leukomalacia.

Abstract Number: 855

Title: What's in a name? Rett Syndrome - 38 years later

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Purpose: Rett syndrome is frequently associated with loss-of-function mutations in *MECP2* gene but the use of NGS technology is expanding the genetic background of this behavioral phenotype. This study aimed at investigating the genetic and clinical characteristics of Rett and Rett-like patients in current clinical practice.

Method: Observational, descriptive, retrospective study of patients with Rett and Rett-like syndrome, followed in a tertiary hospital's Neurology Department. Data collected by reviewing clinical files.

Results: The sample is composed of 28 patients (83.3% females). Average age at presentation and genetic diagnosis was 13 months and 6 years, respectively. Fifteen patients have *MECP2* genetic defects (point mutation in thirteen). Other genetic variants were found in *CDKL5* (n=3), *KCNQ2* (n=2), *FOXG1*(n=1) and *MEF2C* (n=1). Six patients remain without genetic diagnosis. In 32,1% of cases, considered Rett-like, the revised diagnostic criteria of 2010 were not fulfilled, mainly due to lack of developmental regression (6/9).
Almost all patients have epilepsy (92.9%), classified as focal and generalized (42.9%), focal (32.1%) and generalized (10.7%). Epilepsy was or is refractory in 71,4%. The median number of anti-epileptic drugs tried was 4 (IQR 3-7).
Non-*MECP2* patients presented earlier and developed epilepsy earlier – 4 (IQR 1-12) vs. 14 (IQR 8-35) months (p=0,011) and 3 (IQR 1-18) vs. 33 (IQR 17-69) months (p=0,008), respectively – but this did not impact on functional outcome (per Clinical Severity Score).

Conclusions: About half our sample has non-*MECP2* genetic defects, reflecting the increasingly recognized contribution of developmental epileptic encephalopathies to this behavioral phenotype and supporting the pertinence of a Rett-like gene panel.
A third of our patients does not fulfil diagnostic criteria.
Younger age at presentation of epilepsy may suggest non-*MECP2* aetiology in these patients.
Our delay in diagnosis was 5 years. An effort should be made to shorten this, especially when gene therapy is on the pipeline.

Abstract Number: 868

Title: Modified Atkins diet versus Levetiracetam in children with refractory epilepsy: a randomized controlled trial

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Purpose: This study was performed with the purpose to compare the efficacy and tolerability of the modified Atkins diet versus levetiracetam in a children with refractory epilepsy in a randomized controlled trial.

Method: Children aged 2-12 years who had daily seizures despite the appropriate use of at least three anticonvulsant drugs in appropriate dosages were enrolled. Children were randomized to receive either add-on modified Atkins diet or levetiracetam. The on-going anti-seizure medications were continued unchanged. The primary outcome was seizure reduction at the end of three months. Adverse effects were assessed by parental reports in both groups.

Result: : A total of 101 children were enrolled, 51 were in the diet group and 50 in the levetiracetam group. The mean percentage of seizure frequency at 3 months when compared to baseline, was significantly more in the diet group 47.33% and 31.15% in levetiracetam group with p value= 0.03. When the diet and levetiracetam group compared, the proportion of children with >50% seizure reduction was significantly higher in the diet

group (52.9% vs. 22.0%, p < 0.001). Both treatments were well tolerated. The most common adverse effect among children on the diet was constipation (41.1%) and sedation being in the levetiracetam group (18%).

Conclusions: The modified Atkins diet was found to be more effective than levetiracetam in children with refractory epilepsy. Both treatments were reasonably well tolerated.

Abstract Number: 869

Title: Genetic testing in unexplained developmental and epileptic encephalopathy at Chiang Mai University Hospital

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Purpose: To determine the diagnostic yield of genetic testing and clinical characteristics in the patients with unexplained developmental and epileptic encephalopathies (DEEs).

Method: We retrospectively reviewed medical records of children with unexplained DEEs between July 2002 to July 2020 at Chiang Mai University Hospital. Children with major brain malformation and inborn error of metabolism were excluded.

Result: Forty-five patients were identified: 24 girls; 21 boys. Median age of seizure onset was 90 days (range 1 day - 1 year). After reviewing phenotype and clinical history, 10 underwent to have a single gene analysis for SCN1A mutation. Eight showed positive result. All of these children had history or presented with hemiclonic or generalized tonic clonic seizures provoked by fever. Trio whole-exome sequencings were performed in 35 patients including their parents. Results were finished in 17 families (50%). Pathogenic or likely pathogenic variants were identified in 12 children (70%) including SCN1A (2), STXBP1 (2), DARS2 (2, siblings), KCNQ2 (1), KCNT1 (1), GNAO1 (1), CASK (1) BOLA3 (1), and ALDH7A1 (1). Children who found pathogenic variants had seizures onset within 3 months (p<0.05). Nearly all of children (83.7%) in this study had refractory seizures. Two third required at least two antiepileptic drugs. One child with ALDH7A1 mutation presented with generalized tonic clonic seizure at twelve days of age. She has infrequent seizures and her first EEG showed mildly abnormal background.

Conclusions: Clinical correlation and patient selection increase the yield of genetic testing in children with unexplained DEEs. This approach can reduce the cost of investigation in resourced-limited areas. However, many genes had phenotypes heterogeneity. Trio whole exome sequencing helps to identify causative pathogenic variants which can be benefits in treatment plan and family counselling.

Abstract Number: 891

Title: Molecular dynamic modeling for predicting the functional significance of pathogenic variants in sodium channels

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Purpose: Functional impact of pathogenic variants in sodium channels is important for correct phenotype prediction and treatment selection. Patch-clamp studies are required for the assessment, but they are not clinically available. Molecular dynamics (MD) is a bioinformatic tool predicting impact of variants upon protein 3D-structure and function. We present the use of MD in predicting the functional impact of variants in voltage-gated sodium channels.

Method: We performed MD on six patients with genetic variants, using the Schrödinger® platform. After predicting the 3D-structure of mutated proteins by homology modeling, time dependent MD simulations were performed, using the Schrödinger algorithm, allowing the determination of the exact position of atoms at each point in time. The opening of the channel, including the binding of the sodium ion to the ion sensitivity filter (DEKA motif) and the passage time through the pore, were assessed. The pathogenicity of missense variants was evaluated in three patients: a 7-year-old boy with autism (p.Thr155Ala, ***SCN2a***), a 4-year-old girl with neonatal seizures (p.Ala263Val, ***SCN2a***), an 8-year-old girl with drug resistant epilepsy (p.Ile251Arg, **SCN8a**). Two patients with Dravet syndrome and missense variants known to cause complete loss-of –function from previous patch-clamp analysis, served as control (p.Gly177Ala and p.Ser259Arg , ***SCN1a***).

Result: In the **SCN2a^{T155A}** channel MD simulation, the ion remains attached to the DEKA motif and does not pass through the pore, causing severe loss-of-function, consistent with autistic phenotype. In the **SCN2a^{A263V}** and **SCN8a^{I251R}**channels, there was a was a quicker passage through the pore, consistent with gain-of-function and epileptic phenotype. In the **SCN1a^{G177A}** and **SCN1a^{S259R}** channels, MD simulation elicited loss-of-function, consistent with previous electrophysiologic studies and Dravet phenotype.

Conclusions: MD can be useful in predicting pathogenicity of variants and the disease phenotype, as well as selecting targeted treatment based on channel dysfunction.

Acknowledgement: Studies were performed by QR Genetics commercially.

Abstract Number: 907

Title: SCN1A pathogenic variants associated with epilepsies: beyond Dravet syndrome and unmasking patients responding to sodium channel-blockers

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Purpose: *SCN1A* pathogenic variants may result in a wide spectrum of phenotypes, ranging from self-limited epilepsies to developmental epileptic encephalopathies (DEE). Dravet syndrome (DS) is the prototypic DEE linked to *SCN1A*, most mutations cause loss of channel function making sodium-channel blockers (SCB) drugs contraindicated.

Method: We performed a retrospective multicenter cohort study, collecting patients carrying pathogenetic variants of *SCN1A* gene with an epileptic phenotype other than DS.

Result: We selected 11 patients (6 female) with current age of 10 years (range 8 months – 2 years; interquartile range (IQR) 1.2-13.9). Nine patients had seizure onset in the first year of life; overall, the median age at seizure onset was 2 months (range 1 day – 5 years, IQR 2 days -9 months).
All patients presented with multifocal motor seizures, with a clonic or tonic component, nine patients had high seizure frequency, featuring episodes of status epilepticus in three of them. Three patients also had epileptic spasms. Nine had developmental delay, ranging from mild to severe, associated in five with pyramidal and extrapyramidal signs.
Two siblings had seizures onset at 5 and 4 years old respectively, featuring focal epilepsy with auditory features, they also had migraine attacks and normal cognitive functioning. Eight patients were treated with SCB including phenytoin, lamotrigine, lacosamide, and carbamazepine and gained seizure freedom (37.5%) or significant seizure reduction (62.5%). Nine patients carried de novo missense *SCN1A* pathogenic variants, the remaining two were siblings harboring a familial mutation.

Conclusions: Here, we described epileptic phenotypes related to *SCN1A* pathogenetic variants readily distinguishable from DS varying from a severe phenotype with early-onset multifocal seizures, developmental delay, and associated pyramidal and extrapyramidal signs to a childhood-onset focal epilepsy with auditory features. Most patients benefited from SCB treatment, suggesting a possible gain of function effect of the channel.

Abstract Number: 908

Title: Stereotactic laser interstitial thermal therapy corpus callosotomy for the treatment of atonic seizures in pediatric refractory epilepsy

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Purpose: Corpus callosotomy has demonstrated efficacy in reducing atonic seizures and seizure frequency and improving overall quality of life for patients with drug-resistant epilepsy, with relatively low morbidity overall. While open approaches have been used successfully to date, laser interstitial thermal therapy (LITT) is an emerging technique that offers a minimally invasive treatment option for corpus callosum ablation. Here we present 8 pediatric patients, ages 7-21 years (M=14.4, SD=5.1 years), who have undergone MRI-guided LITT callosotomy at our institution for the treatment of drug-refractory primary generalized epilepsy with atonic seizures.

Method: Three patients underwent complete LITT callosotomy, 2 patients underwent anterior two-thirds LITT callosotomy, and 2 underwent LITT for completion of previously performed partial anterior two-thirds callosotomy. LITT callosotomy was completed with 3-4 trajectories in total for complete and anterior two-thirds callosotomy and 1-2 trajectories for callosotomy completion of the posterior one-third corpus callosum.

Result: LITT callosotomy was performed successfully, without intraoperative complications in all cases. Post-operatively, 4 patients experienced transient neurologic deficit, however no patients experienced permanent deficit. Surgery length ranged from 4-8 hours (M=5.8, SD=1.7). Patients were discharged after a median of 3 days (range 1-6). 66.7% of patients with frequent pre-operative atonic seizures and adequate follow-up (N=6) were free from drop attacks at most recent follow-up. A total of 83% of patients experienced a worthwhile improvement in overall seizure frequency by 3-month follow-up (N=6, Engel score II, N=1; III, N=4; IV, N=1), 67% at 6-month follow-up (N=6, Engel score I, N=1; III, N=3; IV, N=2), and 50% at 1-year follow-up (N=2, Engel score III, N=1; IV, N=1). We identified an imaging pattern of DWI/FLAIR/T1 changes characteristic of successful laser ablation.

Conclusions: LITT callosotomy is safe for the treatment of drug-resistant epilepsy in children and may offer advantages to open callosotomy, particularly minimal invasiveness.

Abstract Number: 918

Title: Stereotactic laser interstitial thermal therapy for the treatment of pediatric drug-resistant epilepsy: Indications, techniques, and safety.

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Purpose: MRI-guided laser interstitial thermal therapy (LITT) is a promising alternative to open surgery for treatment of drug-resistant epilepsy, offering significant advantages over traditional approaches for candidate patients, including minimally invasive approach, shorter hospitalization, and decreased patient post-operative discomfort. LITT uses a stereotactically-placed fiber optic laser probe to ablate neural tissue with thermal energy under real-time imaging using MRI thermometry to induce coagulative necrosis in the targeted volume. Here we present our experience performing MRI-guided LITT in 19 pediatric patients with various epilepsies over 2 years at a large tertiary academic center.

Method: Retrospective chart review of intraoperative and perioperative characteristics was performed for 19 pediatric patients, ages 7-21 years old (M=15 years, SD=3.8), who underwent LITT at our institution in the last 2 years. LITT ablation of seizure foci was performed in 14 cases (73.7%) and for corpus callosotomy in 5 cases (26.3%).

Result: Complications of LITT ablation included hemorrhage (26.3%) and permanent neurological deficit (5.3%). Specifically, a single patient who underwent insular ablation experienced moderate hand weakness that improved to mild hand weakness. 71.4% of patients with generalized epilepsy achieved complete seizure freedom with medication at follow-up. Of the remaining patients (N=4), 25% had experienced a notable improvement in seizure frequency. 75% of patients with atonic seizures and adequate follow-up (N=4) experienced complete cessation of drop attacks following callosotomy. Median length of hospitalization was 2 days (range 1-6), including a median ICU stay of 1 day (range 0-5).

Conclusions: This series demonstrates the safety of LITT and efficacy of this approach for seizure control. We provide additional evidence that LITT is an effective procedure that is well-tolerated by pediatric patients and is accompanied by a low rate of complications and short hospital stay.

Abstract Number: 920

Title: Clinical case of diagnosis of X-linked early infantile epilepticencephalopathy, atypical Rett syndrome with CDKL5 mutations in the girls 3 months

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Purpose: Early epileptic encephalopathy (EEE) is a group of diseases characterized by drug-resistant epileptic seizures, manifesting in infancy and leading to a delay in psychomotor development. The most common

genetic variant with X-linked dominant inheritance caused by mutations in the CDKL5 gene. The aim of the work is to present the early clinical and genetic diagnosis of this disease.

Method: neurological examination, night long-term video electroencephalography, neurosonography, magnetic resonance imaging, metabolic examination, genetic testing (next generation sequencing).

Result: The 3-month-old girl started having seizures for the first time and she was hospitalized in our department. Seizures were first characterized by myoclonic seizures in the legs and then epileptic spasms. According to neurosonography and magnetic resonance imaging, we found no pathology. Metabolic examination was performed: lactate, ammonia, proteins, urinolysis - were normal. During the night long-term video of EEG monitoring, interictal and ictal epileptiform activity in the form of flashes of sharp waves and delta waves with bilateral synchronization were obtained. We got a positive result genetic testing - one Pathogenic variant identified in CDKL5 (A Pathogenic variant, c.527G>A (p.Trp176*). After the appearance of epileptic spasms, Vigabatrin with increasing the dose to 110 mg / kg / day - with a positive effect for 1 month. However, the spasms continued for 2 series per day. ACTH was recommended.

Conclusions: For the first time in the hospital we gained experience in clinical and instrumental diagnostics X-linked early infantile epileptic encephalopathy, genetic sequencing, as well as the selection of anticonvulsant therapy.

Abstract Number: 930

Title: Deep brain stimulation of the centromedian thalamic nucleus for the treatment of FIRES

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Purpose: Febrile infection-related epilepsy syndrome (FIRES) is a rare, life-threatening complication of febrile illness in previously healthy children. Patients with FIRES present with non-specific febrile illness often followed by a prolonged clinical course of super-refractory status epilepticus, characterized by lack of response to numerous anti-seizure medications, with long term sequelae including intractable epilepsy and severe neuropsychological impairment. Deep brain stimulation (DBS) has been demonstrated to be a promising therapy for the treatment of drug-refractory epilepsy. Here we present a pediatric patient with FIRES whose epileptic encephalopathy was successfully mitigated with deep brain stimulation (DBS) of the bilateral centromedian thalamic nucleus (CMTN).

Method: Retrospective chart review was conducted to collect patient details. A previously healthy 11-year old female presented emergently with altered mental status, fever, and malaise after 1-week of lethargy, anorexia, fever, and abdominal pain. The patient's seizures began shortly after admission. After thorough work-up for encephalitis and other potential etiologies, this patient was diagnosed with FIRES, which consisted of super-refractory status epilepticus and chronic drug-resistant epilepsy.

Result: The patient's status epilepticus persisted despite aggressive pharmacologic management and vagal nerve stimulator placement. DBS of the bilateral CMTN was pursued after 56-days of hospitalization and super-refractory status epilepticus. Seizure frequency improved and she demonstrated considerable improvement in baseline mental status 30-days after DBS insertion, including verbalizing and following simple commands. Anti-seizure medication doses were reduced and she was discharged to inpatient rehab 41-days post-DBS insertion, where she made tremendous improvements in global functioning and sustained improvement in seizure frequency.

Conclusions: This report highlights the second patient treated with DBS of the CMTN for super-refractory status epilepticus in FIRES. This region has been shown to modulate neural networks contributing to seizure propagation and consciousness, therefore neurostimulation is a potential therapeutic intervention for patients with super-refractory status epilepticus.

Abstract Number: 942

Title: Epileptic drop attacks associated with focal structural epilepsy may worsen with valproate, a report of three cases.

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Purpose: Atonic seizures were traditionally thought to be generalized seizures until recently; they are now classified as either focal or generalized. Valproic acid (VPA) is efficacious against generalized and focal seizures. Seizure aggravation by VPA has been reported mainly as part of a toxic encephalopathy. We report a clinical summary on three patients whose epileptic drop attacks were correlated with focal epilepsy; after introduction of VPA, the attacks became more severe and frequent and substantially improved with VPA cessation.

Method: Three epileptic patients were investigated very carefully with video EEG, MRI epilepsy protocol and extended metabolic profile to classify their seizures and epilepsy types. After initiation of VAP for treatment of drop attacks and worsening of them in our three patients, serial serum level of VAP (peak and trough) were withdrawn, beside full liver functions and serum level of ammonia to exclude hepatic encephalopathy.

Result: We include two females and one male. Developmental delay and learning difficulties observed in two of the patients, while the third was normal. Imaging of the three patients showed focal structural lesions, unilateral right frontotemoral lesion in one patient and bilateral in the other two patients, bifrontal in one and bioccipital in the last. Long-term video-EEG and EMG showed that the falls are slow (2-5 seconds), atonic seizures were emanating in relation to focal structural lesion in each patient. A high voltage spike and slow wave discharge invariably coincided with the onset of atonic seizures with successive EMG silent period caused by epileptic discharge. Serum level of VAP were within therapeutic range (for both peak and trough). Hepatic encephalopathy was excluded by normal liver functions, including serum ammonia.

Conclusions: This report describes a paradoxical, VAP –induced seizure exacerbation in three children with atonic seizures associated with focal structural lesion, without any evidence of encephalopathy.

Abstract Number: 944

Title: Presence and impact of symptoms in SCN2A-related disorders

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Purpose: Individuals with *SCN2A*-related disorders have seizures and developmental delay/intellectual disability (DD/ID). Other symptoms are reported, but their frequency and burden have not been determined.

The aim of this study was to identify parental experience of frequency of symptoms for their child and the impact on their lives.

Method: Parents of 61 individuals (median age 6.7 years) in an *SCN2A* Natural History Study were asked to rate the impact of seven symptoms (seizures, DD/ID, behaviour, irritability, sleep, movement disorders and gastrointestinal symptoms) on their child and family currently, using a scale of zero (not a problem) to 10 (biggest problem they could imagine). For each individual, the number of symptoms present (i.e. with score>0) and biggest current problem were identified.

Result: The median number of symptoms present in each individual was 5/7. 37/61 rated DD/ID as the biggest (or equal biggest) problem. Irritability, behaviour, sleep and gastrointestinal symptoms were each a problem in >60% of individuals; 34/61 rated a symptom other than seizures or DD/ID as the biggest (or equal biggest) problem currently.

Conclusions: Symptoms other than seizures and DD/ID are present in most individuals and can be severe. Recognising the polysymptomatic nature of *SCN2A*-related disorders is important for clinical practice and clinical trial design.

Abstract Number: 949

Title: Functioning in children and adolescents with epilepsy

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Purpose: According to the World Health Organization (WHO), functioning is a term that covers all functions and structures of the body, activity and participation, while disability consists of impairments, activity limitations or participation restrictions. The aim of the present study is to evaluate the functioning of children and adolescents with epilepsy without moderate or severe disability and its relationship with demographic/seizure-related variables, intellectual quotient (IQ) and caregiver burden.

Method: The following scales were used: Pediatric Evaluation of Disability Inventory Computer Adaptive Test (PEDI-CAT), Abbreviated Wechsler of Scale of Intelligence (WASI) and Burden Interview. The sample consisted of 42 patients with epilepsy in regular treatment in a tertiary facility in São Paulo, Brazil. The inclusion criteria were: age between 4 and 18 years old, of both sexes and active epilepsy; and the exclusion criteria were: the presence of physical disabilities and/or severe comorbidities (clinical or neuropsychiatric) that prevented the application of tests.

Result: Mean age of patients was 10.4 years old (± 3.72), disease duration 5.9 years (± 3.94) and seizure onset 4.5 years (± 3.43); classification of epilepsy was focal in 69% and with unknown etiology in 49%; mean number of antiseizure medications was 1.8 (± 1.06) and IQ 73.4 (± 16.93). Functioning was impaired in the Social/Cognitive (z-score = -2.20) and Responsibility (z-score = -2.07) domains of PEDI-CAT. Negative correlations were observed between the four domains of PEDI-CAT and the duration of epilepsy and with Burden Interview results. Positive correlations were observed between the domains of PEDI-CAT and IQ.

Conclusions: In conclusion, patients with epilepsy without moderate or severe disability presented deficits mainly in the areas related to Social/Cognitive and Responsibility domains of the PEDI-CAT scale. Higher scores of PEDI-CAT were correlated to higher IQ values and were inversely proportional to the duration of the disease and caregiver burden.

Abstract Number: 952

Title: Validation of the Heath-Related Quality of Life in Childhood Epilepsy Questionnaire (QOLCE-55) to Portuguese-Brazil

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Purpose: The present study aims to validate the Health-Related Quality of Life in Childhood Epilepsy Questionnaire – 55 items (QOLCE-55) into Portuguese-Brazil, and to evaluate the relation of its results with clinical data and the caregiver burden.

Method: The QOLCE-55 was submitted to translation, back-translation and cultural adaptation in a pilot sample with 20 subjects. In order to ensure psychometric properties of validation, QOLCE-55 was carried out in a sample of 45 patients with epilepsy aged between 4 and 18 years old and their parents or caregivers, and compared with the results of other Quality of Life instruments, namely QVCE-50 and QOLIE-AD-48, as well as with SDQ, a brief behavioral screening questionnaire. WASI and SON-R 2½-7 [a] were used for evaluation of Intelligence Quotient (IQ) and Burden Interview for the caregiver burden.

Result: Internal consistency measured by the Cronbach's alpha coefficient was moderate (0.692; p=0.264) and the test-retest reliability analyzed by the Intraclass Correlation Coefficient was satisfactory when compared with the results by different examiners in the same day (0.951; p=0.001) and in different moments (0.778; p=0.001). This version of QOLCE-55 presented strong correlation with QVCE-50 (0.904; p<0.001) and SDQ (-0.428; p=0.004), but low correlation with QOLIE-AD-48 (0.094; p=0.729). It also presented correlation with IQ (R=0.456, p=0.003) and inverse correlation with the Burden Interview (-0.390; p=0.012). Low quality of life was associated with the presence of tonic-clonic seizures (p=0.005), polytherapy (p=0.003) and low socioeconomic conditions (p=0.005).
Conclusions: The Portuguese-Brazil version of QOLCE-55 was confirmed as a reliable and valid scale in order to assess quality of life in children and adolescents with epilepsy. Behavioral problems, caregiver burden, tonic-clonic seizures, polytherapy and socioeconomic precariousness were associated with low quality of life values, while IQ was correlated positively with the quality of life in this population.

Abstract Number: 958

Title: The knowledge gap of managing childhood epilepsy among primary and emergency care medical officers in Galle district Sri Lanka

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Purpose: To assess the knowledge gap of medical officers working in paediactric and emergency care units in Galle district Sri Lanka in relation to management of epilepsy in children.

Method: All eligible Medical Officers working in paediatric and emergency units of primary(Primary care units and Divisional hospitals) , secondary (Base hospitals) and tertiary care (Teaching hospitals) institutions in Galle district have been evaluated using a self-administered questionnaire.

Result: 190 medical offices have been evaluated. 128 from Primary, 28 from secondary and 34 from tertiary care units. Most of medical offices (63%) had more than 10 years working experience and only 29 % had less than 10 years working experience.
58% medical officers in secondary and tertiary care hospitals showed at least satisfactory knowledge level, whereas only 17% of primary care medical offices had satisfactory level, which is statistically significant ($P < 0.05$).There was significant positive correlation of knowledge gap and working experience. (Only 22 % satisfactory level with more than 10 years' experience and 72% satisfactory level with less than 3 yeses experience)
There was a no significant knowledge difference with exposure of epileptic children.
Only 36% medical officers in primary care hospital had good knowledge of managing status epilepticus. Most of the medical officers had lack of knowledge of differentiation between epileptic from non-epileptic events (69%).

Conclusions: There was a significant knowledge gap in relation to management of epilepsy in children among medical offices especially in primary care level. This is more significant in most senior medical offices, most probably due to lack of continuous education to get updated knowledge.
It is recommended to have continuous education training programs in recognition and management of childhood epilepsy mainly for primary care doctors to narrow down epilepsy knowledge gap in order to achieve better outcome of childhood epilepsy.

Abstract Number: 976

Title: Parental Knowledge and Attitude Towards Pediatric Epilepsy in Latvia

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Purpose: To investigate parental knowledge and attitude towards epilepsy of their children.

Method: In a cross-sectional study (November – December, 2020) Latvian parents of children with epilepsy answered to survey using internet or during outpatient visit to Paediatric Neurologists. Data was analysed using IBM SPSS 26.0. Mann Whitney, Fisher Exact Test and Chi square were used.

Result: Final sample consisted of 93 parents (93.5% female). Mean age was 37.7±6.0 years, 58.1% had higher education, 44.1% lived in Riga. Mean age of children was 9.0±4.1 years (55.9% male).
Overall, 43% of children received mainstream education (12.9% attended kindergarten, 30.1% - school).
Majority of children (54.8%) had presumably severe epilepsy (refractory and/or structural/genetic).
Overall, parental knowledge of epilepsy was good. However, substantial part of respondents considered several unproved factors to be the cause of epilepsy (vaccination – 12.9%, changes in moon phase – 18.3% or weather – 5.4%, physical activity – 21.5%).
Out of 15 correct seizure management strategies only four were performed by more than 50% of parents (remaining calm, supporting child, timing the seizure, waiting till the seizure subsides).
Higher education level was statistically significantly associated with belief that epilepsy is not incurable (75.9% vs 48.7%, $p<0.023$), some epilepsy types could be treated surgically (96.3% vs. 81.1%, $p<0.03$), and children with epilepsy should be vaccinated according to the national vaccination plan (75.9% vs 53.8%, $p<0.012$).

Conclusions: Although overall parental knowledge of pediatric epilepsy is adequate, several myths and misinformation are still present in epilepsy patient families. Ensuring education and support in community should be one of main epilepsy care priorities.

Abstract Number: 993

Title: Role of dietary therapy in intractable epilepsy in children: Emerging paradigms

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Purpose: Ketogenic diet(KD), modified Atkin's diet(MAD) and Low Glycemic index treatment(LGIT) are efficacious in reducing seizure frequency in children with drug resistant epilepsy(DRE). Our division has completed ten clinical studies including seven RCTs analyzing dietary therapies in childhood DRE over last 15 years and has been actively involved in evolution of dietary therapy services by innovative measures, making them less restrictive, without compromising efficacy.

Method: Around 1,500 children from infancy to adolescence have received various dietary therapies (indigenous recipes) over last 15 years. More than 700 children have been enrolled in ten trials: KD(2006),KD 4:1 vs 2.5:1(2008),MAD vs AED(2009), LGIT vs AED(2011),MAD vs KD(2013), KD vs MAD vs LGIT(2016), Daily vs Intermittent LGIT (2018), MAD vs LGIT (2019). Role of various biomarkers like PUFA, HbA1c, Beta Hydroxy Butyrate (BHB) and gut microbiota are being evaluated. Caregiver Satisfaction with Dietary Therapy (CSDT) questionnaire and Dietary Therapy Evaluation of Compliance (DTEC) algorithm have been developed.

Result: KD 2.5:1 was shown equally efficacious as KD 4:1(p=0.78), with less adverse effects. Later, MAD and LGIT were found to be effective(p=0.003 and 0.03 respectively). Subsequently LGIT and MAD were observed to have comparable efficacy to KD with less adverse effects(p=0.18). In another RCT MAD and LGIT was found to have equal efficacy, with LGIT having less adverse effects(58% vs 59% seizure reduction). Recently, intermittent LGIT(liberalized diet two days a week) has been found to be non-inferior to daily LGIT, with better compliance and caregiver satisfaction. Percentage reduction in HbA1c and BHB levels were found to have good positive correlation with seizure frequency reduction in LGIT. We have also initiated enrollment of children for another RCT exploring efficacy of KD in NCSE.

Conclusions: Although KD is most efficacious among dietary therapies for DRE, MAD and LGIT are other acceptable less restrictive and better tolerated options.

Abstract Number: 999

Title: Comparison of Efficacy of Low Glycemic Index Therapy and Modified Atkins Diet in children with DRE: A Randomized Non-inferiority Trial

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Purpose: Ketogenic diet has been the mainstay of treatment of drug-resistant epilepsy (DRE). No large comparative trials have been conducted to assess the efficacy of the two less strict ketogenic diets; Modified Atkin's Diet(MAD) and Low-Glycemic-Index-Therapy(LGIT). This study assesses the non-inferiority of LGIT compared with MAD.

Method: The study was an open label randomized non-inferiority trial (NCT03764956). Children with DRE were randomized to receive either MAD or LGIT as an add-on to the ongoing anti-epileptics. The non-inferiority margin of -15% was predefined to calculate the sample size. The primary endpoint was percentage seizure reduction at the end of 24 weeks of therapy compared to the baseline. Cognition, behavior and quality of life of subjects and caretakers were assessed using VSMS, CBCL, PedQL, QOLCE-55 and WHOQOL BREF scales.

Result: 113 children(92 boys) with mean age of 6.2 years (1.2 - 15 years) received MAD (n=56) or LGIT (n=57). 94 children completed 24 weeks of therapy and one child in the LGIT group expired due to reasons unrelated to therapy. Intention to treat analysis done at the end of 24 weeks of therapy showed mean(±SD) percentage seizure reduction of 58.4%(69.1 to 47.6) in the MAD sub-group and 59.2%(68.9 to 49.6) in the LGIT sub-group and the difference was statistically not significant. The absolute difference between the means of percentage seizure reduction was 0.86(-13.4 to 15.2); p=0.9056 and crossed the non-inferiority margin of -15%. Adverse effects occurred in 30.9% subjects in the MAD group and 21.8% in the LGIT group. There was no statistically significant improvement in cognition scales. Significant improvement in behavior was seen in MAD arm. Caretakers in both arms had significant improvement in quality of life.

Conclusions: LGIT is non-inferior to MAD in the treatment of children with DRE with the advantage of increased acceptance and fewer adverse effects.

Abstract Number: 1005

Title: Febrile infection related Refractory Epilepsy Syndrome - A retrospective cohort study from North India

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Purpose: Acute onset recurrent seizures or refractory status epilepticus preceded by febrile illness without evidence of infectious encephalitis is defined as FIRES (Febrile infection related Refractory Epilepsy Syndrome). It is a poorly understood entity, usually with grave outcome. This study describes a retrospective cohort of the same.

Method: Case records of subjects fulfilling diagnostic criteria of FIRES, presenting to a tertiary care teaching centre in north India, from 2014 to 2020, were retrospectively reviewed. Clinical features, therapeutic response and outcome of the cases have been described in the current study.

Result: Overall, 20 cases (median age: 6 years, range:1-13 years) presented during the study period with majority being males (12, 60%).Fever, altered sensorium and seizures (generalised tonic-clonic in 65%) were present in all, with a quarter of them presenting in shock (5). Lumbar puncture was non-contributory with neuroimaging showing basal ganglia involvement (5, 25%) and diffuse cerebral edema (2,10%). Raised intracranial pressure (ICP) was seen in 10(50%) and 18 (90%) required mechanical ventilation and 2 or more anti- seizure medications to achieve seizure control. Overall, 8 died (40%) and 9 out of the 12 discharged(75%) developed neurodevelopmental sequelae and epilepsy. Raised ICP at presentation (8/8 versus 2/12, p=0.0004)

and need for midazolam infusion in refractory status epilepticus (5/8 versus 1/12, p=0.01) differed significantly between those who died and survived respectively.

Conclusions: Overall, FIRES, has a poor outcome in terms of morbidity and mortality. Certain clinical features like raised ICP at presentation and need for midazolam infusion in refractory status epilepticus may be associated with mortality. Further studies are needed for better understanding of pathophysiology leading to development of potent therapeutic strategies.

Abstract Number: 1038

Title: Daily Fat and Caffeine Intake and Seizure Free Phase in Children with Epilepsy at Dr. Sardjito General Hospital, Yogyakarta, Indonesia

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Purpose: To investigate the correlation between daily fat and caffeine consumption with seizure free phase of children with epilepsy.

Method: A retrospective cohort study was performed by collecting data from medical records of 23 children in Dr. Sardjito Hospital from 2019 to 2020. Additional data were collected via direct interview when subjects visited the hospital for routine follow-up. A validated Food Frequency Questionnaire was used to collect dietary intake, especially fat and caffeine rich food and drinks. Daily fat and caffeine consumption were then categorized into ≤ 37.9% and > 37.9% , and ≤ 7.43 mg and > 7.43 mg, correspondingly. Meanwhile, seizure-free phase was defined into 3 categories i.e. onset of seizure freedom (≤6 months and >6 months), duration of seizure freedom (<2 years and ≥ 2 years), and recurrence incidence.

Result: There were no statistically significant association observed between either of daily fat or caffeine intake with seizure-free phase. However, the group consuming fat ≤ 37.9% had greater number of subjects who achieved seizure freedom in ≤ 6 months and lower incidence of relapse compared to those with fat intake of > 37.9% (92% vs 82% and 33% vs 64%, respectively). Furthermore, the group with caffeine intake of ≤7.43 mg had more subjects with duration of seizure freedom ≥ 2 years and lower incidence of relapse (38% vs 29% and 44% vs 57%, correspondingly) compared to those with caffeine intake of > 7.43mg.

