ABSTRACT BOOK

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P-01

Re-analysis of Exome Sequencing Data of Undiagnosed Epilepsy cases

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INTRODUCTION

Many types of epilepsies have a genetic aetiology. The number of single genes causing epilepsy is in the hundreds, and it is a number that continues to grow. As a result, large gene panels, clinical exomes, or whole exomes are commonly used in clinical practice for the genetic diagnosis of epilepsy. A genetic diagnosis can have a major impact on a patient’s clinical management in terms of treatment choice, avoiding unnecessary further testing and informing future reproductive decisions. Establishing new strategies for genetic testing that aim to increase the diagnostic yield is essential because of the rapidly changing landscape of epilepsy genetics. Salinas et al. (2021) have demonstrated the importance of periodic re-interpretation and re-analysis of genetic data to achieve this. Re-analysis of exome data of previously unsolved developmental and epileptic encephalopathy cases (complex paediatric epilepsies) was shown to further increase the diagnostic yield by ~15%. The objective of this current study is to evaluate the diagnostic potential of exome sequence re-analysis in our cohort of undiagnosed epilepsy cases and to assess the accuracy and impact of Congenica-AI (Artificial Intelligence) for the analysis of SNVs.

METHODS

Patients with a presentation of epilepsy (including the following terms on the referral card: epilepsy, seizures, infantile spasms, hypsarrhythmia, focal cortical dysplasia) were seen by the Clinical Genetics team at St George’s University Hospitals NHS Trust, London. DNA extracted from blood was enriched using Agilent SureSelect Clinical Research Exome V2 (CRE V2) or Nonacus ExomeCG and sequenced on Illumina NextSeq 500 or NovaSeq. Secondary and tertiary analysis of DNA sequences and review of SNVs and CNVs was undertaken using the Congenica clinical decision platform. Re-analysis was performed 6 - 48 months after initial interpretation, using 1) an updated curated epilepsy gene panel, and 2) gene agnostic prioritisation using Congenica AI.

RESULTS

Through original exome sequencing analysis, a diagnosis was achieved in 34/129 patients (26%). Of 59 cases assessed for CNVs, 2 had pathogenic variants (3.4%). Re-analysis was performed on 95 unsolved cases. After re-analysis, an additional 17/93 (18.3%) cases were found to have a causative variant and were re-categorised as diagnosed. This increases the overall diagnostic yield to 40.9%. In addition, Congenica-AI accurately identified 85.7% of causative SNVs (within the top 10 variants) in this undiagnosed cohort.

CONCLUSION

This study illustrates the diagnostic utility of re-analysing exome sequencing data in previously unsolved epilepsy cases. The successful application of Congenica-AI in this re-analysis cohort demonstrates the value of this tool for periodic re-analysis of undiagnosed cases. Using Congenica-AI provides an efficient approach that makes routine re-analysis much more feasible.

P-02

Efficacy and Safety of Cannabidiol (CBD) Dose Adjustment in Patients With Lennox-Gastaut Syndrome: Post-Hoc Analysis of Phase 3 Trial GWPCARE3 and Open-Label Extension Trial GWPCARE5

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INTRODUCTION

In this post-hoc analysis of a randomised controlled trial (RCT; GWPCARE3; NCT02224560) followed by an open-label extension (OLE; GWPCARE5; NCT02224573), we evaluated the effect of dose adjustments on the efficacy and safety of cannabidiol (CBD).

METHODS

In GWPCARE3, patients received plant-derived highly purified CBD medicine (Epidyolex®; 100 mg/mL oral solution) at 10 mg/kg/day (CBD10) or 20 mg/kg/day, or matched placebo for 14 weeks. Patients who completed the RCT were invited to enrol in the OLE, during which CBD dose was titrated to an initial target of 20 mg/kg/day, with subsequent adjustments based on response and tolerability (maximum 30 mg/kg/day). Analyses included patients from the CBD10 group of GWPCARE3 whose dose was titrated up in the OLE and maintained at a modal dose of ≥12.5 mg/kg/day. Weekly median percent change from baseline in drop seizure frequency was assessed through 96 weeks.

RESULTS

Median (range) age of patients was 12 (3–38) years. At the end of the RCT, cumulative weekly median seizure reduction from baseline was 47%. In the OLE portion, an additional 14% reduction was observed, which was maintained throughout the trial. Reduction in seizure frequency during the OLE was greater in patients (25/43 [58%]) who did not have ≥50% reduction in drop seizures during the RCT than in patients (18/43 [42%]) who had ≥50% reduction. AEs were reported in 36/43 (84%) patients during the RCT and 42/43 (98%) patients during the OLE. Most common AEs: somnolence, decreased appetite, and upper respiratory tract infection (8/43 patients [19%] each) during the RCT; convulsion (22/43 patients [51%]), diarrhoea (18/43 [42%]), and pyrexia (16/43 [37%]) during the OLE.

CONCLUSION

This post-hoc analysis emphasises the importance of titrating to each patient’s therapeutic dose, as dose adjustments may improve seizure reduction in some patients. FUNDING: GW Research Ltd., now part of Jazz Pharmaceuticals, Inc.

P-03

Effect of Add-on Cannabidiol (CBD) on Seizure Frequency and Seizure-Free Intervals in Patients With Seizures Associated With Tuberous Sclerosis Complex: Phase 3 Trial GWPCARE6 Post-Hoc Analysis

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INTRODUCTION

This post-hoc analysis of a randomised, placebo-controlled phase 3 trial (GWPCARE6; NCT02544763) evaluated seizure frequency reduction to determine the proportion of patients with tuberous sclerosis complex (TSC), treated with cannabidiol (CBD) or placebo, who reached all continuous responder rate thresholds and the longest seizure-free intervals.

METHODS

Patients received plant-derived highly purified CBD medicine (Epidyolex®; 100 mg/mL oral solution) at 25 mg/kg/day (CBD25) or 50 mg/kg/day, or matched placebo for 16 weeks. Efficacy of CBD25 (n=75) vs placebo (n=76) was evaluated by percent reduction from baseline in TSC-associated seizure frequency and longest seizure-free intervals.

RESULTS

In the 4-week baseline period, median (Q1, Q3) TSC-associated seizure frequency was 56 (21, 101) for CBD25, 54 (26, 102) for placebo; mean (standard deviation [SD]) longest seizure-free interval was 3 (3) days for CBD25, 2 (2) days for placebo. CBD produced significantly greater reduction in TSC-associated seizures vs placebo (treatment ratio [95% CI], 0.699 [0.567–0.861]; P=0.0009). Response rates for ≥25%, ≥50%, and ≥75% reduction: 68%, 44%, and 19% for CBD25; 43%, 22%, and 0% for placebo. Mean (SD) longest seizure-free intervals: 11 (17) days for CBD25 and 6 (6) days for placebo. CBD25 vs placebo 7-, 14-, 21-, and 28-day seizure-free intervals: 45% vs 33%, 24% vs 14%, 12% vs 0%, and 8% vs 0%. AE incidence: 93% for CBD25 and 95% for placebo; 8 patients (11%) on CBD25 and 2 (3%) on placebo discontinued treatment because of an AE. Most common AEs: diarrhoea and decreased appetite, occurring more frequently with CBD than placebo. ALT/AST elevations (>3× ULN) occurred in 9 (12%) patients on CBD25 and none on placebo; 78% were on concomitant valproate.

CONCLUSION

CBD was superior to placebo, reducing seizures and producing longer seizure-free intervals in patients with TSC-associated seizures. FUNDING: GW Research Ltd., now part of Jazz Pharmaceuticals, Inc.

P-04

Parent-reported seizure provoking factors and strategies to limit seizures in children with Dravet syndrome

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INTRODUCTION

Introduction: Previous research suggests that caregivers often identify precipitants to the occurrence of seizures in individuals with Dravet Syndrome (DS) but there is limited population data on this and limited population data on measures taken by caregivers to limit the frequency and severity of seizures in children with DS.

METHODS

Methods: Caregivers of 42/48 children with DS born between 2000 and 2018 in Sweden, consented to participate in an interview, focusing on the frequency of previous and current seizure precipitants and preventive strategies employed to limit seizure occurrence and severity of seizures. Frequency of current precipitants and preventive strategies were compared between older children born 2000-2009 and younger children born 2010-2018 and between children with severe and less severe epilepsy using a Chi square test. The Epilepsy and Learning Disabilities Quality of life (ELDQOL) scale was used to estimate epilepsy severity.

RESULTS

All children had experienced seizure precipitants and in all, measures had been taken to avoid seizures. Seizures had been provoked by a median of seven (range 2-11) out of 13 factors asked for, leading to avoidance of a median of five (range 1-10) out of 11 factors. The most common precipitants were fever (n=42, 100%), afebrile infections (n=39, 93%), physical activity (n=35, 83%), tiredness (n=32, 76%), warm weather (n=29, 69%), strong emotions (n=27, 64%), sleep (n=25, 60%), crowding (n=22, 52%), reduced temperature (n=20, 48%) and bright light (n=19, 45%). Afebrile infections (X2(1,n=41)=6.05, p=0.014) and reduced temperature (bathing in cold water or being out during winter) (X² (1,n=40) =7.42, p=0.006) were more common current triggering factors in younger children. Bright light was a more common current triggering factor in children with severe epilepsy (X² (1, n=39)=6.109, p=.013). The most common factors avoided were warm weather (n=35, 83%), physical activity (n=27, 64%), infections (n=25, 60%), tiredness (n=25, 60%), crowding (n=23, 55%), strong emotions (n=20, 48%), bright light (n=18, 43%) and reduced temperature (n=15, 36%). Some caregivers spontaneously reported that they avoided spontaneous meetings with the grandparents or limited favorite activities, to avoid making the child too excited, as strong feelings usually provoked a seizure. It was currently more common to avoid strong emotions (X² (1, n=41)=4.4, p=.035), and reduced temperature (X² (1,n=40), p=.002) in younger children, and to avoid infections (X²(1,n=40)=5.105, p=.024) and crowding (X² (1, n=38)=3.979, p=.046) in children with severe epilepsy. Other current or previous preventative measures were emergency seizure medications (n=42, 100%), personal cooling devices (n=22, 52%), seizure alarm (n=20, 48%), home pulse oximetry (n=13, 31%), Port-a-cat (n=11, 26%), intravenous immunoglobulin or antibiotics to prevent infections (n= 10, 24% for each) and home oxygen (n=8, 19%). To avoid contagious infection 16/34 (47%) siblings and 28/42 (67%) children had stayed home from school/day-care.

