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ABSTRACTS

REFRACTORY STATUS EPILEPTICUS – A CASE REPORT OF A PATIENT WITH FIRES

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Febrile infection-related epilepsy syndrome (FIRES) is a very rare syndrome manifested by newly developed refractory status epilepticus during febrile illness in children without previous neurological disease and without a proven acute nervous system infection, structural, toxic, or metabolic disorder. Fever may begin 24 hours to 14 days before status epilepticus, but may not be present at the time of onset. This paper presents a case of a previously healthy five-and-a-half-year-old boy who was hospitalized for recurrent seizures and disorder of consciousness. The symptoms were preceded by a febrile state that had started three days before, and at the time of hospitalization he was afebrile. Due to the rapid development of refractory status epilepticus, the patient was treated in the Intensive Care Unit. The seizures were focal with secondary generalization, as well as refractory to anticonvulsant drugs, and between seizures the boy did not regain consciousness. He was intubated and mechanically ventilated with a continuous infusion of midazolam, then thiopental. Extensive diagnostic processing was performed, which did not clarify the etiology of epilepsy syndrome; no acute central nervous system infections, structural abnormalities, traumatic brain injury, hypoxic-ischemic stroke, metabolic disorders, intoxications, autoimmune or paraneoplastic encephalomyelitis were identified. He was treated with acyclovir, ceftriaxone, azithromycin, then immunotherapy (pulse dosing of methylprednisolone, therapeutic plasmapheresis, intravenous immunoglobulins, anakinra). A ketogenic diet and antiepileptic drugs (levetiracetam, clobazam, lacosamide, topiramate, phenobaribital) were gradually introduced. Magnetic resonance imaging of the brain showed progression of bilateral periventricular lesions of the white matter, and serpiginous hyperintensities of the signal along the corticomedullary border began to gradually regress. Subsequent examination of literature revealed that the described radiological changes may correspond to encephalopathy within FIRES. Control of epileptic seizures was gradually achieved after the applied treatment, however, severe psychomotor impairment remained. After long-term multidisciplinary care, there was an almost complete recovery of cognitive functions, speech, and social interaction.

EPILEPTIC SEIZURE OR MOVEMENT DISORDER?

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Epileptic seizure represents a transient period of motor or/and non-motor symptoms due to abnormally excessive or synchronous neuronal activity in the brain. Movement disorders are characterized by abnormal increased or decreased voluntary or involuntary activity including hyperkinetic disorders (chorea, dystonia, myoclonus, tremor, tic, ataxia) or hypokinetic disorder of parkinsonism. Clinical picture of epileptic seizure can resemble different movement disorders, especially myoclonus and different paroxysmal movement disorders including kinesigenic and non-kinesigenic dyskinesias and episodic ataxias. Diagnostic algorithm in differentiating epileptic seizure from movement disorder includes obtaining family and patient's history data, defining specific clinical syndrome and detailed evaluation of attacks. Further diagnostic approach is excluding symptomatic etiology of attacks such as metabolic, structural, autoimmune or other disorders. We will present three cases of patients with long-time history of epilepsy in whom later detailed clinical and diagnostic evaluation revealed that the attacks were part of a specific movement disorder.

EPIPREHRANA PROJECT

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The EpiPrehrana (EpiDiet) project has been launched by the Dravet Syndrome Croatia Society gathering parents/carers of children/adults affected with Dravet syndrome. The project has been launched in partnership with the Croatian Association for Epilepsy and in cooperation with the Referral Centre for Childhood Epilepsy and Convulsive Disorders, Division of Child Neurology and Child Psychiatry, Department of Pediatrics, Rijeka University Hospital Centre and Matthew's Friends from the UK. The aim of the project is to facilitate implementation of ketogenic diet as a successful method of treatment of refractory epilepsy in the Republic of Croatia. Ketogenic diets have been used in clinical practice for 100 years now, and their effectiveness has been proven in many prospective and randomized clinical trials. The main goals of the project are to raise awareness of health professionals, patients and their families, and public at large of the importance of this diet and its therapeutic effects in patients with refractory epilepsy and neurometabolic diseases, as well as to provide education on ketogenic diet and its variants and specifics of diet in patients with refractory epilepsy in the previously mentioned groups. Following the project team's goals and activities, diet counseling has been organized for patients with refractory epilepsy. The team consists of a nutritionist and physicians. The purpose of counseling is to provide patients with the possibility of alternative treatment, i.e. ketogenic diets under supervision of the expert team and in cooperation with attending physicians, which can ultimately lead to better seizure control and improve the patient quality of life.

