In the Name of

God

the Compassionate,
the Merciful

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۱۳۷۴
انجمن صرع ایران
حمایت از بیماران مبتلا به صرع

16th International Epilepsy Congress

22-24 January 2020

National library,Tehran,Iran

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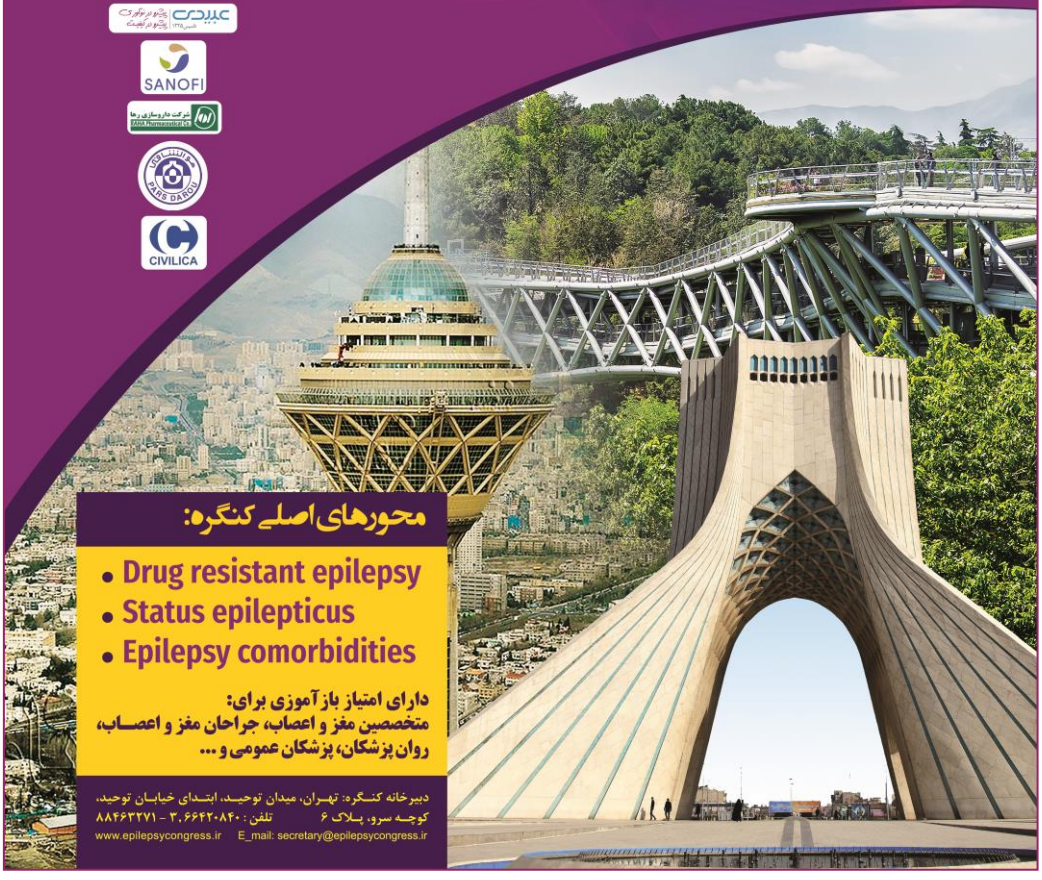

محورهای اصلی کنگره:

- Drug resistant epilepsy
- Status epilepticus
- Epilepsy comorbidities

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Iranian Epilepsy Association

16th International Epilepsy Congress

22 – 24 January 2020
National Library, Tehran, Iran

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Hossein Pakdaman, MD
President of Iranian Neurological Association

Dear Colleagues and Friends,

On behalf of the scientific committee of the 16th International epilepsy congress, it is with great honor I invite you to participate in this congress which will take place on January 22-24 January 2020 in Tehran, Iran.

Participants will join in a stimulating and capable social occasion program including symposia, oral and poster sessions and workshops. It is a unique opportunity for face to face interaction with the experts in the field. It also allows delegates to gain insight into the latest research and to get in touch with the many different nationalities that will be in attendance. I believe that such a scientific meeting is one of the high quality events in an excellent atmosphere and the welcoming spirit.

It is with great pleasure we invite you to take part in this year's Congress, which I hope it will be a scientifically and socially rewarding, memorable and enjoyable experience. we are looking forward to see and welcome you on January 22.

Yours sincerely,

Welcome Messages

Behnam Safarpour Lima, MD

Congress chairperson

Dear Friends and colleagues,

On behalf of the scientific advisory and organizing committee we would like to welcome you to the 16th Iranian International Epilepsy Congress held from January.22nd .2020 to January.24th .2020 in Tehran. This event has been planned and organized by collaboration of the Iranian Epilepsy Association, Iranian chapter of ILAE and Shahid Beheshti University of Medical Sciences.

It is our great pleasure to inform the participants that we have tried our best to organize a memorable event that includes the most novel subjects on various aspects of epilepsy. Furthermore, many sessions have been designed on topics such as epilepsy in different age and sex, status epilepticus, drug resistant epilepsy, epilepsy surgery, epilepsy comorbidities, epilepsy neuroimaging, psychological aspects of epilepsy and pediatric epilepsy which will be discussed by some of the most knowledgeable experts in the field.

Several well-known specialist speakers have also been invited from many parts of the world such as European countries and Japan to take part in this event.

Finally, it is our great hope to be able to accomplish our objectives of discussing and exchanging the most recent developments in the field of epilepsy. We are looking forward to meeting everyone in the congress and wish you a pleasant stay in the beautiful city of Tehran.

Best Regards,

Welcome Messages

Kurosh Gharagozli, MD
Professor of neurology
IEA President

Dear Colleagues,
I am delighted to welcome you to 16th international Epilepsy Congress 2020, to its host city, Tehran.

The Epilepsy Congress is the most important gathering of the Iranian neurologists, epileptologists, Iran chapter of ILAE and IBE and is now an outstanding international meeting. The Scientific Programme this year will once again take in fundamental, clinical, Neuro imaging and electrophysiological issues in Epilepsy and seizure disorders, with experts from around the world travelling to Tehran to make this a stimulating arena for the discussion of ideas and experiences. We will also enjoy posters and oral communications from our emerging and early career researchers.

I would like to thank all those who have worked so hard to organise this Congress, both in the International League against Epilepsy , international bureau of Epilepsy and scientists from around Iran who've given their time freely. I am also very grateful to the many generous sponsors of the meeting and participants of the technical exhibition.

All of my colleagues in Iranian Epilepsy association look forward to an exciting meeting that promises great scientific debate and enjoyable social interaction. We very much hope you enjoy the Conference and your visit to the great city of Tehran despite pollutions!!

We look forward to welcoming you to the Congress in January 2020!

Welcome Messages

Dr. Dariush Nasabi Tehrani, MD
CEO and founder of epilepsy association of Iran

I am so glad and satisfied that with our dear expert neurologists and epileptologists help we are holding 16th epilepsy international congress.

Although epilepsy is maybe seems like a well known disease ,as we know,it has ambiguous and complex angles from different directions that most of the time it makes diagnosis harder for specialists so treatment becomes more difficult.

Obviously the way of neurology and epileptology approaching to the neuro science made many differences in diagnosis and classification of this disease so it shows we need more research and experience transfer between specialists and clinicians.

In this few days, neurology teammate international gathering, I hope we can add more to the neurology science about epilepsy and take steps in the path of curing and diagnosing and partly reduce some problems of patients and their families.

For my part, I specially thank Iranian association of neurology chairing by Pro. Pakdaman that are always with us.Also thanks Iran ILAE representation, Dr. Motamedi and his colleagues, who did their best for holding this scientific space and say thanks to my great and sympathetic partners in epilepsy associationvof Iran that in the last two decades tried hard to promote the epilepsy knowledge and education in our country.

Welcome Messages

Dr. Mahmoud Motamedi, MD
Head of the constituent's members of IC-ILAE

On behalf of the constituent's members of Iranian chapter of ILAE (IC-ILAE). It is my pleasure to welcome your attending in 16th international epilepsy congress of Iran which will be held in Iran National Library.

This congress is actually organized by coordinated joint cooperation of Shahid Beheshti University of Medical Sciences, Iranian Neurological Association, Iranian Epilepsy Association and IC-ILEA.

The scientific program is very exciting covering the most important field of epilepsy, in addition to main topics, focused workshops and scientific symposia are organized, so that everybody can find sessions of personal interest to attend. We look forward to meet you all in this scientific congress.

Congress Organization

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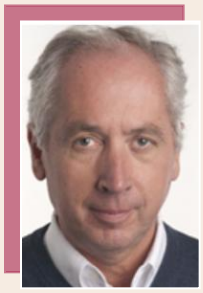

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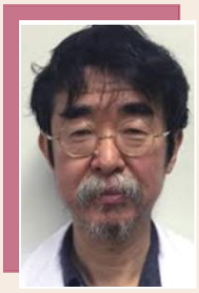

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Medical University, Nagakute,Japan

Dr. Bernhard Schuknecht, MD
Medical Radiological
Institute Zurich Switzerland

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Abstracts

16th International
Epilepsy Congress

Comparison of Severity of Seizure Activity in Acute and Chronic Induction Model in Male Rats

Sara Abedi[1], Narges Zeinalzadeh[2], Leila Mehdizadeh[3], Yousef Panahi[4]
1, 2, 3- Department of Animal Sciences, Faculty of Natural Sciences, University of Tabriz, Tabriz, Iran.
4- Department of Basic Sciences, Faculty of Veterinary Medicine, University of Tabriz, Tabriz, Iran.