CONCLUSION

Parent-reported seizure precipitants and strategies to avoid seizures, also involving siblings, are common in DS, restricting the life of all family members. There is a need for further studies to investigate how effective these strategies are.

P-05

Persistent knowledge gaps between 2005 and 2020 in women with epilepsy: Comparison of multicenter studies from Germany

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INTRODUCTION

Epilepsy is typically a chronic condition that can affect patients of all ages. Women with epilepsy (WWE) require access to specific counseling and comprehensive information regarding issues related to contraception, pregnancy, and hormonal effects on seizure control and bone mineral density. Within the context of informed consent, patients are increasingly involved in medical decision-making and should be provided with sufficient information regarding the potential effects of epilepsy. However, several international and national studies conducted during the last two decades have revealed major knowledge deficits among WWE(Bell et al., 2002; Dierking et al., 2018; May et al., 2009; Vazquez et al., 2007). This study investigated the knowledge among WWE regarding their condition, their needs for information and counseling, and whether epilepsy-specific knowledge has improved over the last 15 years.

METHODS

A total of 280 WWE aged 18 to 82 years participated in this multicenter, questionnaire-based study. The study was conducted at epilepsy centers in Frankfurt am Main, Greifswald, Marburg, and Münster, Germany, between October 2020 and December 2020. Sociodemographic and epilepsy-specific data for participating women were analyzed and compared with the results of a similar survey performed in 2003–2005 among 365 WWE in Germany (May et al,2009). We asked in detail questions regarding their knowledge of epilepsy and women’s issues and asked them to self-rate their level of knowledge. The questionnaire on epilepsy-specific knowledge among WWE included 16 items (e.g., “Some antiseizure medications may cause the birth control pill to become ineffective.”). The response options were “True,” “False,” and “Don’t know.” The total number of correct answers was used to determine a knowledge score, with possible results ranging from 0 (no correct answers) to 16 (correct answer provided for every item).

RESULTS

The questionnaire-based survey revealed considerable knowledge deficits without significant improvements over the last 15 years, particularly among those with less education and with regards to information on the more pronounced effects of epilepsy in older WWE (>50 years), including interactions with menopause and osteoporosis. No significant differences in mean knowledge scores were detected between the 2005 and the 2020 cohorts (2005: mean: 6.19, median: 6, SD: 3.39, range:

0–15; 2020: mean: 6.49, median: 7, SD: 3.51, range 0–15). In WWE ≤29 years, a significant increase in the knowledge score was observed in 2020 compared with this age group in 2005 (mean 7.42 vs. 6.5, p =.036). Mothers with epilepsy frequently reported epilepsy-related concerns regarding childrearing, particularly the possibility of seizures scaring their child and the need to rely on other people.

CONCLUSION

WWE continue to demonstrate inadequate epilepsy-related knowledge and the interactions of epilepsy with pregnancy, parenthood, and hormonal balance. Despite increasing information availability and the aspiration toward better awareness among medical professionals, overall knowledge has not increased sufficiently compared with the levels observed in recent studies.

P-06

Genotype-Phenotype correlations in focal cortical dysplasias (FCD): a large cohort study.

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INTRODUCTION

Genetic malformations of cortical development (MCDs), such as mild mMCDs, focal cortical dysplasia (FCD), and hemimegalencephaly (HME), are major causes of pediatric refractory epilepsies subjected to neurosurgery. FCD type 2 are characterized by neuropathological hallmarks that include enlarged dysmorphic neurons and balloon cells. We provide a comprehensive assessment of the contribution of germline and somatic variants in a large cohort of surgical MCD cases.

METHODS

We enrolled in a monocentric study 80 children with drug-resistant epilepsy and a postsurgical neuropathological diagnosis of mMCD, FCD1, FCD2, or HME. We performed targeted gene sequencing on matched blood–brain samples to search for low-allele frequency variants in mTOR pathway and FCD genes.

RESULTS

We were able to elucidate 29% of MCD/FCD1 patients and 63% of FCD2/HME patients. Somatic loss-of-function variants in the N-glycosylation pathway-associated SLC35A2 gene were found in mMCD/FCD1 cases. Somatic gain-of-function variants in MTOR and its activators (AKT3, PIK3CA, RHEB), as well as germline, somatic and two-hit loss-of-function variants in its repressors (DEPDC5, TSC1, TSC2) were found exclusively in FCD2/HME cases. Analysis of microdissected cells demonstrated that dystrophic neurons and balloon cells carry the pathogenic variants. We further observed a correlation between the density of pathological cells and the variant-detection likelihood. Single-cell microdissection followed by sequencing of enriched pools of dystrophic neurons unveiled a somatic second-hit loss-of-heterozygosity in a DEPDC5 germline case. After surgery, 66.3% of the children are Engel 1 and up to 100% in case of somatic TSC1/2, RHEB or PIK3CA mutations. PIK3CA mutation is responsible for a neonatal onset of the epilepsy whereas RHEB/AKT3 mutations are responsible for a later onset of seizures, around 6 months of age. Infantile spasms are more frequent in case of RHEB/PIK3CA and SLC35A2 mutations. Autism spectrum disorder is particularly frequent in the SLC35A2 sub-group.

CONCLUSION

This study indicates that mMCD/FCD1 and FCD2/HME are two distinct genetic entities: while all FCD2/HME are mosaic mTORopathies, mMCD/FCD1 are not caused by mTOR-pathway-hyperactivating variants, and ~ 30% of the cases are related to glycosylation defects. Targeted therapeutic approaches should be considered in the future, especially in patients not eligible for surgery or after an incomplete resection. In our pediatric cohort, chances of a succesfull surgery are identical whereas a mutation is found in neurons or not.

P-07

Epileptic seizure as first symptom of brain tumours

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INTRODUCTION

Association of brain tumours and epileptic seizures is well known. The risk and impact of preoperative seizures on postoperative care and seizure recurrence in patients with various tumours types remains an topic of active research. Here we present single centre retrospective cohort study of the patients operated for brain tumours between 2015 and 2020 in Vilnius University Hospital Santara Clinics – reference centre for epilepsy care in Lithuania.

METHODS

We analysed consecutive adult patients who underwent first craniotomy for the indication brain tumours confirmed by postoperative pathology. Underage and patients with long-standing epilepsy unrelated to brain tumours were excluded. Data collected included age, sex, tumours histology, grade, affected lobe, date of diagnostic MRI, date of surgery, date of the first pre-operative seizure and date of onset of non-seizure symptoms for patients who did not experience seizures, date of first post-operative seizure, data on pre and postoperative antiseizure medications, last follow-up date. Group of patients who experienced epileptic seizure as first symptom of tumours was analysed versus the groups who experienced any other or no symptoms before diagnosis. Key results summarized as odds ratios for the risk of seizures across tumour types, grades and locations.

RESULTS

696 patients - 412 females (59,2%) and 284 males (40,8%) were included. Mean age at surgery was 57,8±15,0 years. Pre-operative seizure as first symptom of brain tumour was recorded in 164 patients (23,56%). Patients who experienced seizures were 5,88±2,75 years younger, slightly predominantly males 51%.   Brain MRI performed sooner in patients with seizures (0,8 ± 0,03 months) versus non-seizure patients (1,6 ± 0,03 months). Brain surgery respectively performed after 1,85 ± 0,50 months and 2,5 ± 0,50 months following initial symptom. The risk of pre-operative seizure was significantly higher in oligodendroma (n=19, OR=13,0, p < 0,001), diffuse astrocytoma (n=31, OR=5,2, p<0,001), anaplastic oligodendroma (n=13, OR=3,7, p=0,02) as opposed to glioblastoma (n=104, OR=0,61, p=0,05), any type of meningioma (n=166, OR=0,61, p=0,02) and metastatic brain tumours of any type (n=128, OR=0,61, p=0,03). Grade II and III tumours had significantly higher risk for seizures OR=3,93, p<0,001 and OR=2,76, p=0,012 respectively. Most frequently tumours were located in frontal (190), temporal (88), parietal (52) and occipital (20) lobes alone, 168 patients had multilobar, 175 patients had infratentorial Involvement. Significantly higher seizure risk observed in patients with frontotemporal (OR=1,65, p=0,02) and temporoparietal (OR=1,5, p=0,03) as opposed to occipital (OR=0,37, p<0,001) involvement. The average follow-up was 7,62±0,23 months with first post-operative seizure occurring in the first 3,43±0,17 months. 87 patients experienced post-operative seizures, with risk 5,5 times higher in those with pre-operative seizures.

CONCLUSION

1 in 4 brain tumours manifest with epileptic seizures as first symptom, with tendency to occur in younger patients. Certain tumour types have higher risk of seizures. Post-operative seizures risk is significantly higher in patients with pre-operative seizures.

P-08

Stiripentol inhibits status epilepticus in a mouse model of metabolic epilepsy

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INTRODUCTION

Stiripentol (STP, Diacomit©) is an antiepileptic drug indicated for the treatment of generalized tonic-clonic seizures in patients with Dravet syndrome. The complex mechanisms of action of STP suggest that it may be active against various types of epilepsies, including metabolic epilepsy. Methionine sulfoximine (MSO), a powerful glycogenic agent, causes an increase of brain glycogen level and ammonemia, and induces tonic-clonic convulsions, status epilepticus and death (Szegedy et al., 1978; Cloix and Hevor, 2009). Our goal was to evaluate the effect of STP in a mouse model of MSO-induced convulsions (Picard et al., 2011).

METHODS

For this purpose, EEG and video recordings were performed in male CBA mice injected with MSO (50 mg/kg, ip), according to Picard’s method (Picard et al., 2011). Electroclinical seizures were assessed according to an adapted Racine score (from 0 for no sign to 6 for death) every hour for 8 hours. STP (200 to 400 mg/kg, ip) was administrated 30 minutes before MSO. Blood and brain were collected to measure ammonia plasma level and cerebral glycogen level, respectively.