Conclusions: Daily fat and caffeine consumption were not statistically associated with seizure free phase. Nevertheless, there appeared to be clinical benefits of controlling fat and caffeine intake on onset, duration of seizure freedom and relapse incidence in children with Epilepsy.

Abstract Number: 1050

Title: Effect of Multivitamin (B1, B6, B12) Supplementation on Seizure-Free Phase in Epilepsy Children in Dr. Sardjito Hospital, Yogyakarta, Indonesia

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Purpose: To investigate effect of multivitamin (B1, B6, B12) supplementation on the seizure-free phase in children with epilepsy.

Method: A retrospective cohort study was performed by collecting data from medical records of 88 children with epilepsy admitted to Dr. Sardjito Hospital between year 2015-2019. Seizure freedom was defined as no seizure in minimal 1 month duration, while recurrence was defined as seizures occurrence episode after seizure freedom was achieved. Seizure-free phase consists of 3 indicators; onset of seizure freedom, that categorized into ≤6 months and >6 months; duration of seizure freedom, classified into <1 year and ≥1 year; and recurrence. All clinical characteristics, including: age, gender, type of seizure, standardized treatment received, were recorded and compared. Statistical analyses of association between supplementation status and seizure-free phase were done by *Chi-square* test, where p<0.05 was determined as statistically significant.

Result: Among the subjects, 44 (50%) children were supplemented with multivitamin, and the rest were without multivitamin. Duration of seizure freedom ≥1 year occurred in 27 subject (30.7%) with multivitamin and 9 subject (10.2%) without multivitamin (95% CI 1.60-5.62). Almost all subjects (97,7%) achieved seizure freedom in ≤ 6 months with multivitamin 44 (50%), without multivitamin 42 (47.7%) (95% CI 0.67-1.84). Recurrence occurred in 25 (28.4%) of the subjects with multivitamin and 27 subject (30.7%) without multivitamin (95% CI 0.67-1.84). Statistical analyses showed significant association between duration of seizure freedom with addition of multivitamin with p = 0.000.

Conclusions: Addition of multivitamin supplementation had a effect in achievement of a longer duration of seizure freedom but not achieved seizure freedom and reccurence children with epilepsy in Dr. Sardjito Hospital.

Abstract Number: 1055

Title: Association of Nutritional Status with Seizure-Free Phase in Children with Non-syndromic Epilepsy in Dr. Sardjito Hospital, Yogyakarta, Indonesia

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Purpose: To investigate association between pre-treatment nutritional status and seizure-free phase in children with non-syndromic epilepsy.

Method: A retrospective cohort study was conducted in Dr. Sardjito General Hospital, a tertiary academic hospital, in Yogyakarta, Indonesia. Of 70 children who were newly-diagnosed as non-syndromic epilepsy in 2015 were enrolled. Nutritional status was measured on initial diagnosis. There were 3 nutritional status indicators: weight/height (for children age 0-5 years) or BMI/age Z-score (for children age >5 years), weight/age Z-score (for children age 0-10 years), and height/age Z-score and all was divided into two groups, Z-score <-2 and Z-score ≥-2. Seizure-free phase was defined as no seizure episode during minimal duration of 1 month, while recurrence was defined as seizures occurred after seizure-free phase. Seizure-free phase consisted of 3 indicators: onset of seizure-free which divided into ≤6 months and >6 months; duration of seizure-free that divided into <1 year and ≥1 year; and recurrence of seizure divided into yes or no. Statistical analysis of association between nutritional status and seizure-free phase were conducted using *Chi-square* test, where p<0.05 was determined as statistically significant.

Result: Almost all subjects (97.1%) gain seizure free phase in less than 6 months and experienced recurrence in 38 (54.3%) of the subjects. Seventeen (24.3%) children were wasted, 15 (25.4%) were underweight, and 23 (32.9%) were stunted. On 55 of 70 subjects with minimal follow-up of 1 year, 30 (54.5%) had duration of

seizure-free phase ≥1 year. There were no significant association between all nutritional status indicators and seizure-free phase indicators. Stunted children had a considerably higher proportion than non-stunted children in term of recurrence (69.6% vs 46.8%).

Conclusions: Nutritional status might not be associated with seizure-free phase in children with non-syndromic epilepsy, however there may be a 1.2x increase in risk of having recurrence in stunted children.

Abstract Number: 1060

Title: The Effects of Salt and Sugar Intake Patterns on Hyperactivity and Seizure Remission in Epileptic Children

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Purpose: To investigate the correlation between salt and sugar consumption with seizure free phase of children with epilepsy and their incidence of hyperactivity.

Method:A retrospective cohort study was performed by collecting data from medical records of 23 children in Dr. Sardjito General Hospital from 2015 to 2019. Additional data were collected via direct interview when subjects visited the hospital for routine follow- up. A validated Food Frequency Questionnaire was used to collect dietary intake, especially salt and sugar rich food and drinks. Salt and sugar consumption were then categorized into ≤2000 mg and >2000 mg, and ≤50 gr and >50 gr, correspondingly. Seizure-free phase was defined as no seizure episode during minimal duration of 1 month, while recurrence was defined as seizures occurred after seizure-free phase. Seizure-free phase consisted of 3 indicators: onset of seizure-free which divided into ≤6 months and >6 months; duration of seizure-free that divided into <1 year and ≥1 year; and recurrence of seizure divided into present or absent.

Result: The average salt intake was 874.1 mg, and the average sugar consumption was 62.7 grams. There was no significant difference in sugar consumption between < 6 months and > 6 months onset of seizure free groups (p=0.539), between short (<1 year) and long duration of seizure free groups (p=0.142), between recurrence incidence group (p=1.000), and between hyperactivity groups (p=1.000). There was no significant difference in salt consumption either between duration of seizure free groups (p=0.438), recurrence groups (p=0.486), and hyperactivity groups (p=1.000), respectively. However, salt consumption was found to be significantly higher in children with seizure free onset less than 6 month (p= 0.012).

Conclusions: Salt consumption may influence seizure-free onset but not its duration, recurrence frequency, and increased hyperactivity. Sugar consumption may pose no effect either on increased hyperactivity, seizure-free duration, seizure-free onset, or seizure recurrence.

Abstract Number: 1072

Title: Direct and indirect costs and cost drivers of Tuberous sclerosis complex in children, adolescents, and caregivers: A multicenter cohort study

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Purpose: Tuberous Sclerosis Complex (TSC), a multisystem monogenetic disorder, is characterized by growth of benign tumors in several organs. This German multicenter study estimated the disease-specific costs and cost drivers associated with various organ manifestations in TSC.

Method: We assessed sociodemographic and clinical characteristics, organ manifestations, direct, indirect, out-of-pocket, and nursing care-level costs by a validated, three-month, retrospective questionnaire, completed by caregivers of individuals with TSC.

Result: The caregivers of 184 individuals (mean age 9.8 ± 5.3 years, range 0.7 – 21.8 years) responded. TSC disease manifestations included epilepsy (92%), skin disorders (86%), structural brain disorders (83%), heart and circulatory system disorders (67%), kidney and urinary tract disorders (53%), and psychiatric disorders (51%). Pathogenic variations in *TSC2* were reported in 46% and *TSC1* in 14% of individuals.
Mean total direct health care costs were EUR 4,949 per individual over three months (median EUR 2,062, 95% confidence interval [CI] EUR 4,088–5,863). Medication costs were the largest single direct cost category (54% of total direct costs, mean EUR 2,658), with the largest share due to mechanistic target of rapamycin (mTOR) inhibitors (47%, EUR 2,309). The cost of antiseizure medication (ASM) accounted only for a mean of EUR 260 (5%). Inpatient costs (21%, EUR 1,027) and ancillary therapy costs (8%, EUR 407) were further important direct

cost components. The mean three-month-cost of nursing care was EUR 1,163 (median EUR 1,635). Indirect costs were higher for mothers than for fathers.
ASM polytherapy (≥2 ASM) and the use of mTOR inhibitors were independent drivers of direct costs, disability and psychiatric disorders were independent drivers of indirect costs and of nursing care costs.

Conclusions: This study demonstrates the substantial direct, indirect, medication, and nursing care costs associated with TSC over three months, highlighting the spectrum of organ manifestations and treatment needs in the German healthcare setting.

Abstract Number: 1075

Title: Autoimmune encephalitis in children with new onset seizures: Outcomes of a historical cohort

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Purpose: Seizures are a common but inadequately analysed manifestation of autoimmune encephalitis (AIE). This retrospective chart review describes the clinical features and treatment response in children and adolescents with AIE with new onset seizures and compares the same with those without seizures.
Method: Cases with AIE, aged 2-15 years, presenting to a tertiary care teaching hospital in north India between Jan 2015 and Dec 2020 were retrospectively reviewed and followed. Clinical features, immunotherapy details and therapeutic responses were chronicled.

Result: Fifty-seven children with AIE were identified during the study period; 53 (92.9%) of them had seizures. Among those presenting with seizures, the underlying seropositive etiologies included: anti-N-methyl-D-aspartate (NMDA) (n=26), anti-glutamic acid decarboxylase (GAD) (n=7), anti-thyroid-peroxidase (TPO) (n=2), anti-Yo (n=1) and anti-Ma (n=1 encephalitis). Sixteen patients with AIE who presented with seizures were seronegative. Two patients each with anti-NMDA encephalitis and seronegative encephalitis presented without seizures.
Among seropositive AIE patients with seizures, 27/37 and 10/37 patients had generalized and focal seizures respectively compared to 11/16 and 5/16 in the seronegative with seizure group (p = 0.74). In the seropositive AIE patients with seizures, 27/37 responded to first-line treatment compared to 14/16 in the seronegative with seizures (p=0.3). Overall, 17/26 anti-NMDA receptor encephalitis cases with seizures responded to first-line treatment, compared to 24/27 in the non-anti-NMDA receptor encephalitis with seizures (p=0.017). Within the seropositive group, 17 (45.9%) responded to first-line treatment in the anti-NMDA receptor encephalitis with seizure cases compared to 10 (27%) in the non-anti-NMDA receptor encephalitis cases (p=0.8).

Conclusions: Immune dysfunction and related AIE is an important treatable cause of seizures. It is vital to identify it early for appropriate therapeutic decisions.

Abstract Number: 1077

Title: Continuous spike and wave during sleep in Prader-Willi syndrome

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Purpose: To report a case of epileptic encephalopathy with continuous spike and wave during sleep (CSWS) in a patient with Prader-Willi syndrome**.**

Method and Results: : A 9- year-old boy presented to our sleep center for evaluation of daytime sleepiness and cognitive dysfunction. He was followed from infancy for hypotonia, motor and speech delay connected with a phenotype of Prader-Willi syndrome. Genetic testing found no deletion in 15q11-q13 region. His intellectual level was within the normal range (low average). From the age of 7 years he developed frequent seizures classified as absences and atypical absences. Nocturnal polysomnography revealed CSWS. Treatment with corticosteroids, ACTH, valproate and topiramate led to an improvement of sleep EEG and to a reduction of seizure frequency. Brain MRI was normal. At the age of 10 years he had focal motor seizures and a recurrence of CSWS was apparent in polysomnography. Control of seizures and suppression of CSWS was achieved on therapy with clobazam and sultiam. Neurocognitive regression to a level of moderate intellectual disability was apparent. A detailed genetic testing revealed a rare cause of Prader-Willi syndrome – imprinting defect.

Conclusions: To the best of our knowledge this is the first report of continuous spike and wave during sleep in a patient with Prader -Willi syndrome. Sleep EEG should be considered in cases with uncontrolled epilepsy and/or cognitive decline.

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Abstract Number: 1079

Title: Ictal tachycardia is linked to higher age and focal seizures during sleep in children

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Purpose: Ictal heart rate (HR) changes have been used as a marker of ictal onset and HR variability has been discussed in the context of SUDEP.
We here aim to assess the frequency and timing of ictal tachycardia in children with epilepsy grouped in different age groups as well as the influence of seizure characteristics on the HR changes.

Method: We retrospectively reviewed 732 seizures of 195 patients aged 0 to 14 years (median 6.91) with epilepsy of any cause. Patients were grouped according to the age in groups (1) <1 year; (2) 1-2 years; (3) 3-6 years; (4) 7-10 years; and (5) 11-14 years. HR was assessed visually during the seizures and compared with the baseline HR 1 min before seizure onset. The time from seizure onset to ictal tachycardia, defined by convention as an increase in the HR by at least 33%, was described. Data related to seizure and patient characteristics were collected.

Result: Ictal tachycardia in at least one seizure was present in 70.25% of patients. It was more frequent in patients older than 7 years. 31.3% of patients had ictal tachycardia in all their seizures, this being also more frequent in older than 7 years. Ictal tachycardia was present in 51.09% of seizures. It was more frequent in focal seizures, in longer seizures and in seizures occurring in sleep. Ictal tachycardia occurred a median of 5 s after seizure onset. Early ictal tachycardia was more frequent in older than 7 years and in seizures during sleep.

Conclusions: Children older than 7 years especially with focal seizures during sleep could be ideal candidates for warning devices or stimulation therapies triggered by tachycardia detection. Future studies should aim to assess whether ictal HR changes in sleep might be a sign of autonomic vulnerability and increase risk of SUDEP.

Abstract Number: 1085

Title: Time lag to therapy and response to treatment in West Syndrome: A comparison between two cohorts - a decade apart

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Purpose: To compare clinico-etiologic profile, treatment lag and outcome in two cohorts of West syndrome a decade apart.

Method: A retrospective case analysis of hospital records of children registered in our weekly clinic between July 2018 to December 2020 was performed. Diagnosed cases of West syndrome/Infantile spasms were reviewed. Missing data on EEG findings, treatment and outcome was retrieved by telephonic interview. Cases with incomplete data were excluded. Data was compared with our previous cohort (2009-2012).

Result: A total of 218 cases of West syndrome were identified, data was complete for 164 cases who were finally analyzed. Median age of presentation in our current cohort was significantly younger (14 months (IQR 12-30) vs 18 months (IQR 9-22.5) in the old cohort, ($p \leq 0.0005$). Majority of cases had a structural etiology with perinatal hypoxic ischemic brain injury being the single largest contributor in both the cohorts (51% vs 55%). The median lag time in starting appropriate first line therapy (hormonal/vigabatrin) had decreased from 12 months (IQR 5-22 months) in old group to 5.5 months (IQR of 2-11 months). ACTH stayed the preferred (48% vs 45% in old cohort) first line agent. Vigabatrin usage increased to 17% from 5%. The two cohorts did not differ significantly in terms of outcome (complete electroclinical cessation of spasm) (overall response rate 67 % vs 68 % old cohort, p value - 0.8).

Conclusions: Age of presentation and lag time to definitive therapy significantly improved over the last decade. However, the same did not culminate into improvement in outcome of West syndrome. Investigation of additional factors in prospective multicentric studies is needed to improve outcome.

Abstract Number: 1094

Title: Epilepsy meetings experience from a public pediatric hospital in a resource-limited country.

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Purpose:
A proportion of epilepsy patients in resource-limited countries don't receive appropriate treatment.
Our Hospital is a public Paediatric Health Center, with fifteen general child neurology physicians and only one epilepsy specialist, without neurosurgeons nor MRI scans; both supplied within our public health network. To overcome our shortage of epileptologists we developed weekly epilepsy meetings aimed to advise diagnosis

and treatment, and to identify patients who would benefit from epilepsy surgery. We summarized our experience and assessed the impact of meeting groups in patients with epilepsy.

Method: Epilepsy meetings were carried out to analyze clinical, EEG and neuroimaging patients data. We included patients discussed from June 2019 to August 2020. We selected patients from our daily EEG Laboratory work. Clinical data of patients with EEG abnormalities were quickly reviewed and scheduled for the next meeting, with the following:-EEG focal abnormalities (epileptic and/or slow activity).-EEG generalized abnormalities in patients with and without antiepileptic drug (AED).Additionally, we included patients with normal EEG with suggestive epileptic seizures events, and others with any diagnostic doubt.Clinical characteristics, suggestions, and follow-up data were collected and analyzed.

Result:
A total of 107 patients were discussed. AED modifications were suggested in 39/107 (36.4%), including switch-off, add-on or start-on AED, with positive seizure outcome. In 6/107 (5.6%) we concluded non-epileptic paroxysmal event, take-off AED, was advised. In 11/107 (10,3%) we considered presurgical evaluation: 2/11 focal cortical dysplasia, 7/11 extensive unilateral lesion and 2/11 diffuse lesions with drops-attacks. 3/11 were hemispherectomized at our specialized referral centers. Remaining are waiting for surgery.
Conclusions: Epilepsy management can be optimized through meeting group discussion to attain accurate diagnosis and favorable seizure outcomes, including AED modification and presurgical evaluation. EEG findings were a key tool to identify goal patients.

Abstract Number: 1123

Title: Non-Convulsive Febrile Status Epilepticus mimicking a Nonepileptic Twilight State after a Febrile Seizure: Ictal Electroclinical and Evolutive study

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Purpose: Febrile Status Epilepticus (FSE) evolves from a Febrile Seizure (FS) in 5% of cases. Its prompt recognition is challenging, especially when motor manifestations are absent (Hesdorffer DC et al. Epilepsia 2012Sep;53(9):1471-80.). We describe the ictal electroclinical features of Non-Convulsive Febrile Status Epilepticus (NCFSE) following an apparently concluded FS, initially misinterpreted as postictal obtundation and in some way mimicking the “Nonepileptic twilight state” (Yamamoto N Epilepsia 1996Jan;37(1):31-5. Miyahara H et al. BrainDev 2018Oct;40(9):781-785. Specchio N et al. Epilepsia 2006Jun;47(6):1079-81.).

Method: We provide the electroclinical study of 18 children, collected in our Unit, that presented NCFSE after an apparently resolved FS, longitudinally followed-up for 1 year to 7 years 9 months (mean: 4 years 6 months).

Results: The age at first NCFSE ranged between 13 months and 5 years 8 months (mean: 2 years 8 months). Patients were examined after the spontaneous or rectal diazepam-induced resolution of a FS, while showing persisting awareness impairment. Absent responsiveness to painful stimulation, abnormal posturing and aphasia were present in all cases, perioral cyanosis in 10, hypersalivation in 12, automatisms in 3, gaze deviation and other lateralizing signs in 9; eyes were open. The EEG recording, started 15 to 140 minutes after the apparent resolution of the FS, was invariably characterized by delta or theta-delta pseudorhythmic activity, mainly involving the fronto-temporal regions, with hemispheric predominance in 12 (67%). The electroclinical condition, lasting 45 to 197 minutes, quickly recovered after intravenous diazepam. The follow-up revealed a normal neurodevelopment and EEG in almost all (behavioural disturbances emerged in 3, interictal EEG abnormalities in 1). In 5 subjects NCSE relapsed (twice in 2). None presented afebrile seizures.

Conclusion: Our series highlights the electroclinical features of a focal NCFSE. Distinctive elements are absent reactivity, cyanosis, lateralizing clinical and EEG signs, and the global improvement clearly tied to benzodiazepine administration.

Abstract Number: 1137

Title: Unusual case of drug-resistant epilepsy in patient with MED13 gene mutation

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Purpose: It is often difficult to differentiate between epileptic syndromes, due to many overlapping characteristics they present. Versatile clinical appearance, inconclusive tests and unreliable response to treatment often prevent physicians from establishing diagnoses and choosing the right therapeutic approach.

Method: We present the case of a 2-year-old female patient, first admitted in our clinic at the age of 6 months due to arrest of neurological development associated with spasms/myoclonia. Initial EEG indicated hypsarrhythmia, generalized polyspike-wave discharge, with difficulties in differentiating between Infantile Benign Myoclonic Epilepsy and West Syndrome. Normal blood tests, metabolic screening and cerebral MRI ruled out neurometabolic and structural causes. There was no family history of similar disease. Epileptic encephalopathy was the initial diagnosis made and Valproate treatment was administered. This aggravated the aspect of seizures by presenting sustained muscle contractions. Cortisone treatment was initiated and the patient responded positively, with complete remission of seizures, EEG path normalization and resumption of neurological development. After treatment cessation, seizures returned with uncertain aspects of myoclonia/spasms. Levetiracetam, Topiramate, Clobazam and Vigabatrin treatments were subsequently initiated, with no long-term success. In time, the developmental gap between the patient and her age category widened, which tilted the diagnosis towards West Syndrome. Genetic testing was recommended and cortisone treatment reinitiated, alongside a ketogenic diet, temporarily managing symptoms.

Result: Genetic testing using the Epileptic Encephalopathy Panel was inconclusive; the test was extended to Whole Exome Sequencing, identifying a heterozygous missense variant MED13 c.1867A>G, p.(Lys623Glu). Currently, there are no other individuals with such variants in the ExAC reference population cohort.

Conclusions: What is unusual about this case is the expression of the MED13 gene variant through recurring, drug-resistant epileptic seizures. While 13 other affected individuals with MED13 variants have been recorded, presenting developmental delays, intellectual disability and dysmorphisms, only one other patient developed severe drug-resistant epilepsy.

Abstract Number: 1140

Title: Felbamate role in intractable pediatric epilepsy- should we keep on using it as the last resort?

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Purpose: Felbamate is an approved anti-epileptic drug, however, concerns regarding adverse events may withhold its wide use in children. We aimed to examine the efficacy and safety of felbamate in children with drug resistant epilepsy and delineate the subjects that may benefit the most from treatment.

Method: We retrospectively reviewed files of all patients who received felbamate in our tertiary epilepsy clinic. Efficacy was determined following three months of treatment according to seizure reduction rate and electrographic improvement. Adverse reactions were monitored by reported symptoms and routine blood tests.

Result: Our study included 75 children (mean age 8.9 years± 3.7 years), of whom 53 were treated for seizures, 16 for electrical status during sleep (ESES) and 6 for both. The most common causes for epilepsy were genetic (29%) and acquired structural damage (18%). The median number of previous antiepileptic drugs (AEDs) was six (interquartile range 4-8), and a third were previously treated with other modalities. Response ≥50% was documented in 37/75 patients (49%) of patients at a usual dose of 40 mg/kg/day and 9/75 (12%) had complete response, of whom 3 for ESES, 4 for epilepsy and 2 for both. The median follow- up time of 18 months. Adverse reactions were seen in 19/75 patients (25%), among them three cases of elevated liver enzymes that later normalized and one case of neutropenia with normal bone marrow aspiration, all continued treatment. We did not find significant predicting factors for treatment success. However, we noticed that 3/4 of children with epilepsy following herpes encephalitis showed a clinical and electrographic dramatic response.

Conclusions: Felbamate is an efficient antiepileptic drug in children. No elevated rate of adverse reactions was seen compared to other AEDs. The positive findings in patients following herpes encephalitis and in some patients with steroid resistant ESES mandate further investigation.

Abstract Number: 1163

Title: Telemedicine, health disparities and seizure control in pediatric epilepsy during the COVID-19 pandemic

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Purpose: The COVID-19 pandemic resulted in an unprecedented shift towards, and rapid introduction of, telemedicine. However, how the shelter-at-home orders and switch to telemedicine have affected pediatric epilepsy remains unknown. Documentation of seizure frequencies through Common Data Elements (CDE), embedded into many Electronic Medical Record (EMR) Systems shortly before the pandemic, allowed us to compare seizure control in children with epilepsy seen in-person or by telemedicine.

Method: This study was a retrospective comparison of 26986 in-person encounters and 8919 telehealth encounters from September 6th 2019 through September 11th, 2020, with seizure frequency assessed through CDE according to the formats suggested by the Epilepsy Learning Health System and Pediatric Epilepsy Learning Health System. Using EMR extraction methods followed by statistical analysis, we compared seizure frequencies in both groups and assessed improvement or worsening in patients with more than one visit assessed by CDE.

Result: We did not find differences in seizures frequencies in 1094 in-person and 544 telemedicine visits with documented seizure frequency. However, we did find that patients with household income less than the

median of $72,484 were more likely to have seizures worsen over time (OR 3.42, 95% CI 1.54-8.61, p<0.01). Hispanic/Latino patients who were below the median household income were more likely to experience any seizures (OR 2.39, 95% CI 1.30-4.73, p<0.01) and more likely to experience worsening seizures (OR 3.46, 95% CI 1.60-7.08, p<0.01).

Conclusions: Implementation of standardized documentation allowed us to examine the effects of telemedicine on disease severity in childhood epilepsies. While rapid adaptation of telemedicine amid the COVID-19 pandemic did not result in worsened seizure control, barriers in access to healthcare for children have been exacerbated by the pandemic, resulting in increased seizure burden in underrepresented minorities. Adequately addressing health disparities in telemedicine will remain an important task for the future.

Abstract Number: 1177

Title: Early off-label treatment with Fenfluramine in Dravet syndrome: benefits and possible influence on the outcome.

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Purpose: Dravet Syndrome (DS) is characterized by frequent episodes of status epilepticus (SE), which can lead to severe sequelae (De Liso et al. 2020). Randomized clinical trials have demonstrated the efficacy of fenfluramine (FFA) as add-on therapy in patients with DS. The use of FFA is approved in children aged >2 years old, and its efficacy has been reported elsewhere (Nabbout et al. 2020; Specchio et al. 2020). We report the off-label early use of FFA in a DS patient treated from the age of 12 months.

Method: FFA was given in a 12 months boy with DS, with a de novo SCN1A pathogenic variant (c.1277A> C; p.Tyr426Ser). Since the age of 4 months, he presented monthly focal hemiclonic seizures, with or without fever, lasting between 5-10 minutes. At the age of 11 months, while he was on VPA, CLB and STP, he presented two episodes of SE, that required ICU admission. At the age of 12 months, we added FFA up to 0.4 mg/kg/day.

Result: During the 6 months of follow-up, he presented 2 brief (<5 minutes) febrile seizures, with spontaneous remission. FFA was well tolerated, except for a mild loss of appetite. Echocardiogram was unremarkable.

Conclusions: To our knowledge this is the first DS patient treated with FFA below the age of 2 years. Add-on FFA, after 6-months follow-up, prevented further afebrile seizures and status epilepticus, and reduced febrile seizures. Experimental data show that chronic FFA administration in zebrafish model of DS before the seizure onset decreased arborization in GABAergic neurons, acting on the neurobiological process (Tiraboschi et al. 2020). FFA administer very early in the disease course might act as a disease modifying drug (Schoonjans and Ceulemans 2021). Based on these experimental data, it would be interesting to understand if longitudinal data confirm the latter hypothesis.

Abstract Number: 1212

Title: Effective ketogenic diet in CACNA1A–related 'epilepsy of infancy with migrating focal seizures (EIMFS)'

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Purpose: Ketogenic diet has been braodly used in different types of developmental and epileptic encephalopathy. The mutations of the gene enconding calcium channel, voltage-dependent, P/Q type, alpha 1A subunit (*CACNA1A*) have been recently reported in the patients with developmental and epileptic encephalopathy whose seizures occur in early infancy and are multidrug-resistent. In a 3-month-old boy with epilepsy of infancy with migrating focal seizures (EIMFS) whose seizure were effectively controlled on ketogenic diet, we performed whole exome sequencing (WES) to find a genetic cause.

Method: Clinical data in the patient were retrospectively reviewed. WES was performed in the proband.

Result: A 3-month-old boy presented status epilepticus. His perinatal and family history were non-specific. He was globally delayed with normal growth. The patient had different types of focal motor seizures. On ictal electrocephalogram, migrating focal epileptiform discharges from unilateral hemisphere to the contralateral one were recorded. The proband had recurrent seizures, despite multiple antiepileptic drugs (e.g. lorazepam, fosphenytoin, levetiracetam, phenobarbital; midazolam, ketamine; pyridoxine and clonazepam). Brain magnetic resonance imaging was normal. Metabolic screening, chromosomal analysis, and chromosomal microarray study reveal no abnormalities. On 11th day, ketogenic diet was started. He became seizure-free. Ketogenic diet were tapered after 6 months of treatment, being completely discontinued in 11 months. On his last visit 3 months after discontinuation, he was seizure free on levetiracetam, clonazepam and pyridoxine. WES revealed the two likely pathogenic and novel variants, c.899A>C and c.2808del of *CACNA1A*. They were verified with Sanger sequencing in the proband. The second variant was found in his mother.

Conclusions: This case with *CACNA1A* epileptic encephalopathy presenting as EIMFS had rare bialleic muations, either of which were noble mutations not yet reported. Through this report, ketogenic diet can be another option to control seizures in *CACNA1A* epileptic encephalopathy.

Abstract Number: 1234

Title: Fetal outcome in anti-NMDAR encephalitis during pregnancy: a systematic review.

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Purpose: Anti-NMDA receptor encephalitis is an autoimmune inflammatory disease which mainly affects young women, causing psychiatric and neurological manifestations. Pathogenic antibodies target extracellular domain GluN1 subunit receptor. An increasing number of reports show that anti-NMDAR encephalitis can occur also during pregnancy leading to maternal and fetal distress. In this systematic review we analyzed fetal outcome after maternal anti-NMDAR antibodies exposure during pregnancy, summarizing the available data.

Method: We realized a systematic search of the literature to identify epidemiological, clinical, serological data of pregnant women with anti-NMDAR encephalitis and their children, analyzing pregnancy outcome. Mothers' neurologic outcomes were assessed using the modified Rankin Scale (mRS). We examined the age and neurologic symptoms of the mothers, presence of an underlying tumor, immunotherapies used during pregnancy, duration of the pregnancy, and type of delivery. Outcomes of the infants were based on clinical features, developmental abnormality, atypical behavior, the APGAR score and magnetic resonance imaging.

Result: Twenty articles were included with a total of 37 cases of Anti-NMDAR encephalitis during pregnancy. The incidence of anti-NMDAR encephalitis was higher during the first trimester of pregnancy. Ovarian teratoma was found to be the underlying cause of encephalitis in 2/37 cases. Immunotherapy was used in 20% of cases.

Pregnancy outcome was positive in 80% of cases with less than 10% of newborn suffering from transient neurological or respiratory symptoms. Prematurity was found in 40% of cases. At the follow-up, children's neurocognitive development impairment was found in less than 20% of patients. Data actually showed transplacental antibodies transition. Infants with neuropsychiatric symptoms often had anti-NMDAR antibodies serum positivity.

Conclusions: Anti-NMDAR encephalitis can be a severe comorbidity during pregnancy. Pregnancy and fetal outcome is usually positive, though children neurocognitive development impairment can occur. Long-term effects of fetus anti-NMDAR antibodies exposure have to be better explored.

Abstract Number: 1238

Title: PRRT2-gene mutation causing epilepsy in a 2-year-old patient with bilateral periventricular heterotopia - a case report

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Purpose: PRRT2 gene is located on chromosone 16p11.2, encoding the proline-rich transmembrane protein 2. PRRT2 mutations are responsible of numerous neurological disorders, but mostly of self-limited infantile epilepsy and paroxysmal kinesigenic dyskinesia. This paper aims at presenting a case of PRRT2-gene mutation causing epilepsy in a patient with bilateral periventricular heterotopia.

Method: We will present a case of a 2-year-old girl that at the age of 1 yo had 4 febrile seizures over 24h. Mild elevation of CSF cell count correlated with slow EEG activity raised suspicion of encephalitis. VPA was initiated. Repetitive EEG patterns were normal over the following 6 months so the antiepileptic treatment was discontinued. After 4 months she was admitted to our clinic for 5 focal to bilateral epileptic seizures over 24h.

Result: The EEG performed was normal. Neurological examination: mild left leg pyramidal syndrome and expressive language delay. Brain imaging identified mild left occipital leukoencephalopathy and bilateral periventricular heterotopia. Treatment with VPA was restarted. We performed DNA testing that showed heterozygosity of a 398 kb deletion seq[GRCh37] del(16p11.2), chr16:g.29801995_30199957del. She has no seizures after the reinitiation of VPA.

Conclusions: This case is worthy of note since PRRT2-gene mutation is often associated with a type of benign, age- and self-limited epilepsy that mostly does not associate with any MRI abnormalities.

Abstract Number: 1290

Title: Perampanel for intractable epilepsy in children and adolescents: an online survey from India

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Purpose: To determine the clinical indications of perampanel in pediatric patients, its efficacy in achieving seizure control, adverse effects and retention rate from a real-world pedaitric cohort.

Method: We designed a Google form based survey containing questions regarding use of perampanel in children, its dose, clinical indications, proportion of patients with favourable response and adverse effects in last 2 years in patients aged 4-18 years. It was electronically disseminated in May 2020 among paediatricians and paediatric neurologists practicing in various states of India.

Result: 108 doctors responded to the survey, out of which 23(21%) urban practitioners agreed to have used perampanel in 97 patients (10.4±3.2 years, 71% boys, median number of previous ASMs tried 3 (range-2-6), follow up duration-11.4±5.2 months, dose 3.2±1.1 mg/day [range-2-8 mg]). Clinical indications were structural epilepsy (68%), probable/definite genetic aetiology (22%) and probable autoimmune aetiology (10%). Predominant focal onset, generalized onset and both types of seizures were present in 53%, 26% and 21% of patients. The response rates (defined as at least 50 % seizure reduction) was 45 % after 6 months of treatment and at least 75% reduction in seizure frequency and freedom from seizures was reached in 14 % and 11% respectively. The retention rates were 79% and 71% at 6 and 12 months, respectively, but only 4 patients (4%) discontinued due to serious adverse effects. The other causes for discontinuation were ineffectiveness of the drug and excessive cost. Adverse events reported were dizziness (10%), somnolence (9%), fatigue (7%), irritability (7%), gastric upset (7%), nausea/vomiting (6%) and gait instability (3%). Clinically patients with focal seizures and non-structural aetiology responded more favourably to perampanel, although not statistically significant (p=0.13 and 0.24 respectively).

Conclusions: As a real-world paediatric cohort from Indian subcontinent, our survey demonstrated the efficacy and tolerability of perampanel in children with intractable epilepsy.

Abstract Number: 1296

Title: Utilising genetic investigations in a secondary paediatric epilepsy service to aid diagnosis and management

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Purpose: Genetic epilepsies in childhood comprise disorders associated with genetic mutations that cause epilepsies with variable phenotypes and co-morbidities. The high costs and technical complexity of classical genetic testing for 'rare' genetic epilepsies has historically led to the reservation of such testing for patients with strong family history in tertiary settings.