Background: This study aimed to compare the number of spikes induced by acute and chronic intraperitoneal injection of pentylenetetrazol in adult male rats.
Methods: In this study, 22 adults male Wistar rats (200-250 g) were used in the control (n=6), acute (n=6) and chronic group (n=10). After anesthesia with the combination of ketamine (80 mg/kg) - xylazine (eight mg/kg), the animal's head was held fixed using a stereotaxic device and after longitudinal incision in the scalp and wiping the tissue and determining the Bregman point, the intracranial recording electrode was inserted into the CA1 hippocampal striatum layer and seizure activity was induced by intraperitoneal injection of pentylenetetrazol (80 mg/kg). After digestion, the recording electrode was inserted into the CA1 hippocampal striatum layer and seizure activity was induced by intraperitoneal injection of pentylenetetrazole (80mg/kg). Animals were anesthetized with the combination of ketamine (80 mg/kg) - xylazine (eight mg/kg) and after fixation using a stereotaxic apparatus, followed by longitudinal incisions in the scalp and wiping the tissues on the skull, intracranial recording electrodes were placed in the CA1 hippocampal striatum layer, and seizure activity were induced by intraperitoneal injection of pentylenetetrazol (80 mg/kg). In the control group, after recording the activity in basal condition, normal saline and in the acute, group were injected intraperitoneally with pentylenetetrazole and the number of spikes was evaluated by eTrace software. However, whereas in the chronic group for eight weeks on Saturday, Monday and Wednesday, 30 mg/kg pentylenetetrazole were injected intraperitoneally and after the end of this epileptic activity period, similar to the grave group. Diazepam 10 mg/kg was used to suppress epileptic activity induced by pentylenetetrazol.
Results: The results of the present study showed that no spike activity was recorded in the control group and the number of spikes in the acute group compared to the chronic group did not show a significant difference, although the number of spikes in the chronic group in compared with the

acute group had been decreased. Data were analyzed by SPSS software version 22 using one-way ANOVA and Tukey post hoc test. P <0.05 were considered significant.
Conclusion: The decrease in the number of spikes in animals that are chronically affected by epilepsy is likely to reflect the role of specific biological pathways in the pathophysiology of epilepsy, which requires further study to identify these pathways.
Keywords: Acute, Chronic, Rat, Epilepsy, and Pentylenetetrazol.

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Sleep and Epilepsy

Mohsen Aghaee Hakak,MD
Neurologist, Epilepsy Monitoring Unit, Razavi Hospital, Mashhad,Iran

Sleep and epilepsy are closely related. Hypersynchronization occurs during sleep and this phenomenon exacerbates epileptic seizures and epileptiform activities in some epileptic syndromes. Certain epilepsies are associated with sleep, especially in children. Epilepsy may aggravate by both sleep and sleep deprivation. Sleep disorders, on the other hand, are commonly seen in patients with epilepsy. Effective treatment of sleep disorders, especially sleep apnea, can improve the control of seizure attacks. In addition, the quality and quantity of sleep can be affected by seizures or antiepileptic drugs. Some sleep disorders, such as parasomnias, can mimic epileptic seizures and make it difficult to differentiate from epilepsy.
Given the above, screening, diagnosis and treatment of sleep disorders are an important part of the treatment and care of epileptic patients.
Keywords: sleep, epilepsy, parasomnia

Novel Hesperetin Solid Lipid Nanoparticles Attenuates Inflammatory Gene Expression and Astrocyte Activation in Pentylenetetrazol-Induced Kindling Model of Epilepsy

Seyed Raheleh Ahmadian[1]*, Maryam Ghasemi[2], Mitra Pourgholi[1], Hanieh Yavarpour[1]

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Introduction: Epilepsy is one of the most common chronic neurological disorders, which provoke progressive neuronal degeneration and memory impairment. In recent years, application of herbal compounds with anti-inflammatory properties, such as hesperetin has been introduced as useful agent in reducing of the epilepsy symptoms. Despite the numerous pharmacological activities of hesperetin, its biomedical application has been hampered, because of poor water solubility and low oral bioavailability. we fabricated a novel form of hesperetin solid lipid nanoparticles (SLNPs).
The effect of these prepared NPs was evaluated on inflammatory gene expression, neuronal density and astrocyte activation in pentylenetetrazol (PTZ)-induced kindling model.
Method and material: hesperetin-loaded NPs were prepared using a propylene glycol with stearic acid and pluronic F68 polymer. Male NMRI mice have received the daily injection of hesperetin and hesperetin-loaded NPs at dose of 10 and 20 mg/kg. All interventions were injected intraperitoneally (i.p.), 10 days before PTZ administration and the injections were continued until 1 h before each PTZ injection. Animals have received their last injections of PTZ and then, brain tissues were removed. Immunostaining against NeuN and GFAP respectively as mature neuronal and astrocyte markers were performed on brain sections. QRT-PCR was done for inflammatory gene expression in hippocampus.
Result: Our data showed successful fabrication of hesperetin-loaded NPs. In comparison to free hesperetin, hesperetin NPs markedly reduced seizure behavior, neuronal loss, and astrocyte activation in a PTZ-induced kindling model. Results showed that hesperetin administration attenuates inflammatory gene expression in fully kindled animals.
Conclusion: Overall, the results of this study suggest that hesperetin NPs administration effectively ameliorates inflammatory gene expression and

alleviates the level of neuronal death and astrocyte activation in PTZ-induced kindling model.
Keywords: Epilepsy; hesperetin NPs; inflammatory gene expression; Neuronal loss; astrocyte activation

❊ ❊ ❊

Effect of Curcumin-Loaded Nanoparticles on Hippocampal Neuronal Density and Cognitive Impairment in Chemical Kindling Model of Epilepsy

Seyed Raheleh Ahmadian[1]*, Shahram Ghasemi[2], Atefeh Akbari[1]
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Introduction: Epilepsy is considered one of the most common neurological disorders, and is characterized by recurrent and unpredicted epileptic seizures. Although numerous antiepileptic drugs have been designed in recent years, available therapies are in efficient for control of seizure attacks in around 30% of patients. Therefore, several approaches have emerged to design novel drugs for treatment of epileptic patients. Most recently, in order to overcome the side effects of existing chemical drugs, natural products with anti-inflammatory agents such as curcumin has been regarded to reduce the epilepsy symptoms. But its medical application has been hampered due to low water solubility. To improve the aqueous solubility of curcumin, it has been loaded on chitosan -alginate nanoparticles (NPs). In this study, the effect of curcumin NPs on memory improvement and glial activation was investigated in pentylenetetrazol (PTZ)- induced kindling model.
Method and material: Male NMRI mice have received the daily injection of curcumin NPs at dose of 12.5 or 25 mg/kg. All interventions were injected intraperitoneally (i.p), 10 days before PTZ administration and the injections were continued until 1 h before each PTZ injection. Spatial learning and memory was evaluated using Morris water maze test after the 7th PTZ injection. Animals have received 10 injections of PTZ and then, brain tissues

were removed and immunostaining method was performed against NeuN and GFAP/Iba1 for assessment of neuronal density and glial activation respectively

Result: Behavioral results showed that curcumin NPs exhibit anticonvulsant activity and prevent cognitive impairment in fully kindled animals. The level of neuronal cell death and glial activation reduced in animals which have received curcumin NPs compared to those received free curcumin.

Conclusion: To conclude, these findings suggest that curcumin NPs effectively ameliorate memory impairment and attenuate the level of activated glial cells in a mice model of chronic epilepsy.

Keywords: Curcumin nanoparticles; Memory improvement; Anticonvulsant; Glial activation; Pentylenetetrazol

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Fabrication and Evaluation of Novel Quercetin Conjugated Fe3O4–β-cyclodextrin Nanoparticles for Potential Use in Epilepsy Disorder

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Introduction: Despite the numerous pharmacological activities of quercetin, it's biomedical Application has been hampered, because of poor water solubility and low oral bioavailability.

In the present study, we fabricated a novel form of quercetin-conjugated Fe3O4–β cyclodextrin (βCD) nanoparticles (NPs), and the effect of these prepared NPs was evaluated in a chronic model of epilepsy.