RESULTS

A single dose of MSO induced electroclinical seizures starting from the 4th hour following injection, with a progressive increase of the Racine score (5.5±0.2) and mortality (84%) at the 8th hour. Single administration of 200, 300 and 400 mg/kg STP inhibited MSO-induced seizures with Racine scores of 5.1±0.5, 3.1±0.4 and 1.4±0.6, respectively. Likewise, percentages of death were 70%, 30% and 0%, respectively. Ammonemia was strongly increased by MSO: 763±70 µM in the MSO group versus 183±12 µM in the control group. Compared to the MSO group, STP 300 mg/kg significantly reduced hyperammonemia (448±65 µM), while having no effect in the control group. MSO significantly increased cerebral glycogen level: 3.4±0.6 µg/mg protein versus 1.4±0.1 µg/mg protein in the control group. STP did not affect brain glycogen levels increased by MSO.

CONCLUSION

These results show that STP administration has a potent antiepileptic effect in a mouse model of status epilepticus induced by MSO. Although STP was able to prevent MSO-induced hyper-ammonemia, it did not reverse MSO-induced brain glycogen increased level. Future studies are needed to identify the mechanism of action of STP in this model.

P-09

Epilepsy Seizure Network Model for Pre-Surgical Evaluation

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INTRODUCTION

With nearly 30 - 40% of people with epilepsy be resistant to drug therapies, resecting the hypothesized epileptogenic zone (EZ) through surgery provides an effective way to render seizure-free outcome. Accurate and safe localization and delineation of EZ is a crucial step in pre-surgical evaluation. To achieve this, stereo-electroencephalography (SEEG) has become available in some hospitals, where multiple electrodes (with 25-40 mm recording depth and up to 20 contact points each) are implanted inside the brain and can provide spatial and temporal information. The application of SEEG during pre-surgical evaluation has recently led to the development of epilepsy seizure network, by which the suspicious EZ are modeled as physically distributed areas with complex interactions over time, rather than isolated zones that trigger seizures. Understanding both the spatial and temporal properties of epilepsy network are essential to comprehend the dynamic organization and properties of EZ related to initiation, spread and termination of seizures.

METHODS

The basic concept of epilepsy seizure network model is described as follows. (i) First, using a machine learning method pre-trained on annotated clinical data, a few electrodes and contact points (e.g., 10 contact points from 3 electrodes) are ranked and selected. This selection minimizes expert’s time and effort for visual inspection of signals by providing a list of suspicious EZ sites (spatial information) and relevant justification to aid experts in diagnosis and decision making. (ii) Next, SEEG waveforms from selected contacts are chosen for temporal analysis. To give a comprehensive picture on the temporal origin, onset, propagation and termination of ictal events, it is necessary to combine the time duration before and after ictal periods (e.g., 1-3 minute before/after ictal events). (iii) Finally, the spatial-temporal relationship is modeled as a graph, where the nodes represent spatial distribution of the selected contact points, and edges capture the temporal relationship by their directions (propagation and sequencing) and weights (degree of impact).

RESULTS

As a proof of concept, we have so far analyzed SEEG data of only one subject. 17 out of 20 contact points selected by ML matched clinical annotations. A seizure network graph with 9 nodes and 14 directed edges was constructed. We are now working to verify this graph offers information and/or alternatives to predict the surgical outcome.

CONCLUSION

The seizure network model can be effective in pre-surgical evaluation. First, it confirms or helps to identify the EZ candidate sites by providing accurate spatial-temporal information. Second, assessment of the personalized seizure network allows experts choose the most effective site(s) to disrupt/suppress the seizure and achieve a render seizure-free outcome. While some EZ sites are identified as triggering/onset points, others may contribute to seizure propagation (i.e. the hub nodes in the network model). Third and more importantly, the knowledge captured by seizure network allows

expert to assess the chance of success versus the risk of side effects in such surgeries. For example, if the target sites are too close to areas that impact memory or language control, another zone in the network with a lower risk can be selected for resection.

P-10

Applicability of a screening tool for attention and executive functions (EpiTrack Junior®) in pediatric patients at a specialized epilepsy center

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INTRODUCTION

Cognitive function is more frequently impaired in children and adolescents with epilepsy than in the general population. Specifically, attention and executive functions (EF) are often impaired, as these functions rely on complex networks that are vulnerable to conditions interfering with neural networks, such as epilepsy. Early identification of cognitive dysfunction in children with epilepsy is crucial, as such deficits may have a negative impact on the child’s school performance, social functions, self-esteem and quality of life. In a clinical setting it is not feasible to carry out extensive neuropsychological examinations of all children and adolescents with epilepsy, thus sensitive screening tools are needed. The present study evaluates the applicability of EpiTrack Junior® (EpiTrackJr) as a screening tool for attention and executive functioning in children and adolescents at a specialized epilepsy center.

METHODS

The present paper included 235 patients admitted to the National Centre for Epilepsy at Oslo University Hospital, Norway, between 2017 and 2020. EpiTrackJr was administered as a screening of cognitive function, primarily in relation to planned changes in anti-epileptic drug medication, or as part of a more extensive neuropsychological examination.

RESULTS

Of the 235 patients, 29.3 % had an “average/unimpaired performance”, 23 % had a “mildly impaired performance”, and 47.7 % had a “significantly impaired performance”. A substantial higher percentage of the patients in our sample (70.7%) scored below the 16th percentile compared to the original normative data. There was no difference in EpiTrackJr performance between patients with focal versus generalized epilepsies, nor between different etiologies (structural, genetic or unknown), but patients with an early epilepsy debut (≤ 5 years) performed poorer compared to patients with later debut. Furthermore, there was a statistical significant group difference between the different epilepsy types, where patients with developmental epileptic encephalopathy had the lowest mean EpiTrackJr score. We also found that EpiTrackJr performance was related to AED load, comorbidity and IQ.

CONCLUSION

The majority of pediatric patients in the present study show impaired executive functioning, as measured by the EpiTrackJr. These findings were anticipated, given that our study population mainly consists of children and adolescents with complex epilepsy, which is a population where cognitive impairment is highly frequent. The distribution of overall age-corrected EpiTrackJr score shows a satisfactory spread, indicating that EpiTrackJr does detect variability in this patient population.

Impaired performance was associated with grater AED load, comorbidity and lower IQ. Our results indicate that EpiTrackJr is a sensitive and time-efficient screening tool for attention and executive function in children at a specialized epilepsy center. In the case of impaired scores, a more comprehensive neuropsychological evaluation including patent interviews might be indicated, in order to identify the cognitive difficulties more specifically.

P-11

Therapeutical options in MOGHE (mild malformation of cortical development with oligodendroglial hyperplasia in epilepsy)

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INTRODUCTION

Mild malformation of cortical development with oligodendroglial hyperplasia and epilepsy (MOGHE) is a rare, yet increasingly recognized histopathologic entity in patients with early onset focal epilepsies, poor responding to anti-seizure-medication (ASM), described first by Schurr in 2017. This new entity will be included in the 2022 update of the ILAE classification of FCD (Najm et al. 2022, accepted for publication). MRI in young children affected often show radiological features specific for this entity (Hartlieb et al. 2019), whereas MRI abnormalities of adult patients more often resemble changes associated with FCD IIa (Mendes Coelho et al. 2020). Seizure free rates following epilepsy surgery ranging from 25 – 55% (Mendes Coelho et al. 2020; Gaballa et al. 2021). The detection of somatic SLC35A2 mutations in resected brain tissue of MOGHE patients (Bonduelle et al. 2021; Blümcke et al. 2021), which encodes a UDP-galactose transporter in the Golgi membrane, offers a potential therapeutic option by oral galactose supplementation, following the positive treatment results in SLC35A2 positive CDG syndrome (Dörre et al. 2015; Kimizu et al. 2017). We report on the results of different therapeutical interventions (ASM, epilepsy surgery, nutritional supplementation) in patients with MOGHE, diagnosed at our center.

METHODS

Retrospective analysis of therapeutical interventions (ASM, epilepsy surgery, nutritional supplementation) and results in 45 pediatric MOGHE patients. Response to ASM was reported by parents in terms of a) seizure reduction, b) no effect or c) aggravation of seizures. Postoperative seizure freedom was classified according to Engel`s classification. Response to nutritional supplementation is reported in terms of seizure reduction and cognitive performance following treatment.

RESULTS

1. Medical treatment: all patients had refractory epilepsy. Average ASM per patient prior to surgery was 7.1 (3 - 16). Corticosteroids, VGB, VPA, LEV and OXC showed the best effect.   2. Epilepsy surgery: most common operation (22/45) was subtotal frontal lobe resection, followed by subtotal functional hemispherectomy, lesionectomy, posterior disconnection, multilobar resection and hemisperotomy. In subtotal frontal lobe resection, anterior to middle cingulum was resected in 95% of cases, anterior to middle insula in 59% and suprasylvian pre/postcentral gyrus in 32%, due to extension of the pathology into these cortical areas. 60% of all 45 patients were seizure-free postoperatively (Engel Class 1). In the subgroup of patients, in which the MRI-visible lesion was resected completely (curative approach) 78% (21/27) were seizure-free.   3. Nutritional

supplementation: in 2 patients with ongoing seizures since surgery (Engel 4a/4b) oral galactose supplementation improved cognitive performance in both and autistic behavior and sleep quality in one patient, according to the parental reports. One patient showed gastrointestinal side effects (flatulence / diarrhoea) and allergic skin rash, which did not lead to discontinuation of therapy.

CONCLUSION

Therapeutic options for MOGHE patients include ASM, epilepsy surgery and oral galactose supplementation. In drug-resistant epilepsy, surgical approach is the most successful treatment option, in particular when the lesion is located within the frontal lobe. Whether oral galactose supplementation turns out to be a promising therapeutic option for MOGHE patients (with/without somatic SLC35A2 mutation) needs to be proven in further clinical multi-center trials.