Method: Clinical and genetic information (including chromosomal arrays and epilepsy gene panels) were analysed in 100 patients from a database of well-phenotyped children with epilepsy as of 7th September 2020 in a secondary epilepsy service. Epilepsy classification and etiological diagnosis were based on clinical presentations before genetic testing.

Result: Data is presented from the first 100 patients to illustrate the efficacy of genetic testing in a secondary epilepsy service. Just over one-third of patients, (35%) had been referred for genetic testing. Of these patients, almost two-thirds, 63% (22/35) had genetic findings providing a cause for their epilepsy. The remaining 32% (11/35) had negative screening results.
In the sub-group of 22 patients that received a positive genetic diagnosis, only 18% (4/22) had a positive family history with 81% (18/22) having no reported family history of epilepsy or seizures.
Notably, 3 sets of siblings were identified among patients with family history of epilepsy including one instance of clinically suspected parental mosaicism wherein siblings were diagnosed with identical 'rare' *de novo* mutations.

Conclusions: The use of high-throughput technologies such as next-generation sequencing has improved the ability to sequence DNA and detect a wider range of mutations contributing to early-onset epilepsies, with

targeted gene panels yielding upto 30% genetic diagnoses for paediatric cohorts. By providing genetic investigations to children with epilepsy in secondary epilepsy services, positive genetic diagnosis yield is ~63% among tested individuals, highlighting the emergence of genetics as a useful tool for epilepsy diagnosis and management in a secondary epilepsy service.

Abstract Number: 1302

Title: Prolonged EEG recording in the evaluation of paroxysmal events at a tertiary paediatric neurology centre: Is it worth it?

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Purpose: To evaluate the indications and diagnostic value of Prolonged EEG recordings in children at a tertiary centre and determine whether it affects clinical outcome.

Method: Children aged 0-18 years who had an EEG recording of > 1 hour duration over a 6-month period were included in the study. EEG reports and electronic patient records were retrospectively reviewed and analysed.

Result: 146 patient notes were reviewed. The mean patient age was 4.6 years, with 43% being less than 1 year. 49% were outpatients and 51% were inpatients, including 23% from ITUs. 53% of prolonged EEG recordings were requested to determine the nature of paroxysmal events. The majority (69%) of EEG recordings were of less than 6 hours duration (range 1-68 hours). 66% (96/145) of EEG recordings were abnormal. A habitual event was captured in 45% (65/145) of recordings, of which 37% (24/65) seizures and 63% (41/65) were other events. 69% of confirmed seizures were captured within 6 hours, most often in children < 1 year. Motor features were most common in those with confirmed seizures. 69% of clinical management decisions related directly to the findings on EEG. In those with a confirmed seizure the most common outcome was a change in their medication (23/35 - 66%). In patients with other events, this led to a weaning of anti-seizure medications or commencing treatment for dystonia.

Conclusions: Prolonged EEG is a very useful diagnostic tool which can help identify seizures, especially in sick children, thus aiding management. It helps recognise seizure mimics, preventing misdiagnosis and inappropriate treatment. We found EEG recordings of 6 hours or less to be sufficient in the majority of patients for capturing events and to answer the clinical query in line with other studies. This has important management and resource implications.

Abstract Number: 1305

Title: Prevalence of the EEG abnormality in overnight polysomnography of children.

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Purpose: The overnight polysomnography (PSG) is used as one of the diagnoses of sleep disorders. In addition to the evaluation of sleep and respiratory physiology, it is possible to find abnormal findings such as epileptic discharges and asymmetry by electroencephalography (EEG). It is known that the detection rate of epileptiform discharges during sleep is high in children, but there is little information on the pathological significance and treatment. We examine EEG abnormalities detected by PSG.

Method: The subjects were children under the age of 15 who underwent PSG from April, 2015 to March, 2020. EEG wearing site in PSG; F3, F4, C3, C4, O1, O2. Clinical information was collected by retrospective examination of medical records.

Result: Of the 1300 patients who underwent PSG, 68 patients(5.2%) detected epileptic discharges. Of these, 12 patients who had already been diagnosed with epilepsy and 27 patients who had not undergone general EEG were excluded. EEG was performed in 29 of 68 patients, and abnormal waves were found in 19 patients.

Conclusions: EEG abnormalities in PSG were observed in 5.2% excluding the history of epilepsy, and the results were similar to those reported in the past. There are two purpose of the PSG: (1) classification and severity of sleep apnea, and (2) diagnosis and evaluation of sleep disorders. Therefore, detection of epileptic discharges are incidental findings. There is some report suggesting a relationship between EEG abnormalities and transient cognitive impairment, and it is necessary to examine the pathological significance.

Abstract Number: 1331

Title: Use of phenytoin as a rescue drug in Dravet syndrome: a retrospective study and a systematic review

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Purpose: Dravet syndrome is an infantile-onset epileptic encephalopathy characterized by several types of seizures as well as cognitive, behavioral, and motor impairment. Status epilepticus episodes in the first years of life are very common. Sodium channel blockers are usually avoided due to worsening effect. We evaluate the use of phenytoin as a rescue drug for status epilepticus in patients with Dravet syndrome and summarize the state of the art by a systematic review.

Method: A 9-year retrospective study on the management of status epilepticus of Dravet syndrome patients focusing on the effect of phenytoin on the seizure and in the following days. We also conducted a systematic review (PubMed/Medline). Articles were selected based on the title and abstract as well as the type of publication.

Result: We identified 59 status epilepticus episodes in a total of 23 patients. We looked at treatments given and concluded that, as far as phenytoin is concerned, it has been used 21 times; phenytoin stopped the status epilepticus without relapse, in 15/21. It also helped in stopping the seizure but with a relapse in 1 out of 21 cases. Phenytoin did not stop the seizure in 5 cases out of 21. None of the patients experienced any worsening. Few articles state that sodium channels blockers should be avoided. They state that phenytoin should be avoided as well without reporting any data or citing pervious work.

Conclusions: We did not observe any worsening or any absence of efficacy of phenytoin as a rescue drug for status epilepticus in Dravet syndrome. There is no similar report limiting the comparison of our data with other study. The use of phenytoin for status epilepticus management should not be excluded. Further studies are needed

Abstract Number: 1333

Title: Predictive factors of seizure reduction due to ketogenic diet therapy in childhood epilepsy

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Purpose: To identify children with epilepsy showing a seizure reduction to ketogenic diet therapy (KDT) and to find predictors for its effectiveness.

Method: We analyzed data from our single-center prospective longitudinal database on childhood epilepsy treated with KDT. Outcome measures included seizure reduction (in %) and seizure reduction > 50% at 3 months. Predictive factors studied were: age at KDT start, epilepsy duration before KDT, gender, known etiology, epilepsy syndrome, number of seizure types, presence of focal seizures +/- generalized tonic clonic seizures, serum levels of beta-hydroxybutyrate (BHB) before and after KDT start, and number of antiseizure drugs (ASD) before start. A final regression model included 4 factors.

Result: The final analysis was performed on 183 patients. At 3 months, absolute seizure reduction was median 67%. Relevant correlations coefficients to seizure reduction at 3 months in percent were observed for: number of ASD before start (- 1.63; p = 0.027), BHB at dismissal (after 1 week of KDT) (0.156; p = 0.061), BHB after 3 months (- 0.414; p = 0.000), fat/ non-fat ratio at 3 months (0.195; p = 0.010), and age-appropriate neurological development before start (- 0.210; p = 0.004). Regression analysis revealed that age-appropriate neurological development, higher BHB at 3 months, shorter duration before KDT, lower ratio and lower number of ASD positively predicted outcome (p=0.04). A best model included epilepsy syndrome and higher BHB at dismissal (p=0.006).

Conclusions: We were able to identify age-appropriate development at start, shorter duration of epilepsy, lower number of ASD, epilepsy syndrome and a higher BHB level at dismissal as predictive factors. However, a reliable individual prediction model before starting KDT has to be validated in a larger patient cohort.

Abstract Number: 1351

Title: treatment of Electrical Status Epilepticus during Sleep in children: an online survey from India

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Purpose: To determine the current status of various treatment options for children with Electrical Status in Slow-Wave Sleep (ESES) according to Indian physicians.

Method: We designed a Google form based survey containing questions regarding clinical, electrographic characteristics, preferred treatment options and their efficacy/safety in children with ESES aged <18 years. It was electronically disseminated in May 2020 among paediatricians and paediatric neurologists practicing in various states of India.

Result: Total 83 doctors responded to the survey, out of which 26 agreed to have treated 61 children with ESES in the last two years (72% boys, 9.6±2.8 years, 84% CSWS, 10% Landau Kleffner syndrome and 6% malignant BCECTS, 65% had structural abnormality in neuroimaging, mainly the cases with CSWS). While 81% of the cases with CSWS were already on anti-seizure medications (ASM), none of the patients with LKS were on ASM at the time of diagnosis and all patients with malignant BCECTS were receiving carbamazepine/oxcarbazepine at the time of diagnosis. Cognitive decline (84%), neuropsychiatric features/behavioural abnormalities (67%), memory impairment (56%) and acquired aphasia (10%) were predominant presenting symptom.

Most preferred first-line treatment in those who were not on ASMs, was to start anti-seizure medications (82%) or optimization of ASM (like changing from carbamazepine to valproate in malignant BCECTS (18%) and in those who were already receiving ASMs was oral/intravenous corticosteroids (89%) or concomitant corticosteroid and IVIG (11%). However, none of the patients responded completely to ASMs alone and ultimately required corticosteroids. Overall, 62% and 51% patients showed meaningful response in EEG and cognitive/behavioural features, 25% had adverse effects of corticosteroid, but only 4% required discontinuation. Normal neuroimaging (p=0.02) and absence of pre-existing seizures (p=0.01) were good prognostic factors.

Conclusions: Corticosteroids along with ASMs are the most preferred treatment for ESES, which causes improvement in at least half of these cases.

Abstract Number: 1363

Title: atypical evolution of epilepsy with myoclonic-atonic seizures

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Purpose: To describe the atypical evolution of cases with epilepsy with myoclonic atonic seizures (EMAS) to idiopathic generalized epilepsy with photosensitivity in pubertal age and / or generalized electroencephalographic activity with photosensitivity.

Method: Retrospective descriptive study carried out based on a review of 12 clinical cases, of which, 4 patients evaluated before EMAS in preschool age were selected; who underwent clinical and electroencephalographic follow-up until adolescence and who progressed to generalized epilepsy and / or generalized paroxysmal activity with photosensitivity.

Result: The 4 patients (33,3%) identified presented EMAS in childhood and required management with combination therapy; 2 of them with difficult seizure control, but 4 (100%) with complete clinical control and finally resolution of the condition; withdrawal of medication after 3 crisis-free years, only one patient with mild cognitive impairment in his evolution. Reappearance of myoclonic seizures and / or typical absences and / or generalized tonic-clonic seizures at pubertal age were identified in 3 (75%) of the 4 patients; electroencephalographic findings in all patients of generalized interictal slow sharp wave activity at 3.5 Hz, frontal maximum, were found. The discharges were facilitated with photostimulation. Normal brain MRI in all patients (100%). Genetic panel was performed in 2 patients with negative results.

Conclusions: EMAS is a controversial epileptic encephalopathy with variable prognosis, from clinical resolution to drug resistance with variable cognitive impairment. An unusual evolution was found in the patients, after EMAS control to idiopathic generalized epilepsy and / or generalized paroxysmal activity with photosensitivity. This evolution should be studied in greater depth, in order to allow a better understanding of the pathophysiology and a better classification.

Abstract Number: 1364

Title: Vigabatrin and oral steroids given sequentially or combined for infantile spasm syndrome: comparison of two real-life populations

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Purpose: Infantile spasm syndrome (SSI) is a challenging infantile epilepsy syndrome without international consensus guidelines. A prospective study in 2017 (O'Callaghan randomized clinical trial) showed that combination of oral steroids and vigabatrin resulted into more spam free patients as compared to oral steroids alone

Method: We compared two real-life cohorts of infants with ISS: a first multicenter, retrospective cohort of 40 children treated by vigabatrin and steroids sequentially and a second prospective single-center cohort of 50 children treated by a combination of vigabatrin and steroid.

Result: The two cohorts were comparable for main epidemiological and electro-clinical characteristics at diagnosis. In the retrospective cohort, 11 patients were spasm-free after the first line of treatment (i.e. vigabatrin) (27.5%), 11 became spasm-free with the second line (i.e. oral steroids) (38%). Together vigabatrin and oral steroids given sequentially resulted into 55% of spasm-free infants 2 to 4 weeks after the diagnosis of ISS. In the prospective cohort, 34 patients (68%) were free from spasms after the combined treatment (vigabatrin and oral prednisolone) no later than 14 days post-diagnosis. In this prospective cohort, 70% of patients are still free from spasms in June 2021

Conclusions: In this real-life evaluation, combination of vigabatrin and oral steroid seems to result into an earlier arrest of epileptic spasms than a sequential treatment. Several studies have pinpointed that treatment delay is associated with an increased risk for a worse epilepsy and cognitive outcome. While it is not yet clear whether the combination treatment globally changes the cognitive impact of ISS, the impact at the individual level could be beneficial as suggested by the long-term follow-up of the O'Callaghan randomized clinical trial

Abstract Number: 1373

Title: Language ominance in children with epilepsy using near-infrared spectroscopy

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Language ominance in children with epilepsy using near-infrared spectroscopy

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Purpose: There are some studies using near-infrared spectroscopy (NIRS) to investigate language lateralization, especially in presurgical localization of the dominant hemisphere in adult epileptic patients as an alternative to the Wada test. But there are few studies in child epileptic patients.

Method: In the present study, NIRS data were obtained from ten epileptic and ten normal children to determine language dominance. Each child was allotted a word-generation task for 30 s. The targeted regions of NIRS were nearby bilateral inferior frontal areas.

Result: In 9 of 10 normal children, who were all right-handed, the language functions with NIRS were lateralized to the left hemisphere. In all 4 epileptic children evaluated by Wada test, the results of the NIRS study were completely consistent with those of the Wada test. In 8 of 10 epileptic children, the NIRS findings

are consistent with the side opposite to the handness. 4 cases at left-side epileptic focus that had seizure onset from less than 3 years showed right dominance, namely, atypical language dominance.

Conclusions: Although all epileptic children were intellectual disable and had the anxiety of tests, they could test NIRS in relief beside their parents or on their parents' lap. As
NIRS is non-invasive and tolerant to movement artifacts, NIRS is well suited to study language function in children, especially with intellectual disability.

Abstract Number: 1374

Title: Clinical characteristics of MOGHE patients with SLC35A2 mutations compared with FCD patients with mTOR pathway mutations

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Purpose: Mild malformation of cortical development with oligodendroglial hyperplasia in epilepsy (MOGHE) is a distinct clinical entity from focal cortical dysplasia (FCD), with a different molecular etiology. However, before surgery and pathologic investigation, it is hard to differentiate patients with MOGHE and FCD due to its similar appearance on brain MRI. Therefore, we aimed to investigate clinical characteristics of patients with MOGHE and FCD.

Method: A retrospective chart review was done to collect clinical characteristics of patients who received epilepsy surgery in Severance Children's Hospital, and belonged to either one group: 1) FCD patients with somatic mutations in mTOR pathway, or 2) MOGHE patients with mutations in *SLC35A2*.

Result: Of the total 39 patients included in the study, 24 patients were FCD patients with somatic mTOR pathway mutations (16 *MTOR*, 6 *TSC1*, 1 *TSC2*, and 1 *AKT3* mutations) while 15 patients were MOGHE patients with *SLC35A2* mutations. While the age at seizure onset, the age at surgery, the lead time from seizure onset to surgery, the surgical outcome scale did not differ significantly between FCD and MOGHE patients, significantly higher proportions of MOGHE patients showed generalized seizures (100% vs. 18.8%, $p < 0.001$) and developmental and epileptic encephalopathy (100% vs. 18.8%, $p < 0.001$). Also, MOGHE patients showed significantly poorer developmental

Conclusions: Patients with MOGHE present with generalized seizures from the initial onset of seizures, present with developmental and epileptic encephalopathy such as West syndrome or Lennox-Gastaut syndrome, and hence receive more profound deleterious effect on development than patients with FCD. Therefore, earlier surgical intervention is crucial in patients with MOGHE.

Pandemic Response

Abstract Number: 790

Title: The impact of the Covid-19 pandemic on children and families undergoing epilepsy surgery

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Purpose: The COVID-19 pandemic has had a significant impact on how healthcare is delivered to patients with epilepsy. Epilepsy surgery is a strategy with high reported satisfaction rates but can be a stressful road for

patients. We aimed to determine significant challenges faced by the families of children undergoing epilepsy surgery during the pandemic.

Methods: Cross-sectional quality assessment study that included pediatric patients (<18 years) that underwent epilepsy surgery at Children's Hospital/LHSC comparing two groups (1. March 2020-February 2021, 2. March 2019-February 2020).
We collected data at follow-up using a prespecified questionnaire (five quality assurance questions, one open-ended question) asking to evaluate difficulties on a scale of 0-4. Questions focused on seizure activity, concerns over procedure delay, changes in hospital regulations, fear of exposure to COVID-19 and virtual appointments.

Results: Thirty-five surgeries were planned from March 2020 to February 2021, but only 12 (34%) were performed (a 60% decrease vs. 2019). Out of the 12 families, 11 answered the survey. The most challenging aspect was ongoing seizure activity while waiting for surgery expressed by 10/11 families. Four caregivers ranked it as considerably or extremely challenging. The limitations in the number of allowed-in-hospital visitors were deemed significantly or extremely challenging by 5/11 (45%), and the fear of being exposed to COVID-19 was low by 6/11 (54%) families. Two families reported extreme challenges while telemedicine consults.

Conclusions: These findings show how the pandemic impacted our epilepsy center regarding surgery. The number of surgical procedures was reduced considerably throughout the pandemic, with subsequential increased seizure activity and emotional burden on patients. Parents with no additional support expressed the most challenges but felt safe with the implemented COVID-19 measures. Most families were comfortable using telemedicine protocols. Limitations include a small sample size and recruitment from a single-site.

Abstract Number: 795

Title: Epilepsy during the COVID-19 pandemic: Our Experience from a single center

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Purpose: The first reported case of COVID-19 in Albania dates in March 2020. The new coronavirus has spread rapidly throughout the world to become a pandemic and its effects in the nervous system are still being investigated. In some cases seizures and epilepsy have been reported as a neurological complication of COVID-19. We aim to analyze all the cases with epilepsy during a 2 month period in the pandemic and compare them with pre-covid period of time in order to see if there is a relationship between SARS-Cov-2 virus and increased number of epilepsy patients.

Method: We collected all the data from the medical records of epilepsy inpatients of our hospital from January-February 2021 and compared the data to the same period of time in 2020.

Result: Of all 215 hospitalized patients during January-February 2021, 41 patients(19%) resulted with focal/bilateral epilepsy, with a male: female ratio of 14:2 and the mean age of 34±2 years old. Whereas in January-February 2020, 76 patients(11%) resulted with the same diagnosis.

Conclusions: An increased ratio of epilepsy cases is reported at our epilepsy center. There is still need to further investigate if there is a direct effect of COVID-19 and Epilepsy, but the analyzed data triggers a correlation. The follow up of our patients through telemedicine will give us further information to make adjustments in our results since this is an issue that needs further investigation.

Abstract Number: 835

Title: Incidence of status epilepticus in people with epilepsy during covid-19 pandemic

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Purpose: To determine the incidence and factors that associated with status epilepticus (SE) in people with epilepsy (PwE) before and during the Covid-19 pandemic.

Method: It was a retrospective study which obtained data of SE that occurred from March 2019 to February 2021 at Cipto Mangunkusumo General Hospital. Inclusion criteria was PwE who had SE. Subjects were divided into two groups which were before (between March 2019 and February 2020) and during the pandemic period (between March 2020 and February 2021). Demographic data, seizure classification, and antiepileptic drug (AED) history were analysed.

Result: There were 63 PwE who had SE between March 2019 and February 2021, the median age was 42 (18-80) years old with female predominance (66.7%). Most subjects had focal seizures (74.6%) caused by intracranial/structural lesion (63.5%), AED withdrawal (30.2%), and extracranial etiology (6.3%). SE cessation achieved in 55.6% subjects using polytherapy; phenytoin (52.4%), valproic acid (41.3%), levetiracetam (34.9%), topiramate (30.2%), and phenobarbital (1.6%). The incidences of SE before and during the pandemic were 61.9% and 38.1%, respectively. There were no significantly characteristics different between the two groups. Moreover, in the AED withdrawal etiology analysis subgroup, male tended to experience SE more frequent (66.7% vs 30%, p=0.13), as well as the use of polytherapy during the pandemic (55.6% vs 30%, p=0.25).

Conclusions: The incidence of SE did not increase during pandemic. There were no differences in characteristics. However, there was a tendency in male and polytherapy used within subjects who had AED withdrawal.

Abstract Number: 858

Title: New Onset Rare Para-Sagittal Seizures In the Setting of Covid-Related Acute Encephalopathy

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Purpose: Coronavirus is the third leading cause of death in the year 2020 per CDC report. Early landmark studies from Wuhan, China found that upwards of 36% of hospitalized patients with Covid-19 experienced neurologic manifestations of the disease, ranging from acute cerebrovascular accidents to impaired consciousness and muscular injury5. Since then, further studies have detailed other neurological symptoms: loss of smell and taste, agitation, confusion, seizures, and corticospinal tract signs such as enhanced tendon reflexes and clonus3. These occur with particular frequency when the burden of Covid-19 disease is severe enough to necessitate inpatient and intensive care stays There has been reports of underlying exacerbation seizure disorder but new onset onset epileptiform discharges are still rare

Method: Electronic medical records of an interesting patient prestening with atypical neurological manifestations in the setting of acute onset covid related encephalopathy at our institution

Result: We describe an interesting case of 79 year old woman with episodic acute onset right sided paresthesias with stiffening in the setting of covid related encephalopathy. The patient has no prior history of seizures and negative magnetic resonance imaging. . EEG showed presence of epileptiform discharges emanating from the left fronto central parietal regions. New onset left para-sagittal seizures were diagnosed

on the basis of clinical semiology and EEG data. Treatment with anticonvulsant resulted in normalization of EEG and resolution of focal deficits with improvement in mentation back to the baseline

Conclusions: Screening for ictal phenomena should be considered as a differential for all covid positive patients presenting with acute encephalopathy with atypical neurological presentation.

Abstract Number: 915

Title: Rethinking epilepsy trajectories and needs during COVID-19 pandemic

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Purpose: To evaluate care needs, emotional and behavioral changes, and parental stress indices in a cohort of pediatric patients with epilepsy and neurocognitive and emotional comorbidities at the time of the coronavirus disease 2019 (COVID-19) pandemic.

Methods: A prospective monocentric observational study involving 23 pediatric patients with epilepsy with neurocognitive and emotional comorbidities followed at Fondazione Mondino, University of Pavia, was carried out. Included patients were evaluated for epilepsy and neuropsychiatric assessment at t0 (from August 2019 and February 2020), and then at t1 (April-May 2020) and t2 (April- May 2021). At t1 and t2 patients accepted to participate to a phone follow-up visit and to refill CBCL and Parenting Stress Index-Short Form (PSI-SF) questionnaires. Descriptive statistics for demographic and clinical data, seizure frequency change, sleep and CBCL questionnaire scores before and during the COVID-19 pandemic, and PSI-SF scores have been computed. Moreover, results of a survey on the psychological burden during COVID lockdown will be reported.

Results: This study provides the parental-proxy report of emotional and behavioral profile changes of 23 pediatric patients with epilepsy and neurocognitive or emotional comorbidities during the COVID-19 pandemic. At t1 concerns for therapy monitoring at the time of lockdown emerged in 43% of families, and 30% of patients showed worries for an altered contact with the referring medical team. Patients with neurocognitive comorbidities were more likely to exhibit behavioral problems, especially externalizing problems compared with patients with a diagnosis of anxiety/depression. Data of follow-up at t2 will be presented.

Conclusion: Preliminary data and observation during the last year suggest the importance to monitor disease trajectory and behavior and affective symptoms, to rethink patients' needs and to make available telehealth strategies to provide effective care to patients and their families.

Abstract Number: 936

Title: Impact of COVID-19 pandemic on patients with epilepsy in Argentina

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Purpose: The COVID-19 pandemic and social preventive and mandatory isolation generated difficulties in the care of patients with epilepsy, being necessary to modify the access to the health system. The aim of this study

was to define the impact of the pandemic on epilepsy patients and how it affects the access to medication and the seizure-control during quarantine.

Method: This is a multicenter cross-sectional study, conducted in two centers of Argentina from April to August 2020. An electronic self-administered questionnaire was distributed to epilepsy patients by e-mail. The variables included were demographic and baseline clinical characteristics (age, gender, health insurance), change in seizure control, the difficulty in obtaining medications and accessing to the health care professional.

Result: Were contacted 488 patients (response rate of 49.6%), 58% were women, mean age of 37,6 years. Regarding to the health care system, 41,2% reported having prepaid health insurance, 22,3% regular medical care while 36,5% do not have medical insurance at all. An increase in seizure frequency was reported by 28.8% of de patients, and because of that, 9,4% of the patients had to go to the emergency room.
The main contact method used was the e-mail (35%) follow by the phone (15.4%) and attend the clinic in person (14.5%). Regarding to the prescription of antiseizure medications, 58% received it by e-mail and WhatsApp, 27,5% received it at the clinic while 13% were unable to receive it. However, 47% had problems accessing to the medications.

Conclusions: During the pandemic, medical care has had to incorporate new ways of communication, allowing most patients to continue with their treatment and control of the disease. Although approximately half of them had difficulties accessing to the medication. Our results indicate the importance of generating different strategies to guarantee a not in person patient-physician contact using alternative channels.

Abstract Number: 943

Title: Multi-centre development of a secure, cloud based, patient to clinician, neurology video transfer, classification and management syste

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Purpose: A government funded, interactive cloud storage platform (www.vcreate.tv/neuro) allowing patients and carers to upload video and linked metadata for neurological diagnosis was established during the Covid-19 pandemic. We describe the utility for epilepsy and paroxysmal disorders in 16 centres with the first centre active from 01/05/2020.

Method: Users are invited to register and utilise a password and passcode for access. Videos are uploaded with a structured history. The clinician classifies seizure type, syndrome, aetiology or other diagnosis using drop-

down menus. Users and clinicians complete online evaluations. Postcode allows linkage to user index of deprivation score. Consents for teaching by the local clinical team and research within a national neurology video research database with research ethics approval are optional. All data, except the video file, transfer to the electronic patient record.

Result: To 24/03/2021, 4582 video uploads (4024 paediatric, 558 adult), 1889 patients (1594 paediatric, 295 adult). 400-600 new videos per month. 323 physician and nurse users. Deprivation scores indicate equitable use across socio-economic groups. Paediatric classification: non-epileptic 55%, epileptic (36.5%), unknown (8.5%). Adult: non-epileptic 73.5% (34% dissociative, 41% movement disorders), epileptic 11%, unknown 15.5%. Paediatric seizure types include: focal impaired awareness (19%), generalised tonic clonic (18%), focal clonic (17%), epileptic spasms (13%). Non-epileptic events: tics (13%), normal behaviour (12%), sleep myoclonus (10%) gratification (8%), dissociative (5%). >95% carers ranked the system positively. Clinicians report video prevented face-to-face review in 57%, investigations in 44% and reduced time to diagnosis in 97%. Median time to review video and classify was 5 minutes.

Conclusions: Remote care is facilitated, investigations prevented or prioritised, with rapid diagnosis and efficiencies in the patient pathway. A rapidly growing teaching resource and research database for semiology and machine learning diagnostics for paroxysmal disorders has been established. We plan to establish the system in low-income countries without cost.

Abstract Number: 965

Title: Indonesian neurologist understanding and experience in epilepsy care during covid-19 pandemic

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Purpose: To gather information from Indonesian Neurologist understanding and experience about impact of Covid-19 pandemic on epilepsy care.

Method: Survey using ILAE's COVID-19 questionnaire for clinicians about impact of COVID-19 on epilepsy care, was conducted on June and November 2020 during Neurologist National webinars. All participants were Indonesian Neurologist. ILAE's COVID-19 questionnaire for clinicians consist of 4 open-ended and 2 closed-ended questions about their understanding, experience and research priorities.

Result: There were 381 participants. Most participants (75.33%) had sufficient understanding of how COVID-19 infection may present and affect seizure frequency and management in epilepsy. The top 3 urgent research priorities suggested from participants to cover current gap in clinical knowledge were COVID-19 treatment in epilepsy (32.5%), correlation between COVID-19 and epilepsy (24.7%), and association COVID-19 with heart disease (9.4%).
In experience section, 71.9% had never experience nor reported about new onset epilepsy as a neurological presentation or outcome related to COVID-19. Concerning these matters, 23.9% considered important research in clinical neurophysiology, neuro-intensive care, psychiatry problems and encephalitis in COVID-19. Furthermore, 60.4% participant could not anticipate disruptions in epilepsy care and supply of antiepileptic drugs (AED). Participants were aware about changes in patient's mental health, psychosocial and epilepsy

severity especially in nonadherence to AED (82.7%), anxiety (79.3%), depression (77.9%). Sleep patterns changes, increased risk of seizure-related accidents, and discriminations were less expressed by patients and their families/partners; 67.7%, 59.8%, and 59.6%, respectively. Fewer problems reported in alcohol/substance abuse (36.8%), isolation (35.4%), and suicidality (30.9%).

Conclusions: Indonesian Neurologist had sufficient understanding about impact of Covid-19 pandemic on epilepsy care. They were aware of patient's psychiatric problems and nonadherence to AED, but could not anticipate any disruptions in epilepsy care and AED supply. COVID-19 treatment in epilepsy was considered as priority research.

Abstract Number: 1135

Title: Pediatric patients with epilepsy showed elevate rate of anxious depressive symptoms during COVID-19 pandemic: preliminary findings of monocentric a cross-sectional study

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Purpose: Children and adolescents with epilepsy are a vulnerable group for anxious-depressive disorders. The mental health conditions of this population during COVID-19 pandemic is still unknown. The aim of this study was to assess the prevalence of anxiety and depression during COVID-19 pandemic (August 2020 – March 2021) in a pediatric sample of patients with epilepsy.

Method: We conducted a cross-sectional study among 64 hospitalized patients with epilepsy (31F; 33M, mean age: 14.6; range: 11-18 yrs, mean age at diagnosis 10.1 yrs; SD ± 4.2). Our sample included youth with focal epilepsy (65.6%), generalized epilepsy (14.1%) and others (20.3%). Patients with drug-resistant epilepsy were 23.4%. We performed face-to face interviews and assessed depressive and anxiety symptoms with the Patient Health Questionnaire (PHQ-9) and the Generalized Anxiety Disorders (GAD-7) questionnaire during scheduled day-hospital (70.3%), hospitalization (26.6%) and outpatient follow up checks (4.7%).

Result: Results showed a rate of mild-to-severe anxious depressive symptoms by 52.3% and 55.4% respectively. In detail: 27.7% mild, 15.4% moderate and 9.2% of severe anxiety (mean score 6.7; SD ± 5). Meanwhile 30.8% mild, 18.5% moderate and 6.1% of severe depression (mean score 6.6; SD ± 5). The prevalence of comorbid depressive and anxiety symptoms was 41.5% among the entire sample. When compared with Scott et al. (2020) review and meta-analysis, that found an overall pooled prevalence of anxiety disorders in youth with epilepsy of 18.9% and for depression of 13.5%, our sample showed +33.4% of anxiety and +41.9% of depressive symptoms during COVID-19 pandemic.

Conclusions: Our sample showed very elevate rates of anxious depressive disorders during COVID-19 pandemic. These findings reveal that pediatric patients with epilepsy need urgent attention from governors and clinicians as well as mental health protocols of screening and treatment during and after COVID-19 pandemic.

Abstract Number: 1142

Title: Impact of COVID pandemic on Ketogenic diet service in a tertiary setting – A comparison of retention rates

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Purpose: To study the effect of the COVID pandemic-related restrictions on a tertiary paediatric Ketogenic Diet (KD) service by comparing the retention rates of those started on KD during and prior to the pandemic.

Method: Patients started on KD post-COVID (Group A) from March 2020 to December 2020 and pre-COVID (Group B) from May 2019 to February 2020 were identified. Data from follow-up at 3 and 6 months, retention rates, seizure outcomes, virtual/in-person method of dietetic education, and reasons for weaning KD were collated.

Result: Thirteen patients (Group A) and 16 patients (Group B) were included with six months follow-up data for 11/13 patients in Group A. Retention rates at 3 and 6 months were: Group A 92 % (n=12/13) and 63.6% (n =7/11) respectively; Group B 81.3% (n=13/16) and 68.8% (n=11/16) respectively. In Group A, at 3 months 61.5% had >50% seizure-reduction of which 23% had >90% reduction; at 6 months 54% had >50% seizure-reduction of which 23% had >90% reduction/seizure freedom. In Group B, at 3 months 44% had >50% seizure-reduction of which 12.5% had seizure-freedom; at 6 months 44% had > 50% seizure-reduction of which 18.8% had seizure-freedom. The initial education was done in person for 38.4% of Group A and 93.8% of Group B patients. The average time from the referral date to the start of diet was significantly longer in Group A compared to Group B (22.6 weeks versus 9.5 weeks). Reasons for weaning were lack of patient compliance or poor response despite similar rates of target ketosis.

Conclusions: COVID-related restrictions and the resulting changes in our service did not have a significantly negative impact on retention rates or dietary compliance, as evidenced by comparable rates of target ketosis in the two groups. However, time from referral to commencing KD was longer.

Abstract Number: 1167

Title: Status epilepticus and COVID-19: a systematic review

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Purpose: In March 2020, the World Health Organization declared the SARS-CoV-2 infection related coronavirus Disease (COVID-19) a pandemic. During the first and second wave of the pandemic spread, there have been several reports of COVID-19 associated neurological manifestations, including acute seizures and status epilepticus (SE). In this systematic review, we summarized the available data on clinical features, diagnosis, and therapy of COVID-19 related SE.