Method and material: Quercetin-loaded NPs were prepared using an iron oxide core coated with βCD and pluronic F68 polymer. The chronic model of epilepsy was developed by intraperitoneal injection of pentylenetetrazole (PTZ) at dose of 36.5 mg/kg every second day. Quercetin or its nanoformulation at doses of 25 or 50 mg/kg were administered intraperitoneally 10 days before

PTZ injections and their applications continued 1 hour before each PTZ injection.Immunostaining was performed to evaluate the neuronal density and astrocyte activation of hippocampi.
Result: Our data showed successful fabrication of quercetin onto Fe3O4–βCD NPs. In comparison to free quercetin, quercetin NPs markedly reduced seizure behavior, neuronal loss, and astrocyte activation in a PTZ-induced kindling model.
Conclusion: Overall, quercetin–Fe3O4–βCD NPs might be regarded as an ideal therapeutic approach in epilepsy disorder.
Keywords:quercetin, Fe3O4 nanoparticles, anticonvulsant, neuroprotection, astrocyte activation

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Ictal SPECT and Rule of Nurse During this Procedure

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Ictal SPECT is a safe and non-invasive procedure in determination of seizure focus and for evaluation of seizure focus extension in good selected patient.
This method is usually done in pharmaco resistant patients before they become candidate for epilepsy surgery. This method is based on the phenomenon that blood perfusion to the seizure focus is rising during a seizure attack as double. Expert nurses inject Technetium 99 with proper dose through IV less than 30 seconds after starting Ictal EEG onset in selected patient during monitoring in LTM ward. Afterward, 10cc of Normal saline injects due to washing the vessel.
After this step, related physician should be informed for starting over of anticonvulsant drugs. The surface electrodes must be removed and the patient conduct to Gamma Scan ward for doing SPECT at the end of Ictal injection.
The second step of this procedure is Interictal SPECT. As its name shows, it will be done 24 hours after Ictal SPECT if no seizure occurred.
Although ictal SPECT shows hyper perfusion of seizure focus, Interictal SPECT shows hypo perfusion of this zone.

SPECT is a good radiologic method for cases that ictal onset zone of EEG is not completely clear or brain MRI with epilepsy protocol shows more than one lesion as epileptogenic zone.

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Precision Medicine in Epilepsy

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Modern Medicine has served patients during the three eras of intuitive medicine (1950s-1980s), evidence-based medicine (1980s-200s) and precision medicine (2010-present). In the intuitive medicine or symptom therapy era, doctors treated symptoms in patients without really understanding or addressing the actual underlying etiology. In the evidence-based medicine or empirical therapy era, science produced from the randomized controlled trials was used to treat the underlying disease as a global entity. For instance, data from RCTs can provide the statistical success rate of a certain treatment "X". If the rate is justifiable, treatment "X" will be used for all patients with that certain disease. However, there is always a small percentage of patients who will not respond to treatment "X". Precision medicine investigates how an individual's unique genome interacts with their unique invioronment and thus focuses on individual patients instead of the disease and the etiology. Therefore, in the case of our given example treatment "X" , the non-responders will not be neglected. Precision medicine tries to find out why a certain individual is susceptible to a certain disease and how to prevent and cure. It uses, clinical genomics, pharmacogenetics and immunology to achieve this goal. So far, Precision medicine has been mostly used in cancer and genetic disease with success.
In epilepsy treatment, it is well known that some patients respond to AEDs better than others. It is believed that the genetics of epilepsy is the most determining factor in how a patient responds to therapy. The best example would be in patients with Dravet syndrome who will respond to stiropentol due to their unique mutation in sodium channel gene. Or, screening for HLAA 3101 in the asian population before initiating carbamazepine, which is

another example of using precision medicine in order to prevent a drug adverse effect in certain individuals. Precision medicine has also stepped into the field of epilepsy surgery. There are ever-growing modalities of presurgical evaluation that can be utilized to more accurately define the epileptogenic zone. With precision medicine we can choose from these options according to each patient's unique characteristics.

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Accelerating Orphan Drug Discovery Using Zebrafish Models of Rare Diseases

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There are approximately 7000 rare diseases, yet to date only a very limited number of orphan drugs are marketed. Developing new drugs requires significant funds and time, and in the case of rare diseases, the commercial return is often insufficient for the pharmaceutical industry. For many rare diseases, drug repurposing would represent a faster, cheaper and less risky option to identify drugs that would be of immediate therapeutic benefit to patients. A key obstacle currently in the way of a systematic evaluation of approved drugs for their potential to treat a large number of different rare diseases is the availability of suitable screening models to perform drug repurposing screens. Because 80% of rare diseases are genetic in origin, it is possible to create animal models that have similar genetic defects and that mimic the human pathological conditions. Zebrafish, with their high genetic, physiological and pharmacological similarity with humans, offer the possibility of performing rapid drug repurposing screens using microscale, *in vivo* models of human diseases. To date, we have generated zebrafish models for a number of rare neurodevelopmental disorders, including Dravet syndrome, Lennox-Gasteaux syndrome, Otahara syndrome, Batten disease, and Zellweger syndrome. Drug repurposing and drug discovery screens using some of these zebrafish models has led to the identification of

both approved drugs and new drug candidates, one of which will enter a Phase 2a clinical trial in 2020.

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Cognitive Impairment in Epilepsy; Determination, Causes and Risk Factors

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Cognitive dysfunction is detectable in different domains and severity among considerable portion of epileptic patients and even in uncomplicated cases. Several etiology for cognitive decline in epileptic patients has been reported that major categories consist of brain underlying pathology, seizure attacks, epileptic dysfunction, psychiatric problems and therapeutic modalities, in which seizure characteristics and treatments are more dynamic variables.
However epidemiological and clinical evidences reveal that cognitive impairment are prevalent already at the onset of epilepsy and even before. Consequently progress during the years that disorder persist or progress.
Attention, executive function, memory, learning, academic performance, language and behavioral are more involved. Types and severity of dysfunction are

linked to underlying pathology and also type, severity and chronicity of seizure, prior brain functional reserve, age, level of education.

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Identification of People with Epilepsy in West of Kabul City

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Introduction: epilepsy is a common neurological condition that affects about one person in every 103. It is caused by recurring disruptions to the brain`s usual activity, which are generally short lived. Epilepsy is most commonly diagnosed in childhood and in people over 60 years of age, but it can affect anyone. The outward signs of epilepsy are known as seizures, and these vary in appearance depending upon the part of the brain that is affected and how far the disruption has spread. The aim of this study was to evaluate the status of epilepsy patients in west of Kabul city

Material and method: the study was conducted in 1398. Epileptic patients attending the outpatient neurology clinic at the Alemi hospital one of the hospitals in the west of Kabul- Afghanistan. We provided questionnaires and asked them their first We collection the information and analyzed them. data were analyzed by using SPSS.

Result: The number of patients enrolled in the study were 49 persons (35 women and 14 men), (44 hazara, 3 Tajik and 2 Pashtuns), 28 persons single and 21 persons married, that from this number. That of these 37 people had specific symptoms before the onset of the attack, 28 of them had limbs jumping during the day (that causes objects to be thrown), 36 of them suffered from trauma during the attack, 38 of them complained of unilateral weakness after convulsions, 6 of them had anti-epileptic spices, and unfortunately, 44 of them had epilepsy limiting in their lives, the triggers for seizures were one tone of color imaging, 7 of them insomnia, one of them hunger, seven of them fatigue and seven of them sound, and the frequency of attacks was eleven daily, eight weekly, seven monthly, one every three months and eighteen unknown.

Conclusion: Afghanistan has many health problems. One of these problems is epilepsy. Lack of public and private health centers, lack of facilities, specialist doctors is one of the most important reasons for increasing the number of these patients at the population level. Increasing specialized health centers, holding specialized workshops and training seminars for professionals and patients are helpful strategies.

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Psychogenic Nonepileptic Seizures

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Psychogenic nonepileptic seizures are commonly diagnosed at epilepsy centers. The diagnosis of PNES relies on a multidisciplinary evaluation and is usually based on different combinations of data. Recording a seizure, while under video-EEG monitoring, is the most reliable diagnostic test. The neurobiology of PNES is still poorly understood. They may be the result of neurobiological dysfunctions at specific brain networks. Treatment of PNES includes multiple phases. Fewer than 50% of newly diagnosed adults could be expected to become seizure free within five years after diagnosis.

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Intracranial EEG and High-Frequency Oscillations

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Invasive (Intracranial) EEG studies are often recommended in:

- Nonlesional cases without a clear epileptogenic area

- Ambiguous localization by imaging and scalp EEG
- Bilateral temporal lobe epilepsy
- An epileptogenic focus in proximity to the eloquent cortex, thereby necessitating functional mapping

High-Frequency Oscillations (HFOs):

- Events with at least 4 consecutive oscillations between 80Hz and 600Hz that clearly rise above baseline.
- Ripple (> 80–200 Hz), fast ripple (> 200–600), and sigma (≥ 600 Hz)

Significance of HFOs

- The identification of HFOs appears capable of improving presurgical diagnosis and surgical outcome, and it seems reasonable to add a ripple and fast ripple zone to the presurgical diagnosis.

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Selecting Appropriate Candidates for Epilepsy Surgery

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While roughly 2/3 of patients with epilepsy are successfully treated with anti-seizure medications, the remaining continue to have seizures and may be candidates for surgical treatments. For selecting appropriate candidates for epilepsy surgery an extensive presurgical evaluations is mandatory. At least five different specialties should be involved in the epilepsy presurgical assessment including epileptologist, radiologist, neuropsychiatrist, neurosurgeon and nuclear medicine. During the presurgical evaluation, five different brain areas are determined including irritative zone, symptomatogenic zone, seizure-onset zone, functional deficit zone and epileptogenic lesion. These five zones may not be exactly identical but are overlapped. The aim of presurgical evaluation is finding epileptogenic zone defined as the minimum amount of cortex that must be resected surgically to produce seizure freedom. Since the epileptogenic zone (EZ) could not be determined directly, it should be found indirectly by defining the other zones discussed above. If the patient is

seizure-free after surgery, we conclude that the epileptogenic zone must have been included in the resected cortex.
Irritative zone is area of cortex that generates interictal epileptiform discharges. Seizure onset zone is area of cortex that initiates clinical seizures. Symptomatogenic zone is area of cortex that produce seizure semiology. Usually the ictal semiology is due to spread of the discharge from an EZ located in a symptomatically silent area to a distant area of eloquent cortex that is outside the epileptogenic zone. Functional deficit zone is the area of cortex that is not functioning normally in the interictal period. This area could be assessed by neuropsychiatric test, ictal SPECT and interictal PET.
The purpose of electrocorticography recording is to refine the presumed physical boundaries of following zones: the eloquent cortex and the irritative zone.
Ictal SPECT has a higher sensitivity of interictal SPECT and if the isotope is injected within the first 20 seconds after seizure onset, it could be significantly correlated with localization of EZ.
In patients with epilepsy FDG-PET scan is typically performed in the interictal state with the goal of detecting focal areas of decreased metabolism, that are presumed to reflect focal functional disturbances of cerebral activity associated with epileptogenic tissue. PET is more valuable in temporal lobe epilepsy rather than extratemporal ones.