P-12

Vigabatrin-associated brain abnormalities on MRI in patients with tuberous sclerosis complex are asymptomatic and reversible

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INTRODUCTION

The goal of the study is to assess T2- and DWI- MRI changes in the basal ganglia observed in pediatric patients with epilepsy associated with tuberous sclerosis treated with vigabatrin. It has been uncertain whether these lesions should be regarded as pathological and are ADC values of any clinical importance.

METHODS

MRI brain examinations of 54 TSC patients were analyzed. 32 were male (59 %) and 22 female (41 %). Their age varied from 7 weeks to 11 years, median 15 months. All children were treated with vigabatrin. The control group consisted of 10 age-matched children with no known history of neurological disorder or brain MRI pathology. The ADC was measured with a manual placement of regions of interest (ROIs) in the thalami. The signal intensities of the thalami, basal ganglia, midbrain, dorsal brainstem, and dentate nuclei were analyzed visually. ADC values of the thalami were measured and compared with control.

RESULTS

9 patients (17 %) demonstrated at least one focus of abnormal MRI signal, 4 were female and 5 male. In 88 % of patients the lesions were observed in thalami, in 66% in midbrain in 88 % in tegmentum, in 66 % in globi pallidi and 22 % had abnormal signal in dentate nuclei. 2 patients out of 9 (22 %) had lesions in all analyzed regions. We detected no correlation between these lesions and sex, TSC type, VGB dosage, treatment duration or clinical state of patients. ADC values were notably lower in children with DWI/T2WI signal abnormalities therefore seem unlikely to be a variant of physiological development.

CONCLUSION

MRI abnormalities in infants with TSC treated with VGB are relatively common, benign findings. Lesions are most frequently found in the thalami. ADC has proven to be a useful and objective parameter in evaluating these lesions when they are not clearly visible on DWI/T2WI.

P-13

Predicting outcomes in childhood and juvenile absence epilepsy: A retrospective cohort study

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INTRODUCTION

Evidence relating to baseline clinical and EEG predictors of seizure and neurodevelopmental outcome in absence epilepsy is conflicting. We therefore conducted a retrospective cohort study to determine whether baseline clinical or EEG characteristics were associated with seizure remission, number of AEDs and presence of learning difficulties or neurodevelopmental diagnoses at 2 years from diagnosis.

METHODS

Patients with absence epilepsy were identified from records of clinic appointments between January 2015 and December 2019 at the RHCYP, Edinburgh. Clinical features and EEG reports were identified from their initial clinic visit and outcome data collected from records of follow-up appointments at 2 years.

RESULTS

58 patients with absence epilepsy, 40 with CAE and 18 with JAE, were included in the study. At follow-up 70.7% of children had achieved seizure remission, 93.1% were taking AEDs, 8.6% were taking multiple AEDs and 32.8% had documented learning difficulties or a neurodevelopmental diagnosis. Univariate analysis found no significant difference in age at onset, diagnosis, sex, history of febrile seizures, first-degree relative family history or frequency of seizures on baseline EEG between groups for any outcome. A binary logistic regression model including diagnosis, sex, history of febrile seizure, first-degree relative family history and frequency of seizures on EEG for prediction of seizure remission at 2 years was not significant compared to the null model (χ2 (7) = 8.709, p = 0.274). None of these individual factors were predictive of seizure outcome however, patients who exhibited no absences on baseline EEG were less likely to achieve seizure remission at 2 years than those who exhibited 3 or more (OR = 0.072, 95% CI [0.005-0.947]).

CONCLUSION

There is a high prevalence of cognitive and neurodevelopmental comorbidity in patients with absence epilepsy. Seizure frequency at baseline may be a more valuable prognostic indicator than initial diagnosis for predicting long term seizure outcome.

P-14

Therapeutic drug monitoring of Levetiracetam in the Republic of Kosovo

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INTRODUCTION

Through the results obtained from the measurements of plasma levels of Levetiracetam, we aim to obtain accurate data, the interpretation of which can directly affect the current patient adherence and dosage prescription in patients with Levetiracetam. Creating a stable and cost-effective method of detection of Levetiracetam on High-Performance Liquid Chromatography was our priority, given the fact, that there is no direct assay of Levetiracetam provided by either the clinic or the private sector within the country. Moreover, we aimed to evaluate the possible impact of drug interactions at plasma concentrations of Levetiracetam.

METHODS

All the procedures in this study were conducted according to guidelines in the Declaration of Helsinki and the study design was approved by local Ethical Committee (Nr. 586, 10.03.21). For a period of 6 months, 27 epileptic patients who use Levetiracetam from December 2020- to June 2021, were recruited and monitored. After classifying the data 20 patients (75%) of which 10 (50%) were female and 10 male (50%) were selected as suitable for research and monitoring the Css levels. EDTA K3 tubes were used to store the patient’s blood. Mobile phase extraction and separation of LEV from plasma were done through OASIS HLB Cartridges. Sample measurements were performed by High-Performance Liquid Chromatography (Shimadzu Prominence) through the Inertsil ODS-3 column (5µm 150 x 4.6mm LEV). For Levetiracetam detection KH2PO4 and Acetonitrile 91/9 (v/v) with a flow rate of 1.5mL/min. LEV was detected in 4.2 min in wavelength 205 nm. Internal standard used in our study was caffeine and with optimal calibration curve and recovery.

RESULTS

Out of the total number of patients, 23 were detected as adherents (88%), and 4 non-adherent (12 %) with an additional 3 of them excluded due to non-adherent and renal/hepatic problems. Normal plasma levels were detected in 80% of patients, from the 72.7 % of them were seizures free on monotherapy and 22.22 % with add-on therapy-polytherapy. However, the seizure was still present in 27.3 % in monotherapy with 66.7 % normal plasma levels and 77.7 % in polytherapy with 72.42 % normal plasma levels in which the rate number of seizure was higher than during polytherapy. Moreover, the concentration dose-response ratio mcg/L per mg/day was not different between resistant vs sensitive patients in our study, indicating that plasma levels do not have an impact on the seizures incidence or pharmacoresistant.

CONCLUSION

New method of built-in High-Performance Chromatography is reliable, and cost-efficient for transition, and in growing countries like ours is very applicable. We achieved satisfactory results, real plasma levels of patients were detected and measured as we anticipated. The data provided by our study dictated whether patients with seizures were nonadherent or the treatment was not responding to

the selected drug rather than providing levetiracetam as a biomarker for pharmacokinetic pharmacoresistant

P-15

The role of ubiquitin C - terminal hydrolase and protein S100 - B in differentiation of patients with epileptic seizures and psychogenic non-epileptic seizures

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INTRODUCTION

Psychogenic non-epileptic seizures (PNES) are functional neurological disorders or a subtype of conversion disorder where an individual exhibits paroxysmal convulsive and / or behaviour symptomatology with changes of state of consciousness that resemble epileptic seizures but are not associated with changes in cortical activity. Video-EEG monitoring is the gold standard method for differentiating epileptic seizures (ES) from PNES. However, it has the limitations of high cost, low accessibility and long hospitalisation. Laboratory tests may provide a more accessible way in differentiating ES from PNES. Recently there has been increasing interest in the use of different biomarkers to help better understanding underlying mechanism of neurological diseases. Ubiquitin C-terminal hydrolase L1 (UCH - L1) and S100-B are considered as important biomarkers which release following neuronal and glial damages. Various experimental and clinical studies have shown increased serum and cerebrospinal fluid UCHL-1 and S100-B levels in patients with ES.

METHODS

Patients will be included in this study according to the following criteria a) patients with generalised ES and focal ES with evolution to bilateral tonic - clonic seizures and with normal brain MRI (30 patients), b) patients with PNES with normal brain MRI who underwent video - EEG monitoring (30 patients) and control group of 30 healthy controls (healthy individuals without chronic therapy, without psychiatric comorbidities). This study is approved by ethic comity of our hospital.

RESULTS

So far, the study included 20 patients with PNES, of which 15 women and 5 men and 21 patients with epileptic seizures, of which 5 women and 14 men. The average age of patients with PNES is 25 years, and patients with epilepsy 30 years. The average blood sampling time is 1 hour for both PNEN and epileptic seizures. All patients admitted to our Department for video EEG evaluation had previously diagnosed epilepsy (focal seizures with evolution to bilateral tonic – clonic seizures or generalised epilepsy).

CONCLUSION

This study will be conducted in patients with ES and PNES with normal brain MRI, and a venous blood sample will be taken between 30 minutes to 3 hours, and studies with this methods were not published so far. At the moment we have 41 patient included in study from which 20 patients with PNES and 21 with epileptic seizures and median of blood sampling is one hour. Once we conduct our study with all patients and have results of ubiquitin C - terminal hydrolase and protein S100 - B we will be able to compare them and conclude if they could be used as new biomarkers for the diagnosis of PNES.

P-16

A screening pathway for people with epilepsy

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INTRODUCTION

Although there is international consensus that screening for depression in people with epilepsy (PWE) is important, it does not appear to occur universally in clinic settings (1), leaving depression potentially undetected. Depression is associated with suicide, one of the leading but preventable causes of death in PWE. Here we describe the introduction of a standardised questionnaire-based outpatient screening pathway for depression and suicidality in PWE, share a ‘traffic light’ triage system used for psychological support decision-making, and provide results of interval change in questionnaire scores between sequential screenings. We predicted that at re-screening, PWE would have benefitted from psychological support services, as reflected in improvement in scores. Feedback for each support service was collected in relation to engagement and perceived usefulness.

METHODS

From November 2020, PWE receiving care from the NHS Lothian (Scotland) Epilepsy Service were sent the Patient Health Questionnaire (PHQ-9) by post two weeks before outpatient appointments. In the event of no response, an assistant psychologist attempts to carry out screening by telephone. PHQ-9 scores are triaged according to a ‘traffic light’ system and PWE are offered different support services according to the severity of their symptoms (0-4: Green; 5-9: Amber-1; 10-19: Amber-2; >20 or positive for suicidal ideation: Red). Support services were self-help resources (Amber-1), computerised Cognitive-Behavioural Therapy (cCBT) or Epilepsy Scotland (charity delivered) Wellbeing Service , (Amber-2), or Neuropsychology (Red). We re-screened 9-months later. Scores and support plans were shared with consultant neurologists ahead of appointments. We used dependent t-tests for paired samples to assess for change in PHQ-9 scores.