Method: We performed a systematic search of the literature to identify data on demographics, clinical, neurophysiological, and neuroradiological data of patients with COVID-19 related SE. The following electronic databases and data sources were systematically searched: MEDLINE (accessed through PubMed), EMBASE, and Google Scholar (from December 2019 to January 2021). In all databases we used the following search strategy: ('epileptic state'/exp OR 'epileptic state') AND ('coronavirus disease 2019'/exp OR 'coronavirus disease 2019'). We included all studies reporting cases of SE in the context of COVID-19 syndrome in patients with or

without a previous history of epilepsy, published in English, and reporting individual patient data. Non-peer reviewed papers were excluded. We used regression models (linear or logistic) with a stepwise forward method to identify features associated with mortality or severity of SE.

Result: Thirty-nine articles were included with a total of 47 cases of SE associated with COVID-19. Age, time between the acute respiratory phase of SARS-CoV-2 infection and SE onset, and hospitalization correlated with a higher SE severity as assessed by quantitative validated scales.

Conclusions: SE can be a neurological manifestation of SARS-CoV-2 infection. Although a possible association between SE and COVID-19 has been reported, the exact mechanisms are still not fully understood. Systemic inflammatory syndrome due to cytokine release could play a role in COVID-19 related SE.

Abstract Number: 1222

Title: Attitude towards Telemedicine use in patients with epilepsy during the pandemic COVID-19 in Mexico, according to a survey.

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Purpose: Assess the level of acceptance and satisfaction of patients with epilepsy treated through telemedicine during the pandemic COVID-19, and to identify the main barriers to the proper use of telemedicine in patients with epilepsy in Mexico.

Method: Observational, descriptive, cross-sectional study carried out with patients from the Epilepsy Clinic of the National Institute of Neurology and Neurosurgery in Mexico, aged 16 years or older, who were treated via telemedicine during the COVID-19 pandemic.
After a video consultation, a survey and informed consent were sent to all patients by email. The responses of the patients who answered the complete survey and gave their consent were recorded and analyzed.

Result: 83 surveys were obtained, the mean age of the patients was 35.4 (± 11.7), 46 patients (55.4%) were female and 37 (44.6%) were male. 67.5% (56 patients) responded that they do not have difficulty accessing the internet. 85.5% (71 patients) stated that they felt safe receiving medical care from a distance.
Regarding acceptance, 83.1% (69 patients) agreed to be seen again through teleconsultation. 85.6% (71 patients) of the patients had a high degree of satisfaction. An association between satisfaction and ease of internet access was identified.

Conclusions: The population with epilepsy treated via teleconsultation shows a high degree of satisfaction with the care received and accepts this tool with a form of continuous care.

Psychiatry

Abstract Number: 72

Title: Moderators of treatment effects and predictors of outcome in the CODES randomised controlled trial for adults with dissociative seizures

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Purpose: We investigated moderators of CBT treatment effects and predictors of outcome over a 12-month follow-up period in the CODES Trial which compared cognitive behavioural therapy (CBT) plus standardised medical care (SMC) vs SMC-alone for dissociative seizures (DS).

Method: We examined whether baseline variables (including DS-related measures, socio-demographic characteristics and psychological distress/psychiatric diagnoses on the Mini–International Neuropsychaitric Interview – M.I.N.I.) moderated treatment effects at 12 months post-randomisation. Outcomes examined were: monthly DS frequency, psychosocial functioning (Work and Social Adjustment Scale - WSAS), quality of life (Mental Component Summary (MCS) and Physical Component Summary (PCS) scores from the SF-12v2). Where moderating (interaction with treatment) effects were absent, we explored whether baseline variables predicted overall outcome.

Result: At $p<0.05$, the effect of CBT on DS frequency was moderated by somatic symptoms and current M.I.N.I. diagnosis. Greater reductions in DS frequency were associated with more baseline somatic symptoms and the presence of ≥1 M.I.N.I. current diagnosis.
Adjusting for baseline levels worse WSAS scores, irrespective of treatment, were predicted by longer DS disorder duration, older age at DS onset, unemployment status, receiving state benefits and having higher somatic symptom, anxiety and depression scores or lower educational qualifications.
The effect of CBT on PCS scores was moderated by gender. Women in the CBT+SMC group showed greater improvement than men. Adjusting for baseline levels, predictors of PCS scores, irrespective of treatment, were similar to those for the WSAS.
Adjusting for baseline levels, worse MCS scores were predicted by receipt of state benefits, higher anxiety and depression scores and having a weaker belief in the diagnosis and in CBT as a logical treatment for DS.

Conclusions: Somatic symptoms and comorbid psychiatric diagnoses interacted with treatment whereby CBT was more likely to reduce DS frequency. Accessing treatment earlier may help in reducing psychosocial deterioration.
Funding: NIHR HTA 12/26/01

Abstract Number: 76

Title: Polytherapy, frequent seizures, and bilateral tonic-clonic seizures influence on higher depressive and anxiety symptoms in temporal lobe epilepsy

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Purpose: Epilepsy is a connectivity disorder and affects brain functions and behavior. Depression and anxiety are the two most common psychiatric conditions in epilepsy. Patients with temporal lobe epilepsy caused by hippocampal sclerosis (TLE-HS) present a higher frequency of psychiatric disorders than other epilepsy types. Studies demonstrated that the impact of psychiatry conditions could be beside the presence/absence of psychiatry disorder. This study aimed to verify the severity of interictal depressive and anxiety symptoms in patients with TLE-HS and investigate epilepsy-related factors' impact on these symptoms.

Method: 35 patients with TLE-HS and 90 healthy volunteers were evaluated. All participants underwent psychiatric and neurological evaluation. Those patients who met the criteria for a psychiatric disorder

according to DSM-IV were excluded. The Beck Depression Inventory (BDI) and the State-Trait Anxiety Inventory Trait and State (STAI-T and STAI-S) were used to assess symptoms.

Result: Patients with TLE-HS had higher symptoms on BDI (p=0.007), STAI-S (p=<0.001), and STAI-T (p=<0.001), even without any psychiatric disorder and adjusted by sociodemographic variables. Considering the impact of epilepsy-related variables on depressive and anxiety symptoms: (i) numbers of antiseizure medication (ASMs) impacted on BDI scores (p=0.026), patients on polytherapy had higher BDI scores than those on monotherapy; (ii) current seizures frequency (p=0.036) and numbers of ASMs (p=0.021) impacted on STAI-S scores, patients with frequent seizures presented higher scores on STAI-S; and (iii) patients on polytherapy had higher STAI-S scores; (iv) presence of bilateral tonic-clonic seizures (BTCS) was a predictor of STAI-T scores (p=0.041), patients with BTCS obtained higher scores on STAI-T.

Conclusions: Even without the presence of a diagnosis of depressive and anxiety disorder, patients with TLE-HS had higher symptoms on BDI, STAI-S, and STAI-T than the control group. Polytherapy impacted on higher depressive and anxiety symptoms. Frequent seizures and the presence of BTCS predicted higher anxiety symptoms.

Abstract Number: 192

Title: The impact of anxiety and depressive symptoms on quality of life in patients with temporal lobe epilepsy caused by hippocampal sclerosis

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Purpose: We aimed (i) to verify the presence of subsyndromic depressive episodes (SDEs) and subsyndromic anxiety episodes (SAEs) in persons with temporal lobe epilepsy caused by hippocampal sclerosis (TLE-HS) compared to healthy controls and (ii) to determine the impact of depressive and anxiety symptoms on QOL in TLE-HS.

Method: We prospectively evaluated 35 persons with TLE-HS and 90 healthy controls. Those with psychiatric disorders according to DSM-IV were excluded. QOL was assessed by the Epilepsy Surgery Inventory (ESI) and QOL in Epilepsy Inventory-31 (QOLIE-31). The Beck Depression Inventory (BDI) and the State-Trait Anxiety Inventory (STAI-X) were used to assess symptoms, and the presence of SDEs and SAEs were made considering the total scores of BDI (<9) and STAI-Trait (<49), respectively.

Result: Even though the symptoms do not meet the criteria to be considered a "disorder" and adjusted by sociodemographic variables, persons with TLE-HS had 3.011 greater odds of presenting SDEs (p=0.027) and 7.056 times odds, SAEs (p=0.001). The symptoms of depression and anxiety, added in the model with epilepsy-related factors, accounted for a significant increase in the variance in several aspects of QOL. Regarding each factor's contribution, the higher anxiety-trait symptoms were associated with poorer in distinct QOL measures: Overall; Emotional and Mental Well-being; Pain; Energy and Vitality; Cognitive Function; Social Function; Global.

Conclusions: The persons with TLE-HS had greater odds of presenting SDEs and SAEs than the control group. They had greater odds of presenting SAEs than SDEs. Anxiety and depressive symptoms impacted on the QOL. The anxiety-trait symptoms were the individual strongest predictors of QOL. It is essential to be aware of psychiatric symptoms, even if these are not characterized as a "disorder". Screening psychiatric symptoms through brief structured instruments as part of the usual treatment offered to people with epilepsy is important.

Abstract Number: 274

Title: Validation of the Russian version of ultra-short screening for major depressive episode in patients with epilepsy

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Purpose: Patients with epilepsy (PWE) are at higher risk of depression than the general population, and every PWE demand screening for major depressive episodes (MDE). The Russian version of the 6-item Neurological Disorders Depression Inventory for Epilepsy NDDI-E (NDDI-E) is an accessible, straightforward and cost-effective screening instrument for MDE in PWE (Zinchuk M et al. Epilepsy Behav 2020;113:107549). Shorter versions of the NDDI-E could facilitate rapid screening by busy clinicians and be more accessible to patients with mild cognitive or language impairments. One shorter version of the questionnaire - 2 item NDDI-E (NDDI-E-2) was suggested as a valid measure to screen for MDE (Micoulaud-Franchi JA et al. J Affect Disord 2017;210:237-240).
We aimed to investigate the potential effectiveness of the NDDI-E-2 in screening for MDE in PWE.

Method: A consecutive PWE cohort was assessed with the NDDI-E-2 and the MDE module of the Mini International Neuropsychiatric Interview (MINI) as the gold standard. Demographic and clinical variables were collected. Receiver operating characteristic (ROC) analysis of NDDI-E-2 scores, with the identification of higher Yuden's index, was used as statistical methods**.**

Result: The cohort consisted of 174 PWE: 56 (32%) male; mean age was 41.5 (15.19%); 160 (91.4%) had focal epilepsy; mean duration of epilepsy was 16.33 (12.07), and 99 (56.65) patients had current MDE. ROC analysis showed the area under the curve (AUC) of 0.842, a sensitivity of 81.58%, a specificity of 70.71%, a positive predictive value of 45.6%, a negative predictive value of 86.3%, and the largest Youden index of 0.522 for a cutoff score of >3**.**

Conclusions: Our results suggested that MDE screening properties of the NDDI-E-2 are acceptable, but not as good as 6-item NDDI-E (AUC=0.919) (Zinchuk M et al. Epilepsy Behav 2020;113:107549).

Abstract Number: 308

Title: Development and verification of reliability and validity of Epilepsy Self-stigma Scale (ESSS) in Japan

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Purpose: Self-stigma refers to internalized social stigma, and is commonly experienced by patients with epilepsy (PWE). A higher level of self-stigma is associated with lower self-esteem and hindered therapeutic behavior . We developed the Epilepsy Self-Stigma Scale (ESSS) to measure self-stigma in PWE. The aim of this study was to determine the reliability and validity of the ESSS.

Method: We created an 18-item questionnaire based on the results of the basic stigma scale and a qualitative analysis with 200 PWE in four medical facilities in Japan. Participants completed the Rosenberg Self-Esteem Scale (RSES) and Beck Depression Inventory (BDI-II), which were distributed and collected between September and December 2020.

Result: The response rate was 51%, and data from two further participants were excluded owing to incomplete questionnaires . We analyzed data from a total of 100 PWE (mean age: 39.86 years; SD = 17.45 years). Factor analysis was performed on all 18 items using the maximum likelihood method. To determine the number of factors, three factors (internalized stigma, incomprehension of society, and confidentiality) were assumed with reference to an eigenvalue of 1 or more and a scree plot. Four items that did not show a sufficient factor loading were deleted, and exploratory factor analysis was performed again using maximum likelihood ProMax rotation; this resulted in an 8-item ESSS. Using data from the 35 individuals who completed the second survey , we calculated the total ESSS score and Pearson's product moment correlation coefficient between the subscales, and found a strong significant positive correlation, which confirmed the reliability of the scale. Furthermore, the ESSS score was correlated with the RSES and BDI-II scores, thus confirming the scale's constructive validity.

Conclusions: The ESSS can be make it easier to examine factors associated with patients' self-stigma, which could inform effective interventions for reducing stigma .

Abstract Number: 410

Title: Have the mood disorders any influence over seizure control in patients with epilepsy?

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Purpose: To study the prevalence of mood disorders in patients with epilepsy and their relationship with seizure control.

Method: An observational and cross-sectional study of patients with epilepsy who were followed in neurology outpatient clinics was performed. Patients were classified into two groups according to seizure control: good control (≤1 seizure/month) and poor control (>1 seizure/month) and demographic variables (age, sex, employment status and civil status), clinical (epilepsy type, crisis type, years of evolution of epilepsy), therapeutic (antiepileptic, antidepressant and anxiolytic drugs), presence of depression (NDDIE scale), anxiety (GAD7 scale) and quality of life (QOLIE10) were compared between both groups.

Result: 152 patients were included. 53% were men with a mean age of 44±11 years. 68% (n=103) had good seizure control and 32% (n=49) poor seizure control. 37,6% had depression (NDDIE>15) and 42% anxiety (GAD>10). 60% of patients with depression and 54% with anxiety did not receive antidepressant and/or anxiolytic treatment. The factors associated with poor seizure control were the presence of depression (OR 2,3, p = 0,02) and a worse quality of life (OR 1,8, p = 0,01).

Conclusions: The presence of altered mood in patients with epilepsy is frequent. In our series, depression and a worse quality of life were related to worse seizure control.

Abstract Number: 491

Title: Psychogenic non epileptic seizures and Major Depression Disorder: a cortical thickness study

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Purpose: To investigate neuroanatomical changes in patients with psychogenic non epileptic seizures (PNES) patients compared to Major Depressive Disorder (MDD) patients.

Method: Forty-two PNES patients (mean age 42, 46 ± 13,86 years; 9/42 males) and 25 MDD (mean age 42,53± 11,99 years; 6/25 males), matched depression degree measured by BDI-II (Beck Depression Inventory-II), were consecutively recruited. Patients performed a wide neuropsychiatric assessment, including the following tests: Hamilton Anxiety Rating Scale (HAM-A), Toronto Alexithymia Scale (TAS-20) and Somatoform Dissociation Questionnaire (SDQ-20). All patients, together with 78 healthy matched controls, underwent a brain 3T MRI followed by surface-based morphometry.

Result: Cortical thickness analysis showed a significant bilateral cortical thinning in the medial orbitofrontal cortex (OFC) and left rostral anterior cingulate cortex (ACC) in patients with MDD compared to patients with PNES and controls. PNES patients showed significantly higher scores in the SDQ-20 ($p < 0.001$) with respect to the MDD group and this clinical evidence was corroborated by neuroimaging data, where somatoform dissociation scores correlated with morphological changes in the left medial OFC.

Conclusions: Our results show selective cortical thinning over the medial OFC in patients with PNES compared to wider neurodegenerative cortex in patients with MDD. Somatoform dissociation was the only psychopathological construct able to discriminate PNES from MDD in the contest of atrophic OFC.

Abstract Number: 590

Title: Depressive symptoms in patients with epilepsy during COVID-19 pandemic and its correlation with adequate medical care

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Purpose: We aimed to evaluate the prevalence of depressive symptoms in persons with epilepsy (PWE) during the COVID-19 pandemic lockdown in Brazil and its correlation with epilepsy features and access to treatment.

Method: We conducted a cross-sectional study, under the lockdown period and surveyed PWE regarding symptoms of depression using the NDDI-E. We assessed demographics, epilepsy-related variables, social attitudes/ behavior, and access to treatment.

Result: We assessed 320 PWE (77.6% women; mean age of 37.05 years [± 13.77]) with a mean epilepsy duration of 18.46 (± 13.42) years. One hundred and twelve (35%) patients reported increased seizure

frequency; 80 (25%) had difficulties obtaining antiseizure medication (ASM); 43 (13.4%) could not obtain prescription; 140 (43.7%) had difficulties contacting their physicians; and 31.3% (100) reported cancelled appointments due to COVID-19 pandemic. The mean NDDI-E score during the lockdown was 13.15 [± 5.50]. Higher scores were documented in women ($p < 0,000$), in patients who experienced increased seizure frequency ($p < 0.002$), difficulties accessing their physician ($p < 0.01$), and obtaining ASM ($p < 0.000$).

Conclusions: The COVID-19 pandemic affected PWE access to the healthcare system. Depressive symptoms were more severe in patients with higher seizure frequency who had difficulties to obtain proper medical care. PWE are at higher risk for behavioral and psychiatric disorders that may be aggravated during stressful times and guarantee their continuous care is of utmost importance and a challenge during COVID-19 pandemic.

Abstract Number: 621

Title: Alexithymia in adult patients with epilepsy

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Purpose: The concept of alexithymia refers to difficulty perceiving, identifying and describing emotions. We aimed at evaluating the prevalence of alexithymia in a sample of adult people with epilepsy (PWE) with and without psychogenic nonepileptic seizures (PNES) and healthy control subjects (HC) and identifying major factors able to affect it.

Method: We enrolled consecutively 91 PWE (12 of which with PNES in addition to seizures) and 146 HC age- and gender- matched. Both groups' subjects completed the following questionnaires: TAS-20, Beck Depression Inventory-II (BDI-II), Difficulties in Emotion Regulation Scale (DERS) and the Italian translation of Stigma Scale of Epilepsy (SSE), able to evaluate stigma related to epilepsy both in epileptic and non-epileptic subjects. Moreover, PWE completed the Jacoby's Stigma Scale (JSS), dedicated to the evaluation of stigma only by patients with epilepsy and QOLIE-31 (Q31) for evaluating the quality of life. We analyzed correlations between alexithymia and several epilepsy-related (seizure frequency, antiseizure medications-ASMs) and psychosocial factors. Finally, a stepwise multiple regression analysis was performed to identify major factor affecting alexithymia.

Result: Alexithymia was prevalent in PWE compared to controls without discriminating epileptic subjects with and without PNES. This predominance disappeared when depressive symptoms (DS) were controlled for. The difficulties of identifying emotions (DIE) resulted to be clearly higher in PWE, even when DS are controlled for, and significantly correlated with stigma perception. Alexithymia in PWE was also strongly associated with lower quality of life and education and greater number of ASMs and difficulties in emotion regulation (ER), that turned out to be the main factor affecting alexithymia in both groups (PWE and HC).

Conclusions: Alexithymia is prevalent in PWE, mostly influenced by DS and significantly associated to worse quality of life and higher emotion dysregulation and stigma perception. The latter finding could be explained by DIE that selectively characterizes PWE.

Abstract Number: 635

Title: Utility of prolonged EEG in Autism Spectrum Disorder with and without epilepsy

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Purpose: Children with Autism Spectrum Disorder (ASD) with epilepsy and/or abnormalities in EEG are known to have worse behavioural issues. The frequency of inter-ictal epileptiform discharges (IEDs) on routine EEG in ASD can range from 5-30%. We hypothesized that prolonged EEG increases the yield and influences management in ASD. The objectives are:

- To measure the incidence of IEDs in ASD with or without epilepsy in the first 20 minutes and in 20 minutes to 2 hours of EEG recording
- In those with IEDs, to compare the spike frequency between awake state and sleep states

Method: 55 children with ASD aged 2-18 years underwent 2 hour video-EEG recording in a 64-channel Philips Geodesic EGI 400 system, performed with a saline-based net electrode system that conforms to the standard international 10-10 system. EEGs were reviewed by a Neurologist, blinded to clinical data, for the presence of IEDs, and to estimate their frequency in awake and sleep states.

Result: IEDs were detected in 4 (7%) in the first 20 minutes and in additional 6 (10%) in 20 minutes to 2 hours. The spike frequency increased from rare in awake state to very frequent or continuous in sleep. 9 out of 10 children had posterior quadrant IEDs. 6/10 children with IEDs had no history of epilepsy. Anti-seizure medication resulted insignificant improvement in behavioural issues at two months.

Conclusions: Prolonged EEG recording increases yield of IEDs in children with ASD and demonstrates enormous spike burden in some. A high spike burden in sleep could contribute to behavioural problems in children with ASD. Prolonged EEG provides a window of opportunity for a trial of anti-seizure medication for behavioural management in ASD.

Abstract Number: 856

Title: Atypical limbic encephalitis – a case report

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Purpose: To present a rare case of probably paraneoplastic LE, associated with anti-GAD antibodies, with an atypical clinical picture (associated cerebellar signs and eating disorder), still under investigation at this time.

Method: We will present all sociodemographic data, clinical picture, paraclinical results and treatment response in a patient with limbic encephalitis, as case report.

Result: A 29 years old female was admitted in our department with seizures, severe short-term memory impairment, an unusual alimentary behavior, nystagmus, ataxia in all limbs and brisk tendon reflexes. Brain magnetic resonance imaging (MRI) revealed bilateral hippocampal lesions. Serial surface electroencephalographic recordings showed slowing over both temporal regions, multifocal interictal epileptiform discharges and frequent electric seizures with focal onset. Patient presented slightly elevated fasting blood glucose levels and high values of CA-125. Cerebrospinal fluid (CSF) analysis demonstrated pleocytosis and we found high titers of anti-glutamic acid decarboxylase (GAD II) antibodies in the serum. Other autoimmune/onconeural antibodies (in serum and/or CSF) are negative (anti-GAD II antibodies in CSF were not tested because the amount of CSF obtained was considered insufficient by laboratory staff). Pelvic MRI showed a left ovarian cyst, with mixed content and peripheral gadolinium enhancement. Treatment included pulse

therapy with methylprednisolone, followed by the administration of IgIv (with a mild improvement in short-term memory). Patient is currently being considered for exploratory laparotomy.

Conclusions: LE can be associated with ovarian teratoma and anti- NMDA-R antibodies. So far, in our patient we were able to detect a possible ovarian tumor associated with serum anti-GAD II antibodies. Classically, these antibodies are associated with other paraneoplastic syndromes or with diabetes mellitus. Recent literature reports an association with LE, but less than 100 cases were reported till the end of 2020 and even less exhibited other neurological signs. (Vrillon A et al., Neurosci Biobehav Rev, 2020 Dec;119:128-137).

Abstract Number: 1037

Title: Functional neuroanatomy underlying psychogenic non epileptic seizures. An Ictal SPECT study

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Purpose: The physiopathology and the neuronal networks involved in the psychogenic non-epileptic seizures (PNES) disorder still poorly understood. Recent studies have suggested that perception of autonomic changes such as heart rate and the level of attention changes prior to the PNES[1,2].
Ictal brain single-photon emission computed tomography (SPECT) is a very useful tool to characterize brain regions involved in the episodes of PNES [3,4].
We hypothesize that changes of brain areas that are involved in the control and perception of autonomic changes together with changes in the attention networks and motor control networks will be seen during the ictal SPECT compared to the interictal SPECT.

Method: Retrospective study conducted in patients admitted for characterization of seizures at the Epilepsy Monitoring Unit in whom an ictal SPECT was obtained during a PNES were included.
Whole brain analysis, as well as hypothesis based analysis on networks of interest of ictalSPECT vs interictal SPECT was performed using SPM.
Additionally, the brain regions related to other parameters such as the level of motor activity during the PNES (static vs motor PNES) and the level of EEG desynchronization were investigated using regression models in SPM.

Result: Nineteen patients were identified (13/19 female, 42±10 years old). Ten patients had both PNES and epileptic seizures. Fifteen patients had psychiatric comorbidities. PNES were classified as motor (7/19), non-motor (6/19) and mixed (6/19).
Whole brain positive and negative uptake changes as well as changes in the autonomic control regions (insula, amygdala, cingulated gyrus) and attention control networks (salience network, frontal and dorsal attention networks) related to PNES will be discussed.

Conclusions: Brain network activity identified with Ictal SPECT during PNES can contribute to identify the neural mechanisms associated to this disorder as well as to understand the different patterns of attacks seen across patients.

Abstract Number: 1165

Title: Ictal Aggression, A Rare Phenomenon: A Case Report and Review of the Literature

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Purpose: An association between aggressive behaviour and epilepsy has been previously described and is thought to be particularly prevalent among patients with temporal lobe epilepsy. Episodes of aggression in people with epilepsy can be categorised by their temporal relationship to seizures as either interictal, ictal or post-ictal. Ictal aggression is thought to be a rare phenomenon. To the best of our knowledge, there is only one previously documented case of an episode of ictal aggression captured on video EEG monitoring.

Method: We report the case of an episode of ictal aggression that was observed in a 34 year-old left-handed male patient with longstanding refractory localization related epilepsy. In addition, we review the existing literature regarding the phenomenon of ictal aggression.

Result: He had been admitted to our epilepsy monitoring unit (EMU) for a sustained period of monitoring while being considered for potential resective epilepsy surgery. We provide video EEG evidence of the ictal events associated with the aggression captured in our EMU. In one such event, he was noted to attack the nursing staff member that was caring for him. 3T MRI did not identify a potentially causal lesion. Some interictal aggressive behaviours have been reported by the patient and his family, and he has had regular neuropsychiatry reviews as an outpatient.

Conclusions: Ictal aggression is a rare feature in epilepsy and provides significant challenges for diagnosis and clinical management.

Abstract Number: 1172

Title: Evaluation of suicidal ideation in adult people with epilepsy and caregivers in a tertiary center

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Purpose: To determine the frequency and predictors of suicidal ideation (SI) in adult people with epilepsy (PWE) and caregivers in a tertiary center.

Method: We included 548 consecutive adults PWE (60% women; median age 41 [18-83]) and 191 caregivers (72% women; median age 47 [18-82]) followed at Outpatients' epilepsy clinics from a tertiary center (HC-UNICAMP/Brazil). We used "item nine" (scores ≥ 1 were considered positive for SI) of the Beck Depression Inventory-II (BDI-II) to determine the presence of SI. The presence of symptoms of anxiety (with Beck Anxiety inventory) and depression (with BDI-II) was defined with scores ≥ of 14 for both PWE and caregivers. The presence of anti-seizure drugs (ASDs) adverse effects was defined with the "Liverpool Adverse Events Profile" score ≥ of 46. Epidemiological factors and anxiety symptoms were investigated as predictors of SI in both PWE and caregivers' groups. Seizure frequency and epilepsy type were also included as predictors of SI in PWE.

Result: Depression was present in 41% of the PWE and 32% of the caregivers (p=0.04). Anxiety was observed in 37% of PWE and 33% of caregivers (p=0.32).
The SI frequency was higher in PWE (19%) compared to the caregivers (11%; Chi-square test, p=0.02). A logistic regression analysis was performed to identify SI predictors in both groups separately. The PWE model

accounted for between 17% and 27% of the variance of SI. The most significant predictors were anxiety symptoms (OR 4.4, p<0.001), presence of adverse effects of ASDs (OR 2; p=0.021), recurrent seizures (OR 3, *p*<0.004), and younger age (OR 0.98, *p*<0.037). For the caregivers (model accounted for 18-37%), only anxiety symptoms (OR 43, *p*<0.001) predicted suicidal ideation.

Conclusions: Identifying predictors of suicidal ideation is equally necessary for PWE and caregivers, as both live under chronic emotional distress.

Abstract Number: 1231

Title: Efficacy and tolerability of anti-seizure drugs in the treatment of brain tumor repated-epilepsy (BRTE): a real-world study

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Purpose: Brain tumour related-epilepsy (BRTE) is a condition characterized by the development of seizures in the context of a brain tumour pathology. In 40% of cases, seizures represent one of the onset symptoms of brain tumour. According to some studies, the high incidence of BRTE in patients with brain tumour would justify the use of a prophylactic therapy for seizures which in turn would not lead to major side effects (SE) assessed by the AEP (adverse events profile) scale. However, such studies do not make an appropriate assessment of neuropsychiatric SE of anti-seizure therapy.

Method: Thirty-two patients with brain tumour were consecutively selected from 2017 to 2019 and divided into two groups: patients with BRTE on anti-seizure treatment (EPI + T +) and patients with brain tumour on prophylactic anti-seizure treatment (EPI-T +). Demographics, clinical, neurophysiological, and neuroradiological data of patients in both groups were collected. BRTE features, including seizure type, seizure frequency and anti-seizure therapy were evaluated. Neuropsychiatric SE of anti-seizure therapy were assessed using the Neuro-psychiatric Inventory Questionnaire (NPI-Q) at the baseline visit and at 6-month follow-up. The evaluation of the efficacy of the anti-seizure treatment in subjects with BRTE was evaluated according to the percentage reduction in the frequency of seizures at 6 months.

Result: 17 patients in the group (EPI + T +) and 15 patients in the group (EPI-T +) were included. The drug most commonly used in the two groups was Levetiracetam. The mean scores obtained on the NPI were significantly higher in the EPI-T + group (p <0.05) as were the scores on the depression (p <0.02), motor activity (p <0.03) and sleep disturbances (p <0.05).

Conclusions: Prophylactic treatment with anti-seizure medication in the context of brain tumour can have a deleterious effect on the psychiatric sphere.

Abstract Number: 1262

Title: Comorbid impulsivity and depression a year after epilepsy surgery

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Purpose: Psychiatric comorbidity in patients with resistant epilepsy is very common and often develop post-surgical psychiatric disorders. Affective disorders are the most frequent. Impulsivity may be present and deepen the disorder's severity, boosting risky behaviors. The objective of this study is to analyze post-surgical evolution and degree of impulsivity in patients with resistant epilepsy.

Method: Patients operated between July 2016 and September 2019 were included and assessed with a protocol comprising of neurological, neuropsychological, psychiatric assessment, vEEG, MRI. The psychiatric evaluation was performed with the following instruments: SCID-I, SCID-II, GAF, Beck Depression Inventory. One year after surgery, Barratt Impulsivity Scale was added to the patients' follow-up. Student's t-test and chi-square were performed.

Result: Thirty-eight patients were included (21 women). Twenty-four patients (63%) presented pre-surgical psychiatric disorders, either current or past, of which 19 were diagnosed with depression. Six patients had more than one psychiatric comorbidity.
A pre-surgical psychiatric diagnosis was associated with the development of post-surgical psychiatric disorders ($p = 0.014$). Lower GAF scores were correlated with higher impulsivity scores ($p < 0.05$). A post-surgical diagnosis was associated with higher motor ($p= 0.011$) and total ($p= 0.018$) impulsivity scores.
The evolution of postsurgical epileptic seizures, according to the Engel classification, was as follows: Engel I (58%), II (21%), III and IV (21%). Worse postsurgical outcomes were associated with a higher impulsivity score in the non-planning factor ($p =0.005$).

Conclusions: Post-surgical psychiatric comorbidities are more frequent in epileptic patients with a psychiatric history, being depression the most frequently diagnosed. Additionally, de novo postsurgical psychiatric disorders are infrequent. Surprisingly, lack of planning is strongly correlated with seizure outcome following surgery.

Abstract Number: 1272

Title: insights from video-eeg monitoring: semiological features of psycogenic nonepileptic seizures buenos aires argentina

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Purpose: Categorize semiological features observed in psychogenic non-epileptic seizures (PNES) during Video-EEG (VEEG) monitoring to improve clinical diagnosis.

Method: Retrospective observational study in patients(p) admitted to VEEG Unit. Hospital El Cruce and Hospital de Agudos Ramos Mejía (2016-2020). Recording of patients with PNES, with or without epilepsy, were reviewed. We evaluated the semiology and the presence of 19 semiological signs to classified it in four groups: Hypermotor, Akinetic, Focal Motor and subjective symptoms. Following psychiatric assessment was used: DSM-IV, SCID-I and SCID-II structured interview, EEAG and Beck Depression Inventory.

Result: 330 Video-EEG studies were evaluated, 61p met the inclusion criteria, 47 (77%) women; mean age was 33y (14 to 74), Educational level: Elementary or High school in 44 (83%). Singles 37 (61%) currently employed 12 (20%); 41p (67%) were classified in the PNES-only group and 20p (33%) in the PNES and Epilepsy group.

Mean onset of PNEs was 26yr. Average time before diagnosis was 6yr, depression 32p(53%), anxiety 18p (30%). 98% were on medication with AEDs, mean 4 AED´s. Number of PNES on VEEG were 4 (1 to 30), average time on PNES was 8,33mn (1-60mn) According to the semiological signs, 40p (621%) presented Hypermotor, Focal motor in 15p (25%), Akinetic in 14p (23%) subtypes. Multiple types of seizures were presented in 34p, (56%). Major semiological signs in PNES were closed eyes, asynchronous movements, closed hands, head movements, stiffness or generalized tonic clonic posture and body rocking ($p<0.05$). Focal motor PNES were predominant in females ($p<0.05$); we found a proportion 3:1 with female gender

Conclusions: V-EEG is the study of choice for the diagnosis of PNES, since it is a dependent operator study, defining the semiological features of PNES results in a most precise diagnosis; we found that most of the patients presented with multiple and non-stereotyped events.

Social Issues/Nursing

Abstract Number: 48

Title: Ambulance assignments for seizures and socioeconomic deprivation: a regional GPS-based analysis

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Purpose: Associations between socioeconomic level and epilepsy prevalence have been described in several countries, but studies of emergency care service utilization for seizures in relation to socioeconomic standing are scarcer. We recently found that geographical areas with lower income had more ambulance assignments for seizures in the city of Gothenburg, Sweden. Conditions in urban areas may be confounded inner city-specific factors, rather than reflect national epilepsy care. We therefore analyzed data for the entire region of Western Sweden, with 1.7 million inhabitants, encompassing rural as well as city areas.

Method: Data on ambulance assignments for seizures, including GPS-coordinates of each call, for the years 2013-2018 were collected from the Emergency Medicine Database Ambulink. To adjust for epilepsy prevalence, geographical statistics on epilepsy was obtained from the National Patient Register, and data on mean age and proportion of inhabitants in relative poverty in geographical areas (parishes) was obtained from the Region of Western Sweden. Correlation and regression analyses were performed. Ethics Review Authority-approval-no:2019-803.