EPILEPSY IN PRETERM INFANTS WITH WHITE MATTER INJURY

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The aim was to evaluate the relationship between neonatal epileptic seizures and epilepsy, and signal-intensity visibility of the frontal and parietal periventricular crossroads of pathways on brain magnetic resonance imaging (MRI) in preterm infants at term-equivalent age. The study enrolled 64 preterm infants born between 2012 and 2016. The signal-intensity characteristics of the frontal and parietal periventricular crossroads were evaluated and classified into four grades. Unfavorable outcome was defined as a motor and functional disorder with developmental delay and/or cerebral palsy. Neonatal seizures, pathologic electroencephalogram and brain MRI abnormalities were mostly found in neonates with non-favorable outcomes. Visibility of the frontal and parietal periventricular crossroads was associated with a lack of neonatal epileptic seizures (p=0.03; p=0.02). Not-visible or slightly visible periventricular crossroads were associated with non-favorable outcomes in the case of both frontal and parietal crossroads (p=0.001; p=0.015). In conclusion, poor visibility of the frontal and parietal crossroads of pathways on MRI is associated with neonatal epileptic seizures and poor neurological outcomes in preterm infants at term-equivalent age.

DOES CONTINUOUS EEG MONITORING ENABLE BETTER OUTCOME IN CRITICALLY ILL PATIENTS WITH ALTERED CONSCIOUSNESS?

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Electroencephalography (EEG) is a noninvasive diagnostic procedure that can investigate cerebral activity in real time, easily recorded at bedside. It allows identification of subclinical epileptic seizures and status epilepticus in intensive care unit (ICU) patients, identifies cerebral ischemia following subarachnoid hemorrhage, as well as treatment adjustment under general anesthesia, and is part of prognostication after cardiac arrest. Continuous EEG monitoring detects ictal and interictal abnormalities more efficiently than routine EEG. It is recommended as a diagnostic procedure by the European Society of Intensive Care Medicine and American Clinical Neurophysiology Society for critically ill patients with altered consciousness. However, the lack of human and technical resources makes this method still insufficiently available in the ICUs. Given these shortcomings, many researchers have tried to determine whether there is a statistically significant difference in the outcome of treatment of critical patients with altered consciousness whose brain activity was monitored by continuous EEG compared to those in whom routine EEG was frequently recorded.

CLINICAL CHARACTERISTICS OF PATIENTS WITH EPILEPSY CORRELATED TO THE LEVEL OF PHYSICAL ACTIVITY – THE FIRST INSIGHTS (EPICRO)

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Epilepsy is a chronic neurological disease that affects 1% of the general population. People with epilepsy often have comorbidities such as cognitive and psychological problems but also social difficulties. Although it is well known that physical activity (PA) has a protective effect on most chronic non-communicable diseases, people with epilepsy have, for protective reasons, often been discouraged from playing sports. Primarily for fear that sporting activity may cause injuries in case they get an epileptic seizure while playing sports. In 2016, the International League Against Epilepsy published a consensus paper that recommends "safe sports activity". We conducted a prospective, cross-sectional study on 280 patients, where, in addition to clinical characteristics of epilepsy, we examined the level of PA using a validated instrument (International Physical Activity Questionnaire-Short Form (IPAQ-SF), Croatian version). All patients were adults diagnosed with epilepsy and they signed informed consent to participate in the study. Inclusion criteria were met by 279 respondents of whom 270 answered all questions correctly. The study involved 131 male and 139 female respondents, average age 41 years. There was a statistically significant difference between the groups of patients with low PA intensity and groups with moderate and high PA intensity according to clinical outcome of the disease (number of epileptic seizures related to the number of years from diagnosis). In the group of patients with epilepsy and high-level PA, a mean of 0.4 epileptic seizures *per* year were recorded as compared to the mean of 1.8 epileptic seizures *per* year recorded in the group with epilepsy and low-intensity PA. In conclusion, these results support our hypothesis on a positive effect of PA on the clinical manifestation of the disease. However, more comprehensive results and firm conclusion require investigation in a larger sample of respondents and inclusion of confounding factors such as anthropometric measures, effect of antiepileptic therapy, etiology of the disease, and age structure of the study group.

FULMINANT ACUTE CEREBELLITIS – A RARE INFLAMMATORY DISEASE WITH SEVERE COMPLICATIONS, OBSTRUCTIVE HYDROCEPHALUS, ENCEPHALITIS, AND STATUS EPILEPTICUS

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Fulminant acute cerebellitis is a rare inflammatory disease with a high risk of mortality and morbidity. Complications of the disease are due to acute edema of the cerebellum, which causes compression on the structures of posterior fossa and brain stem and leads to development of obstructive hydrocephalus, intracranial hypertension with disturbance of consciousness, status epilepticus, and fatal outcome due to cerebellar tonsillar herniation. Children usually have serious generalized symptoms with nausea, headache, disturbance of consciousness, often without cerebellar signs. There is pleocytosis in the cerebrospinal fluid, while neuroimaging shows significant cerebellar atrophy in progress. If the treatment is not urgent, fatal outcome is almost inevitable. In the majority of cases, the etiology remains unknown, being postinfectious in one-third of cases (rotavirus, Epstein-Barr virus, coxsackievirus B3 or *respiratory syncytial virus*). For now, there is no pediatric consensus about diagnostic and therapeutic algorithm. In this case report, we present a previously healthy 5-year-old girl with fulminant acute cerebellitis. She presented with acute dyskinesias, ataxia, irritability, vomiting, mutism, and progressive disturbance of consciousness to coma within 12 hours of admission. Neuroimaging showed generalized edema of the cerebellum with rapid development of obstructive hydrocephalus which needed to be drained, and encephalitis with development of seizures and epileptic status. The girl was intubated and administered antiepileptic drugs and other supportive therapy. She was treated with acyclovir, ceftriaxone, immunomodulatory therapy (IVIG), and corticosteroids. After 12 days, radiologic finding progressed, however, without significant deterioration of neurological status. After 45 days, she was discharged without change in the neurological status and stationary medical rehabilitation was started. In conclusion, the diagnosis of fulminant acute cerebellitis is very hard to establish because there is a lack of cerebellar signs and the possibility of a broad differential diagnosis. Considering rapid progression of the clinical picture, which can lead to fatal outcome, urgent therapy is necessary.