RESULTS

220 of 339 PWE (65%) who attended clinic were screened. 192 (87%) were re-screened. At re-screening, 76 people screened Green (vs 68 at initial screening), 45 screened Amber-1 (vs 51), 45 screened Amber-2 (vs 54) and 26 screened Red (vs 47). PHQ-9 scores were found to significantly decrease among those people who initially screened as Amber-1 (p <.01), Amber-2 (p <.01) and Red (p<.01), while there was a small, but statistically significant increase among those people who screened Green and received no support services (p<.01).Feedback was most positive for Epilepsy Scotland and Neuropsychology, and least positive for cCBT. Main challenges incurred were logistics with mailing and lack of time for attempting telephone screening.

CONCLUSION

Our data confirm the feasibility of carrying out systematic questionnaire-based screening and providing appropriate psychological support, as part of routine outpatient services for PWE. Further, they suggest the need for more than annual screening, as proposed by ILAE. Future mental health screening pathways should consider more time-effective delivery methods (e.g. electronic screening). If our findings are replicated in other settings, then widespread adoption would be encouraged.   This work was funded by the Juliet Bergvist Memorial Fund. “For the purpose of open access, the author has applied a Creative Commons Attribution (CC BY) licence to any Author Accepted Manuscript version arising from this submission.” (1) International League Against Epilepsy (2019). The black dog in your waiting room: Screening for depression in people with epilepsy. Epigraph, 21(4).

P-17

Task-related electrocorticography activity in auditory cortex during music performance

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INTRODUCTION

Music testing is generally not performed in patients undergoing presurgical evaluation for epilepsy. However, it may be relevant in musicians who will undergo resective brain surgery in order to cure epilepsy and preserve musicality. Data from electrocorticography during music performance is sparse and may provide useful insights in the neuroscience of music cognition due to its high temporal resolution. If areas are identified that show specific changes of activities during music performance, it may even be used as diagnostic test to localize brain function that is critical for this task in a same way task-related activity can localize language- and sensorimotor areas.

METHODS

A musician (guitar playing singer-songwriter) with refractory epilepsy underwent invasive presurgical evaluation with subdural grid electrodes (spatial resolution 1 cm) covering right (nondominant) frontotemporoparietal cortex including the pre- and postcentral gyrus (sensorimotor cortex) and posterior part of the superior temporal gyrus (auditory cortex). He performed ‘Here comes the sun’ (The Beatles) in three different conditions: 1) singing while playing guitar accompaniment, 2) instrumental (only guitar accompaniment) and 3) acapella (only singing). Trends of power of electrocorticography activity (frequency band 65-95 Hz) were studied for the electrodes on the superior temporal gyrus during music performance and normal conversation.

RESULTS

Several areas (four electrodes) on the superior temporal gyrus showed changes of power related to music performance and normal conversation. Two adjacent electrodes showed increase of power during singing while playing the guitar, singing acapella and normal conversation and decrease of power during instrumental music performance. There are two electrodes that show increase of power during normal conversation and decrease during all conditions of music performance. Relative to aforementioned area, one of these electrodes is located two centimeters anteriorly and the other electrode is located one centimeter posteriorly.

CONCLUSION

Discrete areas in auditory cortex on the superior temporal gyrus show specific changes of activities during performance of music. Such areas may be important for music processing and critical to music performance which may be especially relevant to musicians. Hence, music performance may be used to identify these areas. These results need to be confirmed in other patients and future research using cortical stimulation and postoperative behavioral music testing should clarify the clinical significance of these findings.

P-18

Continuous EEG: How long time to screen for non-convulsive seizures? Importance of early epileptiform discharges.

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INTRODUCTION

 Continuous EEG (cEEG) is applied in an increasing number of unconscious patients in the neurocritical care unit. A 24-48 h monitoring period is often recommended to demonstrate or exclude non-convulsive seizures (NCSz). This is resource-demanding and the benefit for the patient’s outcome is uncertain. We investigated the delay between early epileptiform discharges (EDs) and subsequent seizure patterns in cEEG. We also assessed the interobserver agreement for EDs and investigated the change in NCSz diagnosis before and after application of the Salzburg criteria. The main purpose was to investigate if the absence of EDs in the first hour of cEEG recording is a reliable predictor of absence of seizure patterns in the subsequent >20h. 1)

METHODS

In a retrospective study, we included 101 consecutive cEEG recordings of more than 20 h duration from 101 patients obtained in 2013-2015. Exclusion criteria were patients with postanoxic or epileptic encephalopaty. The initial four hours of the recordings were analyzed to identify the first ten interictal spikes or other EDs. The recordings were screened for rhythmic patterns fulfilling the Salzburg criteria for seizures. These results were then compared to the original (pre-Salzburg) evaluation of the recordings. Finally, we compared the delay between first occurrence of EDs and seizures.

RESULTS

The clinical data from 98 adult patients were described elsewhere 2), we further included three children. Median age of patients was 64 years (range 1-87 years). Median duration of cEEG monitoring was 39 h (range 21-374 h). In the 59 patients who eventually had seizures, 90 % had their first ED within 10 min, and all, but one recording showed either interictal EDs or seizure within 1 h. The median time to first seizure was 10 minutes and 90% started before 110 min. In the 42 patients without seizures, 42% never showed any EDs. When EDs occurred they did so within 10 min in 83% of recordings, and all but one had EDs within 1h. In the actual cohort, 1 h of cEEG was sufficient to determine if EDs occurred in all, but two EEG recordings (98%) and to detect actual seizures in 88% of those who eventually had seizures. The interobserver agreement on EDs vs no EDs was 87% (Cohen/Conger's Kappa: Substantial: 0.6125). The agreement between original and Salzburg criteria guided diagnosis of seizures was 76% (fair: 0.1621). A benzodiazepine test was performed in 26 patients. The concordance between original and new seizure diagnosis in this subgroup was 73 %.

CONCLUSION

Our findings support that 1 h of EEG is sufficient to decide if further monitoring is required based on occurrence or absence of EDs. Only one patient with seizures (occurring after 7 h) out of 59 patients would have been missed using this approach. 1) Struck AF et al. Association of an electroencephalography-based risk score with seizure probability in hospitalized patients. JAMA

Neurology 2017 December 1, 74 (12): 1419-1424
 2) Holm-Yildiz S et al. Does continuous electroencephalography influence therapeutic decisions in neurocritical care? Acta Neurol Scand. 2021 Mar;143(3):290-297.

P-19

Long-Term Clinical Outcomes and Quality of Life in Children with Rasmussen's Encephalitis

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INTRODUCTION

Rasmussen’s encephalitis (RE) is a rare, progressive epilepsy syndrome characterised by inflammation of one cerebral hemisphere causing pharmacoresistant focal seizures, hemiparesis and cognitive decline. Typically affecting children, treatment aims to reduce seizure burden and therefore long-term effects on neurological development. Some patients are suitable for hemispheric surgery (either disconnective or resective), but this carries the inevitable consequences of contralateral hemiparesis and hemianopia. Due to its rarity and complex neurological deficits, there have been few studies on long-term seizure and functional outcomes and no studies on long-term psychosocial outcomes in adequately sized cohorts to guide management and prognosis. We present the long-term seizure, functional and psychosocial outcomes of children with RE at a single institution.

METHODS

Records of RE patients discussed in the Epilepsy Surgery multidisciplinary team meetings between 1993 and 2018 at Great Ormond Street Hospital were retrospectively reviewed for demographic information and seizure history. Data on long-term seizure, functional and quality-of-life outcomes were collected by telephoning participants and asking them or a parent to complete a questionnaire in 45-minute semi-structured interviews.

RESULTS

The cohort included 32 patients, comprising 26 patients who had undergone epilepsy surgery and 6 who had not. Mean age at data collection was 22.95 years (±9.04) and mean age at seizure onset was 7.01 years (±3.06). Among the surgical cohort, mean age at surgery was 10.62 years (±4.62) and mean time to surgery from seizure onset was 3.59 years (±2.52). Mean length of post-operative follow-up was 12.32 years (IQR = 5.06 – 9.03). No non-surgical patients had experienced seizure freedom since last follow-up. Among surgical patients, seizure freedom was achieved in 84%, 80%, 73% and 55% at 1, 5, 10 and 15 years, respectively. Median time to post-operative seizure recurrence was 36 weeks. Surgical patients took significantly fewer anti-epileptic drugs than non-surgical patients in the long-term (p<0.01). There was no statistically significant difference in age at seizure onset, age at surgery or time to surgery between patients who experienced post-operative seizure freedom and those who did not. Rates of seizure freedom were non-significantly higher in surgical patients who had undergone hemispherotomy compared to other forms of epilepsy surgery and in those with left-sided RE. Surgery was associated with significantly worse upper and lower limb function (both p<0.05), but 96% of patients could ambulate and 62% had normal speech following surgery. Surgery was associated with significantly better quality of life (mean PedsQL score = 100.50 in surgical patients vs. 85.42 in non-surgical patients, p<0.05; mean IPES score = 15.38 in surgical patients vs. 85.42 in non-surgical patients, p<0.05). 63% attended a special needs school and 25% had a psychiatric co-morbidity.

CONCLUSION

We demonstrate high rates of seizure freedom in RE patients after surgery at long follow-up intervals, challenging previous studies suggesting that hemispheric surgery can only be seen as a palliative treatment rather than a cure for seizures in RE. Our results provide valuable information to support shared decision-making with patients and their families considering surgical treatment for RE.

P-20

Beware of nonconvulsive seizures in prolonged disorders of consciousness: long-term EEG monitoring is the key

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INTRODUCTION

The purpose of this study was to the prevalence of epileptic seizures (ES) and epileptiform discharges (EDs) in patients with prolonged disorders of consciousness (DOC), and potential influence of amantadine on epilepsy.