Result: The prevalence of epilepsy increased with the proportion of inhabitants in relative poverty ($r = 0.139$, $p=0.025$). The number of ambulance assignments for seizures per capita were was significantly associated with the proportion of inhabitants in relative poverty ($r=0.31$, $p<0.001$) and the proportion of inhabitants with an epilepsy diagnosis ($r=0.165$, $p=0.008$). In multiple regression, including mean age, proportion of inhabitants with an epilepsy diagnosis, and proportion of inhabitants in relative poverty, a significant association between the latter variable and number of ambulance assignments remained significant ($p<0.001$).

Conclusions: In the Region Western Sweden, ambulance assignments for seizures were more common in socioeconomically weaker areas, also when epilepsy prevalence was taken into account. Whether this represents epilepsy severity, access to epilepsy care, or different utilization of emergency services should be studied further.

Abstract Number: 66

Title: Epilepsy Safety - Patient Familiarization Act

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Purpose: According to the WHO, reducing injury deaths from seizures is a priority even compared to finding a cure for epilepsy. The deaths of patients in conditions of social maladaptation and indifference of state structures dictate the need to develop strategies for the prevention of fatal injuries in this group of patients. The goal: to identify ways to inform about risks during the treatment of epilepsy patients.

Method: Surveys of patients on a social network were conducted in a sample from a patient group to inform about the risks of epilepsy. Requests for measures were sent to the Ministry of Health, 84 regional health departments, Centers for Medical Prevention, Centers for Hygiene and Epidemiology, First Aid Department, Rospotrebnadzor, Department of Social Protection of the Population, Ministry of Emergencies, Ministry of Internal Affairs, manufacturers of antiepileptic drugs, and baths, as the main source of risk at home.

Result: Patients with epilepsy for the most part did not receive information from doctors and other sources on how to reduce deaths from seizures. Responsible authorities show passivity in improving the situation. There are no safety sections for epilepsy on the websites of medical organizations and in clinical recommendations. Only individual regional departments respond to the call with practical cases. The First Aid Department refuses to separate seizure first aid from first aid in the absence of consciousness, which harms patients with epilepsy. In Russia, the epilepsy patient community is in its infancy.

Conclusions: Familiarizing the patient with the risks of epilepsy is a complex and multidisciplinary task. The full-scale introduction of safety in epilepsy can save about a thousand lives a year in Russia.

Abstract Number: 71

Title: Comparison of the quality of life of patients with epilepsy from the Ukrainian study with results of studies from USA and India

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Purpose: To evaluate quality of life (QoL) in patients with epilepsy in Ukrainian study and compare them with results of similar studies from USA and India.

Method: 74 patients of an average age of 36.99±1.10 years old (including 43 female ones) from Kharkiv Region (Ukraine) were examined using the QOLIE-31 (Version 1.0).

Result: According to our data, the overall QoL score of patients from Ukrainian study is lower (overall 56.05±17.4 points), than in the USA study (62.87 ± 16.31 points) (Vickrey BG et al. Quality of life in epilepsy QOLIE-31 (Version 1.0) points Scoring manual. Santa Monica, California. 1993. 9 p.) and in the Indian study (64.61±13.13 points) (Pimpalkhute SA et al. Assessment of quality of life in epilepsy patients receiving anti-epileptic drugs in a tertiary care teaching hospital. Indian J Pharmacol 2015; 47 (5): 551–554).
The same was demonstrated for all individual QoL indicators. Comparing with data from India, the biggest differences were for Medication Effects (49.74±28.63 and 67.0±12.34 points, respectively), Energy/Fatigue (49.8±16.93 and 65.73±12.4 points respectively), Emotional Well-Being (55.30±18.29 and 70.53±11.12 points respectively), and Social Functioning (52.88±18.96 and 66.74±12.46 points, respectively). Differences with the

data from USA were even higher: for Social Functioning, for example, it was 52.88±18.96 and 67.25±26.88 points, respectively.
In the Ukrainian study, QoL was higher if seizures were controlled, and usually ameliorated with decreasing of seizure frequency, except for rare seizures. Also, the QoL was better in patients who lived in city and lower in those, who had idiopathic epilepsies.

Conclusions: The overall QoL in Ukrainian patients with epilepsies is noticeably worse as compared with patients from USA and India. Among the most
vulnerable areas were Medication Effects, Energy/Fatigue, Emotional Well-Being, and Social Functioning. The results confirm a necessity of development of social and psychological support for these patients.

Abstract Number: 91

Title: Employment in people with epilepsy: A cross sectional study

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Purpose: Employment is indispensable to people with epilepsy (PWE) in financial, psychological and social aspects. Hong Kong is a well-developed economy which depends very much on tertiary industry. We aimed to investigate the factors that associate with employment among PWE.

Method: A cross-sectional questionnaire-based study was conducted in our institution. PWE within 18-65 years old without intellectual disability were eligible. A self-administered questionnaire was given to each subject. Recruited PWE were divided into employed group and unemployed group depending on current employment status. Various demographic and clinical parameters were individually compared between both groups. Finally, selected variables were further analyzed by binomial logistic regression model. Statistical significance was set at $p<0.05$.

Result: A total of 138 PWE were recruited. Mean age was 42, sex ratio (Male: Female) was 1:1.1, drug-resistant epilepsy was 34% and median Charlson's comorbidity index was 0. Secondary school or above level accounted for 93%. Unemployment rate was 33%. Education level ($p=0.003$), drug-resistant epilepsy ($p=0.042$), psychiatric comorbidities ($p<0.001$) and Charlson's comorbidty index ($p=0.042$) were significantly correlated with unemployment. Other variables including current age, sex, epilepsy onset age, epilepsy classification, number and generation of anticonvulsant did not reach statistical significance. Selected variables were then further analysed by binominal logistic regression model to correlate with employment status. These included current age, sex, epilepsy onset age, education level, Charlson's comorbidity index, drug-resistant epilepsy and psychiatric comorbidities. The model was statistically significant ($p<0.001$). Sensitivity was 65%, specificity was 92%. Among the predictor variables, 3 were statistically significant: Charlson's comorbidity index, drug-resistant epilepsy and psychiatric comorbidities.

Conclusions: PWE with drug-resistant epilepsy, psychiatric comorbidities, high Charlson's comorbidity score and low education level tend to be unemployed. Job counselling service may need to target to these groups who are mostly in need.

Abstract Number: 231

Title: The Ottawa Epilepsy Program: region-wide coordinated and community integrated care in the 21st century

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Purpose: Epilepsy is the most common chronic neurological illness worldwide, affecting more than 330, 000 people in Canada, 10, 000 of which reside in the Ottawa area. Despite facing higher mortality, stigma and social barriers, people living with epilepsy (PLE) incur treatment gaps even in high income countries like ours. Our goal was to address this burden locally with the creation of novel, community-integrated, care delivery for PLE in our area; we describe its inception.

Method: Despite traditionally siloed, care for PLE became part of a continuum of care for patients in our region. In 2017, a transition program bridging pediatric and adult institutions was created to address the care continuity gap. Following a retreat of key stakeholders in 2019, the community education and patient advocacy group was integrated into our model of care and the region-wide program was created incorporating adult, pediatric, transition and community pillars. A patient friendly website was launched in 2020 (ottawaepilepsyprogram.ca). Community pillar programs such as UPLIFT[1] (a mindfulness-based cognitive behavioural therapy program that improves depression, anxiety, and overall psychological quality of life in people with epilepsy) and clinic to community (C2C)[2] (an education program with access to resources, programs, services, and an epilepsy community) were disseminated rapidly to adult and pediatric pillars. Referrals were tracked and patient/caregiver satisfaction informally surveyed.

Result: 170 patients were followed in the transition program since 2017. Adult and pediatric pillars have referred 70 patients to the community program between 2019-2020, 48 between 2020-2021. PLE are able to access C2C and UPLIFT programs for social support services and mental health, respectively. These services are highly rated by patients/caregivers.

Conclusions: An interconnected region-wide program can support PLE and foster care integration across disciplines. Synergism between pillars of the program allow for rapid dissemination of innovations such as C2C and UPLIFT.

Abstract Number: 278

Title: Margiad Evans' inside history of epilepsy.

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Purpose: History

Method: Narrative

Result: Welsh poet, memoirist, novelist and nature writer, Margiad Evans (1909-1958) was by many considered one of the most interesting writers in English language when at the age of 41 she was struck by epilepsy. Her description of that episode, the time leading up to it with a long preamble of isolated auras, and its sequel, in her autopathography A Ray of Darkness (1952, new edition in press)1 was appreciated by Lennox. In his textbook, he amply quoted from it as a unique authentic document of typical challenges epilepsy inflicted on the affected patients2, and made friends with the author. Although from early on, she received expert care by Prof. Golla in Bristol her seizures continued and were eventually discovered to be caused by an inoperable gliomatous tumour from which she died, 49 years old.
Conclusions: As long as she was able to write in an organized way, she continued to document her inside experience of epilepsy, including a non-convulsive status epilepticus. Her desire was "to put into physicians' hands a book of clues to the sensations of such an epileptic as myself."3 This manuscript she named The

Nightingale Silenced. It remained unfinished and was only recently published by one of us3. Evans "represents the rare example of a professional writer who described, analyzed and commented the symptoms and consequences of her own epilepsy fully keeping her literary standards. … Together [the two books] seem to represent the only comprehensive inside case history of epilepsy",4

1) Evans M. A Ray of Darkness. Reprint. Honno: Aberystwyth, in press.
2) Lennox WG, Lennox MA. Epilepsy and related disorders. Little, Brown: Boston 1960.
3) Evans M. The Nightingale Silenced and other late unpublished writings. Ed. Jim Pratt. Honno: Aberystwyth 2020
4) Wolf P. Epilepsy & Behavior 2020; 102: 106677.

Abstract Number: 471

Title: The effect of fear of COVID-19 on quality of life in patients with epilepsy

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Purpose: In the COVID-19 pandemia period, the effect of COVID-19 fear on quality of life was uncertain. This present study aimed to examine the effect of fear of COVID-19 on quality of life in patients with epilepsy.

Method: This single-center, cross-sectional study was conducted with a total of 319 adult patients with epilepsy. Data were collected online between 15 December 2020 and 5 January 2021. COVID-19 Fear Scale (FCV-19S), Beck Depression Inventory (BDI), Worry and Anxiety Form (WAQ), and Epilepsy Quality of Life Scale-10 (QoLIE-10) were used for data collection. Serial mediation analysis was used to determine the indirect effect of COVID-19 fear on quality of life.

Result: The mean age of the 319 patients with epilepsy was 36.0 (± 11.1), and %53 were male. The mean duration of diagnosis was 16.0 (± 10.6) years, and more than half of the patients (52.4%) were using two or more antiepileptic drugs. The mean scores were found to be 19.2 (range: 0-35) for FCV-19S, 40.2 (range: 0-80) for WAQ, 16.4 (range: 0-63) for BDI and 52.1 (range: 0-100) for QoLIE-10. Although there was a binary correlation between them, the fear of COVID-19 did not directly affect the quality of life. However, it was determined that the fear of COVID-19 increased anxiety and depression; consequently, the increase in negative mood decreased the quality of life.

Conclusions: It was found that the fear of COVID-19 experienced by patients with epilepsy did not have a significant direct effect on the quality of life. However, it was determined that it had been an indirect effect on the quality of life by increasing mental health problems such as anxiety and depression that negatively affect the quality of life. In particular, this indirect effect was mostly on anxiety.

Abstract Number: 496

Title: COVID-19 pandemic in Istanbul: Seizure Frequency and Psychosocial Outcomes in Patients with Epilepsy

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Purpose: The aim of this study is to examine the effect of the COVID-19 outbreak on seizure frequency and psychosocial outcomes in patients with epilepsy (PwE).

Method: This cross-sectional study was conducted with a total of 319 adult PwE. Data were collected online between 15 December 2020 and 5 January 2021. Data were obtained using the patients' information form (sociodemographic, psychosocial and clinical characteristics), Worry and Anxiety Questionnaire (WAQ), Beck Depression Inventory (BDI), and Pittsburg Sleep Quality Index (PUQI) scales**.**

Result: The mean age of the 319 patients with epilepsy was 36.0 (± 11.1), and 53% were male. It was found that more than half of the patients were seizure-free before the pandemic (55%), and this situation was almost unchanged in the pandemic period (54%). It was observed that the COVID-19 pandemic mostly affected the social (80%) and psychological (67%) areas in the life of the patients, and the rates of patients with anxiety, depression, and sleep problems were also quite high (61%, 57%, and 37%, respectively). Nonlinear canonical correlation analysis revealed that pre-and post-pandemic seizure frequencies were closely located, and this implied that the Covid-19 outbreak did not directly increase the frequency of seizures. Moreover, PwEs who have problems in drug supply during the pandemic period, have more than 4-6 seizures a year, have the anxiety to intervene in a seizure and experience a depressive mood are more psychologically affected by the pandemic.

Conclusions: It was determined that the frequency of seizures before and during the pandemic was similar, and the COVID-19 pandemic did not have a direct effect on the frequency of seizures. However, it has been observed that the psychology of patients who have anxiety about their seizures and medications and who cannot receive support from a health professional was negatively affected.

Abstract Number: 574

Title: Caregiver burden, quality of life and related factors in caregivers of patients with epilepsy (PwE) in Turkey

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Purpose: This study aimed to evaluate caregiver burden and quality of life (QoL) and their predictors in caregivers of **patients with epilepsy** (PwE).

Method: A descriptive cross-sectional survey was carried out with a sample of 107 patients and their family caregivers. While the Zarit Caregiver Burden Inventory (ZCBI), Short Form-36 (SF-36), Hospital Anxiety and Depression Scale (HADS), and Ways of Coping with Stress Scale were used for caregivers, Montreal Cognitive Assessment, HADS, Quality of Life in Epilepsy-31 (QoLIE-31), Stigma scales were used for patients.

Result: A total of 107 caregivers participated, of whom 57.9% were females, 67.3% parents, 42.1% housewive. Half of the caregivers (54.2%) reported mild-moderate levels of burden (mean ZCBI score 31.10, SD 19.29). The mean age of the patients was found to be 31.9 (± 13.7) and 38.3% of them had more than one seizure per month. The burden was higher in caregivers of male patients (p=0.047). Mean scores of SF-36 sub-domains varied between 54.39 and 74.44. There were correlations between caregiver burden and age of seizure onset (p=0.025), stigma level (p<0.001), cognitive function (p<0.001), quality of life (p<0.001), anxiety (p=0.001), and depression (p=0.005). Also, the total ZCBI score was correlated with caregivers' depression (p<0.001), anxiety (p<0.001), and quality of life (p<0.001). It was determined that caregivers' styles of coping with stress were frequently the self-confident approach method and this was negatively correlated with care burden (p <0.021).

Conclusions: It has been determined that the majority of caregivers are composed of parents, and gender is an important factor in caregiver burden. Also, it was found that psychosocial state, as well as the clinical characteristics of the patient, were correlated with caregiver burden. In order to reduce the caregiver burden in epilepsy patients, providing psychosocial support to the patient along with medical treatment will be of great benefit.

Abstract Number: 591

Title: A peer support group intervention to decrease epilepsy related stigma in an onchocerciasis endemic area in Mahenge, Tanzania

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Purpose: To improve the quality of life of persons with epilepsy (PWE) in Mahenge, an onchocerciasis endemic area in Tanzania. We established a peer support group (PSG) in two out of four rural villages (Mdindo, Msogezi, Mzelezi and Sali). One year later, we compared the degree of perceived epilepsy related stigma among PWE.

Method: Between February and July 2020, we carried out a baseline cross-section survey among PWE identified in our previous surveys and their caregivers in the four rural villages. Perceived stigma was measured using the validated Kilifi stigma scale of epilepsy (KSSE) and logistic regression was used to identify factors associated with perceived stigma.

Result: A total of 162 PWE participated in the study, 76 (46.9%) from villages with PSG intervention. The proportion of perceived stigma among PWE was 32.7%; with no difference between villages with and without PSG (P=0.903). The median stigma score was 2.0 ranges from 0.0 to 25.0. A history of seizures during the last month, a history of physical abuse and sexual harassment (adjusted OR (aOR)=1.7, p<0.001; aOR=1.2, p=0.003 and aOR=2.7, p=0.349 respectively) were associated with a high perceived stigma score among PWE.

Conclusions: Perceived stigma in rural villages in Mahenge is a major public health problem. A follow-up study is planned after one year to determine the effect of the PSG intervention on perceived epilepsy related stigma.

Abstract Number: 664

Title: The impact of COVID-19 vaccines in patients with epilepsy: a review

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Purpose: The coronavirus disease 2019 caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a pandemic worldwide. The most efficient solution to end this pandemic is a safe and

efficient vaccine. Whether patients with epilepsy should get instant vaccination has become a frequent asked question in the clinic.

Method: We reviewed all 13 currently approved COVID-2 vaccines listed by WHO, with a particular interest in mechanism(s) and adverse effect(s) through their published academic paper from January 1, 2020, up to February 28, 2021. The search systematically made in PubMed and medRxiv using the brand name and previous reported name of vaccines products. Reviews, editorials, and animal studies were excluded.

Result: Forty-eight was selected for detailed reviewing. No major or significant neurological adverse effect was reported in these data. One seizure and one tonic convulsion cases were reported in the ChAdOx1 nCoV-19 vaccine.

Conclusions: Preliminary results suggest that seizure related incidence is rare. Fever was one of the most frequent effects on all platforms, particularly in the mRNA platform. It could lower the seizure threshold, as the international league against epilepsy warns. There was no evidence suggesting an increased risk of side effects in patients with epilepsy from the COVID-19 vaccine. A cautious optimism towards the vaccine's safety in terms of patients with epilepsy is appropriate.

Abstract Number: 730

Title: People with epilepsy still feel stigmatized

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Purpose: Those affected with epilepsy have long been subject to stigmatization. Stigmatization and discrimination can have manifold negative effects from social isolation, low self-esteem, to reduced quality of life and worsening of seizures.
In Norway educational programs have been arranged at the National Centre for Epilepsy, aiming at reducing stigma and shame associated with epilepsy, and thereby increase the quality of life for those affected and their families. Thus, we wanted to explore the extent of self-reported perceived stigma and experienced discrimination in a Norwegian cohort with epilepsy.

Method: We conducted a web-based questionnaire survey in Norway. Participants were asked to report background and epilepsy-related information. In addition,
they were encouraged to answer questions regarding felt stigmatization in different situations and to rate stigma according to the Jacoby stigma scale.
Result: Of 1182 respondents, 56% reported to have felt being stigmatized, and 35% reported to have experienced discrimination solely on the ground of the disease. Living alone was significantly associated with reporting stigmatization. After controlling for gender, age, perceived depression, cohabitation, seizure freedom, and occurrence of tonic-clonic seizures, reports of experienced stigmatization was a statistically significant predictor for reduced quality of life.

Conclusions: A considerable proportion of people with epilepsy in Norway feel stigmatized and/or subject to discrimination, and it reduces their quality of life.

Abstract Number: 823

Title: epilepsy advocacy best practices from africa

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Purpose: There is a pressing need for low-cost intervention models to promote epilepsy prioritization at national level. The aim of this study conducted between December, 2020 and March 2021 was to provide information on best practices at national level for addressing issues of persons with epilepsy in relation to advocacy of persons with epilepsy in all aspects of development efforts. It also aimed at identification of what constitutes best practices in mainstreaming epilepsy and illustrates this through diversified approaches based on a needs based approach. The study also presents recommendations and input to the development of a best practice guide to compliment the Epilepsy Advocates Toolkit (International Bureau of Epilepsy (IBE), 2021).

Method: The case studies included have been collected through key contacts and the IBE network. 10 countries[3] were purposively selected and submitted institutional or individual cases. Additional information was collected through a best practice workshop. All submissions were triangulated to identify key themes.

Result: Three thematic areas were identified namely: Advocacy (evidence based advocacy, self-advocacy), capacity building, and partnerships were identified. Across the countries there is evidence that a three legged approach can be used in engagement with duty bearers and any supporter for an epilepsy cause. The approach is summarized as Capacity Building, Advocacy, and Partnerships (CAP) model to represent the core themes of the study. The model being proposed can used to strengthen systematic engagement of organisations of persons with epilepsy and individuals when advocating and lobbying duty bearers to put epilepsy on the agenda. Each step has supporting steps Capacity Building (Self-Assessment, Training/Empowerment, and Resources), Advocacy (self-advocacy and evidence based advocacy), and Partnerships (formal or informal).

Conclusion: The study highlights that a holistic and sytematic approach needed to engage duty bearers.

Abstract Number: 897

Title: Survey on the effectiveness of a training course for school staff on seizures management: semi-structured interview after 12 months

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Purpose:
School staff do not have specific training on epilepsy and the management of seizures resulting in the use of the ambulance. In Italy, more than 40% of school calls to health emergency number are for seizures. The objective is to assess how seizures have been managed by school staff after a year from a training course on epilepsy.

Method: The study was conducted on 108 people belonging to 81 schools in Rome after 6-12 months from training meeting. Participation in the course took place at the request of the schools. A semi-structured interview was used to assess, in case of seizures, if safety measures have been implemented, whether the rescue medication has been administered, whether the ambulance has been called and whether the child has been admitted. Interview was conducted on 80% of the school staff who attended the meeting. Training and interview were done by epilepsy nurses.

Result:171 seizures occurred at school, 147 (86%) lasting less than 2 minutes and 24 (14%) longer than 2 minutes. The rescue medication was administered 25 times (14.6%). The ambulance was called 22 times (13%) and 17 (9.9%) were the hospitalization. Most of the seizures occurred in children aged 6-13 years (73%) and male (80%). 93% (159/171) of the school staff who managed these seizures that occurred at school had participated in the training course.

[3] Sierra Leone, Zambia, Rwanda, Mauritius, Malawi, Cameroon, Eswatini, Kenya, Uganda, South Africa

Conclusions: Often staff school without a training would have used the ambulance in cases of seizures. So we can say that the training course: increases the safety of the child, reduces calls to health emergency number and improper hospitalizations. This not only reduces costs for the National Health Service but also avoids discomfort for the child and the family.

Abstract Number: 934

Title: Quality of life in caregivers of people with epilepsy in Mexico City

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Purpose: Describe the QoL in caregivers of people with epilepsy (PWE).

Method: Twenty-three caregivers of PWE were assessed with WHOQOLBREF questionnaire. Shapiro-Wilk normality test was performed, measures of central tendency and proportions were used to describe the clinical and sociodemographic data, and Student's T test or ANOVA for inferential statistics.

Result: Mean patient age was 40.56 years ± 9.32. Nineteen (82.61%) were women. Seven (30.43%) finished a degree and nine (39.13%) have an employment. Nineteen (82.61%) of the caregivers were the primary caregiver and only 8 (34.78%) were married. On average 2 people depended financially on the caregiver. The global percentage of the WHOQOLBREF domains were the following: physical 54.73%, with 18 (78.3%) with poor quality of life (pQL); psychological 43.82%, of which 20 (87%) have pQL; social relationships 64.34%, of which 11 (47.8%) have a pQL; and 54.82% in environment of which 15 (65.2%) have a pQL.
When comparing by sex, a difference was found in the psychological domain: men (31.25 ±10.210) versus women (46.47 ±12.62) (p = 0.035), no differences were found between the primary caregiver or another caregiver. Regarding the occupation of the caregivers, differences were found in the physical domain, being greater in unemployed (63%) than in employees 44% (p = 0.010), (OR= 0.039 ; IC 0.003-0.581). Single caregivers had a lower score in the psychological domain (p = 0.032). (OR 1.214 IC 0.974-1.513).

Conclusions: Most of the patients had a poor quality of life in WHOQOLBREF, principally in the psychological domain where differences related to sex and occupation were found.

Abstract Number: 938

Title: Epilepsy Association of Zambia empowered through IBE Promising Strategy Programme

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Purpose:
Empowerment is a cross-cutting issue, from education and health care to governance and economic policy, activities which seek to empower and increase development opportunities, enhance development outcomes and improve people's quality of life. The Association through the Promising Strategy sought to empower its members with skills for sustainability.

Method:

- Establishment of Rehabilitation Centre with training and counseling sessions held

- Establishment of Self Help Groups e.g. Youth Group, Women with Epilepsy, Cooperative, etc.
- To work as a team and think of projects for sustainability
- Train members to identify opportunities: (thinking out of the box)
- Create a psychological safety net to enable team members to grow
- To develop skills and individual social support
- To empower the clients to lead productive lives
- To enhance advocacy programmes; and
- To help people with epilepsy participate meaningfully

Result:
The establishment of a Rehabilitation Centre had been a long term plan for the Epilepsy Association of Zambia since inception. The initiation of the Promising Strategy by the International Bureau for Epilepsy was a great milestone to achieving our dream. In 2010, with funding from IBE the Epilepsy Association of Zambia was able to come up with a longstanding project site, which enables people with epilepsy with little or no capacity to support themselves to pass through the project to learn skills. The proceeds from the production at the project site go towards supporting school going children with epilepsy.

Conclusions:
The Promising Strategy Programme has been the strength for the Epilepsy Association of Zambia in difficult times, making people with epilepsy feel confident and the Association is a reliable support group.

Abstract Number: 970

Title: Marital status of people with epilepsy in indonesia urban cities

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Purpose: The aim of this study was to describe the marital status and its associacted factors in people with epilepsy (PWE) population.

Method: This study was part of descriptive study enrolling PWE in Jakarta, as the capital city of Indonesia, and surrounding satellite areas (Bogor, Depok, Tangerang, and Bekasi) on January to December 2019. Using demographic and clinical characteristics, this study emphasized marital status. Statistics was calculated using SPSS software. Only completion of twelve years-compulsary education was considered as lower education.

Result: We enrolled 154 PWE consisting of 90 (58.44%) females and aged between 18 to 71 years old. Regardless of gender, proportion of PWE who were not married was higher (56.50%). Among married PWE, 65.7% was female while only 34.3% was male. Significantly, higher proportion of married PWE was observed at older age, ≥35 years old (p=0.000) and high education level (p=0.0285). However, 91.3% of married male and 81.8% of married female had descendants. There was no significant correlation between employment status and seizure severity parameters (seizure-free status, seizure onset, seizure duration, and number of antiepileptic drug), and marital status.

Conclusions: Higher proportion of PWE were not married. However, among who were married, majority had descendants. Compared to overall urban Indonesia population, PWE tended to marry at older age. Only higher education level was associated to marital status in PWE.

Abstract Number: 1030

Title: The voice of the youths and young adults with epilepsy in Taiwan

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Purpose: This report summarizes an innovative nationwide, Taiwan Youth with Epilepsy Summit on 2020-11-21 at Tainan. This conference was hosted by the Tainan Epilepsy Association.

Method: The process of the initiation, design and training for the conference was reviewed. Parts of the conference will be demonstrated.

Result: This innovative conference entitled Taiwan Youth with Epilepsy Summit was attended by the invited members of the deputy of Tainan City Mayor and her members, academic leaders in pediatric and adult epileptologists, medical sociologists, educational professionals. The other participants included social workers, medical professional, medical students and people with epilepsy and their care givers from 12 out of 16 organizations of people with epilepsy in Taiwan. In total 153 persons attended the meeting. This is the biggest gathering in Tainan during the COVID-19 era.
Six youths and young adults with epilepsy on behalf of people with epilepsy and their caregivers were the speakers, I firstly addressed the relationship between “Convention on the Rights of Persons with Disabilities, CRPD) and epilepsy. The others proposed some urgent biopsychosocial care and human right needs related to education (one speaker), vocation (two speakers) and traffic regulation (two speakers). Although Taiwan is not a member country of the United Nations, Taiwan is the only country to legislate for the implementation of CRPD. This conference was prepared for the Taiwan State Party Report of implementing the UNs Convention on the Rights of Persons with Disabilities in the last 4 years.

Conclusions: The new paradigm of protecting the human rights and dignity of persons with disability as a national strategy for social welfare created the opportunities of autonomous individuals to participate social policy they concerned. The intelligent youths and young adults with epilepsy in this conference demonstrated their altruistic heart and behavior.

Abstract Number: 1131

Title: The Role of Trained Epilepsy Counselor in Combating Psychological Consequences of Epilepsy in Rural Kenya

Abstract Number: 1173

Title: Tele-education of nurses and social workers for a better management of Epilepsy in Africa

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Purpose: Tele-education, defined as the application of information and communication technologies in the delivery of distance learning, has been used for many years to deliver continuing education. The main modes are audio, video and computer. Epilepsy has a major impact on social, school or professional and family life. Epilepsy is the source of many disabilities: disability related to epileptic disease, social disability, "medical" disability related to the treatment. We aim to highlight the importance of the use of tele-education to empower the social matters related to epilepsy (care, training, care, education, sensitization, management, association support), which remains a new means which can solve several health problems all over the world and mainly in the Remote areas.

Method: We will launch tele-education sessions for nurses and social workers first, in 4 countries: Niger, Rwanda, Cameroon and Malawi, in April 2021. 3 nurses were recruited per country, 3 months ago. This represents a first step that can be generalized to other localities in other countries to benefit more patients. Based on the needs expressed in the field, we have chosen 2 main phases for the implementation of this project.

Result: Tele-education has been in use in South Africa since the 1970s. Several forms of tele-education are in place at the medical schools and in some Provincial Departments of Health. The service has expanded to offer video-conferenced education into Africa using different ways of delivering tele-education, yet major social workers remain distant and inaccessible.

Conclusions: The use of tele-education for nursing and social workers should be encouraged along with guidelines for the use of videoconferencing. It is an ideal solution to allow early support when there is a lack of local resources and would optimize the use of human resources and skills within its scope of application.

Abstract Number: 1180

Title: On the Cusp of a Revolution? Managing Epilepsy in Marrakesh using Telemedicine

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Purpose: Telemedicine is a revolutionary approach to medical care, and presents tantalizing advantages, aside peculiar challenges of implementation. While many developed countries are leading the charge, several developing countries are gaining grounds in this medical evolution.
The purpose is to report our experience in managing epilepsy in Marrakesh using Telemedicine

Method: Our work is a descriptive retrospective study of the telemedicine experience of epilepsy consultation in the Neurology Department, Mohammed VI University Medical Center, Marrakesh, since 2011. Data was collected through the Mohammed VI University Medical Center Telemedicine Commission which includes medical professors, administrative staff, network administrators and computer scientists

Result: Consultants were brought together for managing and monitoring the health status of epileptic patients and encouraging secondary and tertiary prevention. A senior neurologist from our department interviewed and examined patients and prescribed treatment by videoconference.
Our Neurology Department organised specialised video-conferenced consultations on epilepsy, nationally and internationally. Local neurologists or general practitioners carried out these consultations remotely.
Another use of telemedicine is the continuous training of medical staff via the tele-expertise with reference centers and international experts, as well as the south-south collaboration whose goal is to extrapolate our experience to our African colleagues.

Conclusions: Telemedicine retains a central place in our practice. Virtual care is a complement to in-person consultations and needs to be developed, with its application expanded in terms of services and outreach.

Abstract Number: 1192

Title: Application of virtual reality and AI as an education tools to support students with epilepsy in Bosnia and Herzegovina online learning

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Purpose: The paper explores e-learning issues related to the virtual environment reality and artificial intelligence and the importance of application of artificial intelligence for the benefits of students who are diagnosed with epilepsy and autism. The paper presents the advantages and opportunities that contribute to improving e-learning in educational institutions and the benefits for students with epilepsy and other involved parties in the educational process, such as teachers and parents.

Method: A study in this research sought to analyse e-learning potentials by seeking to measure the benefits of e-learning over traditional learning; how different e-learning tools facilitate this approach to learning; examine students' attitude towards e-learning tools and and their preferences; demonstrate how providing education through virtual learning environment encourages. I.T. literacy and offers 10-15 age school students opportunities to succeed in a globally competitive world by leveraging their knowledge through application of virtual reality and AI

Result: Students enrolled in this research have a highly positive attitude towards e-learning. It proves that the use of artificial intelligence has the potential to change the traditional and potentially damaging model of modern teaching that corresponds to a standard that should apply to all, in which all students, regardless of individual differences and preferences, should fit in.

Conclusions: Artificial intelligence tools enable creating global classrooms accessible to everyone, including those who have impairments. It opens opportunities for students who cannot attend school regularly, struggling with chronic illness, students with disabilities- Artificial intelligence provide opportunities for children to learn to suit their personal needs and preferences, and learning styles.

Abstract Number: 1197

Title: Intermittent light stimulation in on-demand streaming television series, accuracy of information and seizure occurrence. The STREAM-LIGHT study.

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Purpose: In about 3% of people with epilepsy, exposure to flashing light sequences (FLS) can trigger seizures. This condition is known as photosensitive epilepsy, which is more common in children and teenagers. Exposure to FLS may as well induce other symptoms l like headache, nausea and dizziness. On-demand streaming platforms (OSP) have become popular given the variety of contents (i.e. films and TV-series) and the easy access. Most binge watching sessions involve the use of laptops and take place in the night-time, in conditions of low ambient light. The purpose our study is to identify the presence of FLS in the content catalogues offered by the main OSP, and to assess any correlation to seizure onset or discomfort symptoms recurrence. The presence of adequate information addressed to PWE was also evaluated.

Method: We carried out a research in online patients' forums, looking for warnings about FLS reports within TV-series and films offered by the main OSP. Data referred to seizure onset, as well as symptoms of discomfort associated with the vision of a specific show and the presence of adequate warnings, were collected. A re-watch of the TV-series/film by an epileptologist was performed to evaluate the definite presence of FLS.

Result: A total of 134 TV-series have been identified, with 3334 FLS warnings (median: 13,5; IQR: 11-29). Recurrence of seizures was reported in 2 TV-series, while 12 were associated with the onset of discomfort symptoms. The platform with the higher number of reports was Netflix. Among all of the analyzed and reported shows, only in one case an FLS information banner was shown.

Conclusions: The presence of FLS was very frequent in the OSP catalogues of films and TV-series. Systematic improvement of the information about FLS presence is necessary for greater safety of the audience suffering from epilepsy.

Abstract Number: 1202

Title: Fighting for epilepsy without barriers: indigenous linguistic inclusion health education in Mexico. Young Epilepsy Section-CAMELICE-ILAE

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Purpose: Develop health educational audiovisual material in native languages in regard to epilepsy for indigenous communities in Mexico.