RESPONSES OF PEOPLE WITH EPILEPSY TO THE COVID-19 PANDEMIC IN THE TIME OF NATIONAL LOCKDOWN

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The aim of our study was to gather information on how people with epilepsy (PwE) responded to the COVID-19 pandemic during national lockdown in the first wave of COVID-19. An online questionnaire was therefore offered to visitors of the Croatian Association for Epilepsy website from April 24, 2020 until May 10, 2020. The 22-item questionnaire was designed to acquire information from adults with epilepsy living in Croatia on demographic data, cognitive, emotional and behavioral responses to the pandemic, and communication problems between patients and their neurologists during the lockdown. Perceived anxiety and fears were expressed with the Likert scale (1-5) and the results of specific fears added to make the Total Fear Score. Out of 186 respondents, only 2.8% did not comply with the lockdown measures, and all of those respondents stated that they did not feel any anxiety related to COVID-19. A canceled neurologist examination during the lockdown was significantly associated with pandemic-related anxiety (2.9±1.28 *vs*. 2.3±1.19, p=0.001) and fears (Total Fear Score 31.4±9.70 *vs*. 28.4±9.79, p=0.036), and 87.4% of respondents expressed the wish to communicate with their neurologist, either by phone/video call (53.0%) or e-mail (34.4%). In conclusion, the results of our survey showed that responses from PwE point to social responsibility appropriate for the existing situation. During future pandemics, telemedicine could have an important role in tackling the fears and anxieties caused by cancelation of examinations, which corresponds to the wishes expressed by the great majority of our respondents.

GENETICS OF EPILEPSY AND EPILEPTIC SYNDROMES – CHALLENGES IN CLINICAL PRACTICE

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In the last two decades, genetic etiology has been identified in over half of all epilepsies, and single gene defects in ion channels or neurotransmitter receptors have been associated with most inherited forms of epilepsy, as well as epileptic encephalopathies. This has led to new insights, describing further the clinical phenotype in these epilepsies. Using these additional clinical data, it may be possible to diagnose patients earlier. We describe two girls with epilepsy and unexpected genetic findings, after years of follow-up. One girl had early developmental delay and seizures accompanied by apnea, while the other one had growth hormone deficiency and childhood partial epilepsy that progressed to the electrical status of epilepsy. The first girl was suspected to have diGeorge syndrome, then tuberous sclerosis, but definitive genetic findings revealed 1p36 microdeletion syndrome and one variant in clinical exome sequencing. The second girl was unexpectedly found to have hypoplastic uterus and was suspected of having Mayer-Rokitansky syndrome. A surprising finding was a marker chromosome, stressing the need for FISH and further molecular testing. Both of them were difficult to treat. In conclusion, genetics is transforming clinical practice in epilepsy, especially in pediatric patients. The large number of different syndromes and seizure types, as well as the highly variable inter-individual response to therapies makes the management of syndromic epilepsy challenging. Sometimes, it takes time to find the genetic etiology, or to associate newly revealed genetic findings with clinical data.

NEUROPSYCHOLOGICAL ASSESSMENT OF CHILDREN WITH EPILEPSY – WHEN LESS IS MORE?

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Neuropsychological assessment is a process that encompasses collecting a patient's detailed medical history, conducting tests to assess various cognitive functions and emotional states, and providing counseling with the aim of supporting an individual and understanding the effects of their illness on their everyday life. The process described thus represents a bridge between functional events in the central nervous system and how they affect manifest behavior in the patient's cognitive, emotional and social life. Taking into consideration that epilepsy is one of the most common chronic illnesses among children, the significance of neuropsychological assessment is further enhanced when combined with the expected development of the brain and how the illness and treatment of the illness can affect it. Neuropsychological assessment therefore represents a major factor in the neurological treatment of epilepsy as it provides a vast source of information relevant for selecting therapy, monitoring the course of treatment, as well as setting expectations regarding the outcome of treatment and prognosis of development. The paper emphasizes the significance of the initial assessment of cognitive and emotional functioning of a child newly diagnosed with epilepsy. The assessment provides an insight into the child's state before starting treatment, which can detect the potentially impaired cognitive functions at the onset of the illness clinical manifestation, as well as the potential presence of primary cognitive deficits. Furthermore, the paper emphasizes the significance of further psycho-diagnostic monitoring after the initial diagnosis and how important it is to conduct re-assessment that can lead to conclusions about the development of cognitive functions and any possible consequences of taking antiepileptic drugs. Additionally, the aim is to show the potential obstacles that prevent creation of an all-encompassing framework for developmental neuropsychology, taking into consideration various moderating variables, the dynamics of development and continuous interaction between numerous psychosocial and environmental factors.