METHODS

We conducted a retrospective study in 34 patients hospitalized in a DOC care unit for prolonged DOC between 2012 and 2018, who received a long-term EEG monitoring (LTM). We reviewed the prevalence of ES, EDs and nonconvulsive seizures (NCSz), the type of DOC recovery treatment administered, and neurological outcome.

RESULTS

LTM was more effective than standard EEGs in detecting EDs (32% vs 21% respectively). Moreover, 12% of the LTM showed NCSz. Among patients with EDs in LTM, 73% showed no EDs in standard EEG recordings, even when performed more than once. The presence of EDs and/or NCSz in LTM was significantly associated with the occurrence of remote clinical epileptic seizures (p=0.017), but did not influence neurological outcome (p=1). Amantadine was not associated with higher occurrence of EDs/NCSz or clinical seizures.

CONCLUSION

In our prolonged DOC population, LTM showed more pathological results (EDs and NCSz) than standard EEGs, which was significantly associated with remote clinical seizures. Therefore, the use of LTM might be advised to rule out NCSz in patients with prolonged DOC.

P-21

Complete callosotomy in children with drop attacks; A retrospective monocentric study

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INTRODUCTION

Introduction : Corpus callosotomy is a palliative neurosurgical treatment for patients with drug-resistant epilepsy and suffering from drop attacks, which are a source of major deterioration in quality of life and can be responsible for severe traumatic injury. The objective of this study is to identify clinical markers that would predict a better outcome in terms of drop attacks and other types of epileptic seizures and to describe more than 20 years of experience with complete callosotomy at the Rothschild Foundation Hospital.

METHODS

Methods: We reviewed a retrospective series of all children who underwent complete corpus callosotomy at our institution, from January 1998 until the end of 2021, and analyzed our series between 1998 and 2019, including all children with a minimum postoperative follow up of 1 year. We studied the neurological and cognitive pre- and postoperative status, the imaging, and the EEG monitoring data.

RESULTS

Results: Sixty-four children underwent a complete callosotomy at our institution, 50 with the required minimum follow-up. In the latter group, mean age at surgery was 7.5 years and median postoperative follow-up was 42.5 months. Concerning drop attacks, 29 (58%) were totally seizure free, and another 13 (26%) had rare events. Statistical correlation analysis between outcome of drop attacks and patient characteristics did not find any trend in terms of age, etiology or developmental level. Regarding the different seizure types, the probability of becoming drop attack-free was significantly higher in children that presented tonic seizures ($p = 0.017$). Transient neurological complications occurred in two patients. A disconnection syndrome was observed in one child with good preoperative cognitive level, which resolved within one week. The mean hospital stay was short (5 -10 days).

CONCLUSION

Conclusions: Callosotomy is a well-tolerated procedure for children with drug-resistant epileptic drop attacks. Aside from a better surgical outcome for children with tonic seizures causing the falls, the lack of any other significant prognostic factor implies that no patient should a priori be excluded from this palliative surgical indication.

P-22

EpiCARE survey on accessibility, availability and common practices of genetic testing for epilepsy across Europe.

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INTRODUCTION

<p style="text-align:justify">The interest in genetic testing in epilepsies is constantly rising. The increasingly rapid pace of advancement may lead to inequalities in technical and human resources and, in certain cases to a downscaling of clinical training in the field. In this view, the European Reference Network for Rare and Complex Epilepsies EpiCARE conducted a survey addressing several aspects of accessibility, availability, costs, and standard practices on genetic testing across European Epilepsy Reference Centers.

METHODS

<p style="text-align:justify">An online Google form was created and sent to 69 representatives of full- or affiliated-members and collaborating centers of EpiCARE during January 2022. SPSS 21.0 was used for statistical analysis.

RESULTS

We received 45 responses (1/center) representing 23 European countries. The majority of the respondents were paediatric neurologists (44,4%), followed by child/adult epileptologists (26,7%) and geneticists (13,3%). Fifty-five percent of the centers have access to all available types of genetic testing (karyotype, specific gene sequencing, Whole Exome Sequencing (WES), Whole Genome Sequencing (WGS), etc.). Thirty-five percent of centers report cost coverage only for some of the available tests, while costs per test vary significantly (i.e., 150 to 3000 euros for epilepsy gene panel or 800 to 6000 euros for WES) across countries. Urgent genetic testing is available in 71,7% of countries, with the time to result varying from 2 days to 2 months. The average time needed for results to be returned to the clinician has a significant variance per test and per country (i.e., 0.5 to 52 months for epilepsy panel or 1.5 to 52 weeks for WGS.) <p style="text-align:justify">Regarding which genetic testing in specific clinical situations the clinicians would choose, the tests selected most frequently were: WES (36,8%) for neurodevelopmental encephalopathy with epilepsy as a secondary feature; epilepsy gene panel for neonatal/infantile epileptic encephalopathy (36%), non-lesional focal epilepsy (38%), electroclinical phenotype suggestive of a specific diagnosis (43%), epilepsy-related to structural/cortical malformations (34.9%), and epilepsy syndromes with an established genetic

heterogeneity (47.8%); no genetic testing (35,5%) for idiopathic generalized epilepsies. There is no association between the country of practice and the first choice of genetic tests in the scenarios proposed.

CONCLUSION

Almost all frequently used genetic tests are accessible in Europe, but WGS is not yet widely available. Availability, in terms of costs and time to deliver the results to the clinician, is highly heterogeneous, even in the setting of an urgent demand. Urgent genetic testing is still not available in around 1/3 of the centers. Regarding choice and prioritization of available genetic tests in common clinical scenarios of everyday practice, there is a considerable variance even among experts with a maximum of 47,8% of agreement rate in the choice per test and scenario, irrespective of the country of practice. <p style="text-align:justify">In conclusion, the harmonization of availability of genetic tests in Europe and guidance for optimal test choices remains essential to avoid diagnostic delays and excess health costs in Genetic Epilepsies. Based on the above results the ERN EpiCARE is working on the development of an algorithm, with the ambition of support both best practices and healthcare policies to be implemented.

P-23

Stereo electroencephalography-guided radiofrequency thermocoagulation treatment in drug resistant epilepsy patients with Periventricular nodular heterotopias: a single center experience.

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INTRODUCTION

Stereo-electroencephalography (SEEG) is an invasive diagnostic procedure for patients with drug-resistant epilepsy (DRE). In selected patients, the diagnostic SEEG- may be converted, during the same admission, into a therapeutic procedure with the aim of radiofrequency thermocoagulation (RFTC) of the epileptogenic zone (EZ) via the already implanted depth electrodes. SEEG-guided RFTC has proven to be a safe method.

METHODS

This study describes a retrospective analyzed cohort of patients with DRE, a follow-up time of at least 12 months after SEEG-guided RFTC and periventricular heterotopias (PNH). The aim is to analyze and describe post-treatment seizure outcome, the 50% responder rate (defined by ³ 50% seizure reduction) and complication rate.

RESULTS

In this study 20 patients with complete follow-up data were included. Patient demographics were as followed: sixteen female, mean age at RFTC 34.2 years (95% CI 28.3-40.0), mean age at onset 18.7 years (95% CI 13.8-23.5), epilepsy duration at RFTC 15.5 years (95% 10.8-20.3), mean seizure frequency (per month) 41.0 (25.4-56.6), mean number of electrodes 14.3 (95% CI 10.8-17.8), mean number RFTC lesions 21.2 (95% CI 12.8-29.7), mean follow-up duration (months) 32.4 (95% CI 23.4-41.4). Location of PNH was parietal N=4, temporal N=2, temporo-occipital N=8, frontoparietal N=2 and temporo-occipital and frontoparietal N=4, and were further grouped in superior (frontal and/or parietal) N=6, inferior (temporal and/or occipital) N=10 and both (superior and inferior) N=4. In 11 patients the PNH was localized unilateral and in 9 bilateral. The number of PNH was expressed as 1 (N=7), 2 (N=2), 3-5 (N=2), 6-10 (N=4), >10 (N=2) and beads (N=3). A total of 10 patients (50%) were seizure free after SEEG-guided RFTC (ILAE 1) and 13 patients (65%) were deemed responders (³50% seizure reduction). Four minor complications (20%) related to RFTC were seen (two patients with mild to moderate visual symptoms and another 2 patients with transient fever after extensive RFTC-lesions in multiple PNH). No major complications were seen.

CONCLUSION

SEEG-guided RFTC is a relatively safe method for treating PNH in DRE patients with promising outcomes, including in patients with multiple and even bilateral PNH's.

P-24

Clinical and Genetic Features of Acute Deterioration with Resulting Neurological Regression in Children with Dravet Syndrome.

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INTRODUCTION

The clinical course of children with Dravet Syndrome is subject to significant variability and current understanding of risk factors for acute neurological deterioration and adverse outcomes is limited. This case series reviews clinical and genetic features of children with Dravet Syndrome with episodes of acute deterioration and resulting neurological regression from 2 tertiary paediatric neurology centres in London.

METHODS

Case notes of children with Dravet syndrome with a history of acute deterioration leading to neurological regression were gathered from 2 tertiary centres in London. Clinical features prior to, during and after their acute deterioration were reviewed including demographics, baseline anti-seizure medication, seizure frequency, seizure duration, rescue medication, neuroimaging and EEG findings. In addition, analysis of each variant within SCN1A using CLINVAR and SCN portal was undertaken including, where applicable, a review of previously reported identical variants. Data was analysed, alongside literature review, to identify ‘risk factors’ predictive of acute deteriorations and resulting neurological regression.

RESULTS

18 children were identified. 17/18 had an episode of status epilepticus; 2/17 had a cardiac arrest during status epilepticus and survived whilst 4/16 had a cardiac arrest and died. One patient had sepsis without status epilepticus leading to sustained regression. All 18 patients had SCN1A variants located in functional locations/domains within Nav1.1 . On initial analysis, no variables were predictive of an acute decompensation and persisting neurological regression.

CONCLUSION

This case series demonstrated no patient characteristics, including SCN1A variants, associated with episodes of acute deterioration and neurologic regression to further inform the management or prognosis for children with Dravet Syndrome. Further analysis is ongoing including comparison to children with Dravet syndrome without acute neurological deterioration.