Method: An initial research of the main indigenous languages in Mexico was conducted. Then 22 downloadable audiovisuals were created in Spanish by medical experts to produce videos and podcasts in the four main native languages. YES-CAMELICE provided an epilepsy training workshop for the indigenous translators. The audiovisual material addressed: "What is epilepsy?", "Symptoms and causes of epilepsy", and "What to do during a seizure" We started a digital-radio broadcast "Neuro-Radar" to facilitate the diffusion of the content. This project was conducted in agreement with the Mexican Government and Armstrong Laboratories.

Result: In Mexico, approximately 364 variants of 68 indigenous languages are spoken. According to population census of National Institute of Economic and Geographic 2020, 7.4 million people speak an indigenous language/Spanish and 865,972 only an indigenous language; the most common are Nahuatl and Maya (1,651,958 and 774,755 speakers, respectively), followed by Tseltal (589 144), Tsotsil (550 274) and Mixteco (526 593). We created 4 videos; 2 Maya and 2 Nahuatl and 8 podcasts in Maya, Tseltal, Nahuatl and Mixteco. Multimedia was available online and shared on social media, an official webpage, Neuro-Radar Radio, medical meetings, local newspapers and TV shows with an estimated impact on 36 million Mexicans.

Conclusions: A collaboration between YES-CAMELICE, a pharmaceutical company and local government is possible to provide high quality educational multimedia in native languages to people with language barriers to understand epilepsy and their consequences. YES-CAMELICE* (Gutiérrez-Cisneros Michel, Callejas-Rojas Rodolfo César, Barrera-Tovar Diego Andrés). Acknowledgement to Armstrong Laboratories for collaboration and funds provided. Acknowledgement to Cessiah-Chuc-Uc, A-Silvano-Jiménez, Cresenciano-Hernández and Fausto-Aguilar for translations.

Abstract Number: 1258

Title: Improvement of public stigmas and sociocultural beliefs towards epilepsy and social identity in the Aseer region, Saudi Arabia: An updated study.

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Purpose: Differences in the sociocultural biases and practices against epilepsy largely contribute to the development of a stigmatizing nature for patients with epilepsy (PWE). In this study, we evaluated factors that impact the stigma evolution and maintenance, changes in the public awareness and cultural practices toward PWE.

Method: A cross-sectional study in which data were collected from a self-administered electronic survey composed of 33 items targeting the population in the Aseer region.

Result: A total of 937 individuals participated in the present study. The majority of responders were Saudis (98.6%) with a mean age (±SD) of 31.24 ± 11.85 years. More than half of the subjects were women (58.3%), while men accounted for 41.7%. Of these, 921 participants (98.3%) had heard or read about the disorder previously. Approximately 84.8% believed that epilepsy was one of the brain disorders, while 95.8% disagreed that it was a contagious disease. Unfortunately, 40.1% of the responders were convinced that it was a result of a spiritual reason, with more than 9% believing in treating epilepsy spiritually. About 75% thought that epilepsy could be a test from God.

Conclusions: In addition to the clinical aspects of epilepsy, it is a social label with a public stigma that influences its social prognosis. Raising awareness through campaigns would improve the knowledge and practices of the population and, therefore, provide a healthier environment for PWE, alleviate their feelings of stigma, and improve their quality of life.

Abstract Number: 1274

Title: Cultural adaptation of the Brief Illness Perception Questionnaire (B-IPQ): preliminary results of patients with epilepsy in Buenos Aires, Argentina

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Purpose: To perform a linguistic and conceptual adaptation of the Brief Illness Perception Questionnaire (B-IPQ, Broadbent, 2006) in patients with epilepsy in Buenos Aires, Argentina. This is a 9-item self-administered instrument that evaluates cognitive and emotional aspects of patients' illness experience in a relatively short time.

Method: The steps suggested by the International Test Commission (ITC) for the cross-cultural adaptation of psychological assessment (2017) were followed: forward translation, content validity through expert judges (through Aiken's V), patient feedback and pilot test with patients with epilepsy. From the pilot test, preliminary analyses were carried out. Association analyses were performed using t-test and ANOVA between sociodemographic and clinical variables (sex, education, time of disease evolution and depressive symptoms [through the Beck Depression Inventory]), and total scores of B-IPQ. All patients signed informed consent.

Result: A preliminary version of the scale was obtained with similar characteristics to the original version, both linguistically and conceptually (AV_{total} = .94). Patients (n=66, 45 women) reported a good understanding of it,

although they suggested few changes in some expressions to facilitate reading. No significant differences were found in B-IPQ total scores according to sex, educational level or time of evolution of the disease. Patients with moderate or severe depressive symptoms reported a higher total score than those with mild or without symptoms (X_{with_depr}= 49,36, t=2,21, p<0,05).

Conclusions: The Argentine version of the B-IPQ is a tool that was positively evaluated by expert judges and patients. Preliminary results indicate that patients with epilepsy and depressive symptoms report a more negative illness perception than those without depressive symptoms. These data are in accordance with other research that affirm that illness perception and mood would be related. Further research in this population is needed.

Abstract Number: 1320

Title: Systematic Review of Frequency of Felt and Enacted Stigma in Epilepsyand Determining Factors and Attitudes Towards Persons Living With Epilepsy

Churl-Su Kwon[1], Ann Jacoby[2], Amza Ali[3], Joan Austin[4], Gretchen Birbeck[5], Patricia Braga[6], J Helen Cross[7], Hanneke de Boer[8], Tarun Dua[9], Paula Fernandes[10], Kirsten Fiest[11], Jonathan Goldstein[12], Sheryl Haut[13], Diane Lorenzetti[14], Janet Mifsud[15], Solomon Moshé[13], Karen Parko[16], Manjari Tripathi[17], Samuel Wiebe[18], Nathalie Jette[1]

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Purpose: To review evidence of felt and enacted stigma and attitudes towards persons living with epilepsy, and their determining factors.

Method: Thirteen databases were searched (1985-2019). Abstracts were reviewed in duplicate and data independently extracted using a standard form. Studies were characterized using descriptive analysis by whether they addressed 'felt' or 'enacted' stigma and 'attitudes' towards persons living with epilepsy.

Result: Of 4,234 abstracts, 358 articles met eligibility criteria for papers addressing tools to evaluate stigma, stigma frequency, attitudes and interventions. Specifically, 132 addressed either felt or enacted stigma and 210 attitudes towards epilepsy, this paper's focus. Stigma frequency ranged broadly between regions. Factors associated with enacted stigma included low level of knowledge about epilepsy, lower educational level, lower socio-economic status, rural areas living, and religious grouping. Negative stereotypes were often internalized by persons with epilepsy, who saw themselves as having an 'undesirable difference' and so anticipated being treated differently. Felt stigma was associated with increased risk of psychological difficulties and impaired

quality-of-life. Felt stigma was linked to higher seizure frequency, recency of seizures, age of epilepsy onset or duration, lower educational level, poorer knowledge about epilepsy and younger age. An important finding was the potential contribution of epilepsy terminology to the production of stigma. Negative attitudes against those with epilepsy were described in 100% of included studies, originating in any population group (students, teachers, healthcare professionals, general public, those living with epilepsy). Better attitudes were generally noted in those of younger age or higher educational status. Studies were generally of poor or fair quality.

Conclusions: Implications for felt and enacted stigma show considerable commonality worldwide. Though some studies show improvement in attitudes towards those living with epilepsy over time, much work remains to be done to improve attitudes and understand the true occurrence of discrimination against persons with epilepsy.

Abstract Number: 1360

Title: Epilepsy-Related Stigma and Attitudes: Systematic Review of Screening Instruments and Interventions

Karen Parko[1], Joan Austin[2], Gretchen Birbeck[3], Churl-Su Kwon[4], Paula Fernandes[5], Patricia Braga[6], Kirsten Fiest[7], Amza Ali[8], J Helen Cross[9], Hanneke de Boer[10], Tarun Dua[11], Sheryl Haut[12], Ann Jacoby[13], Diane Lorenzetti[14], Janet Mifsud[15], Solomon Moshé[16], Manjari Tripathi[17], Samuel Wiebe[18], Nathalie Jette[19]

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Purpose: A systematic review aimed at summarizing the evidence related to instruments that have been developed to measure stigma or attitudes towards epilepsy and on stigma-reducing interventions.

Method: This review followed the PRISMA standards. A broad literature search (1985-2019) was performed in 13 databases. Articles were included if they described the development and testing of psychometric properties of epilepsy-related stigma or attitude scale or stigma-reducing interventions. Two reviewers independently screened abstracts, reviewed full text articles, and extracted data. Basic descriptive statistics are reported.

Result: We identified 4,234 abstracts, of which 893 were reviewed as full text articles. Of these, 38 met inclusion criteria for an instrument development study and 30 as a stigma reduction intervention study. Most instruments were initially developed using well established methods and tested in relatively large samples.

Most intervention studies involved educational programs for adults with pre- and post-evaluations of attitudes towards people with epilepsy. Intervention studies often failed to use standardized instruments to quantify stigmatizing attitudes, were generally under-powered, and often found no evidence of benefit or the benefit was not sustained. Six intervention studies with stigma as the primary outcome had fewer design flaws and showed benefit. Very few or no instruments were validated for regional languages or culture and there were very few interventions tested in some regions. Overall quality of the studies was generally poor.

Conclusions: Investigators in regions without instruments should consider translating and further developing existing instruments rather than the development of new instruments. Very few stigma reduction intervention studies have been conducted, study methodology in general was poor, and standardized instruments were rarely used to measure outcomes. To accelerate the development of effective epilepsy stigma reduction interventions, a paradigm shift from disease-specific, siloed trials to collaborative, cross-disciplinary platforms based upon unified theories of stigma transcending individual conditions are needed.

Status Epilepticus

Abstract Number: 33

Title: New-onset refractory status epilepticus (NORSE) and febrile infection-related epilepsy syndrome (FIRES): More differences than similarities

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Purpose: Febrile infection-related epilepsy syndrome (FIRES) is now considered a subcategory of new-onset refractory status epilepticus (NORSE) that requires a prior febrile infection, applicable for all ages. In the past it has been discussed whether NORSE and FIRES are the same entity, especially, if no cause has been identified despite extensive investigations, often referred to as cryptogenic. Therefore, we test the hypothesis that NORSE and FIRES of unknown cause are one syndrome.

Method: We compared a cohort of 52 children with FIRES of unknown cause to 18 adults with NORSE of unknown cause. We retrospectively examined demographic and clinical data. Statistical analyses were made using Mann-Whitney-*U* and Chi-Square tests. *P* values <0.05 were regarded as statistically significant.

Result: NORSE affected more women (78% vs 44%; *P*=0.01) and was more often affected by previous neurological diseases than FIRES (33% vs. 4%; *P*<0.001). The median acute hospital stay in FIRES was longer than in NORSE (36 days [interquartile range, IQR=37] vs. 20 days [IQR=19]; *P*<0.001). FIRES was treated more frequently with coma therapy (81% vs. 28%; *P*<0.001) and with a higher median number of antiepileptic drugs during acute therapy than NORSE (7 [IQR=6] vs. 4 [IQR=2]; *P*<0.001). FIRES showed an elevated cerebrospinal fluid (CSF) cell count (10 cells/µl; *P*=0.002). In contrast, CSF protein level was higher in NORSE (48 mg/dl [IQR=24]; *P*=0.02) but without differences in oligoclonal bands. Immunotherapy was administered more frequently in FIRES (73% vs. 22%; *P<0.*001). There were no significant differences in number of antiepileptic drugs after hospital stay (*P*=0.23) and in overall mortality (*P*=0.41).

Conclusions: We found more differences than similarities. Therefore, NORSE and FIRES of unknown cause should be compared separately by age and prospectively.

Abstract Number: 101

Title: Refractory seizure secondary to Human Herpes Virus 6 (HHV-6) encephalitis in young immunocompetent adult:Unusual presentation

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Purpose: Human Herpes Virus 6 (HHV-6) encephalitis is usually seen in immunosuppressed patients, particularly in transplanted patients as it remained latent in immunocompetent individuals.
Method: Case-report

Result:34-year-old lady, without prior medical illness, presented with a-week history of fever associated with 3-day history of altered behaviour and confusion. She was somnolence on arrival to the emergency unit. Her husband denied prior history of travelling, seizure, weakness, double vision or significant drugs history. Apart from temperature of 37.7 Celsius and GCS of 10/15, her other examination findings are benign. Her blood investigations were unremarkable. Her lumbar puncture revealed normal opening pressure together with normal CSF analysis. She was empirically treated as meningoencephalitis, with IV ceftriaxone 2g twice daily and IV acyclovir 500mg thrice daily
In the ward, she developed recurrent complex partial seizure, intermittent dejavu and psychic experience despite on initiation of increasing dose of antiepileptic including intravenous phenytoin, sodium valproate and levateracetam. A trial of 5-day IV methylprednisolone 500mg OD was commenced.
Her EEG showed evidence of diffuse encephalopathy. MRI brain displayed T2 flair-hyperintensity over bilateral mediatemporal limbic system which suggestive of limbic encephalitis. CT Thorax/abdomen and pelvis was insignificant. HHV-6 PCR was positive while her CSF autoimmune profile was negative.
Her condition deteriorated, as she developed status epilepticus which later required intubation and mechanical ventilation. On top of continuous IV midazolam, and other antiepileptic agents, Intravenous immunoglobulin (IVIg) was commenced together with IV ganciclovir. Her condition was later improved. She was discharged with tapering dose of oral prednisolone, and sodium valproate, levetiracetam and perampanel tablet. Upon follow up 6 weeks later, she reported no more seizure or behavioural changes.

Conclusions: The case highlights the importance of considering HHV encephalitis an immunocompetent patient presenting with encephalitis with temporal lobe involvement and the role of intravenous immunoglobulin in treating HHV6 encephalitis

Abstract Number: 121

Title: Subacute Herpes Encephalitis With Full Neurological Recovery Post Acycylovir: Unusual Presentation With Unexpected Outcome

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Purpose: Herpes simplex virus-1 (HSV-1) encephalitis is a common cause of lethal sporadic encephalitis and known to cause persistent severe neurological deficits despite some improvement with acyclovir therapy.

Method: A case report

Result: We presented a case of a 54-year-old man with four weeks history of gradual personality changes associated with anterograde amnesia, impaired executive functioning and impaired speech that was initially suspected as a space occupying lesion. He developed non convulsive status epilepticus in the ward with

twitching on left sided of the mouth. Other than being afebrile (37 °C) at presentation, the examination revealed MMSE Score of 15/29, with impaired function mainly in orientation, recall, attention and calculation. Other neurological examinations have been found normal. EEG done shown moderate cerebral disturbance of diffuse theta and theta activity of encephalopathy changes. Cerebrospinal fluid (CSF) by polymerase chain reaction (PCR) and viral culture was positive for HSV-1, and MRI shown typical bilateral temporal lobe encephalitis, and he responded rapidly to empirical treatment with acyclovir 500mg (weight 53kg) every 8 hour, for total two weeks and 48 hours post treatment the MMSE Score improved to 30/30 and patient was asymptomatic without residual neurological significant abnormality noted on the day of discharge, 3 months and 6 months follow-up.

Conclusions: The case underscores the importance of recognizing HSV-1 encephalitis as a differential of non-febrile chronic behavioural changes. As illustrated in our case, the prognosis is good with prompt antiviral treatment despite the knowledge of poor morbidity outcome as majority of patients didn't return to previous neurology baseline.

Abstract Number: 129

Title: A case report of Paradoxical Reaction of Multifocal Leptomeningeal Tuberculoma in an Immunocompetent Individual

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Purpose: To report a case of progressive multi-focal leptomeningeal tuberculoma in the setting of anti-tuberculous paradoxical reaction in an immunocompetent patient.

Method: case-report

Result: 22-year-old, lady presented with severe headache, fever and anorexia for a month. On admission, she developed focal seizure and was febrile. Neurologic examination is nonfocal. Lumbar puncture showed high opening pressure of 35 cmH20, high cerebrospinal fluid (CSF) protein, low glucose count and lymphocytosis. Magnetic resonance imaging (MRI) brain demonstrated right corpus striatum infarction secondary to infective arteritis. EEG showed right hemisphere focal slowing. Patient was treated with Tab levetiracetam 250mg twice daily, ceftriaxone and due to high suspicion of tuberculosis meningitis she received concurrent anti-tuberculosis and dexamethasone. CSF mycobacterium Tuberculosis (MTB) culture, PCR, Gene Xpert were however negative. Despite prolongation of intensive phase at day 80, her symptoms persist, and admitted again for non-convulsive status epilepticus with further weight loss. Reassessment MRI showed multifocal thick wall rim-enhancing leptomeningeal lesions with features of caseating granuloma largest at basal cistern. Worsening right frontotemporoparietal vasogenic oedema and hydrocephalus were noted. Initial consideration suggested progressive brain infection without response towards antituberculosis therapy or paradoxical antituberculosis reaction. In view of the CSF MTB culture and PCR were negative, brain biopsy was performed to exclude other possibility such as neurocysticercosis or fungal infection. Brain biopsy rendered diagnosis of TB with evidence of caseating granuloma and multinucleated giant cell and positive MTB PCR. The anti-tuberculous was intensified with higher dose rifampicin (15 mg/kg) and dexamethasone 0.4mg/kg was reinitiated with slow tapering. Repeated MRI at 6 months shows resolving lesion with resolution of symptoms.

Conclusions: Paradoxical reaction may lead to diagnostic and management dilemma. The case highlights the tough decision made to continue anti-tuberculous drug in the setting of negative CSF MTB culture and MTB PCR with respect of worsening follow up MRI.

Abstract Number: 224

Title: Clinical Phenotyping, MRI and EEG Characteristics in Convulsive Status Epilepticus - a 2 Year Follow up of a Scottish Population Data-linkage Study.

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Purpose: Convulsive status epilepticus (CSE) is a common medical emergency. We have previously reported on a large prevalence cohort study (accepted for publication, DMCN). We followed this cohort for two years studying the detailed phenotype (clinical characteristics and anti-epileptic drug prescriptions) as well as investigation data including EEG and MRI.

Method: This study draws on a cohort of children who presented with CSE to a tertiary children's hospital in Scotland between January 2011 and December 2017.
We linked our CSE cohort using individual identifiers (CHI numbers) to electronic records of emergency care, outpatient neurology care and the EEG and MRI databases to obtain clinical phenotype details, anti-epileptic drug prescriptions, EEG and MRI features.

Result: There were 665 children with 1,234 presentations with CSE. 57.30% were male and the median age was 3.65 years (IQR 6.33). 60.45% of admissions were diagnosed with epilepsy, 24.40% were before the status epilepticus event and 75.60% after. EEG was carried out in 55.67% of admissions (30.28% normal, 40.47% abnormal and specific to epilepsy diagnosis, 29.26% abnormal but non-specific). MRI was carried out in 61.35% of admissions (49.80% normal, 41.08% abnormal and associated with epilepsy, 7.40% abnormal and possibly related to epilepsy, 1.72% unrelated abnormal). Maintenance anti-epileptic drugs were prescribed in 35% of patients. Of those 43.35% require polytherapy; the commonest anti-epileptic drug was levetiracetam.

Conclusions: We describe a clinical phenotype for our large cohort of CSE using data-linkage. Sixty percent of the status epilepticus admissions were amongst children who either already have epilepsy or go on to have a diagnosis of epilepsy. In those investigated further, EEG and MRI abnormalities were specific to epilepsy. Children who have generalised epilepsy and status epilepticus are more likely to be on polytherapy. Overall, these are valuable prognostic factors for emergency and long-term care plans of convulsive status epilepticus.

Abstract Number: 242

Title: The 2HELPS2B scale is useful to predict the prognosis and development of epilepsy in encephalopathic patients with suspected status epilepticus

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Purpose: The 2HELPS2B scale predicts the risk of seizures in patients with encephalopathy who undergo continuous electroencephalography. We evaluated the usefulness of this scale to predict the mortality and functional outcome, as well as the risk of developing epilepsy in encephalopathic patients with suspected status epilepticus (EPSE) in a tertiary hospital.

Method: We designed a retrospective observational study assessing hospitalized EPSE between May 2014 and May 2020. Patients aged 18 years and older were included while patients with post-anoxic encephalopathy were excluded. We analyzed the relationship between the 2HELPS2B scale and the following variables:

development of epilepsy, mortality at discharge and functional prognosis (defined by the mRS scale (modified Rankin scale) in good (mRS 0-2) and poor (mRS 3-6)) at discharge.

Result: 100 patients were analyzed, with a mean age of 60.8 years (SD 16.5). 2HELPS2B predicted the development of epilepsy with a cut-off point of 2 (sensitivity 0.80 and specificity 0.73) and an area under the ROC curve of 0.86, p <0.001. 2HELPS2B predicted higher mortality with a cut-off point of 3 (sensitivity 0.79 and specificity 0.68) and an area under the ROC curve of 0.73, p <0.001. 2HELPS2B predicted worse functional outcome with a cut-off point of 3 (sensitivity 0.73 and specificity 0.72) and an area under the ROC curve of 0.76, p <0.001.

Conclusions: In EPSE, 2HELPS2B has the ability to predict the development of epilepsy at discharge and is predictive of mortality and worse functional outcome at discharge.

Abstract Number: 267

Title: Childhood Status Epilepticus and Epilepsy Determinants of Outcome (SEED): a protocol for a cohort clinical-genomics study in northern Nigeria

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Purpose: To develop a protocol and funding for the largest-to-date cohort study of childhood status epilepticus (SE), with clinical and genomic predictors of outcomes.

Method: We will enroll ~1800 children, ages 30 days to < 15 years, with SE from three hospitals in Kano, Nigeria over 24 months. Deep phenotyping of childhood SE will be performed among children with SE. SE diagnosis and treatment will be based upon a standardized city-wide protocol. Detailed history, family history, pre-morbid history, video-recorded exams, standard laboratory tests, brain MRI, and CNS infection screening will be completed. Epileptologists will phenotype SE, using standardized criteria, including point-of-care EEG-video, MRI, and detailed clinical data. Blood for DNA extraction will be obtained upon enrollment. Genomic risk factors for SE-associated mortality, morbidity, benzodiazepine-resistant SE (BR-SE; continued SE after two weight-appropriate doses of a benzodiazepine) and development of epilepsy will be studied via genome-wide association studies (GWAS). GWAS, identifying SNPs associated with poor outcomes, and candidate gene analyses will be performed using the H3Africa Illumina array of ~2.3 million SNPs, enriched for common African variants, with PCA-matched population controls from H3Africa collaborators. Children enrolled in SEED cohort will be followed for a minimum of 24 months.

Result: The outcomes of this project will include the clinical and genomic predictors of (1) short-term SE-associated mortality, (2) benzodiazepine-resistant (established) SE, (3) long-term SE-associated mortality and morbidity, (4) recurrent SE, and (5) development of epilepsy after surviving a first seizure as SE. Other outcomes will include detailed EEG-video and MRI findings associated with SE in northern Nigeria.

Conclusions: SEED will provide the most detailed-to-date characterization of childhood SE in sub-Saharan Africa, as well as significant insights into the clinical (including EEG and MRI) and genomic predictors of SE-associated outcomes, including the development of epilepsy. Funded by Fogarty International Center, NINDS, NIH (R01 NS118483).

Abstract Number: 461

Title: The Effectiveness and Safety of Tocilizumab in Children with Febrile Infection-Related Epilepsy Syndrome (FIRES) : A Case Series.

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Purpose: There is increasing interest in the use of immunotherapy in the treatment of Febrile Infection-Related Epilepsy Syndrome (FIRES) but outcomes with conventional immunotherapies such as steroids and immunoglobulin have been disappointing. We report the effectiveness and safety of tocilizumab in the treatment of FIRES in children at our institution.

Method: Retrospective review of medical records, electroencephalography (EEG) monitoring and neuroimaging of six children between 2018 - 2021 was carried out. Outcome measures analysed were seizure control and functional outcome using the Modified Rankin Scale (MRS) at 3 months and at last follow up.

Result: The 6 children presented at a median age of 7.5years (range 5 -13years). All were previously normal and had fever and subsequent super refractory status epilepticus (SRSE) 1-2days following seizure onset. Serial EEGs showed frequent or near continuous focal electrographic or electro-clinical seizures often with characteristic shifting ictal foci. All had normal cerebrospinal fluid (CSF) including negative viral studies and autoimmune panel. All had normal acute magnetic resonance imaging (MRI), except one patient with symmetrical and extensive T2/FLAIR hyperintensities involving the deep grey matter structures at day 14 following status epilepticus onset. All patients received a combination of intravenous midazolam, high dose phenobarbitone, therapeutic hypothermia, ketogenic diet, immunoglobulin +/- steroids. Tocilizumab was given at a median time from onset of illness at 35.5 days (range: 7-93 days). Cessation of seizures were seen within a mean of 2.8days (range: 1- 5days). When we assessed for side effects, only two patients had grade 2 leukopenia. No patients suffered from pneumonia, sepsis or death. At 3months follow-up, 3/6 of them were largely seizure free with a dramatic improvement in their MRS scale of 1-3.

Conclusions: Intravenous Tocilizumab shows promising outcomes in our children with FIRES despite later administration with only mild side effects.

Abstract Number: 539

Title: Temporal Trends in Hospital Admissions and Incidence of Status Epilepticus and Epilepsy in England 2003-2018

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Purpose: Previous work using publicly available mortality data from the UK Office of National Statistics (ONS) suggested that Status Epilepticus (and Epilepsy) mortality rates decreased in England and Wales between 2003-2013. This data however was not coupled with the corresponding incidence data. Consequently we wished to determine whether the incidence of status epilepticus (and Epilepsy) hospital admissions had changed over time

Method: Using Hospital Episodes Statistics (HES) NHS Digital anonymised data, we looked at all hospital admissions for Status Epilepticus and Epilepsy in England between April 2003 and March 2018. During this time period, 555,133 Epilepsy hospital admissions and 47,720 admissions, with complete data available in 99.9% of cases.

Result: The incidence of status epilepticus overall increased from 5.1/100,000 persons year to 7.1/100,000 persons year, with a progressive increase in hospital admissions after 2011/12. In contrast, epilepsy hospital admissions increased from a rate 66.7/100,000 persons year to a high of 77.2/100,000 person years, decreasing thereafter year on year to a low of 64.0/100,000 person years in 2017/8. There was significant regional variations in admission rates for both status epilepticus and epilepsy. In-hospital mortality rates for Epilepsy admissions decreased by about one third (0.9% to 0.6%) while mortality rates for status epilepticus remained relatively stable (5.6% to 5.1%).

Conclusions: In the observed time period (2003-18), epilepsy hospital admissions and in-hospital mortality decreased by one-third, while admissions for status epilepticus increased by one-third with relatively stable mortality rates.

Abstract Number: 599

Title: Status Epilepticus – Therapeutic Management at the Pediatric Emergency Department

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Purpose: Status epilepticus is an important cause of pediatric neurological emergency. Immediate treatment is essential to prevent definitive neurological damage. Several antiepileptic drugs are available for the management of status epilepticus. Our aim was to evaluate these patients' management, including compliance with the current treatment guidelines.

Method: Retrospective study of patients admitted at the emergency department of a tertiary hospital for 5 years (2014-2019). We analysed the compliance to the treatment guidelines for pediatric status epilepticus.

Result: One hundred and seventeen admissions were identified, 23.9% of these were febrile status epilepticus. Among the other cases, the most frequent cause was genetic (22.2%). The majority were convulsive status epilepticus (93.1%), 58.7% of which were generalized tonic-clonic seizures. Benzodiazepines were the most used first and second line drug (98.2% and 94.8%). The most frequent third drug used was diazepam (56.4%) followed by phenytoin (18.2%). An infra-therapeutic antiepileptic drug dose was given in 48.7% of cases. 49.6% presented with a prolonged status epilepticus and 6.8% needed intensive care. Incorrect sequence of drugs

and infra-therapeutic doses were associated with prolonged status ($p<0.001$ and $p<0.05$) and an increased number of antiepileptic drugs used ($p<0.001$ and $p<0.05$).

Conclusions: Benzodiazepines were the most frequently first and second line drugs used for status epilepticus management. Surprisingly, the most frequently third line drugs used were also benzodiazepines. These findings were partially explained by the misuse of infra-therapeutic doses of these drugs. Noncompliance with the implemented guidelines was associated with unfavorable outcomes.

Abstract Number: 628

Title: Adjuvant role of vitamin-D supplementation on seizure control and neuronal degeneration in rats after status epilepticus induction

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Purpose: This study investigated the effect of vitamin-D3 (Vit-D3) supplementation with antiepileptic drugs [AEDs- valproate (VPA) and perampanel (PEM)] on seizure control and neuronal injury following status epilepticus (SE) induction in rats.

Method: Male Wistar rats (200-250 g) were divided into 7 groups (n=12): normal-control, SE-control, single drug-treated groups [VPA (370mg/kg/day), PEM (1.5 mg/kg/day), Vit-D3 (6000 IU/kg/day], and combination groups (Vit-D3+VPA, Vit-D3+PEM). Acute and long-term effects were observed in each half of animals (n=6) on day-3 and day-14 after SE-induction using lithium-pilocarpine. Parameters assessed were: seizure (Racene-stage 3-4) latency/frequency, mortality, neurobehavioral impairment [elevated-plus maze (EPM) and passive-avoidance (PA)], oxidative stress, histopathological and electron-microscopic changes in hippocampus/cerebral cortex tissue.

Result: The percentage of rats showing stage 3-4 seizure after SE induction was 91.66, 33.33, 41.66, 50, 25, and 0 % for SE, VPA, PEM, Vit-D3,Vit-D3+VPA, Vit-D3+PEM groups, respectively. The latency to seizure increased in drug-treated groups (VPA, PEM, and Vit-D3+VPA) compared to SE-control ($p<0.001$). PEM group had significantly higher memory impairment on day-3 as compared to VPA, Vit-D3, and Vit-D3+VPA groups. On day-14, VPA and Vit-D3+VPA groups had less memory impairment than SE-control group ($p=0.027$, 0.041, respectively). In EPM test, combination groups had significantly decreased transfer latency compared to single AED-treated groups on day-3 and day-14. Combination groups had lesser malondialdehyde ($p<0.001$) and higher superoxide-dismutase level ($p=0.042$) as compared to SE-control and single drug-treated groups. Combination groups had less ischemic changes in hippocampus and cerebral cortex as per histopathology as compared to single AED-treated groups on day-3 and day-14. On electron microscopy, reduced ischemic changes were observed in combination groups than single AED-treated groups; the severity also decreased on day-14 as compared to day-3 changes.

Conclusions: Vitamin-D3 exerted adjuvant potential with AEDs by better seizure control after SE-induction and reduced sequelae like neurobehavioral impairment, oxidative stress and neuronal degeneration.

Abstract Number: 644

Title: Serum Neurofilaments Light as a biomarker of neurodegeneration in Status Epilepticus.

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Purpose: Neurofilaments (Nf) are members of the family of intermediate filaments specifically expressed in neurons. They maintain the cytoskeleton' structure of the axons establishing cross-bridging with other filaments. Nf might be released from damaged or diseased axons in significant amounts into blood and cerebrospinal fluid (CSF). Thus, their elevated levels in either CSF or serum are used as potential biomarkers of neurodegeneration in different neurologic disorders. Elevation of serum Neurofilaments Light (sNfL) has been reported in drug resistant epilepsy and, recently, in post-anoxic electrographic status epilepticus. The purpose is to evaluate sNfL in patients with Status Epilepticus (SE).

Method: we retrospectively measured the serum NfL concentrations of prospectively collected adult patients with SE and compared them with epileptic patients (EP) and healthy controls (HC).

Result: sNfL concentrations of age and sex-matched 30 SE, 30 EP and 30 HC were measured. SE patients have significantly higher sNfL concentrations compared to EP and HC ($p < 0.001$). In SE patients, sNfL levels have a high correlation with CSF NfL and t-TAU concentrations ($\tau = 0.68$, $p < 0.001$ and $\tau = 0.63$, $p < 0.001$ respectively). SE sNfL levels demonstrated a positive correlation with the duration of SE ($\tau = 0.51$, $p = 0.003$) and were significantly increased in patients with Refractory and Super-Refractory SE (RSE/SRSE) when compared to Responsive SE ($\tau = 0.38$, $p = 0.048$). Moreover, patients with 30-days bad outcome (worsening of clinical conditions compared to the baseline or death) had higher levels of sNfL compared to good ones ($\tau = 0.38$, $p = 0.049$).

Conclusions: These exploratory data suggest the role of sNfL levels as a neurodegeneration biomarker in patients with SE. sNfL is a reliable and an easy obtainable biomarker in patients with SE that reflects CSF NfL and t-TAU levels.

Abstract Number: 700

Title: Status epilepticus outcome in patients with and without MRI abnormalities

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Purpose: Status epilepticus (SE) is a neurological emergency frequently associated with peri-ictal MRI abnormalities (PMA) including diffusion restriction, hyperperfusion and high signal in T2-weighted images (including FLAIR). PMA can be completely reversible or persistent. It can be followed by permanent alterations such as cortical laminar necrosis, mesial temporal sclerosis and focal brain atrophy. We aimed comparing the outcome of SE in patients with and without PMA.

Method: We prospectively recruited 247 patients with SE between February 2019 and November 2020. 142/247 (57%) patients underwent MRI within 48 h after the onset of SE.
SE-outcome scores as well as admission to intensive care unit (ICU) and days spent at the ICU were compared in two groups of patients: those with and without PMA.

Result: PMA was observed in 59/142 (42%) of patients (51% female; mean age 62.0 years, range 19-93 years). In 83 (58%) of patients no PMA were seen (36% female; mean age 64.6 years, range 19-89 years).
Mean values (with range) of STESS, mSTESS and EMSE did not differ in patients with PMA vs. patients without PMA: STESS (2.8, 0-6) vs. (2.8, 0-6) p=0.577; mSTESS (3.3, 0-7) vs. (3.2, 0-7) p=0.629; EMSE (49.1, 4-153) vs. (43.6, 4-113) p=0.631. END-IT score was significantly higher (p<0.001) in patients with PMA (mean 2.4, range 0-5) compared to patients without (mean 1.3, range 0-5). More patients with PMA (38/59; 64%) were admitted to ICU as compared to those without PMA (33/83; 40%) (p=0.004). Patients with PMA spent significantly more days in ICU (mean 4.9, SD 8.3) as compared to those without (mean 3.1, SD 7.2) (p=0.006).