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Post Anoxic Status Epilepticus

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The term “myoclonic status epilepticus” has been used to describe a variety of clinical states that have in common a prolonged period of frequent spontaneous myoclonic jerks. A reasonable general definition might be that myoclonus must occur either (1) at least once every 10 seconds for longer than 10 minutes or (2) at least once a minute for longer than 30 minutes. Myoclonic status may be associated with a wide range of etiologies and the

presentation of and approach to myoclonic status epilepticus depends largely on the underlying etiology.

Acute anoxic myoclonic status epilepticus (MSE)usually starts on the first or second day after the anoxic injury and lasts 1 to 5 days. It is typically considered a poor prognostic sign and it is always associated with coma. The facial muscles are preferentially affected by asynchronous or synchronous small amplitude jerks that may occur at regular or irregular intervals. They often increase in frequency and severity with stimulation of the patient. Prominent eye movements, including paroxysmal eye opening and upward eye rolling, are characteristic, though all muscle groups can be affected.

Chronic anoxic myoclonic status epilepticus, as classically defined, Lance-Adams syndrome (LAS) presents days to weeks after the insult and persists for months to years. It was originally described in patients who have regained mental status but may present while the patient is still in coma or under sedation (Freund et al 2016). It is also most commonly seen in patients who have suffered a primary respiratory arrest with or without a subsequent cardiac arrest. As defined, Lance-Adams syndrome is often associated with good neurologic recovery.

On a practical level the most important distinguishing feature is that acute postanoxic myoclonic status epilepticus is typically associated with other clinical and neurophysiologic signs of severe brain damage, such as absent brainstem reflexes or absent cortical response on somatosensory-evoked potentials.

Neuroimaging, EEG monitoring, somatosensory-evoked potentials, and neuron - specific enolase levels should be considered in all cases of acute postanoxic myoclonic status epilepticus. Repeated clinical exams are also critical because favorable outcomes have been noted despite the presence of postanoxic myoclonic status epilepticus. Pupillary response and absence of bilateral N20 (cortical) responses on somatosensory-evoked potentials and EEG are regarded as some of the most reliable predictors.

Therapeutic hypothermia and targeted temperature management has been shown to improve survival and neurological recovery after cardiac arrest and has become the standard of care for cardiac arrest . In a meta analysis of studies of cardiac arrest conducted when hypothermia was utilized, 211 patients with myoclonus (not necessarily myoclonic status), 9% (18) were considered to have good neurologic outcome (Sandroni et al 2013; Sandroni and Nolan 2015).Also in a retrospective review of The International Cardiac

Arrest Registry, a multicenter cohort of cardiac arrest patients mostly treated with targeted temperature management, Seder and colleagues reported very similar findings (Seder et al 2015). The authors also found that 9% (44) of 471 patients with myoclonus after cardiac arrest were considered to have good functional outcomes .Seder and colleagues found that if myoclonus was not thought to be associated with epileptiform activity on EEG, the likelihood of a good outcome increased to 15% (Seder et al 2015).
There is little agreement on the appropriate management of acute myoclonic status epilepticus following circulatory arrest.Treatment approaches range from adding 1 or 2 anti myoclonic agents in an attempt to suppress clinical jerking to use of IV anesthetics to suppress most or all epileptiform activity. Agents commonly used include benzodiazepines, sodium valproate, and levetiracetam, as well as lacosamide and brivaracetam. For the treatment of refractory cases of LAS, deep brain stimulation surgery has been performed with some initial encouraging results, but only in a few cases and it is still experimental at this time. In a case of perinatal hypoxia, the target of stimulation was the thalamus but in the other two cases the stimulation target was the globus pallidus internus.

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Lennox-Gastaut Syndrome

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The history of Lennox-Gastaut syndrome (LGS) begins in 1939 when a slow (2.5 Hz) spike-and-wave pattern was described by Gibbs, Gibbs, and Lennox . LGS is a severe form of age related epilepsy that typically becomes apparent during infancy or early childhood. LGS belong to the classification of epileptic that are a group of disorders in which seizure activity leads to progressive cognitive dysfunction and constituting 1-4% of childhood epilepsies . Three necessary findings for the diagnosis of LGS are multiple generalized seizure types, a slow spike-and-wave pattern (less than 2.5 Hz) on EEG and cognitive Decline . The most common types of seizures associated with LGS are tonic and atonic seizures. A third type of seizure commonly is seen in Lennox-

Gastaut syndrome is atypical absence seizures. Patients with LGS may develop normally before the onset of seizures, and then psychomotor regression begins. Because the seizures associated with LGS are usually refractory to treatment, intellectual impairment and learning problems may worsen over time. In approximately 70-80 percent of cases LGS has an identifiable cause and called symptomatic Lennox-Gastaut syndrome. Such as perinatal insult, cortical dysplasia, neurometabolic disorders T congenital infections, stroke, trauma, tuberous sclerosis, encephalitis or meningitis. In 17-30 percent of individuals a previous history of West syndrome is present. Lennox-Gastaut syndrome may also be classified as cryptogenic, in which the cause is unknown or cannot be determined after evaluation. Cryptogenic cases are presumed to result from an unidentified condition. Individuals with cryptogenic Lennox-Gastaut syndrome do not have a previous history of seizure activity, prior neurological problems or cognitive impairment before the development of the disorder.

The prevalence of LGS is 0.1 per 1000 population for boys, versus 0.02 per 1000 population for girls. The annual incidence in children is estimated to be 2 per 100,000 children.

A diagnosis of Lennox-Gastaut syndrome is usually made based upon a thorough clinical evaluation, a detailed patient history and a complete physical and neurological evaluation. EEG and MRI is necessary for diagnosis No specific therapy for LGS is effective in all cases and the disorder has proven particularly resistant to most anti-epileptic drugs(AEDs).Ketogenic diet, VNS therapy and epileptic surgery are other options.

Effects of Maternal Administration of Curcumin and Hesperidin on Lipid Peroxidation in the Hippocampus Following Repeated Febrile Seizure in Rat Pups.

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Introduction: Febrile seizures are the most common form of seizures in the early years of a child's life, which affect 2-5% of children. Febrile seizures can predispose children to have subsequent epilepsy and must be taken seriously. It has been reported that induction of oxidative stress is involved in pathogenesis of epileptic seizures and development of epilepsy. Oxidative stress can activate pro-inflammatory mediators, which in turn affect the release of inflammatory cytokines such as IL-1β. Administration of natural antioxidative compounds (such as plant materials) is one of the treatment goals to reduce the oxidative activities.
Curcumin and hesperidin are the major components derived from turmeric rhizome and citrus fruits, respectively. It has been reported that these compounds have antioxidant activity and reduce the production of ROS.
The aim of this study was to evaluate oxidative stress following repeated febrile seizure in the offspring of rats that received curcumin and hesperidin in their pregnancy period.
Material and methods: Curcumin (60 mg/kg) and hesperidin (100 mg/kg) emulsified in 1% carboxymethyl cellulose (CMC) was used for treatment groups. Also, 1% CMC was administered to the vehicle group. Pregnant rats were received the materials via gavage. Male offspring of rats were divided to seizure and normothermia groups. Hyperthermia febrile seizure was induced at postnatal days 9-11, and six-hour after the last hyperthermia induction, rat pups were decapitated and their hippocampi were collected and stored at -80°C until later use.
Malondialdehyde (MDA) concentration, as a biomarker of lipid peroxidation, was measured based on the thiobarbituric acid (TBA) reaction method.
Data were analyzed by one-way ANOVA followed by Tukey's post hoc test.