MICRORNAS AS POTENTIAL BIOMARKERS OF EPILEPSY AND TREATMENT TARGET

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Identification of a molecular biomarker that could be reliably detected in blood would transform epilepsy diagnosis. MicroRNAs (miRNA) are among the leading candidates in this regard with recent studies reporting miRNA biomarkers of epilepsy in serum, plasma and cerebrospinal fluid. MiRNAs are small noncoding RNAs the main function of which is to control gene expression and negatively regulate protein levels in cells. Recent studies show the possibility of using miRNAs as diagnostic biomarkers of epilepsy, as well as novel therapeutic targets. MiRNAs might be suitable biomarkers of epilepsy because of their enrichment in the brain and because individual MiRNAs are present exclusively in certain regions of the brain or cell types. Biochemical characteristics that support the biomarker potential of miRNA is its stability in biofluids such as blood and cerebrospinal fluid. However, the results of multiple studies on miRNAs as biomarkers for epilepsy need to be unified. MiRNAs are involved in the inflammatory response in the nervous system, neuronal necrosis and apoptosis, dendritic growth, synaptic remodeling, glial cell proliferation, impairment of neurotransmitter, and receptor function. All these processes constitute epileptogenesis. Therefore, we can conclude that miRNAs play a key role in epileptogenesis. Studies have shown that manipulating miRNA by its agomir or antagomir can have strong effects on neuropathology, epileptogenesis, and seizures. Therefore, MiRNA-based treatments could be deployed as anti-epileptogenic or disease-modifying treatments.

EPILEPSY AND LONG QT SYNDROME: A CASE REPORT

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There is clinical overlap between seizures and syncope due to cerebral hypoperfusion during cardiac arrest and that of epileptic seizures related to ion channel-mediated changes in brain excitability. One of the causes of syncope may be an electrocardiographically prolonged QT interval, a primary arrhythmic disorder caused by changes in potassium channel activation, which can lead to malignant ventricular arrhythmias and sudden cardiac death. The causes of prolongation could be congenital long QT syndrome (LQTS), hypokalemia, hypomagnesemia, hypocalcemia, hypothermia, myocardial ischemia, condition after cardiac arrest, increase in intracranial pressure, or drugs. We present a case of a 38-year-old woman treated for epilepsy with generalized seizures since the age 14. Treatment of hyperprolactinemia showed a pituitary macroadenoma of 4 cm in diameter, which was transnasally surgically removed, followed by gamma-knife radio-surgical treatment due to the residue. Diagnostic processing of abdominal pain showed Crohn's disease. Because of the repeated epileptic seizures, antiepileptic therapy (AET) was corrected; the last recommended was a combination of valproate and lamotrigine. Three years before, due to change in clinical semiology of the seizures, she was referred to a cardiologist who diagnosed LQTS. Beta adrenergic blocker was introduced. After two attempts of artificial insemination, she conceived naturally. Her AET was corrected from the 7th week of gestation. She gave birth to a female newborn at term by cesarean section. The baby was also diagnosed with LQTS and propranolol was initiated. Genetic analysis of the child revealed a mutation heterozygote for KCNH2, which is one of the genes that cause LQTS. No genetic analysis was performed in the mother. Holter electrocardiography was performed three months after delivery and recorded symptomatic self-interrupting ventricular tachycardia in the patient and implantable cardioverter defibrillator (ICD) was urgently implanted. At the end of 2020, she became naturally pregnant again. Premature delivery occurred at 37 weeks, giving birth to a male child also diagnosed with LQTS. On one occasion, the ICD was activated with the appearance of symptoms. The patient is still taking AET. Previous literature data confirm the need for continuation of therapy because changes in KCNH2-encoded potassium channels can cause, in addition to cardiac disorders, a tendency to recurrent epileptic activity.