Conclusions: MRI abnormalities in patients with SE are associated with worse outcome, need of admission to ICU and longer duration of treatment there. Acute changes in MRI may serve as prognostic biomarker in patients with SE.

Abstract Number: 702

Title: Outcome scores in Salzburg cohort of patients with status epilepticus

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Purpose: Status epilepticus is a common neurological emergency with high mortality. Predicting outcome in SE plays an important role in defining acute treatment strategies. Four outcome scores are widely used for predicting mortality in SE patients: STESS (Status Epilepticus Severity Score), mSTESS (modified STESS), EMSE (Epidemiology-based Mortality score in SE) and END-IT (Encephalitis, Non-convulsive SE, Diazepam resistance, Image abnormalities and Tracheal intubation). We aimed to determine concordance between these four scores with days spent in ICU, admission to ICU and death in our cohort of patients with SE.

Method: We prospectively recruited 254 patients (44% female; mean age 64.3 years, range 18-96) with SE at our institution between February 2019 and January 2021. Each score was correlated with days spent in ICU, admission to ICU and 30-day mortality.

Result: Mean values (with range) of STESS, mSTESS, EMSE and ENDIT were significantly higher in patients who were admitted to ICU vs those who did not need treatment in ICU: STESS (3,3 0-6) vs (2,5 0-6) p<0,0001; mSTESS (3,6 0-8) vs (3,0 0-7) p=0,001; EMSE (57,2 1-185) vs (40,1 0-97) p=0,036; END-IT (2,2 0-5) vs (0,9 0-3) p<0,000. Mean values (with range) of STESS, mSTESS, EMSE and END-IT were also significantly higher in patients who died within 30 days after the onset of SE (47/254, 19%) vs those who survived SE: STESS (4,5 1-6) vs (2,7 0-6) p<0,000; mSTESS (4,7 1-7) vs (3,1 0-8) p<0,000; EMSE (97,7 7-185) vs (39,3 0-124) p<0,000; END-IT (2,4 0-5) vs (1,4 0-5) p<0,000. There were moderate positive correlations of days spent in ICU with scores END-IT (r= 0.586, p<0.0001), STESS (r= 0.355, p<0.0001), mSTESS (r= 0.299, p<0.0001) and EMSE (r= 0.288, p<0.0001).

Conclusions: In our population, all four scores could predict an unfavorable outcome in terms of admission to ICU and 30-day mortality.

Abstract Number: 703

Title: A new exploratory score for determining the prognostic value of MRI in patients with status epilepticus.

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Purpose: Status epilepticus (SE) is a neurological emergency frequently associated with peri-ictal MRI abnormalities (PMA). PMA commonly include diffusion restriction, hyperperfusion and high signal in T2-weighted images (including FLAIR). PMA can be completely reversible or persistent. It can be followed by permanent alterations such as cortical laminar necrosis, mesial temporal sclerosis and focal brain atrophy. We aimed to determine a prognostic value of PMA for the outcome of SE.

Method: We prospectively recruited 268 patients with SE between February 2019 and January 2021. 145/268 (54%) patients underwent MRI within 48 h after the onset. Patients with hypoxic brain injury (n=6) were excluded. An MRI score based on three aspects: 1) location 2) size and 3) distribution of PMA was used. Alterations in different MRI sequences were considered as separate lesions and were divided into cortical and subcortical. Each location scored 1 point; large lesions - 2 points; in case of presence of both cortical and subcortical lesions the sum was multiplied by 2. This score was correlated with other SE-outcome scores, days spent at intensive care unit (ICU) and admission to ICU.

Result: PMA was observed in 53/145 (37%) of patients (51% female; mean 61.7 age 65 years, range 19-93 years). The mean value on an MRI score was 12.6 (range 1-104). Mean values (with range) of other prognostic scores were: STESS (2.7, 0-6); mSTESS (3.2; 0-7); EMSE (45.6; 7-124) and END-IT (2.3; 0-5). Mean days spent in ICU were 5.7 (range 0-45). There were moderate positive correlations of MRI score with a need of admission to ICU (r= 0.299, p=0.031), days spent in ICU (r= 0.374, p=0.006) and END-IT (r= 0.410, p=0.003).

Conclusions: Our new exploratory MRI score correlates with an unfavorable functional outcome in patients with SE, the need of admission to ICU and a prolonged treatment there.

Abstract Number: 712

Title: Phase 2 Open-Label, Dose-Finding Study of Intravenous Ganaxolone for the Treatment of Refractory Status Epilepticus

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Purpose: There remains a need for antiseizure medications (ASMs) that produce rapid status epilepticus (SE) cessation and durable seizure control with a favorable safety profile in refractory status epilepticus (RSE). IV Ganaxolone (IV GNX) is an intravenous formulation of a synthetic neuroactive steroid that acts as a positive allosteric modulator of synaptic and extrasynaptic $GABA_A$ receptors.

Method: The study aims to determine the appropriate IV GNX dosing paradigm and obtain a preliminary assessment of the efficacy and safety in patients with RSE. Three GNX dosing-paradigm cohorts (high (n=8), 713 mg/day; medium (n=4), 650 mg/day; low (n=5), 500 mg/day) for up to 4 days were studied in patients who had failed at least one second-line IV ASM(s). Efficacy assessments included proportion of patients requiring escalation to a third-line IV anesthetic at 24 hours, time to SE cessation, and change in EEG seizure burden (SB).

Result: Eleven patients (65%) enrolled had non-convulsive SE and had failed a median of 3 prior ASMs. No patient required escalation to third-line IV anesthetics during the 24-hour period post GNX initiation. The median time to SE cessation following GNX initiation was 5 minutes with 94% of evaluable patients achieving SE cessation within 30 minutes. In all dose groups, a rapid reduction in SB of ~45% relative to baseline was seen within 0-5 minutes of GNX administration and further decreased to at least an 80% reduction within 10-15 minutes post-GNX initiation. GNX was generally well-tolerated, and no new safety finding emerged. Two treatment-related serious adverse events (sedation) were reported.

Conclusions: IV GNX achieved rapid and durable SE cessation with acceptable safety and tolerability in RSE. A Phase 3 study of IV GNX in RSE is currently enrolling patients in the U.S. A Phase 3 study of IV GNX in RSE to be conducted in Europe is planned.

Abstract Number: 715

Title: Novel approach to treatment of New onset refractory status epilepticus (NORSE)/Febrile infection related epilepsy syndrome(FIRES) in children

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Purpose: New-onset refractory status epilepticus (NORSE) is defined as a clinical condition,with new onset status epilepticus without a clear metabolic, structural, infective of toxic cause in a patient without any pre-existing neurological disorder or epilepsy. In majority of the cases of NORSE proven or possible either autoimmune or immune mediated etiopathogenesis is suspected. Our aim of study is to discuss the implications of early immunotherapy of children with NORSE presented to our centers between July 2017 to January 2021.

Method: During study duration total 18 children with NORSE were included. Their clinical, biochemical, radiological, electrophysiological and treatment details were recorded and short term neurological follow up was obtained.

Result: Out of total 116 children with status epilepticus 11 were presented with NORSE/FIRES. Mean age was 4.7 years. History of preceding or current febrile illness was seen in 4 (22%) patients. All CSF sample were negative for HSV PCR and autoimmune antibody profile were negative. 8(73%) children had mild CSF pleocytosis and 4 (36%) had abnormal MRI study. All 18 children had abnormal EEG with 7(64%) of them had evidence of electrical status epilepticus. All the patients were given immunotherapy and it was timely escalated as per combined clinical and EEG findings (considering burden of spikes and background activity) similarly as we do with antibiotics in treatment of sepsis monitoring sepsis markers. We achieved termination of seizures with median duration of 5 days. With this approach 7(64%) children didn't require ventilation or pharmacological coma at all. Our cohort has no mortality with this novel approach and 8(73%) children was on more than 2 ASMs till last follow up.

Conclusions: Immunotherapy has beneficial role in management of children with NORSE. Our novel approach to treatment of NORSE/FIRES in children seems very promising but need larger population and multi-centre study for further validation.

Abstract Number: 760

Title: Status epilepticus amauroticus in a patient with familial photosensitive occipital epilepsy

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Purpose: To report the electro-clinical and imaging features of status epilepticus (SE) amauroticus in a patient with subsequent resolution of MR abnormalities and visual deficits.

Method: the patient is an 18-year-old-man with photosensitive occipital epilepsy (pOE) that started at the age of 10, with relatively good seizure control, on therapy with valproate and topiramate. His 29-year-old brother had pOE evolving into genetic generalized epilepsy with absences and eyelid myoclonia. Despite a polytherapy with valproate, lamotrigine and topiramate, seizures have persisted, and he had rare episodes of absence status. His 20-year-old sister also had pOE that spontaneously remitted from the age of 12 years. The proband was referred to our outpatient clinic since he had become complete blindness in the last 10 days without any evidence of other seizures.

Result: neurological examination revealed complete blindness with bilaterally spared direct and consensual pupillary light reflex. EEG revealed sub-continuous focal epileptiform discharges over both occipital lobes. Brain 3T-MRI showed bilateral cortical parieto-occipital hyperintensities in DWI, T2 and FLAIR sequences. Subcortical white matter was relatively spared. Extensive laboratory investigation and cerebrospinal fluid analysis including autoimmune and infectious screening, serum lactate levels, antibodies against cell surface and intracellular neuronal antigens, were all unremarkable. The electroclinical findings fulfilled the criteria of SE amauroticus. Intravenous therapy with levetiracetam and methylprednisolone prompted the disappearance of SE on EEG, with complete resolution of MR abnormalities and visual deficits in a week.

Conclusions: SE amauroticus represents a rare cause of potentially reversible blindness and should be considered in patients with acute visual loss and a history of epilepsy. It remains to be elucidated the etiopathogenetic mechanism underlying SE amauroticus as also the pathophysiology of reversible MRI alterations, alongside with the underlying genetic factors.

Abstract Number: 851

Title: Eyelid Myoclonia with Absence Status Epilepticus: 3 Cases

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PurposeEpilepsy with eyelid myoclonia with absences (EMA) is a genetic/idiopathic generalized epilepsy (GGE/IGE) syndrome, which photosensitivity occurs in and might be accompanied by absence seizures, is characterized with eyelid myoclonia (EM) arising with the closing of the eye and 3-6 Hz generalized spike/multiplspike wave paroxysms in electroencephalography (EEG). In this article, it is aimed to review the EMA syndrome and to examine the association of SE in the presence of 3 patients with EMA who were admitted to our clinic with status epilepticus (SE).

Method: To present demographic, clinical and electroencephalographic features of 3 patients with EMA-SE.

Result: All of our cases were women, consistent with the female gender superiority defined in EMA syndrome. The age of onset of the seizures was between 9 and 13 years. The time elapsed between the onset of their seizures and their diagnosis of EMA was 12, 13 and 16 years. The diagnosis of all our cases was made with Video-EEG Monitoring (VEM), which is reported as the gold standard in the literature. In the prolongation of the diagnosis processes of our cases, because of the EMA not seen as a symptom of disease being late to consult a physician, they were not having been examined with VEM before and the EMA syndrome being less recognized by physicians were effective. All of our cases consulted with SE clinical prezentation and the presence of SE was reported in 20% of EMA cases in the literature. It has been reported that seizures will usually continue lifelong and many patients will be drug-resistant in cases with EMA.

Conclusions: EMA syndrome is a condition clinical features of which should be well known in order to be diagnosed and treated early and accurately and in which electrophysiological evaluation with VEM is essential.

Abstract Number: 890

Title: EEG seizure onset patterns in status epilepticus

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Purpose: Seizure-onset (SOn) patterns have been studied especially in isolated seizures in epilepsy surgery candidates. EEG studies characterizing the SOn patterns in status epilepticus (SE) are lacking. We aim to classify the different SOn patterns during SE and to evaluate any differences in mortality, morbidity and treatment response across different SOn patterns.

Method: consecutive EEG recorded from adult patients admitted for focal SE, from January 2015 to August 2019 were reviewed. Five SOn patterns were identified (in accordance with Tanaka et al. 2018): (1) paroxysmal rhythmic slow activity at <13 Hz; (2) paroxysmal rhythmic fast activity at ≥13 Hz; (3) repetitive epileptiform discharge; (4) suppression of background activity to ≤10 µV; and (5) artifacts. For each patient 1 to 5 seizures were analyzed, and each seizure's duration was registered.

Result: 307 seizures were analyzed in 100 consecutive patients/SE episodes (mean age 70 yrs); the most frequent SOn pattern was pattern 3 (39 patients) followed by pattern 1 (34 patients) and pattern 2 (14 patients); pattern 4 and 5 were less frequently observed (1 and 3 patients respectively). Nine patients presented with multiple SOn patterns. Seizures with SOn pattern 3 showed longest duration ($p < 0.05$). No statistical difference in demographics, SE etiology, semeiology and treatment response was observed among the different SOn, while a higher 28-day mortality was observed in SOn pattern 3 ($p = 0.02$; HR 3.00; 95% CI 1.13 – 7.97).

Conclusions: this is the first EEG study on scalp seizure onset patterns in status epilepticus. In SE the pattern characterized by repetitive epileptiform discharges (# 3, spike and waves) was the most frequent, with the longest mean seizures duration, and associated to highest short-term mortality. Analysis of SOn patterns could improve our understanding on SE mechanism and could become a useful EEG biomarker.

Abstract Number: 909

Title: Management and treatment of refractory status epilepticus: a retrospective cohort study

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Purpose: Status Epilepticus (SE) is the second most frequent neurological emergency.
The aim of the present study was to determine responsiveness to therapy in patients with refractory SE (RSE).

Methods: We retrospectively reviewed the medical records of patients with SE admitted to our hospital between 2016 and 2020. Inclusion criteria were age ≥ 18 years and diagnosis of RSE. Successful treatment was scored to the last drug introduced up to 24 hours before RSE termination. Patients were divided into two groups ('Anesth+' and 'Anesth-'), according to anesthetics administration. Clinical information, Status Epilepticus Severity Score (STESS), Glasgow Coma Scale (GCS) and anti-seizure medications (ASMs) were compared between groups.
The primary outcome was the comparative efficacy of ASMs. Secondary outcomes were: 1) ASM response rates in the two subgroups; 2) factors associated with anaesthetics administration.

Results: A total of 244 episodes in 220 patients were assessed. The response rates were 57.6%, 39.8%, 40.7% and 24.7% for phenytoin, valproate, lacosamide and levetiracetam respectively. Anesthetics, administered in 46.7% of cases (114/244), stopped SE in 42.1% of treated episodes.
The overall comparison between the different ASMs showed significant difference ($p<0.0001$). In the post-hoc analysis, phenytoin was more effective than valproate ($p=0.02$) and levetiracetam ($p<0.00001$); valproate was superior to levetiracetam ($p=0.0049$). In the 'Anesth+' group phenytoin was more effective than valproate ($p=0.009$) and levetiracetam ($p<0,00001$). On the other hand, in the 'Anesth-' group phenytoin showed significant higher response rate compared to levetiracetam ($p=0.01$) and valproate was superior to levetiracetam ($p=0.01$).
In the comparison between groups, GCS ($p<0.0001$) and age($p<0.001$) were significantly lower in the Anesth+ group. Treatment with anesthetics was associated with increased mortality ($p=0.01$) and more complications ($p<0,0001$).

Conclusions: In our cohort phenytoin and valproate showed the higher response rates for RSE resolution. Treatment with anesthetics was associated with worse outcome.

Abstract Number: 959

Title: Refractory and Super-Refractory Status Epilepticus Treated with High Dose Perampanel and Topiramate: Case Series and Review of the Literature

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Purpose: Limited evidence exists regarding alternative therapies to the management of refractory and super refractory status epilepticus (RSE/SRSE) once first-line antiepileptic drugs (AED) and coma-inducing agents are proven ineffective. Since glutamate plays a key role in this condition, drugs that counteract its hyperexcitable effect such as Perampanel (PER) and Topiramate (TPM) could provide an answer. They both target the glutamatergic system through AMPA receptors with the latter also inhibits kaïnate receptors.
We present a single-center case series of four patients with RSE and SRSE for which a combination of TPM and PER played a considerable role in terminating SE.

Method: We reviewed medical records of four cases where this combination was administered to RSE/SRSE patients. They were hospitalized between November 2019 and December 2020 at the Hôpital de l'Enfant-Jésus, Quebec.

Result: Three out of four patients were females. and the mean age was 63.5 years old (range: 55-73). They had different etiologies for their RSE; namely left mesial temporal sclerosis, left hemispheric glioblastoma, HSV-1 encephalitis, and anoxic-ischemic encephalopathy. They were all treated with high dose PER and TPM among other agents. Three of them had PER as the last AED used before SE resolution. For the patient with anoxic-ischemic encephalopathy, a well-known refractory form of SE, another AED was used before SE termination. The mean duration of hospital stay was 48 days with complete SE resolution for each case.

Conclusions: Glutamate increased activity through receptor trafficking plays a major role in the persistence of seizures. Our cases support the hypothesis that the action of TPM and PER on glutamate, through different receptors, possibly has a synergistic effect. This renders that combination an interesting alternative to the treatment of RSE/SRSE. To our knowledge, this is the first case series to report this combination. Further studies are needed to evaluate its effectiveness.

Abstract Number: 1051

Title: predictors of outcome in Super Refractory Status Epilepticus

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Purpose: This study was done to determine the predictors of outcome in Super Refractory Status Epilepticus (SRSE).

Method: Data of patients were taken and analysed prospectively from our SE registry between January 2000 and November 2019. Glasgow outcome score (GOS) was used for assessing functional outcome at discharge and was divided into: good i.e. GOS≥3 and bad outcome i.e. GOS<3. The predictors of outcome were determined using appropriate statistical tests by univariate and multivariate analysis, p<0.05 was considered as statistically significant

Result: 28 (8%) out of 384 patients with Status Epilepticus (SE) were diagnosed as SRSE and included in the analysis. The mean age of study population was 20+18.45 years and 67.9% were males. Acute symptomatic SE comprising 15 (53.6%) patients was the most common aetiology of SRSE. Thirteen patients had New Onset Refractory Status Epilepticus (NORSE) and five patients had Febrile Infection Related Epilepsy syndrome (FIRES) as clinical presentation .The preferred first line anaesthetic agent was midazolam (100%) followed by Thiopentone (57.1%).. Multivariate logistic regression analysis showed that independent predictors of poor outcome were: duration of ICU stay (p<0.001); EEG findings such as non-convulsive SE in coma (0.032), spontaneous burst suppression (0.001) and post-ictal diffuse attenuation (<0.001); delay in starting anaesthesia (0.002); and delay in starting immunotherapy in NORSE due to autoimmune encephalitis (0.002). 12 patients (42.9%) had good outcome and 16 patients (57.1%) had bad outcome. The overall mortality of patients in our study was 28.6% and majority (75%) died due to complications

Conclusions: Treatment delay for effective control of SRSE is frequent and electrophysiological prognostic factors such as non-convulsive SE in coma, spontaneous burst suppression and post-ictal diffuse attenuation are associated with predictors of poor outcome .Prognosis is not dismal as thought of and a uniform protocol driven management of SRSE can result in good outcomes.

Abstract Number: 1084

Title: Effect of barbiturate sedation on Non-convulsive Status Epilepticus diagnosis.

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Purpose: Initiating the treatment of non-convulsive status epilepticus (NCSE) as early as possible is well known to improve the outcome. The continuous electroencephalogram (CEEG) is used in the diagnosis of convulsive status epilepticus (CSE) and NCSE. This study aimed to assess the effect of barbiturates use on the diagnosis of NCSE.

Method: The study included four patients (all male and >18 y.o.) with new onset CSE who had not regain consciousness after convulsive seizures were controlled with first or second line treatment. In order to transfer the patients to specialized neurology center all four patients received sedation with sodium thiopental. All of them underwent CEEG in line with the 10-20 international system, 1,5T Magnetic Resonance Imaging (MRI) of the brain and necessary blood and cerebrospinal fluid (CSF) analysis.

Result: After cessation of thiopental infusion the patients remained unconscious. No seizures were seen clinically. MRI, blood and CSF analysis were normal. On CEEG rhythmic delta activity without definite fluctuation and with superimposed beta activity was registered. The differential diagnosis between high-voltage delta coma and NCSE was considered. Diagnostic intravenous antiseizure drug trial didn't improve electroencephalogram (EEG) or patients' clinical state, so EEG findings didn't meet criteria for possible status epilepticus. After 5,5-7 hours (median of 6,5 hours) of thiopental anesthesia cessation the EEG pattern had changed and matched Salzburg criteria for diagnosis of NCSE which allowed us to continue appropriate treatment.

Conclusions: Obtained results indicate that the start of sedation using barbiturate prior to EEG-recording complicates diagnosis and may increase the time of a treatment initiation of NCSE. Further studies are needed to develop an algorithm for NCSE diagnosis after use of barbiturate sedation.

Abstract Number: 1101

Title: NORSE (new onset refractory status epilepticus) in a patient with FASTKD2 mutation: a case report and review of the literature

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Purpose: In half of all cases presenting with NORSE no underlying cause can be identified. Mutations in the nuclear gene encoding for the mitochondrial protein FASTKD2, presumably involved in mitochondrial RNA metabolism, were reported as cause for infantile encephalomyopathy with refractory epilepsy. We report a patient with FASTKD2 mutation presenting with NORSE.

Method: Case report and review of literature.

Result: A previously healthy 14-year old male patient with normal motor and cognitive development presented with super refractory generalised convulsive SE. Emergency diagnostics did not reveal any structural, metabolic, or toxic cause. EEG showed lateralised periodic discharges over the right posterior temporal leads and cerebral MRI revealed a reversible DWI-positive, FLAIR hyperintense lesion in the right temporooccipital region. Lactate levels were normal. Diagnostic work-up did not reveal any evidence for an infectious or autoimmune cause. NORSE resolved after treatment with thiopental and ketamine with full recovery of the

patient. After a seizure free period of 6 years, the patient developed another super-refractory SE and subsequently pharmacoresistant focal epilepsy, a mild myopathy and discrete psychomotor slowing. Whole exome sequencing revealed a homozygous loss of function mutation (c1072C>T) in the nuclear gene encoding for FASTKD2.

Conclusions: This is the first case with NORSE as the presentation of a FASTKD2 mutation. The phenotype of FASTKD2 mutations is heterogeneous, ranging from SE and focal epilepsy in an adolescent with normal cognitive development to severe forms of infantile mitochondrial encephalopathy.

Abstract Number: 1153

Title: Pediatric Non Convulsive Status Epilepticus (NCSE) with favourable outcome in three distinctly different clinical settings

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Purpose: Non-convulsive status epilepticus (NCSE) is a frequently underdiagnosed critical condition with pleomorphic presentation, seen in children with disturbed consciousness. It usually manifests as unexplained behavioural and mental status changes, confusion, sleepiness and continuous epileptiform discharges in electroencephalography.

Method: We present three children presenting with NCSE in different settings, who responded to prompt management.

Results: A 12-year-old pre-morbidly normal girl, admitted with low grade fever, vomiting and diarrhea, had sudden alteration in behavior (decreased speech and interactiveness), with an episode of upward vacant stare, followed by fall in the bathroom. EEG revealed near-continuous 3 Hz spike slow-wave discharges suggestive of absence status epilepticus. MRI Brain was normal. Dramatic clinical and electrographic improvement was noted after initiating Levetiracetam.
An 8-year-old boy, on treatment for Atypical Hemolytic Uremic Syndrome, developed abrupt onset right focal seizures with impaired awareness, preceded by ictal spitting and confusion. He was disoriented despite seizure resolution with anti-seizure medications(ASMs). EEG showed Left focal NCSE, which responded to intravenous Lorazepam bolus. Upon hiking the ASMs, there was complete resolution of encephalopathy. Repeat EEG showed complete resolution of epileptiform activity with persistent slowing in left anterior temporal region. MRI Brain revealed left mesial temporal sclerosis.
A 6-year-old developmentally delayed boy with infrequent seizures from late infancy presented with new-onset fever, altered sensorium, and increased frequency of seizures. He was being managed as a presumed case of epileptic channelopathy. Seizures aborted on intravenous valproate and levetiracetam, however impaired sensorium persisted despite seizure control. EEG showed near-continuous <2.5 Hz generalized spike-wave discharges, with poorly discernible background distinct from his previous baseline EEGs. A prompt hike in anti-seizure medication and addition of clobazam, showed electroclinical improvement.

Conclusions: EEG is advisable in patients with unexplained prolonged disturbed consciousness, considering the possibility of NCSE. Prompt diagnosis and rapid management may dramatically improve the clinical status.

Abstract Number: 1161

Title: Status epilepticus in CFC patients: focus on neuroimaging

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Purpose: Cardio-facio-cutaneous (CFC) syndrome is a genetic condition due to variations of Ras/MAPK pathway genes, associated to neurological impairment, including cerebral malformation and epilepsy. Status epilepticus (SE) is an underreported feature. Resonance imaging (MRI) in these patients has allowed identification of heterogenous neuroanatomic changes related to SE. Different clinical-radiological patterns could be related to different underlying mechanisms.

Method: Among our CFC patients cohort (23 patients), we identified 5 patients (harbouring *BRAF* mutation) with refractory SE (age ranged from 3 to 12 years). All patients underwent electroencephalogram (EEG) and MRI during SE. Baseline MRI images are available for 2/5 patients, follow-up images for 4/5.

Result: The 5 CFC patients presented with long-lasting incoming seizures evolving into SE (focal seizures in 4/5, myoclonic seizures in 1/5). Seizures appeared with minimally clinical signs; EEG recording was needed to establish SE diagnosis. SE was refractory or super-refractory (duration: weeks -months) despite multiple antiepileptic treatment. Acute MRI findings showed in 2/5 cortical focal swelling (T2/FLAIR hyperintensity with restricted diffusion), followed by focal cortical atrophy. Patient 2, because of these findings, that corroborate the hypothesis of vasogenic and cytotoxic edema and autoinflammatory pathway, was treated with high-doses steroids and she was the only one with good epileptic and neurological outcome. 2/5 patients presented periictal MRI abnormalities during acute phase (hippocampal hyperintensity), followed by mesial temporal sclerosis. 1/5 patient did not have acute neuroradiological changes during SE.
Conclusions: CFC syndromes could be a model for studying SE predisposing factors, including pre-existing abnormalities -focal epileptogenic lesion, genetic abnormalities, autoinflammatory pathways. Acute brain edema endorses the use of possible disease-modifying therapeutic intervention (steroids), with good outcome. MRI proved to be the best diagnostic tool to disclosure early abnormalities and can be also harnessed to provide deep insights into the possible pathomechanisms underlying SE and to target rational treatment strategies.

Abstract Number: 1307

Title: intravenous immunoglobulin for pediatric super-refractory status epilepticus cases: an online survey from India

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Purpose: To determine the efficacy and safety/tolerability of intravenous immunoglobulin (IVIG) in pediatric super refractory status epileptic (SRSE) patients with/without probable autoimmune origin.

Method: We designed a google form-based survey containing questions regarding use of IVIG for pediatric SRSE cases, its efficacy, safety, dosing schedule and nature of SRSE. It was electronically disseminated in May 2020 among pediatricians/pediatric neurologists from India.

Result: Total 97 doctors responded to the survey, out of which 29(30%) practitioners from tertiary care centers in urban setting agreed to have used IVIG for total 48 pediatric SRSE cases (64% boys, 11.2±3.1 years, 31 had probable/definite autoimmune etiology, 39 had convulsive status epilepticus (CSE), among which 32 had focal CSE, all were on multiple ASMs and midazolam/barbiturate infusion). Total 91% of these patients also received intravenous corticosteroid (simultaneously in 54% and sequentially in 37% cases). The most common schedule for IVIG administration followed were 0.4 gram/kg/day for 5 days.
The predominant autoimmune etiologies were anti-NMDAR encephalitis (5/31), FIRES (12/31), Rasmussen encephalitis (8/31) and rest were probable seronegative autoimmune encephalitis. Among these patients, neuroimaging was abnormal in 59% of cases (mostly non-specific changes, except Rasmussen encephalitis) and favorable response in terms of seizure freedom or >50% reduction was observed in 19/31 cases.
Predominant etiology in patients without probable autoimmunity was new onset refractory status epilepticus (14/17). In this subgroup, neuroimaging was abnormal in 6/17 cases (mostly non-specific changes) and only 5/17 patients responded favorably to IVIG.
Minor adverse effects were observed in 13% cases, but none required discontinuation or reducing the rate of administration. Overall, patients with autoimmune etiology (p=0.01), CSE (0.09, as compared to NCSE) and focal CSE (p=0.04) responded more favorably to IVIG, although the difference was not significant statistically for CSE.

Conclusions: IVIG is a safe and probably efficacious therapeutic option in pediatric SRSE cases.

Terminology and Classification

Abstract Number: 1014

Title: Investigating the feasibility of automating the differential diagnosis of Transient Loss of Consciousness

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Purpose: Over 90% of presentations with Transient Loss of Consciousness (TLOC) are explained by syncope, epileptic or psychogenic nonepileptic seizures (PNES). The risk of initial misdiagnosis is high. Whereas syncope can be identified with a small number of "yes"/"no" questions, the differentiation of the other two causes of TLOC is more challenging. Previous conversation analysis research has demonstrated that patients with epileptic and nonepileptic seizures typically exhibit different levels of formulation effort in their seizure descriptions. This research investigates whether features reflecting the level of formulation effort can be automatically elicited from audio recordings and transcripts of speech and used to differentiate between epileptic and nonepileptic seizures.

Method: Verbatim transcripts of conversations between patients and neurologists were manually produced from video and audio recordings of interactions with 45 patients (21 epilepsy and 24 PNES). This analysis focussed on patient's description of their first seizure. Seven automatically detectable features were designed as markers of formulation effort and were used to train a Random Forest machine learning classifier using nested leave-one-out cross validation.

Result: Patients with epilepsy used significantly more hesitations and repetitions in seizure description compared to patients with nonepileptic seizures. Although there was no group level difference for the features 'pause frequency', 'average patient pause length', 'average between speaker pause length', 'total patient pause time' or 'use of key words associated with uncertainty', the inclusion of these features in a random forest classifier achieved a classification accuracy or 71% using all features, or 68.9% using hesitations and repetitions alone.

Conclusions: This pilot study provides proof of principle that automatically detectable linguistic features could be used to distinguish between epileptic seizures and PNES. Future research should explore whether this can contribute to the differential diagnosis of TLOC when additional linguistic observations and information about the seizure or medical history are included.

Abstract Number: 1057

Title: Inter-observer agreement between Primary Care Physicians and Pediatric Neurologists in classifying epilepsy in children according to ILAE 2017 scheme

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Purpose: Primary care physicians are generally the first health care contact for children with epilepsy. Correct identification and initiation of appropriate and timely treatment is imperative to reduce morbidity and mortality related to epilepsy. The current study developed and validated a questionnaire-based tool to identify seizure semiologies as per International League Against Epilepsy (ILAE) 2017 classification.

Method: The study was conducted in a tertiary care teaching hospital in north India from October 2017-December 2018. The questionnaire was developed by modifying the existing All India Institute of Medical Sciences (AIIMS) Modified International Clinical Epidemiology Network (INCLEN) Diagnostic Instrument for Epilepsy by content and face validation. Construct validity of the tool was done by calculating interobserver agreement between Pediatric neurologists and primary care physicians (represented by Pediatric postgraduate trainees and medical interns). The Pediatric postgraduate trainees and the medical interns underwent structured training prior to application of the tool. The Pediatric neurologists diagnosed the epilepsy semiologies using their clinical judgement.

Result: Overall 144 children with confirmed epilepsy were enrolled. Kappa agreement was 0.52 (moderate) for the basic version and 0.28 (fair) for the expanded version of ILAE 2017classification between Pediatric postgraduate trainees and Pediatric neurologists. It was 0.45 (moderate) for the basic version and 0.30 (fair) for the expanded version of ILAE 2017 classification between medical interns and Pediatric neurologists.

Conclusions: The tool developed in the current study may be appropriate for broad classification of seizures into generalized, focal, multiple and unclassified seizures as per basic version of ILAE-2017 classification compared to detailed semiology classification as per its expanded version. It thus needs to be applied in the community settings to establish generalisability.

Women's Issues

Abstract Number: 93

Title: Uneventful pregnancy on lacosamide monotherapy.

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Purpose: To report the course and outcome of pregnancy in a woman treated with lacosamide (LCM) monotherapy.

Method: Data on seizure frequency, pregnancy course, delivery and breastfeeding, birth outcome, congenital malformation and development of a newborn were collected.

Result: Our patient was a 36-year-old woman with a history of meningoencephalitis at age 9 months complicated by right spastic hemiparesis and development of epilepsy at age 4. Imaging demonstrated encephalomalacia in right occipital, parietal, and temporal lobes, and EEG revealed frequent focal sharp waves in the left temporal region. She experienced focal seizures with impaired awareness 2-4 per month and rare tonic-clonic seizures. She had tried and failed a variety of antiseizure medication, including carbamazepine, gabapentin, valproate, lamotrigine, levetiracetam, topiramate, oxcarbazepine (OXC). During her first pregnancy (at age 30) she was on OXC 300mg BID and delivered a healthy daughter by cesarean section. Subsequently she tried LCM 200mg BID with improvement in seizure control (1-2 focal seizures per month). Prior second pregnancy OXC had been withdrawn and folic acid 0,4 mg was added. Treatment with LCM was continued throughout pregnancy with no deterioration in seizure control. The patient underwent fetal ultrasound examinations in the first and second trimester. She delivered a healthy daughter at term by cesarean section, birth weight was 4050g and Apgar score 10. The infant was breast-fed up to 7 months postnatally. No medical problems or developmental delays were detected at calendar age of 24 months.

Conclusions: This case corroborates with previous reports on the safety of lacosamide throughout pregnancy and breastfeeding. Futher studies are needed to confirm low teratogenic potential of lacosamide.

Abstract Number: 252

Title: epilepsy and pregnancy

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Purpose: To analyze the mutual influence epilepsy and pregnancy.