Results: Statistical analysis of MDA content showed significant differences between seizure groups and vehicle group (vehicle+ seizure vs. vehicle: P< 0.001, curcumin+ seizure vs. vehicle: P< 0.05, hesperidin+ seizure vs. vehicle: P< 0.001). Also, the curcumin+ seizure group showed a significant difference with the vehicle+ seizure group (P< 0.05).
Conclusion: Repeated febrile seizure in rat pups increased the levels of reactive oxygen species. During inflammatory processes, elevation in a series of oxidative compounds such as ROS is considered as contributing factors in neurological diseases. Agents causing oxidative stress, together with inflammatory cytokines potentiate each other and make a vicious cycle, leading to further damages. It has been reported that curcumin exhibits radical scavenging activity and reduces oxidative stress. Moreover, there are some documents demonstrating the antioxidant activity of hesperidin. Our results showed that curcumin attenuated lipid
peroxidation in rat pups' hippocampus following repeated febrile seizure induction, but hesperidin did not have any effect on reducing lipid peroxidation.
Keywords: Febrile seizure, Curcumin, Hesperidin, Oxidative stress, Epilepsy

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Rolandic Epilepsy and the Spectrum of Idiopathic Focal Epilepsies in Children

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Rolandic epilepsy and spectrum of idiopathic focal epilepsies account for 10% to 20% of epilepsies in children. These epilepsies have a number of common features. They are age dependent. Patients have normal neurologic examination and developmental status. Neuroimaging is usually normal. These epilepsies have characteristic EEG findings with spikes of distinctive morphology and variable location superimposed on a normal background. All of these epilepsies have genetic predisposition and have specific seizure semiology. Almost all of these epilepsies rapidly respond to treatments and

the prognosis is usually good. However, many issues exist around the treatment of these epilepsies because atypical and extreme forms of Rolandic epilepsy such as Landau Kleffner and Continuous spikes and waves during sleep usually could see after treatment with traditional anti-seizure medications. A number of investigators argue the treatment of these epilepsies with anti-seizures medication such as carbamazepine. These investigators believe that treating many of these patients with Rolandic epilepsy and its spectrum could have deteriorating effects on the EEG during NREM sleep and even could deteriorate cognitive function in these children. They believe that many of these children do not need to treat at all, however, if we need to treat them we need to administer anti-seizure medications without deteriorating effects on EEG and cognition. As a practitioner dealing with children with Rolandic epilepsy, we need to know this spectrum of epilepsies enough and update our knowledge about their treatment.
Keywords: Children, Rolandic epilepsy,Treatment

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The Anticonvulsant and Neuroprotective Effect of the Stachys Lavandulifolia Against the Epileptic Model of the Seizures Induced by Pentylenetetrazol in the Male Rats

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Background: Considering the prevalence of epilepsy and the failure of available treatments for many epileptic patients, finding more effective drugs in the treatment of epilepsy s eems necessary. The aim of the present study was to investigate the ameliorative effect of *Stachys lavandulifolia* extract (SLE) against pentylenetetrazol-induced kindling was studied.
Methods: Kindling was produced by sub-convulsant doses of PTZ treatments in rats. Twenty-four Wistar albino rats were divided into 4 groups; PTZ treated (PTZ), PTZ+SLE treated (PTZ+SLE) and PTZ+ phenobarbital treated (PTZ+PB) groups. Extracts were given a dose (25 and 50 mg/kg) 30 min before each PTZ injection. In addition, after the end of the experiment, the rats were killed and their brains were removed for the histological study.

Findings: The obtained data from this experiment demonstrated that compared to the control group, the SLE delayed the initiation and duration of the tonic, clonic and tonic-clonic seizures and significantly reduced the tonic and clonic seizures. Furthermore, the administration of the SLE significantly prevented the production of the dark neurons in different areas of the hippocampus compared to PTZ group.
Conclusion: The results from this study suggest the presence of significant anticonvulsant activity in SLE, in PTZ-induced seizure models, which could be due to its antioxidant activity, as is reflected by the change in oxidative stress markers in the brain.
Key words: *Stachys lavandulifolia*, Epilepsy, Kindling, Anticonvulsants, pentylenetetrazol

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Cannabinoids (THC and CBD) as Controllers of Drug-resistant Epilepsy Syndromes

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Epilepsy is one of the most common neurological disorders, which is spreading more and more every day. Almost one third of epileptic patients suffer from drug-resistant onesets that are known with refractory seizures, leading to decrease in quality of life that will cause inevitable psychological consequences.
According to the population-based national study survey of epilepsy, Iran has the highest prevalence of long life epilepsy that is 2-3 more than the overall worldwide estimation. It has been estimated that 1300000 Iranian people struggle with epilepsy and 400000 of them are diagnosed with drug-resistant syndromes. So nowadays, comprehensive research has been done to find a treatment for drug-resistant epilepsy.

Cannabis sativa as a new hope has been used for epilepsy, pain and anorexia from deep past. This plant has more than 80 canabinoids that among them Δ9-tetra hydrocanabidiol (THC) and canabidiol (CBD) have a high share. From 19th century, the role of THC on treatment of drug-resistant epilepsy has been investigated and from 2 years ago CBD as a new idea has attracted scholar's attention for medical usage especially for drug-resistant syndromes. In many studies, positive effects of phitocanabidiols have been reported; using animal modeling of epilepsy, seizures, epileptogenesis and neuroprotection, however, usage of CBD is preferable due to plethora psychic side effects of THC. CBD is the most frequent molecule used for drug-resistant epilepsy like Lenox-Gastaut and Dravet treatment whereas the mechanism is not understood clearly.

Method: A comprehensive study on cannabinoid's effect on epilepsy has been done, using search engines like Google Scholar and PubMed. Our strategy to find most relevant papers was using key words like "Epilepsy, Cannabinoids" and" seizure, cannabis, THC" without any limitation on year and language.

Cannabis sativa belongs to Urticales order and Cannabaceae family (Ahmed et al., 2008) cannabis has been known as hemp, marihuana, marijuana, Indianhemp, indestrialhemo in Europe. In English, marijuana refers to that kind of Cannabis which is cultivated for drug manufacturing and hemp is used to produce fiber (Sengloung et al., 2009). Cannabis grow in western and middle parts of Asia like Russia, China, India, Pakistan, Iran specially marginal parts of Himalaya toward India.

This plant grows in arid lands mostly (Anwar et al., 2006). Cannabis is known as a herb with miscellaneous potentials that it is utilized as a source of drug, fiber, food and oil around the world (Small et al., 2002Piluzza et al., 2013). More than 480 different metabolites in Cannabis have been reported and most of these secondary metabolites like flavonoids, stilbenoids, terpenoids, alkaloids, and chemicals with Nitrogen, lignans and phenolic amids are found in cannabis tissues (Flores-Sanchez et al., 2008).

Cannabinoids are unique materials which are found only in Cannabis Sativa which are terpenophenolic molecules with 21 carbons. More than 70 cannabinoids have been detected in cannabis that the main 10 among them are CBG, CBC, 9-ΔTHC, and 8-ΔTHC, CBL, CBE, CBN, CBD, CBNT and CBT while the rest are classified as sundries. (Flores-Sanchez et al., 2008, Cascini et al., 2013). 0.3% of these molecules or less is found in root, seed and stalk,

less than 1% in below leaves and 2-3% in the top leaves of female plants (Carpentier et al., 2012). Among Canbinoids, mentioned above, CBD and THC are the most important due to medical usage such as killing pain, appetite increase, migraine, seizure, decreasing nausea between cancerous patients who are under chemotherapy, epilepsy, MS, anti-cancer and so on (Chandra et al., 2010; Sirikantaramas et al., 2004; Van Bakel et al., 2011). Regarding a certain group of epileptic people (almost one third of whole) who suffer from treatment-resistant epilepsy, no proper remedy has been found (Devinsky et al., 2016) these patients have to experience anaemia as a side effect.

Conclusion: Regarding prior arts, studies and experiments mentioned previously, effect of Cannabis as a medication with infinitesimal side effects has been proved. So, Cannabis cultivation and oil extraction in order to combat with a wide range of disease, most importantly treatment-resistant epilepsy has been necessitated. To aim this goal, Scholar's effort to provide the best condition for Cannabis cultivation is in demand to reach the highest amount of oil as a material for drug manufacturing to have a share in decreasing of death from epilepsy.

Key words: Canabidiols, Cannabis, seizure, epilepsy

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Developmental and Epileptic Encephalopathies of Infancy

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Developmental and Epileptic encephalopathies(DEE), define as syndromes in which epileptic seizures and epileptiform activity contribute to or exacerbate underlying brain dysfunction, leading to prominent developmental delay. Developmental impairment originates from a direct consequence of the genetic mutation, in addition to the effect of the frequent epileptic activity on brain development. These mutated genes are commonly responsible for both epilepsy and deviation from developmental milestones. Despite choosing the most appropriate antiepileptic drugs for the seizure type and syndrome, the results are often disappointing, and polytherapy and/or alternative therapy becomes unavoidable. In this lecture, I will discuss the clinical and electroencephalographic characteristics and evolution and management of age-related early epileptic encephalopathies, recognized by the International League Against Epilepsy, as follows: early infantile epileptic encephalopathy (Ohtahara syndrome), early myoclonic encephalopathy, epilepsy of infancy with migrating focal seizures, various early epileptic encephalopathy syndromes, infantile spasms(West syndrome), severe myoclonic epilepsy in infancy (Dravet syndrome) and myoclonic-atonic

epilepsy (Doose syndrome). Precision medicine plays an important role in future management of these epileptic syndromes.