P-25

Epilepsy and seizure related mortality in a tertiary care hospital in Riyadh

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INTRODUCTION

People with epilepsy (PWE) are more prone to premature death from various causes compared to general population. A study showed that mortality rate in individuals with epilepsy are up to 11-folds higher than the non-epileptic matched control. However, epilepsy related mortality was not studied in Saudi Arabia. The aim of this study is to estimate the frequency of epilepsy-related mortality and the causes of death in PWE.

METHODS

All PWE who expired in the period 2016 through 2021 in King Abdulaziz Medical City –Riyadh were included. Demographic data, comorbidities, epilepsy and seizure classification, and cause of death were gathered from the patients’ electronic medical records including death certificates. We used the classification suggested by Devinsky to classify epilepsy related death[.]

RESULTS

We found 128 PWE who expired during the study period. The age mean was 63.5 years with a standard deviation of 19.07. Around half of them were females (50.78%). Five (3.91%) deaths were directly related to epilepsy and all of them were caused by status epilepticus. Forty-nine (38.28%) deaths were indirectly related to epilepsy. Deaths due to acute symptomatic seizures happened in 7 (5.47%) cases and deaths due to underlying neurological disease were observed in 14 (10.94%) cases. Deaths that were not related to epilepsy or seizures were observed in 53 (41.41%) cases. We did not find any death that was attributed to sudden unexpected death in epilepsy (SUDEP).

CONCLUSION

Status epilepticus is the most common cause of deaths that are directly due to epilepsy. The absence of SUDEP cases may be related to the small sample size or referral bias. However, SUDEP as a cause of death had never been considered as possible cause of death by the treating physicians which may indicate a need for increasing awareness about SUDEP among physicians particularly in emergency department.

P-26

Strategies for Pediatric Epilepsy Surgery in Type II FCD

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INTRODUCTION

Epilepsy associated with Type II Focal Cortical Dysplasia (FCD II) constitute a common condition in Pediatric Epilepsy Surgery (ES) practice. We evaluate presurgical and surgical strategies driven to achieve the best possible seizure and neuropsychological outcomes in cases with “small/medium size” FCD II (involving a limited part of one or two gyri/sulci), paying particular attention to the management of “MRI-negative” and “eloquent-area” cases.

METHODS

We revised methodological approaches for presurgical electro-anatomo-clinical definition of the epileptogenic zone (EZ), surgical procedures and post-surgical outcomes, in a series of 53 consecutive patients with this kind of FCD II, most of them classified as bottom-of-sulcus-dysplasia (BOSD), operated on and followed-up in our center between 2010-2022. Comprehensive presurgical evaluation included: 1) “ad hoc” 10-10 system electrode regional arrangements, 2) 3T MRI, FDG-PET, PET-RM fusion, DTI tractography and fMRI if collaborative, 3) longitudinal neuropsychological / neurodevelopmental assessment, 4) invasive evaluation in 32 cases. Surgery consisted of direct lesionectomy or tailored resection of the lesion supported by invasive evaluation, including intaoperative multimodal neurophysiological monitoring in 17 cases. A preliminary analysis of demographic, clinical, neurophysiological, neuroimaging and neuropsychological variables was accomplished.

RESULTS

Median age at seizure onset was 3,9 years (range 0,1-17), median age for epilepsy surgery was 7,5 years (0,5-18), median duration of epilepsy before surgery was 3,4 years (range 0,1-16,4), median postsurgical follow-up was 4 years (range 0,5-12 years). Topographical FCD distribution included: 26 left / 27 right hemisphere lesions, 41(77,3%) frontal, 6 (11,3%) parietal, 3(5,7%) occipital, 3(5,7%) insular/opercular. Relevant results included: 1) Distinctive electro-clinical localized findings, typical epilepsy course and normal neurodevelopment/ intellectual/ neurological status before seizure onset were noted in most cases; 2) Refined individualized neuroimaging approach (mainly PET-MRI fusion interpretation based on video-EEG findings) uncovered small FCD (mostly subtle BOSD) in 29(54%) patients, initially considered “MRI-negative”, 3) Integration of fMR/Tractography and evaluation with intracranial electrodes (mostly depth electrodes) improved resection of the EZ in patients previously considered “difficult” or “poor” candidates for ES, because of unclear/ non-congruent non-invasive findings in 8(15%) or risk of postsurgical motor or language neurological deficit in 24(45,3%); 4) Postsurgical seizure outcome at last follow-up was excellent (seizure free status) in 46(86,8%) cases, good (seizure reduction >90%) in 5(18%), and moderate (seizure reduction>75%) in 2 (3,8%); 5) Postsurgical neuropsychological follow-up showed significant improvement of the median IQ in

respect to presurgical evaluation (91 versus 85), including significant IQ improvement in 12(22,6%) cases, and IQ decline only in one (1,88%).

CONCLUSION

Comprehensive non-invasive multimodal evaluation focused on a refined integration of neurophysiological and structural/functional neuroimaging findings and invasive evaluation in selected “MRI-negative” and “eloquent-area” cases are useful strategies for early and safe epilepsy surgery and favorable neuropsychological outcome in pediatric patients with focal epilepsy associated with “small/medium size” FCD II.

P-27

SCN1A-related developmental and epileptic encephalopathy: First Tunisian experience on Panel sequencing diagnoses two cases

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INTRODUCTION

SCN1A is one of the most common developmental and epileptic encephalopathy (DEE) genes. About 80% of SCN1A gene mutations cause Dravet syndrome. However, with the advent of the new generations of exome sequencing (NGS), other DEE phenotypes are also due to SCN1A mutation. This work aims to describe our first results of the DEE Panel gene sequencing.

METHODS

It is a longitudinal study conducted in the Child Neurology Department of Sfax, Tunisia from 2008 up to now for the genetic diagnosis of DEE (SEED project). The genetic etiology was suspected when the cerebral MRI and the metabolic screening were normal (lactate, pyruvate, blood, and urine chromatography of amino acids and organic acid). A series of 21 unrelated Tunisian patients with different clinical phenotypes of DEE were explored by high-throughput sequencing on a Miseq (Illumina). Sequencing of a panel of 120 genes most involved in DEE using Agilent's Haloplex technology was performed for all our patients.

RESULTS

From 21 patients explored by a panel of 120 genes, we identified two patients with SCN1A pathogenic variants. The first patient is a 4 years old girl with recurrent focal clonic febrile seizures at 38.5°C since the age of 4 months followed at the age of 14 months, by focal afebrile clonic seizures. The neurological evaluation revealed normal motor examination and language delay. EEG and cerebral MRI were normal. The diagnosis of Dravet syndrome was made. The second patient is a 17 years old boy with always normal pregnancy and delivery but he had a cognitive delay from the start. His epilepsy started at the age of 6 months with focal febrile and afebrile seizure (tonic or clonic) occurring sometimes in status epilepticus. He had no other seizure types. He has normal background rhythm with rare right and left spikes in the EEG, and normal cerebral MRI. The diagnosis of Dravet-like syndrome was made.

CONCLUSIONS

SCN1A was a major gene in the exploration of genetic DEE. Mutations in the SCN1A gene are associated with several epilepsy syndromes, ranging from genetic epilepsy with febrile seizures plus

(GEFS) to the severe infantile-onset epilepsy, Dravet syndrome and other DEE phenotypes. The identification of a SCN1A variant not only confirms a clinical suspicion but allows an adapted therapy, an eviction of the aggravating drugs especially for non- classic phenotypes

P-28

First report of Tunisian patients with CDKL5-related encephalopathy

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INTRODUCTION

Mutations in the cyclin-dependent kinase-like 5 gene (CDKL5) are associated with a wide spectrum of clinical presentations. Early-onset epileptic encephalopathy (EOEE) (1) is the most recognized phenotype. Here we describe phenotypic features in 7 Tunisian patients with CDKL5-related encephalopathy.

METHODS

We included all cases with clinical features consistent with CDKL5-related EOEE: epileptic spasm, acquired microcephaly, autism spectrum disorders, movement disorders and visual impairment. We collected data about seizure types, electroencephalogram (EEG), magnetic resonance imaging (MRI), and metabolic analysis (lactic acid, pyruvate, Ammonia, blood and urine amino acid and organic acid). The diagnosis of CDKL5 mutation was made thanks to Sanger sequencing using ABI PRISM 3100-Avant automated DNA sequencer and a Big Dye Terminator Cycle Sequencing Reaction Kit v1.

RESULTS

We collected 7 patients with DEE with confirmed mutation on CDKL5 gene. They were 4 boys and 3 girls aged meanly 10-years-old. Overall, we identified 4 de novo CDKL5 mutations in our 7 patients including three Frameshift mutations and one missense mutation at a mosaic state in 3 boys and a heterozygote state in 1 girl. Out of 7 cases, 4 exhibited two stages epileptic course while epilepsy in the 3 remaining patients progressed on three stages. The mean age at first seizure onset was 3,6 months. The first seizure type was infantile spasm (3/7) with hypsarrythmia on EEG followed by tonic (2/7) and myoclonic seizures (2/7). Regarding development, most cases (5/7) had psychomotor retardation from the start whilst the two others showed psychomotor regression with the onset of seizures. Later, only 2 out of our 7 cases acquired global motor milestones with less improvement in communication skills. Additional clinical features included acquired microcephaly (5/7), dysmorphism (4/7), visual impairment (7/7), hearing loss (2/7), tone abnormalities (6/7), stereotypies (6/7), and movement disorders (3/7). Brain MRI was more often normal (4/7) and showed frontotemporal atrophy in 3 cases and thin corpus callosum in 2 cases.

CONCLUSIONS

Our present report delineates an unusual phenotype of CDKL5-related EOEE mutation with male gender predominance and delayed onset epilepsy. It interestingly described new phenotypic features such as hearing loss, peculiar dysmorphic traits, uncommon benign developmental profiles in boys carrying CDKL5 mutation, different patterns of CDKL5-epilepsy, neuroimaging findings and CDKL5 mutational spectrum. Although some patients showed common clinical features, they seemed to

have heterogeneous seizure types, epilepsy, and developmental course. These findings are in agreement with literature data where no phenotype-genotype correlation was found (2–4).