Method: This is an observational prospective cohort study designed to evaluated the AED therapy during pregnancy, malformations, predictors of seizure, preterm labor, the importance of folic acid supplementation and neurodevelopment of the children. The data we have used, have been provided from the Neurology Department UHC Mother Teresa, Tirana; Albania.
Result: 38 women with epilepsy were enrolled and 43 pregnancies were studied. The mean maternal age was 27.28 years old (±4.905). The etiology of epilepsy was mainly idiopathic, except in 9 cases. The vast majority of pregnancies were unplanned (55.8%) with a significant correlation between low maternal education and unplanned pregnancy (p=0.027). 30 patients (69.8%) were under monotherapy, 4 were under polytherapy and

9 were not treated. The most used AED was CBZ. The use of VPA (from 7% in the first trimester to 4.7% in the third trimester) and phenobarbital (from 4.7% in the first trimester to 2.3% in the third trimester) were decreased, while the use of LMT was increased (from 4.7% in the first trimester to 20.9% in the third trimester). Bilateral seizures were the most common type (66.77%). 32.6% were seizure free during the pregnancy. Prepregnancy seizure situation was the most important predictor of seizures during pregnancy and postpartum. We had only one neonatal death, one myelomeningocele, exposed in utero to VPA, 2 cases of preterm labour, 1 developmental delay, exposed to LVT. The vast majority of patients have taken supplementary folic acid.

Conclusions: Epilepsy patients should be treated with a low-dose monotherapy during pregnancy. New AEDs like LMT are recommended to be used due to their safety. Prepregnancy seizure was the most important predictor of seizures during pregnancy. Epilepsy is not an indication for a caesarean section. Supplementary folic acid is recommended.

Abstract Number: 277

Title: A psychosocial perspective on depression and anxiety in women with epilepsy

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Purpose: To assess the prevalence of depression and anxiety in women with epilepsy and to evaluate their relationships with psychological variables: duration of the epilepsy disease, education, marital status, and urban/rural areas.

Method: 124 women, aged 18-67 years (mean age = 38.4 ± 13.8 years, mean epilepsy duration =15.1 ± 10.9 years), with epilepsy were evaluated with Beck Depression Inventory (BDI) and Hamilton Anxiety Rating Scale (HAM-A). The study took place at National Center of Epileptology, Chișinău, Republic of Moldova in 2020.

Result: This study has demonstrated that 58 % of women suffer from depression and 54% from anxiety. It is evident that with the progression of the epilepsy disease, the symptoms of depression and anxiety are more pronounced – from 50% of women in the first five years of the epilepsy disease and increase till 79% with more the 20 years of the disease. Women with higher education are less exposed to suffer from depression and anxiety. While, the divorced and married women are more affected than the single or widowed. As well, women from the rural areas are more protected from depression and anxiety than the urban.

Conclusions: Based on our study, we recommend to assess psychologically all women with epilepsy and provide psychosocial interventions which may reduce anxiety and depression and improve the quality of life and social competency.

Abstract Number: 326

Title: Lacosamide effects on the human placental barrier: studies in perfused term placentas

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Purpose: Despite the increasingly growing use of lacosamide (LCM) for the treatment of epilepsy in women of childbearing age, data on neonatal outcomes following in-utero exposure to LCM are scarce. In the current project, our goal was to assess the effects of LCM on the placental barrier, which controls the transfer of essential compounds to the fetus, using ex vivo perfused term human placentas.

Method: Placentas were obtained from Cesarean deliveries of women with no known epilepsy. Cotyledons were cannulated and perfused in the absence or presence of LCM at 2.5 µg/mL or 10 µg/mL (representing low and high therapeutic concentrations, respectively) in the maternal perfusate over 180 minutes. Valproic acid (VPA; 83 µg/mL), which was previously shown by our group to affect the expression of placental carriers in the same experimental model, was used as a positive control. A customized gene panel array was used to analyze the expression of carrier genes in the perfused cotyledons.

Result: LCM diffused across the placenta (fetal compartment/maternal compartment ratio = 0.89 ± 0.06). In placentas treated with VPA and 10 µg/mL LCM, the mRNA expression of SLC19A1 (folate transporter 1) was downregulated compared with the vehicle by 38.4% and 44.1%, respectively ($p<0.05$). Exposure to 10 µg/mL (but not 2.5 µg/mL) LCM was additionally associated with significantly ($p<0.05$) reduced levels of SLC6A4 (the serotonin transporter; 30.4%), SLC19A3 (thiamine transporter; 48%), the amino acid transporter LAT4 (42.8%), and the organic cation transporter OCT3 (43.6%) compared with the vehicle.

Conclusions: To our knowledge, this is the first study on the effects of LCM on the human placenta. Our findings emphasized the need for risk assessment while using LCM during pregnancy, avoidance of high ASM doses when possible, and therapeutic drug monitoring.

Abstract Number: 354

Title: Pregnancy, delivery and neonatal outcome in women with epilepsy- a prospective, single center study

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Purpose: This study evaluated obstetric and neonatal outcome in a cohort of women with active epilepsy treated at the university epilepsy clinic in Kraków, Poland.

Method: Information on pregnancy and delivery complications, delivery mode, birth weight, Apgar score, and feeding method were collected prospectively from 122 pregnancies of women with epilepsy. Detailed neurologic data were retrieved from the medical records.

Result: We included 100 cases of maternal epilepsy (122 pregnancies with average maternal age of 30 years old at delivery). Most women were nulliparous. The majority of pregnancies (84%) were on monotherapy, 68% patients had focal epilepsy, and most of women (88%) were prescribed antiseizure medication with low teratogenic potential (lamotrigine, levetiracetam or oxcarbazepine). Epilepsy was diagnosed in two patients during pregnancy (8th and 9th month of pregnancy). In 61.1% pregnancies patients experienced seizures. There were three miscarriages, one induced abortion due to congenital malformations, and one stillbirth among the studied patients. Two thirds of cohort delivered by caesarean section and the majority delivered at term. All but two newborns scored > 7 Apgar points (mostly 9-10 points). The mean birth weight was 3116 grams (range 1870-4400). Major congenital malformation was diagnosed in only one fetus and this pregnancy was terminated. Two thirds of women reported breastfeeding at any time.

Conclusions: Although all patients received antiseizure medication during pregnancy and more than a half experienced seizures in pregnancy, the majority of patients delivered healthy babies. Treatment with medication with low teratogenic potential resulted in very low rate of congenital malformations. The

percentage of women delivering by cesarean section was very high in our cohort. Further studies are needed to find risk factors for adverse pregnancy/neonatal outcomes in women with epilepsy in Poland.

Abstract Number: 378

Title: Pharmacokinetics of brivaracetam, lacosamide and perampanel during pregnancy and lactation - close monitoring in two cases

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Purpose: Changes in pharmacokinetics of new antiseizure medications (AMSs) are poorly described. Here we present pharmacokinetic data during pregnancy and lactation for brivaracetam, lacosamide and perampanel in two cases with close follow-up. Patient 1 used brivaracetam in monotherapy and gave birth to twins. Patient 2 used the combination of brivaracetam, lacosamide and perampanel. The aim was to investigate pharmacokinetic changes of these ASMs during pregnancy and lactation in two cases with multiple measurements in various matrixes.

Method: In both patients, therapeutic drug monitoring (TDM)-data were used. Serum concentrations were monitored throughout the pregnancies. Drug concentrations were also analyzed in umbilical cord blood at birth, in serum from the offspring and in breastmilk after 5 days and 3-11 weeks.

Result: The patients had 10-11 serum, 2 milk and 3-4 infant serum concentration measurements. There were minor changes in concentration/dose-ratios of brivaracetam and lacosamide. The mean milk/serum-ratios of brivaracetam and lacosamide were 0.71 and 0.83, respectively, 5 days and 3-5 weeks after delivery. The perampanel serum concentration increased by up to 80% in Patient 2 during the last part of gestation. The mean milk/serum-ratio of perampanel was 0.13, unchanged from 5 days to 5 weeks after delivery.

Conclusions: These two patients demonstrated only minor changes in serum concentrations of brivaracetam and lacosamide throughout pregnancy, while perampanel concentrations seemed to steadily increase towards the end. The distribution to milk was considerable for brivaracetam and lacosamide and low for perampanel. More studies on mother-infant pairs are warranted to confirm these results in larger groups.

Abstract Number: 464

Title: A Systematic Review of Antiepileptic Drug Exposure during Pregnancy and Neonatal Birth Weight Outcomes and Interim Meta-analysis

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Purpose: Antiepileptic drug (AED) exposure in-utero has been associated with various neonatal outcomes, including adverse birthweight outcomes. The study objective is to systematically summarize and meta-analyse the published evidence on AED exposure during pregnancy and neonatal growth outcomes.

Methods: We searched seven databases (MEDLINE, EMBASE, Cochrane Library, Scopus, CINAHL, IPA, and Global Health) for studies in English and French from inception to October 2020. Experimental and observational studies were included. Random effects models were used for meta-analysis.

Results: We screened 15,720 identified studies, 4279 were excluded after deduplication, 11,380 articles were excluded after title, abstract, and full-text review, and a total of 61 studies were finally included. We identified 26 studies on SGA, including fifteen studies with full data to conduct SGA meta-analysis. The primary meta-analysis included 15 studies comparing women exposed to any antiepileptic drug in-utero vs unexposed women, showing a significant increased risk of SGA; RR 1.55 (95% CI 1.27 to 1.90, I^2= 86%).

Four studies examined the class effect of all AEDs (i.e. unspecified), showing a significant increased risk of SGA; pooled RR=1.38 (95% CI 1.30 to 1.46, I^2 =0%). Ten studies compared exposed vs. unexposed women with epilepsy, showing a statistically increased risk of SGA; pooled RR 1.26 (95% CI 1.05 to 1.51, I^2= 46%). AED polytherapy was compared to monotherapy in 5 studies, showing a significant increased risk of SGA: pooled RR=1.57 (95% CI 1.02 to 2.42, I^2 = 51%).

Conclusion: This meta-analysis demonstrates that women taking AED during pregnancy have a significantly increased risk of SGA compared to unexposed women, among both women with and without epilepsy. Such results demonstrate a potential impact attributed solely to AED exposure. Polytherapy was associated with higher SGA risk compared to monotherapy. Further, this systematic review will report additional birthweight/growth outcomes in infants exposed to AED in-utero.

Abstract Number: 481

Title: New Onset Epilepsy During Pregnancy

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Purpose: Epilepsy is a common neurological disorder that poses challenges in managing women with epilepsy of reproductive age. Both women's and fetal health can be affected by a seizure during pregnancy. Rarely, patients of whom first-ever seizure was during pregnancy may be observed. The aim of the study was to investigate the rate and clinical feature of new onset epilepsy during pregnancy.

Method: We retrospectively evaluated women with reproductive history who were followed in the epilepsy clinic of Haseki Training and Research Hospital Department of Neurology between 1997 and 2019. The patients of whom first-ever seizure was during pregnancy were selected. Women with evidence of preeclampsia or acute symptomatic seizures were excluded. Two hundred and twenty pregnancies of 85 women who were followed in our epilepsy clinic were evaluated.

Result: Of 85 women with epilepsy, five (%5,9) had their first seizure during pregnancy. Mean age at seizure onset was 22,2 (±2,0; 20-25). The seizures occured 1 in the first, 3 in the second and 1 in the third trimester. Most of them had only one seizure during pregnancy. Three women were diagnosed generalized epilepsy while two had focal epilepsy. Three of them had their first seizure in the 1st, one in the 3rd and one in the 6th pregnancy. Only one pregnancy resulted in stillbirth. All children were healthy except one child with hydronephrosis.

Conclusions: New onset epilepsy during pregnancy was rare, however it should be well defined and diagnosed to avoid harm to the health of the fetus and mother.

Abstract Number: 522

Title: The Biology of Juvenile Myoclonic Epilepsy (BIOJUME) consortium: revealing a sex difference in the influence of precipitants on seizure prognosis.

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Purpose: Individuals with juvenile myoclonic epilepsy (JME) display varying clinical features, such as differing seizure types and seizures triggered by a variety of precipitants, and also vary considerably in response to anti-seizure medication (ASM). Here we describe an extensively phenotyped cohort of individuals with JME and investigate their clinical heterogeneity and factors influencing seizure control.

Method: We collected clinical data through the Biology of Juvenile Myoclonic Epilepsy (BIOJUME) consortium across 72 sites in 12 countries. We used the Avignon Class II diagnostic criteria for JME, and a phenotype committee reviewed diagnoses. We collected details of epilepsy, EEG and ASM history, self-reported seizure precipitants (including sleep disturbance, stress, light/visual patterns and menstrual cycle) and any lifestyle modifications. We investigated sex differences in factors influencing seizure control with univariate and multivariable analysis.

Result: 765 individuals met inclusion criteria (female:male, 1.8:1). 59% of females and 50% of males reported experiencing triggered seizures, and in females, this was associated with also experiencing absence seizures (p=0.0006). There was a significant association between reporting seizures triggered by light/visual patterns and experiencing an EEG photoparoxysmal response (PPR) ($p=5.9x10^{-8}$). Absence seizures significantly predicted drug resistance in both males (p=0.001) and females (p=0.000005) in univariate analysis. In multivariate analysis in females, catamenial seizures (p=0.001), absence seizures (p=0.00004) and stress-precipitated seizures (p=0.02) were associated with drug resistance, while PPR predicted seizure freedom (p=0.03). Females with absence seizures and a sensitivity to stress-related precipitants constitute the prognostic subgroup with the highest prevalence of drug resistance (49%).

Conclusions: In addition to absence seizures, experiencing triggered seizures is a common and important predictor of seizure control in JME, particularly in females. Further, there is variable effectiveness of current ASMs for the spectrum of individuals diagnosed with JME, highlighting the unmet need for more effective targeted interventions for female JME patients with triggered seizures.

Abstract Number: 580

Title: Valproate usage in pregnancy: An audit from Kerala Registry of Epilepsy and Pregnancy

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Purpose: To audit the use of valproate (VPA) during pregnancy in Women With Epilepsy (WWE) from Kerala Registration of Epilepsy and Pregnancy (KREP)

Method: We screened all pregnancies in KREP from January 2010 to December 2019 to identify pregnant women exposed to VPA. Seizure count before and during pregnancy, lifetime Anti-epileptic Drug (AED) usage, fetal outcome and Major Congenital Malformations (MCMs) were ascertained from the registry records. The presumed reason for usage of VPA was deducted from standard proforma prepared by abstracting the context in which each AED was initiated or discontinued as well as any AED adverse effects.

Result: There were 221 pregnancies (17.75 %) exposed to VPA during the audit period. The MCM rate for the completed pregnancies exposed to VPA was higher (n= 20, 10.36%) than that of VPA unexposed pregnancies (n=39, 4.96%). The odds ratio for MCM with VPA exposure was 2.2 (95% confidence interval 1.24-3.48, number needed to treat with VPA to result in MCM was 19). This audit revealed various presumed reasons for use of VPA during pregnancy, most common being either other AEDs were ineffective or not tolerated (n=145, 65.6%) and second being VPA was the first AED prescribed and was effective (n=68, 29.06%). Only less than 10% of women were tried on lamotrigine (LTG) or levetiracetam (LVT) before switching to VPA.
Conclusions: With the current prescription rate of VPA, ten MCM per thousand pregnancies can be avoided if VPA is not used in WWE. We suggest there is a need to change the practice policy while initiating the treatment and augment the use of LTG or LVT as first drug of choice in WWE.

Abstract Number: 673

Title: Prenatal exposure to high dose folic acid and risk of childhood cancer: A Nordic Register-Based Cohort Study.

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Purpose: To assess whether prenatal high dose folic acid exposure (maternal daily intake of ≥ 1mg) increases the risk of childhood cancer. This is commonly prescribed among pregnant women with epilepsy.

Method: Data from mandatory, nationwide health- and social registers from Denmark, Finland, Iceland, Norway, and Sweden were linked together using unique personal identification numbers through the SCAN-AED project (www.scanaed.org). Medical birth registries were linked to prescription-, patient, and cancer registries including information from national statistical agencies. Denmark, Norway, and Sweden record high

dose folic acid prescriptions. Cancer was defined as first cancer diagnosis below 20 years-of-age and coded in accordance with The International Classification of Childhood Cancer 3rd revision. Cox proportional hazards model was used to estimate adjusted hazards ratios (aHR) and 95% confidence intervals (95% CI), adjusted for birth year, sex, maternal age- and education, prenatal anti-seizure medication exposure, maternal smoking, major congenital malformations, and birthweight.

Result: We included 3,325,277 children (median observation-time 7.1 years; interquartile range 3.6-10.6 years) with 54,629 (1.64%) children exposed to high dose folic acid between 90 days prior to last menstrual period and birth. In total, 4,532 children were diagnosed with cancer (incidence rate 18.1/100,000 person-years). Prenatal exposure to high dose folic acid was not associated with cancer risk overall (aHR = 1.15; 95% CI: 0.90-1.46), nor was high dose exposure associated with increased risk among the three most common childhood cancer subtypes: Leukaemia (n = 1660, aHR = 1.07; 95% CI: 0.73-1.58), lymphoma (n = 462, aHR = 1.18; 95% CI: 0.52-2.67), cancer in the central nervous system (n = 562, aHR = 1.49; 95% CI: 0.70-3.18).

Conclusions: In utero exposure to high dose folic acid was not associated with an increased risk of childhood cancer.

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Abstract Number: 766

Title: Control of epileptic seizures in the postpartum period in women suffering from epilepsy.

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Purpose: To assess the incidence of epileptic seizures in the postpartum period in women with epilepsy.

Method: The study included 276 cases of pregnancy in women with epilepsy. The analysis of the frequency of epileptic seizures during the last year before the onset of gestation, during pregnancy and in the postpartum period, analysis of antiepileptic therapy, method of delivery, breastfeeding.

Result: Delivery time was 39 [38; 40] weeks. There were no statistically significant differences in delivery time depending on the form of epilepsy (p = 0.26). Increase in epileptic seizures in the early postpartum period was registered in 28 women (10.1%). Disruption of remission of epilepsy in 42% of cases was recorded after changes in antiepileptic therapy during pregnancy, including self-canceling and/or reducing the dose of antiepileptic drugs (AED) (p <0.05). 68% of patients with disruption of remission received antiepileptic therapy. There were no statistically significant differences between AED between the control group and the group with disruption remission. Breastfeeding was carried out by 62% of patients. The causes of breastfeeding refusal included: the prohibition of a neonatologist was registered - 79%, the absence of lactation - 18%, the prohibition of a pediatric neurologist - 3%. A statistically significant effect of the refusal from breastfeeding on an increase in epileptic seizures is not registered.

Conclusions: Control of epileptic seizures in the postpartum period is no less important than control of seizures during pregnancy. Disruption in remission of epilepsy in the early postpartum period was recorded in 10.1% of cases and is associated with some change in the pharmacotherapy of epilepsy during pregnancy.

Abstract Number: 773

Title: Prenatal exposure to antiseizure medication duotherapy and risk of neurodevelopmental disorders - SCAN--AED: a Nordic nationwide cohort study

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Purpose: To investigate the risk of neurodevelopmental disorders after prenatal exposure to antiseizure medication (ASM) in duotherapy.

Method: Population-based cohort study (www.scanaed.org) using linked health-and social register data from Denmark, Finland, Iceland, Norway, and Sweden. We defined prenatal duotherapy exposure as filled prescriptions for two distinct ASMs (only) within the same trimester. We identified child neurodevelopmental disorders by ICD-10 codes for autism spectrum disorders and intellectual disability (F84.0, F84.1, F84.5, F70 to F73, F79, F84.3, F84.4, F84.8, F84.9). Cox regression with adjustment for birth year, maternal psychiatric/somatic morbidity, comedication, and sociodemographic confounders provided hazard ratios (aHR) with 95% confidence intervals (95%CI) for neurodevelopmental disorders in children after prenatal exposure to the five most common ASM duotherapies in comparison with ASM unexposed children.

Result: We identified 4,493,377 singleton births (median follow-up 8 years, interquartile range 4.0-12.1). Of 4,462,358 unexposed children, 67,808 (1.5%) were diagnosed with neurodevelopmental disorders (incidence rate 177/100,000 person-years). Compared with ASM unexposed children, the aHR for neurodevelopmental disorders among children exposed to lamotrigine+valproate was 2.5 (95% CI 1.5-4.1; 3.9%, n=384), for lamotrigine+topiramate 3.5 (95%CI 1.8-6.1; 5.8%, n=155) for levetiracetam+carbamazepine 4.3 (95%CI 1.9-9.6, 4.4%, n=136), for lamotrigine+oxcarbazepine 3.0 (95%CI 1.4-6.2; 5.4%, n=130). Of 417 lamotrigine+levetiracetam exposed children < 1.2% had neurodevelopmental disorders (aHR not calculable). The corresponding aHRs after monotherapy of each ASM were: lamotrigine 1.2 (95%CI 1.04-1.4, 1.7%, n=9,581), valproate 3.3 (95%CI 2.9-3.8, 6.8% n=3,042), topiramate 2.0 (95%CI 1.4-3.0, 2.5%, n=897), levetiracetam 1.4 (95%CI 0.8-2.6, 1.0%, n=1,050), carbamazepine: 1.6 (95%CI 1.3-1.9, 3.1%, n=3,649), oxcarbazepine 1.5 (95%CI 1.2-2.0, 3.3%, n=1,627).

Conclusions: Prenatal exposure to commonly used ASM duotherapies were associated with increased risk of neurodevelopmental disorders. However, risk estimates were in the range of those seen after some monotherapy exposures. The prevalence of neurodevelopmental disorders after exposure to lamotrigine + levetiracetam was low.

Abstract Number: 796

Title: Spontaneous abortion among married women with epilepsy at indonesia national refferal hospital

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Purpose: To determine the prevalence and associated factors for spontaneous abortion among women with epilepsy (WWE) at Cipto Mangunkusumo Hospital.

Method: The cross-sectional study was conducted from August 2020 to January 2021 at Dr Cipto Mangunkusumo General Hospital. The inclusion criteria were married WWE and had experienced pregnancy. The data of demographic characteristic, clinical characteristic of epilepsy (seizure type, history of status epilepticus, aetiology, and seizure control), history of antiepileptic drug (AED), obstetric profile (history of pregnancy, labour, and contraception) was obtained. Spontaneous abortion was defined as the loss of pregnancy at less than 20 weeks of gestation.

Result: There were 67 subjects, mean age was 35.73±7.421 years old. Of total subjects, 76.1% had children, 38.8% were multiparity, and 43.3% were on contraception. There were six subjects (8.9%) had history of spontaneous abortion. Among them, five subjects were multiparity and one subject had abortion during her first pregnancy. None of them had multiple spontaneous abortus. The epilepsy aetiology was intracranial tumour (two subjects), lupus erythematosus (two subjects), and cryptogenic (two subjects). Four subjects still had seizures but none of them had history of status epilepticus. Regarding the AED, the distribution of mono- and polytherapy was equal. Three subjects were on monotherapy with phenytoin, phenobarbital, or levetiracetam. The other three subjects were on polytherapy; two subjects with combination of three AEDs (valproic acid, levetiracetam, and phenytoin; topiramate valproic acid, and clobazam) and one subject on two AEDs (lamotrigine, topiramate). None of them took carbamazepine.

Conclusions: The prevalence of spontaneous abortion among married WWE in our study was 8.9%. This number was not differed from general population. There was no any associated factor to spontaneous abortion among married WWE in our study.

Abstract Number: 830

Title: Menstrual disorders in women with epilepsy at indonesia referral hospital

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Purpose: To know the menstrual disorders and its associated factor in women with epilepsy (WWE) at Dr Cipto Mangunkusumo General Hospital.

Method: The cross-sectional study was conducted from August 2020 to January 2021 at Dr Cipto Mangunkusumo General Hospital. Menopausal WWE were excluded. The data of demographic characteristic, clinical characteristic of epilepsy (seizure type, history of status epilepticus, etiology, and seizure control), history of antiepileptic drug (AED), menstrual profile (menarche, menstrual disorder including menstrual cycle disorders and dysmenorrhea) were obtained. Menstrual disorder was define as having at least one of dysmenorrhea or menstrual cycle disorders. Statistical analysis was calculated to identify associated factor to menstrual disorders using SPSS 20.0.

Result: There were 127 WWE with a median age of 29.5 (min-max 18-51) years old, 51.9% of them had been on polytherapy. The median age of menarche was 13 (min-max 7-17) years old. Menstrual disorders were found in 82.7% subjects (72.4% dysmenorrhea and 31.8% menstrual cycle disorder). Types of menstrual cycle disorders were irregular cycle (24%), polymenorrhagia (4.7%), amenorrhea (2.3%), and oligomenorrhea (0.8%). There was a significant association between history of intracranial infection as epilepsy etiology and menstrual disorder (p=0.048). In subgroup analysis, the significant associated factor to menstrual cycle disorders was topiramate usage (p=0.032) and associated factors to dysmenorrhea were the use of levetiracetam (p=0.029) and lamotrigine (p=0.009).

Conclusions: Menstrual disorders were found in 82.7% WWE; menstrual cycle disorder and dysmenorrhea were 31.8% and 72.4%, respectively. History of intracranial infection was associated with menstrual disorders. The use of topiramate was significantly associated to menstrual cycle disorder while levetiracetam and lamotrigine were associated to dysmenorrhea. Apparently, polytherapy and valproic acid were not associated to menstrual disorders in this study.

Abstract Number: 848

Title: Impact of the EMA regulatory restrictions on the use of valproic acid: prescription trends from 2010 to 2020 in Emilia Romagna Region

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Purpose: Valproic acid (VPA) use in pregnancy has been associated with a significant risk of congenital malformations and neurodevelopmental problems. In 2014 the European Medicines Agency (EMA) recommended restricting the use of VPA for women of childbearing age. New restrictions were issued in 2018. We aimed to evaluate the impact of the restrictions comparing the prescription of VPA and other antiseizure medications (ASMs) in males and females of all ages, in the Emilia Romagna Region (ERR), Northern Italy.

Method: ASMs prescriptions were derived from the reimbursed drug prescription registries from 2010 to 2020 including only ERR residents. We classified as incident all cases with a first prescription of ASMs during the study period. Time series of incident rates by sex and age groups were evaluated for all ASMs. Focusing on VPA, an interrupted time-series analysis was performed to assess the impact of the restrictions.

Result: Incident rates of VPA prescriptions decreased over time, from 32 per 100.000 person-years in the first quarter of 2010 to 27 per 100.000 person-years in the last quarter of 2020.
A significant decrease was recorded only for females, both after the first restriction (IRR=0.89, 95%CI = [0.82; 0.96]) and after the second one (IRR=0.81, 95%CI = [0.71; 0.92]) vs the previous period (2010-2014). The decrease was higher for females of childbearing age, both after the first (IRR=0.85, 95%CI = [0.75; 0.96]) and the second restriction (IRR=0.67, 95%CI = [0.55; 0.82]).
In this group we observed an increase in incidence rates of other ASMs, especially lamotrigine ($p<0.001$) and ethosuximide ($p<0.001$). This trend was not observed in males.

Conclusions: The regulatory restrictions likely influenced a decline in the use of VPA in female of childbearing age in ERR. It can be hypothesized that VPA was at least in part, replaced by lamotrigine and ethosuximide in this subpopulation.

Abstract Number: 1011

Title: Unfolding Few More Parts of Antiseizure Medication (ASM) Effect Puzzle on Placental Carriers; in vitro study in human placental cell line

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Purpose: Recently, we demonstrated that antiseizure medications (ASMs) affect the expression of major uptake and efflux placental carriers essential for fetal growth, both in vitro and ex vivo studies. Our aim was to zoom into still unexplored effects of both older and newer ASMs on the expression of uptake carriers for essential compounds for fetal development, among which glucose and choline.

Method: BeWo cells were incubated with valproic acid (VPA), carbamazepine (CBZ), levetiracetam (LEV), lamotrigine (LTG), lacosamide (LCM) or their vehicles at concentrations that mostly represent their therapeutic range. RT-PCR analyses were utilized to study the effects of ASMs on carriers' mRNA expression. Choline/Acetylcholine quantitative assay was utilized for quantifying choline and acetylcholine in BeWo cell culture supernatant. The function of glucose transporter 1 (GLUT1) was evaluated by a glucose uptake assay.

Result: Compared with controls, VPA and LEV lowered the levels of choline transporter transcript and total choline levels in BeWo cell lysates (n=6/treatment group; $p<0.05$). VPA, CBZ, LEV-treated cells displayed decreased levels of GLUT1 mRNA (n=6; $p < 0.05$). LCM and LTG did not alter expression of any explored transporters. VPA, CBZ, LEV extent of effect on GLUT1 activity is analyzed in these days.

Conclusions: These findings suggest a possible effect of ASMs on placental transport mechanisms for glucose and choline to the fetus. We suggest a novel target of ASMs, both older and newer, the placental carriers. The potential clinical applications of these findings remain to be established. Parallel work is done in our lab to assess these effects *ex vivo*. Nevertheless, these results may be the additional step toward understanding the effects of ASMs on the placental barrier and directing a rational supplemental therapy in pregnant women with epilepsy.

Abstract Number: 1088

Title: Different sex vulnerability in a rodent model of induced epilepsy

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Name: Different sex vulnerability in a rodent model of induced epilepsy

Purpose: In this study we aimed to compare male versus female vulnerability to seizures induced by the same dosage of penthylenetetrazole (PTZ).

Method: Thirty-eight adult rats, divided into four groups: Male PTZ (n =10), Female PTZ (n =12), Male Naïve (n=8) and Female Naïve (n=8) received 18 PTZ applications (30 mg/kg, ip) given every other day. Seizures were observed for 30 minutes after PTZ injection and categorized through the Racine scale (stages 0-5). Seizure scores (SS) are expressed as mean + SE, significance level was set as $P<0.05$. Estrous cycle was examined daily in both female groups.

Result: Our results demonstrate that both Male PTZ and Female PTZ groups had an increase in convulsive activity ($F_{[17,476]}=2.5360$; P=0.00069). Differences were also observed between sexes: male rats who underwent PTZ applications had a larger increase in convulsive activity, which was observed for the first time during the 13th application (D13=4; P=0.002) when compared to female PTZ rats (D13=2.64; P=0.002). Statistically significant differences in seizure score were observed during the 8th application for female rats (D8: 2.67 *vs* D1: 0.67; P=0.0001) and 7th application for male rats (D7:2.21 *vs* D1: 1.05; P=0.02). Male PTZ rats presented SS ≥ 4 for the first time in the 13th day, where female PTZ rats did not reach stage 4 seizures during the entire experiment. No correlation was observed between seizure frequency/intensity and estrous cycle phases for female PTZ rats. Naïve rats received saline instead PTZ and never had a single seizure.

Conclusions: Under the same laboratory conditions, female rats were demonstrated to have higher threshold for PTZ-induced seizures and did not reached the fully kindled stage as the male rats.

Abstract Number: 1196

Title: Quantitative electroencephalography (qEEG) modifications during ovarian cycle in patients with catamenial C1-pattern temporal lobe epilepsy (TLE)

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Purpose: The term ''catamenial epilepsy'' refers to cyclic seizure exacerbation in relation to the ovarian cycle. There are three recognized patterns: perimenstrual (C1), peri-ovulatory (C2) and entire luteal phase in anovulatory cycles (C3). The prevalence of catamenial epilepsy is estimated up to 70% in women with epilepsy. Temporal lobe epilepsy (TLE) represents the most common form of epilepsy in adulthood. Temporal lobe can define a direct influence on the function of the hypothalamic-pituitary axis which is involved in the regulation, production and secretion of sex steroids. Vice versa, sex steroids can modulate brain activity. The aim of this study is to evaluate quantitative electroencephalography (qEEG) modifications during ovarian cycle in patients with catamenial C1-pattern TLE.

Method: Thirty-five women with diagnosis of TLE were enrolled. All patients presented regular ovary cycle (28 ± 5 days). According to the presence of catamenial C1-pattern, patients were divided into 2 subgroups: catamenial TLE (17 patients), non-catamenial TLE (18 patients). Each patient underwent a 30-minute 21-electrods EEG recording during menstrual, follicular and luteal phase of the ovarian cycle. A total of 90 epochs of 2 s-long per patient were processed by a specific software (BrainVision Analyzer) performing a fast Fourier transform (FFT) on each second of EEG acquisition. The mean power spectrum was divided automatically into four frequency bands: delta (1-3.9 Hz), theta (4-7.9 Hz), alpha (8-12 Hz) and beta (13-18 Hz).

Result: During menstrual phase, patients with catamenial TLE showed a significantly lower alpha mean power spectrum and a significantly higher theta mean power spectrum in temporal derivations, as compared to follicular and luteal phases

Conclusions: Reduction of alpha rhythm during M phase may account for seizure exacerbations in catamenial TLE patients. This specific qEEG pattern could represent a biomarker of C1 pattern, supporting diagnosis and aiming to differentiate it from other catamenial patterns.

Abstract Number: 1369

Title: Malformation Risk Prediction with Machine Learning Modelling for Pregnant Women with Epilepsy

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Purpose:
Children of women with epilepsy (WWE) have increased risk of major congenital malformations (MCM). Prenatal exposure to valproate and other antiepileptic drugs (AEDs) and higher dosage of AEDs are critical modifiable risk factors for MCM. It is unclear how demographic and environmental factors influence the risk of MCM. We aimed to develop a machine learning model to predict malformation risk for children of WWE.

Method: Anonymized data set from the Kerala Registry of Epilepsy and Pregnancy was utilized for validation and testing of the machine learning model. The details of maternal socioeconomic background, epilepsy syndromes, AED exposure & dosage, folic acid usage, seizures during pregnancy, and MCM were available in the data set. We balanced the data by synthetic oversampling technique (SMOTE) before classifying with six models based on Decision Tree, Random Forest, Naïve Bayes, Logistic regression, AdaBoost, and stack model. Cross-validation and leave-one-out techniques were used to compare the performance of the model.

Result: There were 148 children with MCM (6.3%) in 2338 pregnancies. AEDs exposed as mono were phenobarbitone (137), lamotrigine (50), phenytoin (119), carbamazepine (490), valproate (341), levetiracetam (106), oxcarbazepine (71) and others (29). The stack model outperformed the other classifiers with 93.52% accuracy when results were compared using cross-validation (70-30). Its predictions were correct in 91.8% and 93.9% of cases with and without MCM. The false positivity (5.3%) and false negativity (7.4%) were low. The Area under the Curve (AUC) for the Receiver Operator Characteristics (ROC) for the stack model was 0.975 indicating high accuracy.

Conclusions: Machine learning models can predict the risk of MCM in pregnancies of WWE. The model captured the relative influence of maternal factors and prenatal AED exposure on risk of MCM.