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Psychiatric Comorbidity in Epilepsy: A Review Article

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background:Epilepsy is a common neurological condition with wide-ranging neuropsychiatric manifestations. Neuropsychiatric problems in epilepsy are difficult to diagnose and they are frequently missed or overlooked. The impact of these comorbidities on patients' seizure control and quality of life suggests that early detection and treatment are of paramount importance. The purpose of this study was to identify and explore these psychiatric comorbidity in epileptic disorders.
Methods:This study reviewed the scientific references of authentic databases and journals, including Medline, Pubmed, Scopuse, SID, Web of science andClinicalkey. Overall,42 scientific studies conducted during 2005-2019 were collected.
results: Data analyses revealed this categories psychiatric comorbidityin epileptic patients: Suicide, generalized anxiety disorder, depressive disorder, social phobia and agoraphobia, autism spectrum disorders and eating disorders.
conclusion: A range of mental health problems can be seen in patients with epilepsy that can lead on to significant distress, dysfunction and impair their quality of life.So special attention should be paid to the impact of psychiatric co-morbidity and disablement. Successful treatment can have a profound effect on a patient's quality of life and may contribute towards better seizure control.
Keywords: epilepsy, Comorbidity, anexiety, depression

The Relationship Between Attitude and Knowledge of Epilepsy Among Students of Hamadanuniversity of Medical Sciences

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Background: Understanding knowledge and attitude with respect to epilepsy is an essential initial step in evolving strategies aimed at dispelling the myths and misconceptions associated with this condition. The purpose of this study is to assess relationship between knowledge and attitudes of students of Hamadanuniversity of medical sciences towards epilepsy.
Methods: This cross-sectional descriptive study was conducted in Hamadan University of Medical Sciences. 266 students completed the self-report questionnaire. This questionnaire consisted of three sections: demographic information, knowledge and attitude questionnaire.To participate in the study, written informed consent was obtained from the participations. Data was analyzed by SPSS-16 software.
Findings: The knowledge of most participants (68.4%) was moderate and only 6% of the subjects had good knowledge about epilepsy. While the attitude of most participants (75.2%) was positive. Our findings confirm the relationship between knowledge and attitudestoward epilepsy among students. This means that there was a significant positive relationship between knowledge and attitude of the participating students.
Conclusion: According to this survey, knowledge about epilepsy is not satisfactory. with respect to the relationship between knowledge and attitude, It is suggested that additional efforts must be made to increase the knowledge of students through education programs.
Keywords: epilepsy, knowledge, attitude, student

Focal Epilepsies

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Focal epilepsies are characterized by seizure arising from a specific part (lobe) of the brain include frontal lobe, temporal lobe, parietal lobe and occipital lobe epilepsy.
Focal epilepsy maybe treated with medication and occasionally with diet, nerve stimulation or surgery. Especially in the condition is due to a scar or other lesion in the brain.
Frontal lobe epilepsy: Frontal lobe epilepsy is the term for recurring seizures beginning in the frontal lobe. Because the frontal lobe is responsive for planning, executing movement and personality. Frontal lobe epilepsy can have a dramatic effect on a patient's quality of life. Frontal lobe seizures are often very brief and tend to occur at nights. They are typically with preserved awareness or impaired awareness and can quickly spread throughout the brain. Because there are so many connections between frontal and temporal lobe. It can be difficult to determine which section of the brain is being affected. Anticonvulsant drugs are the most first common choice for treatment if those do not control the seizures, surgery maybe an option.
Temporal Lobe Epilepsy: Temporal lobe epilepsy is the term for recurring seizures beginning in the temporal lobe. The temporal lobes are areas of the brain that most commonly give rise to seizures. The mesial portion (middle) of both temporal lobes is very important in epilepsy - it is frequency the source of seizures and can be prone to damage or scarring. Because there are so many diverse functions either in or closely related to the temporal lobes, these seizures may have a dramatic effect on the patient's quality of life.
Seizures beginning in the temporal lobes may remain there, or they may spread to other areas of the brain. Depending on if and where the seizure spreads, the patient may experience the sensation of:
Seizures beginning in the temporal lobes may remain there, or they may spread to other areas of the brain. Depending on if and where the seizure spreads, the patient may experience the sensation of:

- A peculiar smell (such as burning rubber)
- Strong emotions(such as fear)

- Abdominal/chest discomfort
- Automatic, unconsciously repeated movements
- Staring
- Loss of awareness

Parietal Lobe Epilepsy: Parietal lobe is the section of the brain on the top and sides of the head. Known as the "association cortex" the parietal lobe is responsible for connecting meaning to the brain's functions. It is here that the brain creates a visual image, that sounds are recognized as words, and that the sense of touch is associated
with a particular object. In some ways, the parietal lobe is where perception meshes with physical reality. Parietal lobe epilepsy is very uncommon. Seizures staring in this area can cause sensory disturbance, such as heat, numbness or electrical sensations, weakness, dizziness, hallucinations, distortions of space and other symptoms.

Occipital Lobe Epilepsy: Occipital lobe epilepsy is the term for recurring seizures beginning in the occipital lobe, the section of the brain in the back of the head that is primarily responsible for vision. Seizures beginning in the occipital lobe rare.

These seizures can cause a person to experience flashing bright lights or other visual changes on the left side of his or her visual field (if occurring in the right cortex), or on the right side (if occurring in the left cortex)

Keywords: focal epilepsy, treatment

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Why is psychogenic nonepileptic seizure diagnosis missed? A retrospective study

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Purpose: The aim of this retrospective study was to scrutinize factors that are associated with a delay in making the diagnosis of psychogenic nonepileptic seizures (PNES).

Methods: In this study, patients with PNES, who were investigated at Shiraz Comprehensive Epilepsy Center, Iran, from 2008 to 2019, were studied. We categorized the patients into the **following:** 1. those with a definite diagnosis

of PNES in less than a year since the onset of their attacks; 2. those with a definite diagnosis of PNES later than 10 years since the onset of their attacks.

Results: During the study period, 330 patients were recorded. In 98 patients (30%), the diagnosis of PNES was made in less than a year since their seizure onset. In 67 patients (20%), the diagnosis of PNES was made later than 10 years since their seizure onset. Taking antiepileptic drugs (AEDs) (odds ratio (OR) = 6) and a history of ictal injury (OR = 3.6) had a positive association, and age at the onset (OR = 0.8) had an inverse association with a delay in receiving a definite diagnosis of PNES (p = 0.0001).

Conclusion: Some demographic variables (i.e., early age at the onset of seizures), patients' clinical variables (i.e., severe seizure manifestations such as ictal injury), and finally, some physician-related variables (i.e., prescribing AEDs) have significant associations with a delay in making a definite diagnosis of PNES.

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Epilepsy, Brain Networks, and Memory

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None of the normal or pathological brain functions solely arise from distinct brain regions, but from interactions between the large scale brain networks. The intrinsic connectivity between saliency network, default-mode network, and central executive network lays the foundation of cognitive processes such as memory. Epilepsy certainly disturbs activity of intrinsic connectivity within and between the networks. Exploring changes of the large scale brain networks associated with focal or generalized epileptic discharges provides information about both transient and permanent memory impairment related to spatio-temporal disruption of brain connectivity. In this lecture, I will try to discuss memory impairments of patients with epilepsy in the brain connectivity paradigm.

Key words: Epilepsy, network, memory

Knowledge, Attitude, And Practice Among The Practitioners Regarding Epilepsy In Bhutan- A Rural And Remote Country

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Background: The correct knowledge and attitude among the practitioners is key to provide good quality patient care on epilepsy. The objective was to assess the knowledge-attitude-practice on epilepsy among various medical workforce in Bhutan.
Methods: A one-day face-to-face training was organized on the "diagnosis of epilepsy and treatment course" with suitable prior advertising and public invitation to participate. Those interested were requested to answer a short questionnaire on various aspects of epilepsy before the start with 17 items related to socio-demography, level and source of knowledge on epilepsy, etiological nature, contagiousness, relation to past life/sins, warning signs and precipitants of seizures, encephalogram, definitions of epilepsy and active epilepsy, first-aid and epilepsy management, treatability of epilepsy, with two feedback questions.
Results: A total of 65 (57.0% males) subjects successfully completed their necessary pre-event questionnaire. Of them 72.0% were lecturer or clinician, 22.0% were nurses, 3.0% were from medical administration, and 3.0% were traditional practitioners.
The positive aspects were: none recognised epilepsy as contagious or epilepsy related to the past life or sins, including traditional medicine participants. All responded favorably to that "they found this event useful" and "this event added something meaningful to them personally or professionally". All participants responded positively to "do you know what epilepsy is", although it was clearly not the case.

The negative aspects were:
38.0% participants reponded electroencephalogram as essential in the diagnosis of epilepsy. For 6.0% participants, inserting an object in the mouth is the first they would do if they see an epilepsy patient. A 48.0% of participants could not identify correct definition of epilepsy, and about 90.0% participants could not recognise the correct definition of active epilepsy. About 68.0% participants recommended modern treatment alone, while 20.0% recommended a mix of both modern and traditional treatment and 3.0% recommended traditional treatment alone. Additionally, after excluding items with low (<0.4) item-test correlation, the alpha coefficient was found to be 0.81. The factor structure showed a two factor model fit with cumulative variance of 81.6%, coefficient of determination of 92.6%, and CFI of 0.81.
Perspectives:(a) Multi-lingual short course structured modules on epilepsy (print and online) for allocation (on fee or free) to institutions in and outside Iran;
(b) Academic-cum-advocacy annual exchange for in-person annual training on epilepsy;
(c) Field exposure on epilepsy through field research projects, as well as
(d) First-ever Iranian Journal on epilepsy, for which the process is underway.
Conclusions: Although all participants reponded that they know what epilepsy is, important gaps on the knowledge of epilepsy were found. Fortunately, there were no stigmatizing attitudes about the nature of epilepsy or its treatment among our participants.Our work emphasizes the need for multi-purpose structured educational-cum-advocacy programs, which can ameliorate knowledge and professional development among the practitioners in order to improve the quality of epilepsy care.