P-29

The Long-Term Effects of Fenfluramine on European Patients With Dravet Syndrome and Their Families: A Qualitative Analysis

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INTRODUCTION

Clinical trial data indicate that fenfluramine (FFA) provides meaningful reductions in seizure frequency and improvements in executive function for individuals with Dravet syndrome (DS). This study sought to assess how FFA treatment affects quality of life (QOL) of individuals with DS and their families.

METHODS

Study participants were European parents caring for a child with DS. Caregivers participated in one-on-one semi-structured interviews and were asked (on a 7-point Likert scale) whether they noticed changes in a number of their child's seizure- and non-seizure-related QOL domains after starting FFA treatment; they were also asked about benefits of FFA treatment to their own lives and the family unit.

RESULTS

The study concluded in March 2022, with 25 parent/caregivers participating. Average participant age was 47.1yrs, and 16 participants (64%) were women. Among the participants' children with DS, average age and number of months on FFA were 11.7yrs (range, 3.0-23.6yrs) and 22.4 months (range, 4.7-55.7), respectively. Caregivers reported improvements after FFA treatment in both seizure-related (ie, reductions in seizure activity, seizure triggers, and post-ictal recovery times, and improved post-seizure function) and non-seizure-related (ie, cognition, focus, alertness, speech, academic performance, behavior, sleep, motor function) QOL domains. Caregivers also reported that they had better mood and more time for things they enjoyed, felt less overwhelmed, and had better sleep quality and less personal and family stress. Most caregivers (96%) said they would “very” or “quite” likely recommend FFA to others with DS.

CONCLUSIONS

Parents with a child with DS reported many seizure- and non-seizure-related FFA treatment benefits for their child, themselves, and their family. Many reported feeling hope for the first time since the child was born or diagnosed with DS. Funding: Zogenix (now a part of UCB)

P-30

Adults With Lennox-Gastaut Syndrome Have Improved Everyday Executive Functioning With Fenfluramine (Fintepla®)

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INTRODUCTION

Most adults with Lennox-Gastaut syndrome (LGS) experience profound intellectual disability, often leading to institutionalization. Patients with LGS aged 5-18 years showed improvement in everyday executive function (EF) after 14 weeks of fenfluramine treatment, but the impact on patients initiating treatment in adulthood needs to be evaluated. Here, we evaluate EF in adults with LGS after treatment with fenfluramine in a 14-week randomized clinical trial.

METHODS

Adult patients with LGS received placebo or fenfluramine (0.2 or 0.7mg/kg/day) for 14 weeks. EF was evaluated at baseline and Week 14 for patients aged 19-35 years with the Behavior Rating Inventory of Executive Function®—Adult Version (BRIEF®-A: Behavioral Regulation Index, BRI; Metacognition Index, MI; Global Executive Composite, GEC). The threshold for clinically meaningful improvement in BRIEF®-A indexes/composite T-scores from baseline to Week 14 was defined as a Reliable Change Index (RCI) of ≥95% certainty; worsening was defined by RCI ≥80%. Clinically meaningful change was evaluated using Somers' D ($p \leq 0.05$).

RESULTS

Data were analyzed for 57 adult patients (placebo, n=23; fenfluramine, n=34; median age, 23 years; 63% male). Median baseline T-scores were clinically elevated across treatment groups (T≥65) for 44% of patients in BRI, 61% in MI, and 60% in GEC. Clinically meaningful improvement at RCI≥95% certainty was observed in BRI (placebo: 1/23, 4.3%; fenfluramine: 8/34, 23.5%; p=0.024), MI (placebo: 1/23, 4.3%; fenfluramine: 9/34, 26.5%; p=0.012), and GEC (placebo: 2/23, 8.7%; fenfluramine: 11/34, 32.4%; p=0.018). No significant or clinically meaningful worsening was observed in any index at RCI≥80%.

CONCLUSIONS

Adults with LGS and a high degree of baseline EF impairment showed improvements in EF over a relatively short, 14-week treatment duration. These data suggest that treatment with fenfluramine, even late in neurodevelopment, confers benefits in EF. Further investigation is warranted to determine the longer-term treatment impact of fenfluramine on EF in LGS. Funding: Zogenix (now a part of UCB)

P-31

Unusual seizure trigger: Seizure triggered by eating

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INTRODUCTION

Reflex seizure is seizure triggered by specific afferent stimuli or specific activity. Reflex epilepsy is a syndrome where epileptic seizure is triggered regularly by somatosensory, visceral, visual, auditory, gustatory, olfactory, or cognitive stimuli. Eating epilepsy is a rare form of reflex epilepsy with prevalence of 0.1-0.05% in epileptic population. Purpose: - The purpose of this case series is to report unusual food triggering epileptic seizure.

METHODS

We report 4 cases of different food trigger epileptic seizure in patients with focal epilepsy from an epilepsy unit of King Abdulla Medical City in Makkah

RESULTS

All four cases had seizure triggered by specific type of food together with other non-specific trigger like lack of sleep. 2 cases had their seizure triggered by eating banana, one with eating specific type of noodles and one patient has seizure triggered by lemon. All patients developed cluster of seizures on the day they ate the specific food. All of the four cases had focal epilepsy. Three cases with temporal lobe seizure and one had a frontal lobe epilepsy. All are refractory epilepsy on multiple medications.

CONCLUSIONS

Eating is a rare under-recognized seizure trigger. Recognizing the specific type of trigger has important role in managements. Hence avoiding the specific trigger will help in better seizure control among those patients.

P-32

Pseudorefractory epilepsy in specialized childhood epilepsy center

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INTRODUCTION

Pseudorefractory epilepsy is defined as the epilepsies in which seizures persist due to inappropriate diagnosis, inappropriate treatment, poor adherence to treatment, or associated comorbidities. It is postulated that this phenomenon occurs in approximately 20% of the patients diagnosed with refractory epilepsy (RE). This study aimed to determine the prevalence of pseudo refractory epilepsy in a Chilean specialized childhood epilepsy center and characterize its population.

METHODS

This is a retrospective observational cohort study. The sample was obtained from patients who presented an RE diagnosis at their admission and were subsequently seizure free from March 2019 to October 2020.

RESULTS

Of the total number of patients controlled in the clinic (811 patients), 117 patients were derived with a probable diagnosis of RE, and 26 patients met the criteria for pseudorefractory (22.22%) classification. Of these 26 patients, 13 were women and 13 men. The pseudorefractory patients corresponded to: 6 non-epileptic paroxysmal disorders, 7 presented an inadequate syndromic diagnosis of epilepsy, 6 used an inadequate antiepileptic treatment for their syndrome, 6 presented indications for curative surgery and only 1 patient presented a paradoxical reaction to a well-chosen antiepileptic, which was resolved by changing this drug. From the total of 26, 7 patients presented psychiatric comorbidity and 4 with mood disorders.

CONCLUSIONS

We would like to highlight that almost a quarter of the patients who were derived to a specialized childhood epilepsy center with probably RE, had pseudo refractory epilepsy and became seizure free once their cause was evidenced. The majority of these patients had a wrong epileptic syndrome diagnosis, resulting in inadequate treatment or not corresponding to the definition of epilepsy.

P-33

Concentration analysis of commercial and artisanal CBD products given as treatment for pediatric refractory epilepsy in Chilean population

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INTRODUCTION

Cannabidiol (CBD) and trans-Δ-9-tetrahydrocannabinol are the known phytocannabinoids with physiological and psychotogenic effects. CBD, the non-toxic compound, has proven antiseizure effects, mainly through binding to endogenous cannabinoid receptors, CB1 and CB2. THC is responsible for the psychoactive and neurotoxic effects. So, according to EU law, CBD products must not contain more than 0.2% THC. Since 2018, it has been established, through Class I evidence, that the pure form of CBD is a therapeutic option for certain types of epilepsy syndromes such as Dravet syndrome, Lennox Gastaut syndrome and Tuberous Sclerosis complex epilepsy. Unfortunately, the misconception that CBD products are “natural and non-harmful" has led to uninformed physicians prescribing and promoting parents with refractory and non-refractory epileptic children to buy non-certified products, sold as “pure CBD”, or manufacture their own CBD oil as antiseizure medication, without knowing the exact compounds and CBD/THC concentration, risking the well-known short and long adverse effects it can have. This study aims to analyze the composition of CBD products that were either home-made or commercially sold as “pure CBD” and used in pediatric patients as antiseizure treatment. All products were voluntarily given by parents for its analysis

METHODS

An open invitation for a free of charge analysis of CBD oil being given to pediatric patients with epilepsy as antiseizure treatment was sent. The analysis of the samples was performed using the High-Resolution Liquid Chromatography (HPLC) methodology, capable of accurately determining the amount of CBD, d9-THC and CBN present in the preparations. Previous analytical validation was carried out according to the FDA’s Handbook of Analytical Validation’s recommendations to determine sensitivity, limit of detection and quantification. The method’s accuracy and precision were certified with pure standards of CBD, d9-THC and CBN. Samples were divided in 3 groups: licensed commercial samples (LCS), non-licensed commercial samples (NLCS) and homemade artisanal samples (HMS). Hemp plant strain and type of oil used as solvent was registered when it was available in HMS. LCPS and NLCS results were contrasted with what was reported in the product's brochure.

RESULTS

Between March 2020 and September 2021, 35 samples were collected: 2 LCS, 6 NLCS and 27 HMS. None of the samples had the declared concentration of CBD (100mg/ml). LCS oils were pure: high concentration of CBD and THC was acceptable (average: CBD 89,15mg /ml /THC 0,015). NLS’s had low levels of CBD and unacceptable levels of THC, but much lower in comparison with HMS. HMS showed much higher and highly variable concentrations of THC, with an average and range of CBD 1,83(0 – 6,6)/16,03 (0- 388mg/ml).

CONCLUSIONS

The medical community must be well informed and make the population realize that Hemp products are not pure and/or innocuous. HMSs are likely to have high levels of THC and very low CBD, far away from therapeutic doses of CBD. CBD used in epilepsy should be restricted to licensed products, especially in children where THC toxicity is greater.