JUVENILE MYOCLONIC EPILEPSY – A WELL-KNOWN DISEASE AND NEW CHALLENGES

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Juvenile myoclonic epilepsy (JME) is a phenotypical spectrum with different combinations of the main seizure types, presence or absence of localized features in semiology or electroencephalography, psychopathology, and varying treatment response. This diversity seems to be due to a combination and interaction of genetically determined endophenotypes along with quantitative differences in the expression of the predominant pathogenic mechanisms. We analyzed our cohort of patients with JME, followed-up during the last 12 months, according to age, gender, duration of epilepsy, seizure types, and therapy. As in other recent studies, the benign course was observed in two-thirds of the patients. Others had pseudoresistance due to problems in lifestyle/compliance, or true resistance to therapy mainly due to the coexistence of all three seizure types and existence of psychiatric problems. We analyzed the proportion of patients on first-line therapy choice such as valproate, or lamotrigine and levetiracetam, when valproate was contraindicated. The failure of valproate or failure of two first-line antiepileptic drugs suggested that combination therapy was indicated. Topiramate is a cost-effective alternative monotherapy, but because of its poor tolerability, it should be add-on treatment only. Zonisamide is a good alternative for patients with compliance problems because of its long half-life; it can be used once daily without significant fluctuation of blood levels. Its mechanism of action, may make it effective in absence epilepsy and JME. Clonazepam can be a useful adjunct for myoclonus. In conclusion, the best suitable choice of therapy should be considered not only according to the types of seizures, but also according to compliance, individual needs, and comorbidities. Unfortunately, there is still no information about the related genes in the great majority of JME patients. The diversity and difficulty to elucidate the JME genes are among the best clues to support that JME is a spectrum with marked genetic heterogeneity.

EPILEPSY IN RARE DISEASES – CASE REPORTS

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Rare diseases are a heterogeneous group of disorders that mainly affect the central and peripheral nervous system and muscles. They usually manifest by neurological symptoms and epileptic seizures. Rare diseases are the result of genetic defects that often lead to metabolic block in a biochemical pathway critical for cellular function or accumulation of metabolite or disturbance of the balance of protein synthesis and degradation at the synapse. The diseases themselves are a rare cause of epilepsy but seizures and epilepsy are common in such patients. Epilepsies in rare diseases can be present throughout life and they are generally resistant to antiseizure medications. They are often associated with comorbid developmental delay/regression, intellectual and behavioral impairments. Some of these disorders are amenable to specific treatment interventions; timely and appropriate diagnosis is critical to improve outcomes. Although epileptic seizures in some conditions are the first presentation of the disease, we will present rare disorders with delayed epilepsy onset and show our approach to clinical recognition, diagnosis, and follow-up.

CLINICAL AND ELECTROENCEPHALOGRAPHIC FEATURES AND OUTCOMES AFTER FIRST UNPROVOKED EPILEPTIC SEIZURE WITHOUT ANTICONVULSANT THERAPY

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About one-fifth of all cases of seizures in children are first unprovoked epileptic seizures that are defined as seizures in the absence of conditions that can cause seizure (febrile illness, metabolic disturbance, rotavirus gastroenteritis, etc.) or beyond the time typical for acute symptomatic seizures (stroke, central nervous system infection, etc.). Use of anticonvulsants or follow-up approach without therapy immediately after first unprovoked epileptic seizure is one of the most common dilemmas in epileptology. The overall risk of seizure recurrence after first seizure is 50% and increases to 70% in the presence of epileptiform electroencephalogram (EEG) abnormalities, previously formed morphological abnormalities of brain, or other neurological signs. In the absence of these factors, the risk is around 30%. The risk of third seizure after two previous unprovoked seizures is 70%-80%, which is similar to the risk of recurrence after first seizure in the presence of risk factors. In this study, we assessed the following clinical and EEG characteristics and clinical outcome in 84 children with first unprovoked epileptic seizure after which anticonvulsant therapy was not introduced: age at the time of first seizure (median age, 7 years), semiology (focal seizures in 55% of cases), and duration of seizure (three-quarters of seizures lasted for less than 5 minutes, equally frequent in wakefulness and sleep). In 75% of children with abnormal EEG after first seizure, we found focal epileptiform discharges. Epilepsy or febrile seizures were found in family history of 42% of children with first seizure, whereas febrile seizures and perinatal neurological risk factors were recorded in personal history in 12% each. Median time to the second seizure was 2 months and anticonvulsants were introduced in 43% of patients after second seizure. Despite the treatment, 62% of patients had recurrent seizures. Potentially epileptogenic structural abnormalities were found in 14% of our patients. We discuss risk factors for seizure recurrence and subsequent epilepsy diagnosis in children with first unprovoked epileptic seizure. Identifying these risk factors in clinical and EEG assessment of patients can help us decide whether or not to initiate anticonvulsant therapy after the first unprovoked epileptic seizure.