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Epilepsy and Down Syndrome and Mental Retardation

Mehrdad Boroon

There has also been epilepsy since the creation of man on the planet.

In the old days, people believed that someone who was in such a state would have enraged the genius or devil in his body. Based on these superstitious

beliefs about epilepsy, various ways were being used to treat the sufferer, so that Satan was driven from within him. To be Sometimes evildoing ghosts would be very cruel.

They were tortured and scratched with pristine instruments like sharp gems, or crackling magic.

The Greeks looked at the disease as a sacred illness and believed that only one of the gods could cause the patient to fall on the ground. He will be shaken and then again before the patient's complete death
Bring him alive.

Hippocrates was the first to disagree with this theory. The Greek physician, about 2450 years ago, believed that epilepsy was one of a variety of diseases that caused brain dysfunction.

key words: Epilepsy, Down syndrome, mental retardation

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Dexmedetomidine as an Analgesic Agent with Neuroprotective Properties: Experimental and Clinical Aspects

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Dexmedetomidine (dexdor or precedex®) is considered as a sedative agent that is widely used as an adjuvant in general anesthesia and critical care medicine practice. There are many evidences indicating its neuroprotective properties especially in various ischemic and hemorrhagic brain injury models of animals. Clinical trials have shown that dexmedetomidine (DEX) can improve outcome of intensive care unit (ICU) patients. Also, DEX is appropriate for use as a non-opioid analgesic therapy whenever minimizing opioid-related side effects is necessary. The underlying mechanism of this drug is related to the activation of alpha-2 adrenergic receptors, causing inhibition of C-fibers and Aα-fibers in the peripheral nervous system. Alpha-2 adrenergic receptors centrally (in the locus coeruleus) prevent nociceptive

neurotransmission through the spinal cord. Alpha-2 adrenergic receptors also presynaptically inhibit the release of norepinephrine, which disturbs depolarization and the pain signaling. In addition, recent studies indicate that in neurons, synthesis and release of acetylcholine and nitric oxide are affected by DEX that could be involved in the regulation of analgesic activity of the drug. Apart from the beneficial effects of the drug on the nervous system, there are potential adverse effects, such as hypotension and bradycardia, which can be treated pharmacologically and must be taken into consideration by clinicians.

Keywords: Dexmedetomidine, Neuroprotection, Pain, Analgesia, Non-opioid

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Evaluation of anticonvulsant activity of Japanese sake yeast (Saccharomyces cerevisiae sake) supplementation in mice: A pilot study

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Introduction:Neuroprotective activity of adenosine receptors in the central nervous system (CNS) has been mentioned in previous studies. On the other hand, it was previously reported that Japanese sake yeast enriched in adenosine analogues in vitro.

Methods: Male C57BL/6N strain mice weighing 20–30 g were selected for this study. Seizure activity and the effect of sake yeast were evaluated in animals during administration of pentylenetetrazol (PTZ). The animals were treated with drugs during 1 week and 60 min after the last dose of all drugs, seizure was induced by the IP administration of 60 mg/kg of PTZ. Each animal was placed separately into a transparent Plexiglas cage and observed for at least 60 min and the following parameters were recorded: 1) Latency to the onset time of tonic-clonic seizures. 2) Seizure frequency.

The experimental design was consisted of 5 groups: vehicle (0.5% methylcellulose in water) + NaCl 0.9%, vehicle + PTZ, vehicle + diazepam

(5 mg/kg), vehicle + sake yeast (100, 200, and 300 mg/kg), and sake yeast (100, 200, and 300 mg/kg) + PTZ. Vehicle, Saline, diazepam and sake yeast were given orally.
Results: Latency times to tonic-clonic seizures were significantly (P <0.05) higher in groups receiving oral sake yeast in comparison with non-treated groups. Also, seizure frequency and seizure stage were significantly (P <0.05) lower during all 3 doses oral administration of sake yeast.
Conclusion: It is concluded that sake yeast can attenuate severity of convulsion in rat and this supplementation can be a good candidate for treatment or prevention of seizure with advantages including the lower adverse effects in comparison with the current chemical drugs in the market.
Keywords: Japanese sake yeast, Convulsion, Rat

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Antiepileptic Activity of Ziconotide as a Neuronal Calcium Channel Blocker: Experimental and Clinical Features

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Epilepsy is a chronic non-communicable neurological disorder with high prevalence that affects around 50 million people worldwide and is caused by abnormal electrical activity in the brain. Normal brain function depends on the proper balance between excitatory and inhibitory neurotransmitters, and their imbalance leads to the abnormalities such as epileptic seizures. The crucial role of the calcium ions and glutamate-induced calcium influx via N-methyl-D-aspartate receptors (NMDARs) in neuropathological conditions is widely mentioned in various studies. During the neuropathological conditions such as traumatic brain injury and its neurobehavioral sequelae including possible seizure and epilepsy, excessive glutamate release and subsequent abnormal NMDA - stimulated calcium accumulation in postsynaptic neurons is thought to contribute to a cascade of cellular events that lead to the neuronal cell death. On the other hand, most epileptic and anxious patients that treated with the first-line drugs demonstrate tolerance, dependency and addiction to the remedy. Therefore pharmaceuticals with lower adverse effects and more efficacies in neuronal disturbance including

seizure and convulsion are highly desired. Ziconotide is the small peptide originated and synthesized by cone snails as a component of paralytic venoms. Ziconotide induces neuroprotection at least by two pathways: (1) direct blocking of calcium entry by acting on the N-type calcium channels and (2) restricting calcium entrance via postsynaptic NMDARs due to inhibition of release of the presynaptic excitatory neurotransmitter, glutamate. Other neuroprotective mechanisms of ziconotide are believed to be competitive inhibition of neuronal nicotinic acetylcholine receptors (nAChR) and blocking N-type VDCC via intracellular signaling mediated by gamma-aminobutyric acid receptors ($GABA_BR$). It is concluded that ziconotide represents neuroprotective including anti-seizure activity in human and animal models of neuronal damages but in human clinical trials, it seems necessary to improve the convenience of peptide drug delivery protocols and attenuate the adverse effects associated with ziconotide-based therapies.

Keywords: Epilepsy; Seizure; Neuroprotection; N-type calcium channel blocker; Ziconotide

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Intravenous Antiepileptic Drugs in Adults with Benzodiazepine-Resistant Convulsive Status Epilepticus

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Generalized convulsive status epilepticus (GCSE) is a time-dependent medical emergency, which requires to be promptly recognized and treated. First-line benzodiazepines effectively control GCSE in two thirds of patients. After their failure, antiepileptic drugs are administered intravenously. A recent systematic review showed that phenobarbital was the most effective and less tolerated second-line treatment for GCSE in adults. Valproate and levetiracetam were less effective than phenobarbital, but associated with lower risk of respiratory depression and hypotension; lacosamide showed a good safety profile. These results probably reflect the doses used in included trials. Phenytoin ranked worst in the likelihood of reaching GCSE cessation, reflecting the long infusion time required to prevent adverse events. The

Established Status Epilepticus Treatment Trial (ESETT) demonstrated equi-effectiveness of levetiracetam, fosphenytoin, and valproate in benzodiazepine - resistant GCSE in adults and children; these drugs had similar incidences of adverse events. Overall, levetiracetam and valproate administered at adequate doses are effective and safe second-line treatments for GCSE in adults.
The effectiveness of phenytoin in benzodiazepine-resistant status is hampered by its long infusion time with delayed onset of anticonvulsant activity. Further studies could evaluate the efficacy and safety of second-line drugs administered immediately after benzodiazepines and irrespective of the initial control of GCSE.

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Progressive Myoclonic Epilepsy

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Progressive myoclonic epilepsies (PME) are a group of rare, inherited disorders characterized by seizures, myoclonus, and progressive neurological degeneration. Patients may also exhibit cerebellar ataxia, dementia, neuropathy, and myopathy.
Myoclonic and generalized tonic-clonic seizures are most common, although absence, atypical absence, tonic, and focal seizures may occur.
Myoclonus in PME occurs separately from seizures and may be focal or segmental and is often asymmetrical and arrhythmic.
Myoclonic jerks are often precipitated by posture, action, or stimuli such as sound, light, or touch; they are most apparent on the face and distal extremities.
The symptoms of PME typically begin in childhood or adolescence and the outcome is generally severe; however, the age of onset, rate of progression, and associated features depend on the PME subtype.
In the early stages of PME, clinical and EEG features may mimic idiopathic generalised epilepsy syndromes, especially juvenile myoclonic epilepsy,but failure of therapy and progressive neurological and EEG deterioration point

to a diagnosis of PME. A full history of the illness,developmental history in children, comprehensive family history when possible, and thorough clinical examination are imperative to obtain clues to diagnosis.
Although laboratory and pathological studies are still required for some of the PME disorders, the revolution in molecular genetics has allowed a definitive diagnosis of some PMEs such as Unverricht-Lundborg disease, MERRF, DRPLA, and most patients with Lafora's disease.
Genetic evaluation panel usually includes 12 genes known to cause Lafora disease, Unverricht-Lundborg disease, the neuronal ceroid lipofuscinoses, and PRICKLE1-associated PME. These disorders are all inherited in an autosomal recessive manner.
Treatment of PME disorders remains essentially that of managing seizures and myoclonus together with palliative, supportive, and rehabilitative measures. Commonly used antiepileptic drugs for management of myoclonus include combinations of valproic acid, benzodiazepines, phenobarbital, and more recently, piracetam, zonisamide, and levetiracetam.
Care must be taken to avoid antiepileptic medications that clearly worsen myoclonus. These include vigabatrin, carbamazepine, phenytoin, and gabapentin. Lamotrogine has an unpredictable effect on myoclonus and must be used with caution.