GRIN2A RELATED DISORDERS – OUR EXPERIENCES

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GRIN2A gene codes GluN2A protein, an NMDA receptor subunit. NMDA receptors are widely disseminated in the brain and their role in normal brain development, neuroplasticity processes, learning and forming memory is well known. Disorders of the GluN2A subunit specially affect signaling in the regions involved in speech and language, and it also affects brain activity during slow-wave sleep. GRIN2A related phenotypic spectrum is very broad, ranging from almost unaffected individuals to patients with severe developmental and epileptic encephalopathy. The most common presentations are connected with epilepsy and speech impairment brought together in the epilepsy-aphasia spectrum. Regarding speech impairment, dysarthria, speech dyspraxia, and both expressive and receptive language delay or regression have been described. As for epilepsy, different seizure types have been described, most common being focal seizures. Epileptic syndromes connected with GRIN2A mutation are benign epilepsy with centrotemporal spikes, atypical childhood epilepsy with centrotemporal spikes, Landau-Kleffner syndrome, and epileptic encephalopathy with continuous spike and wave during slow-wave sleep. We describe phenotypic variety of GRIN2A related disorders by showing experiences at our Department. We will present a case of a 14-year-old boy with normal cognitive development, without speech impairment but with focal epileptic electroencephalogram changes who by this time has never had a seizure. We will also present a case of 6-year-old boy with speech impairment and cognitive delay, and with focal seizures and continuous spike wave during slow-wave sleep and his 4-year-old sister with only mild speech impairment, who presented with isolated myoclonic epileptic status. At the end, we will present a 4-year-old boy with different types of seizures and severe developmental delay. In conclusion, GRIN2A related disorders show phenotypic variety ranging from almost unaffected individuals to patients with severe developmental and epileptic encephalopathy.

EPILEPSY OF INFANCY WITH MIGRATING FOCAL SEIZURES (EIMFS)

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Epilepsy of infancy with migrating focal seizures (EIMFS) is a rare developmental and epileptic encephalopathy beginning with drug resistant focal seizures in the first year of life, predominantly at the age of 6 months. Focal seizures can arise in both hemispheres and migrate from one cortical region to another. Seizures are often prolonged with status epilepticus. Prognosis is poor with severe neurological disability and reduced life expectancy. The cause is mainly genetic with KCNT1 as the major gene but more than 25 genes are linked with this syndrome. Head size and neurological examination are normal at onset but later findings are consistent with severe neurological impairment. Most patients develop microcephaly by 1 year of age. Focal motor clonic or tonic seizures are mandatory for diagnosis. Initially, these are sporadic but their frequency rapidly increases within weeks or months. Focal seizures show a migration pattern on electroencephalography (EEG), which might be missed without prolonged video EEG. Clinically, migration is characterized by unilateral focal tonic or clonic activity at seizure onset, which then evolves to contralateral focal tonic or clonic activity over the course of seizure. Status epilepticus is common. Myoclonic seizures are exclusionary. The EEG background can be normal at onset but diffuse slowing occurs with time with multifocal discharges. Ictal EEG correlates with clinical semiology and there is involvement of multiple independent cortical regions. Neuroimaging is normal at onset. Brain atrophy has been reported on follow up. Familial inheritance is rare. *De novo* gene abnormalities are most common. KCNT1 is the major gene, others are SCN1A, SCN2A, SLC12A5, BRAT1, and TBC1D24. In our presentation, we will introduce two children, a boy and a girl, who met the criteria for the diagnosis of EIMFS. In both patients, a mutation in the TBC1D24 gene was demonstrated.

THE ROLE OF EEG IN THE DIAGNOSIS OF STATUS EPILEPTICUS

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Based on the knowledge of pathophysiology and the need for urgent clinical intervention,the International League Against Epilepsy (ILAE) states that status epilepticus (SE) is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of the mechanisms which lead to abnormally prolonged seizures (after time point t1). Time point 1 (t_1) indicates when treatment should be initiated, and time point 2 (t_2) indicates when long-term consequences may appear, including neuronal injury, neuronal death, and alteration of neuronal networks depending on the type and duration of seizures. Electroencephalography (EEG) correlates are one of the four axes included in the classification of SE proposed by the ILAE Task Force in 2015 (the others are semiology, etiology, and age), that provides a framework for clinical diagnosis, investigation, and therapeutic approaches for each patient. The authors will present their experience from clinical practice of the Referral Centre for Epilepsy of the Ministry of Health of the Republic of Croatia in treating SE patients, with special reference to EEG correlates and American Clinical Neurophysiological Society (ACNS) Standardized Critical Care EEG Terminology from 2013 and 2021 Version. It is important to point out that EEG affects the choice and aggressiveness of treatment, prognosis, and clinical approaches, so an EEG should be performed where possible and as early as possible. However, it is known that the diagnosis of nonconvulsive SE relies largely on EEG findings. As in other acute neurological conditions, the semiology and the EEG pattern in SE are highly dynamic and may change over short time periods in a given patient. In the ACNS 2021 version, recent research findings have been incorporated, definitions of several new terms have been added, most of the old terms have remained unchanged, however, a few definitions of old terms have been clarified.

THERAPEUTIC CHALLENGE IN OBTUNDATION STATUS EPILEPTICUS IN A CHILD WITH DRAVET SYNDROME

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Dravet syndrome (DS) is a genetic encephalopathy characterized by drug resistant epilepsy which appears in the first year of life in previously healthy children; then, neurodevelopmental delay becomes evident, together with motor, language and behavioral problems. Diagnosis is made on the basis of clinical features. Children usually show several seizure types including convulsive, myoclonic, absence, focal and tonic seizures. Obtundation status is a special seizure type in DS and consists of consciousness impairment variable in intensity, with fragmentary and erratic myoclonus of low amplitude involving limbs and face, sometimes associated with drooling. Patient may or may not react to stimuli, according to the degree of consciousness. It may last for hours or days. Although according to the International League Against Epilepsy standard, antiepileptic drug is used 5 minutes from seizure onset, in children with DS it is reasonable to apply emergency treatment immediately rather than wait for a standard time, so it is recommended that such children have an individualized emergency treatment plan. We present a 6-year-old boy with obtundation status and therapeutic option, as well as all the challenges regarding the choice of emergency anticonvulsant treatment.

DYSEMBRYOPLASTIC NEUROEPITHELIAL TUMORS

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According to the WHO classification, dysembryoplastic neuroepithelial tumors (DNET) are classified as neuronal and mixed neuronal-glial tumors. They occur at a frequency of 1.2% of patients up to 20 years of age and 0.2% of patients over 20 years of age. There are four histologic subtypes: complex, simple, nonspecific, and diffuse. DNET are found in about 20% of histologic diagnoses after stubborn epilepsy surgery in adults. The dominant localization of DNET is temporal lobe. They are radiologically characterized by cortical location, lack of compression, and absence of perifocal edema. During the 2012-2020 period, seven patients (four male and three female), mean age 26.2 years, were operated on. All patients presented with focal impaired awareness seizures. Total resection of tumors was performed in all seven patients, including resection of the uncus and amygdala involved. All seven patients were seizure-free postoperatively (Engel 1). In conclusion, complete tumor removal is the most significant prognostic factor. Other major factors are younger age and short duration of epilepsy. Early surgical treatment in patients with epilepsy and DNET is crucial to achieve seizure freedom.

PERIHIPPOCAMPAL TUMOR-ASSOCIATED EPILEPSY

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Pathologic intracranial processes are responsible for 10%-15% of seizures. A large number of patients with glial tumors infiltrating the insular-paralimbic area have refractory epilepsy. Maximal tumor resection with preserved quality of life is the main goal of treatment, but seizure-free outcome is achieved in 60%-70% of patients, especially those with the insular-paralimbic areas involved. During the 2009-2019 period, six patients (three male and female each) with paralimbic-perihippocampal lesions (astrocytoma grade II, glioblastoma multiforme, dysembryoplastic neuroepithelial tumors, ganglioglioma, anaplastic ganglioglioma, focal cortical dysplasia II) were operated on. The mean patient age was 36 years and follow-up period was 12-40 months. Postoperatively, patients were seizure-free at a satisfactory level. After total or subtotal resection, 65%-80% of patients are seizure-free. Duffau *et al*. were the first to show that in patients with insular-paralimbic gliomas, resection of a healthy hippocampus has a significant impact on postoperative seizure occurrence. This small series supports hippocampal resection in patients with limbic gliomas and refractory epilepsy.

SLEEP, EPILEPSY AND ANTIEPILEPTIC DRUGS

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Good-quality sleep is an important and frequently overlooked component of general health, but it is particularly essential to patients with epilepsy. Their sleep can be affected by seizures, concurrent sleep disorders, and seizure treatment. Sleep worsening can result not only in poor daytime functioning but potentially also in exacerbation of epilepsy. The complex interplay and reciprocal interactions between sleep and epilepsy have been known for centuries. The relationship between sleep and epilepsy was recognized by ancient Greeks. In the late 18th century, Gowers recognized that approximately 20% of patients with epilepsy experience seizure solely in sleep. With the dawn of electroencephalography, Gibbs recognized that epileptiform activity increased during sleep. It was recognized that close to half of patients with generalized tonic-clonic seizures had a nocturnal predominance. Sometimes there can be problems differentiating nocturnal seizures from sleep disorders. It is often important to recognize sleep effects on epilepsy, along with comorbid sleep disorders affecting the treatment of epilepsy. The effects of antiepileptic drugs (AEDs) on sleep are of particular concern. Some agents have detrimental effects on sleep, particularly benzodiazepines and barbiturates but also phenytoin and, possibly, carbamazepine. Others, especially gabapentin, seem to actually improve sleep quality. Much research in this area is confounded by the effects of seizures and concurrent conditions on sleep, making it difficult to isolate the direct effects of AEDs on sleep. However, as AEDs have independent effects on sleep quality, the choice of an appropriate agent not only determines whether seizures are completely controlled but also whether the patient performs optimally on daily basis. As there are many potentially appropriate AEDs for most patients, familiarity with the possible effects on sleep is important when recommending the best agent for each individual. Thus, choosing a sleep-friendly AED is of utmost importance in patients with epilepsy.

TREATMENT OF PSYCHOGENIC NONEPILEPTIC SEIZURES – PATIENT EXPERIENCE

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The physician-patient relationship is crucial for the outcome of treatment of psychogenic nonepileptic seizures (PNES). Studies of PNES perception have shown a bidirectional problem. Physicians cite uncertainty in diagnosis and treatment, divided opinions on which physicians should take care of these patients, and seeing PNES as challenging and frustrating. Conversely, patients with PNES often report sparse interaction with physicians, with the impression that they are not being listened to. As part of the Croatian Association for Epilepsy project entitled Educational Internet Platform on Psychogenic Nonepileptic Seizures, people with epilepsy (PwE) and those close to them were offered an anonymous online questionnaire to examine their attitudes and experiences in diagnosing and treating PNES. Preliminary results show that neurologist explained the diagnosis in 60% of subjects and that 67% were referred to a psychiatrist. Seventy percent of respondents were satisfied with the way the neurologist or psychiatrist explained the diagnosis. About 45% of respondents state that they have been treated by medication and talking to a psychologist and/or psychiatrist. In about one-third of patients, treatment led to improvement in the condition in general, reduction in the number of seizures, and shortening of the duration of seizures. Although most respondents were satisfied with the way they were treated, half of them felt that none of the specialists wanted to address their problems seriously and then felt that the physician was motivated to help but did not have enough knowledge, which in 80% of cases referred to the neurologist. In almost two-thirds of cases, a family member (usually a parent) was also involved in treatment. PwE and their relatives agree with the statement that a family member should be involved in the treatment and that a website where they could educate themselves should be used to explain the diagnosis.

MYOCLONIC STATUS EPILEPTICUS AFTER COVID-19

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A case is presented of a male patient aged 55 who was hospitalized for myoclonus treatment. In April 2021, the patient recovered from COVID-19 (the period of isolation lasted from April 19 to April 30, 2021). Immediately upon the period of isolation, the patient experienced twitching of all body muscles, firstly in the arms (mostly fists), and then in the legs. Twitching was constant, regardless of the time of the day. The patient experienced difficulty with walking, and needed support by another person and a walking cane. He provided his personal medical history. He was treated for gout. Upon admission, the patient was unable to walk independently. He could be verticalized with the help of a walking cane and an assistant. Head twitching was noticeable, as well as twitching of both arms (especially fists) and both legs while still. The patient exhibited interrupted, staccato speech. He suffered from obstructive sleep apnea. Test results revealed no abnormalities. Laboratory test results, multi-slice computed tomography of the brain, magnetic resonance imaging and magnetic resonance angiography of the brain, heart ultrasound, *electromyoneurography* of upper and lower extremities, cytologic and biochemical test results of cerebrospinal fluid, *Borrelia burgdorferi* and neurotropic viruses were negative. Immunotyping showed identical IgG strands in cerebrospinal fluid. Chest x-ray indicated regressive dynamics of inflammatory infiltrates. Radiological skeletal survey did not indicate any osteolytic or osteoproliferative changes. Initial electroencephalogram (EEG) showed diffuse dysrhythmia and paroxysmal changes bilaterally, fronto-centro-temporal (FCT) with mild lateralization on the right, with elements of the spike-wave complex and abortive spike-wave complexes of faster variant. Repeat EEG after two weeks showed diffuse dysrhythmia changes, mainly bilateral; FCT with lateralization on the right. The patient was treated with levetiracetam, an antiepileptic drug; antiaggregation therapy; immunoglobulins at a daily dosage of 0.4 g/kg body mass for 5 days; pulse corticosteroid therapy; and physical therapy at the ward. At discharge from the hospital, the patient showed discrete, mild residual amplitude tremor, as well as pronounced obstructive sleep apnea, interrupted speech, and insecure walking. At 2-week post-discharge follow-up visit, minimal speech (interrupted speech) problems remained. Repeat EEG showed bilateral dysrhythmia, frontocentral, better visible on the right, while 6 weeks after discharge no abnormalities were detected, with normal neurological status. The patient responded well to therapy. In our opinion, the patient had the post-COVID-19 syndrome, which was manifested by myoclonic seizures, i.e. myoclonic status epilepticus. His recovery was successful owing to the application of almost all treatment modalities available.

NETWORKS IN POSTERIOR CORTEX EPILEPSIES

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Epilepsy can be defined as the epileptic network disease and precise definition is an important aspect in planning alternative options in the treatment of pharmacoresistant epilepsy. Posterior epileptic network has some specific features. Posterior cortex epilepsies account for about 18% of epilepsy cases, even though parietal, occipital and posterior temporal lobes make about 50% of the brain volume. One of the features of posterior cortex epilepsy is rapid propagation not only to the neighboring brain regions but also to distant brain regions. It is possible that this is one of the reasons why the epileptic network in the cases of posterior cortex epilepsy is not so easily defined. Another reason is that the main parts of posterior cortex are 'silent' and there is no semiology without propagation. Seizures that originate from the occipital lobe can have rapid propagation to the temporal and frontal lobes, without visual aura, which is characteristic for occipital lobe epilepsy. Even though this visual aura is characteristic for occipital lobe type of epilepsy, it can still be found in only 50% of cases, and different visual auras could be the first signs of epilepsy from partial and temporal lobes. This complexity of posterior cortex network is one of the reasons for not so successful outcomes of epilepsy surgery. Good knowledge of the semiology, and appropriate use of noninvasive and invasive methods can still improve results in the treatment of patients with posterior cortex epilepsy.