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Preparation and Evaluation of Nanostructured Lipid Carrier-Based Hydrogel for Intranasal Administration of Lorazepam for Treatment of Status Epilepticus

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Background: Status epilepticus is defined as a condition in which epileptic seizures lasts more than 5 minutes and must be treated aggressively because of the brain damage risk. The benzodiazepine of choice for initial treatment

is lorazepam (LZM). Nasal drug delivery is a non-invasive route of administration for direct nose-to-brain delivery without passing the blood–brain barrier. It delivers the drugs to brain without systemic absorption, thus avoiding the side effects and enhancing the efficacy of neurotherapeutics. The use of nanoparticles for nasal drug delivery cause quick absorption, controlled drug release and enhance residence time in nasal cavity especially if nanoparticles load in a gelling system. In this study, chitosan-thermosensitive hydrogel containing LZM nanostructured lipid carriers (NLC) was prepared and used in pentylenetetrazole (PTZ) induced seizures' rats to evaluate its in vivo performance.

Methods: LZM-NLCs were prepared by emulsification solvent diffusion and evaporation method. The effects of differents factors like lipid/drug ratio, oil content and surfactant concentration were investigated by using Design Expert software (version10, USA). Furthermore, chitosan/β-Glycerophosphate in situ hydrogel containing LZM-NLCs (LZM-NLCs-Gel) were prepared and performance of the optimal formulation was investigated in four groups of PTZ-induced seizures' rats.

Findings:The mean particle size of the LZM-NLCs was found to be71.7±5.2nm with PdI of 0.21±0.23 and negative zeta potential (-20/06±2/70mV). The drug entrapment efficiency of NLCs was 81.80±5.04. In situ hydrogel containing LZM-NLCs were prepared by chitosan (%2 w/v) and β-glycerophosphate (%15w/v). LZM-NLCs-Gel could reduce prevalence of epileptic seizure, duration of symptoms, severity of symptom and increase time of incidence in rats.

Conclusion: Hydrogel containing LZM-NLCs is a novel drug delivery system for delivery of LZM through nose to brain. The system showed to be effective to prevent and treat status epilepticus in rats.

Keywords: Status epilepticus, Nasal drug delivery, Insitu gelling system, Lorazepam, pentylenetetrazole

Side effects of stablished new antiepileptic drugs

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Backgrounds: Epilepsy is considered to be among the most prevalent neurological disorders and one of most important health issues. AED at 20 years for ineffectiveness was 39.3%, for adverse events 8.0%. In contrast, some of the newer AEDs appear to produce fewer adverse cognitive effects. More studies are needed to delineate fully the relative effects of all the new AEDs to each other and to the older AEDs.
Methods: the all of studies founded by search with Google motor, PubMed and Iranian indexes evaluated.
Results: Gabapentin (GBP) and lamotrigine (LTG) have demonstrated fewer cognitive effects than CBZ and minimal effects compared with placebo, but sleepiness in some patients is a problem. Of the new AEDs, topiramate (TPM) appears to have the greatest cognitive side effects, but slow titration during drug initiation reduces these effects. Lamotrigine have many side effects; the most important of which is allergic reactions. The major adverse events that caused discontinue lamotrigine in a study included: cutaneous reactions in 29 cases(3%); Stevens-Johnson syndrome, and severe headache, exaggerated or induced myoclonic jerk, and other rare side effects. Recently a lot patients receive levetiracetam. One of the important side is depression, especially suicide reported frequently. I observed attempt suicide in two patients.
Conclusion: the new anti epileptic drugs have the seriously adverse events; Steven Janson/TEN, depression, suicide.
Keywords: side effects, levetiracetam, suicide, depression. Lamotrigine, skin reactions, cognitive effects, topiramate, gabapentin, sleepiness.

Case Report of Complementary Therapy for Achieving Happiness of a Child with Absence Epilepsy

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Background: Epilepsy is one of the most common neurological disorders in childhood. The research shows that children with epilepsy are more exposed to childhood disorders than healthy children. One of these disorders is anxiety. Anxiety is a common comorbidity in epilepsy. Therefore an epileptic child needs psychological complementary therapy in addition to medication. This complementary therapy is not a substitute for medical treatment but can be associated with medical treatment. The aim of this case report, with Kids' Skills approach, is to illustrate the process of this complementary therapy for achieving happiness of a child with absence epilepsy.
Methods: This case report on a primary school girl, uses the psychological approach of Kids' Skills founded by Ben Forman, psychiatrist and director of the Helsinki Brief Therapy Institute. Kids' Skills sets a plan for children to overcome their behavioral and emotional problems by learning skills with the support of their parents and teachers. The systematic steps of this approach start by agreeing with the child on the skill and end with a happy celebration and planning for teaching the skill to another child. In this report, the Pediatric Quality of Life Inventory (PedsQL™ 4.0) is used to assess the epileptic child's quality of life.
Case Report: Melika is seven years old and a first grade student. This Melika's teacher refers her to the school psychologist because of daydreaming and inattention in the classroom. Parents' interview and psychological tests indicate that Melika has a normal IQ, no learning disability and no attention deficit disorder. Because the child's daydreaming occurs frequently, with staring and interruptions of consciousness, she is referred to a child neurologist for diagnosis. Neurological tests show that Melika has absence epilepsy and needs medication to control her seizures. Starting medication, Melika and her parents come to the Kids' Skills and Health Room in order to prevention of the behavioral and emotional problems. The results of the Quality of Life Inventory, completed by the school health teacher in collaboration with Melika's parents, are reviewed to explore the child's required skills. The results indicate that Melika's emotional

functioning is not satisfactory because Melika feels sad and worry about what will happen to her. Available evidence suggests that she is a subject to generalized anxiety. For this reason, it is agreed with Melika on the two skills for achieving happiness: cooperating with classmates and keeping happy memories diary. After displaying the model and role-playing in the Kids' Skills and Health Room, the class teacher and the health teacher be invited as the child's supporters and a training plan is set for Melika to practice the skills under supervision on her supporters.

Conclusion: The primary goal of treating a child with absence epilepsy, which is realized through the diagnosis and supervision of a child neurologist, as well as the support and care of parents and educators, is to prevent silence seizures attacks and reduce the potential risks that the child may have due to loss of consciousness. In addition to medical treatment and care, for the prevention of generalized anxiety and improvement of the epileptic child's quality of life as the secondary goal, supplementary therapy can be initiated for achieving happiness. This supplementary therapy should be down at the discretion of child neurologist. According to psychological research, one of the most important predictor variables of children's happiness is their cooperative relationship with peers.

Keywords: absence epilepsy, anxiety, complementary therapy, happiness, Kids' Skills.

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Comparison of Defense Mechanisms in Women with Temporal Lobe Epilepsy Versus Ordinary Counterparts

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Background and Purpose: Epilepsy is one of the most prevalent neurological disorders, that being afflicted has numerous physical, psychological and social consequences. On the other hand, defense mechanisms are responsible for protecting (a person) against the stresses, anxieties and pressures of

everyday life. The present study was undertaken with the aim of investigating the defense mechanisms of epilepsy patients and a non-clinical group.
Materials & Methods: The research design was based on causal-comparative case study. The statistical population of the study is consisted of all epileptic women and their normal counterparts referred to Khatam ol anbia Hospital during the first half of 2019. The research sample was selected by means of the convenience sampling approach, for which 40 women with epilepsy were recruited and compared to their 40 normal counterparts, so that the two studied groups were similar in terms of age, education and marital status. Research data were gathered using the Andrews Defense Mechanism Questionnaire (DSQ40) and were analyzed by SPSS24 software employing multivariate statistical analysis of variance.
Results: There is a significant difference ($p<0.05$) between the defense mechanism used in epileptic women and that of healthy women.
Conclusion: This is a subject based study in which some of the psychological factors in epilepsy have been investigated and in line with previous theories regarding the close association between mental components and physical illnesses .epilepsy uses mechanism that psychiatric theorists see as gateway to physical and psychological abnormalities .
Consequently, it can be ascertained that women with epilepsy have different defense and are more likely to use immature mechanisms in comparison with normal women. mechanisms
Keywords: defense mechanisms, epilepsy

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Brain Networks and Seizure Spreading

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In the human brain Information transmission is a fundamentally dynamic network process.Epilepsy is characterized by disturbed dynamics that originate in a local network before spreading to other brain regions.The influence of network topology and the anatomical organization of the epileptogenic process are particularly important in the context of seizure control and epilepsy surgery.Seizures can spread and terminate across brain

areas via a rich diversity of spatiotemporal patterns. The hypersynchronous discharges that occur during a seizure may begin in a very discrete region of cortex and then spread to neighboring regions. Seizure initiation is characterized by two concurrent events: 1) high-frequency bursts of action potentials, and 2) hypersynchronization of a neuronal population. Seizure propagation, the process by which a partial seizure spreads within the brain, occurs when there is sufficient activation to recruit surrounding neurons. This leads to a loss of surround inhibition and spread of seizure activity into contiguous areas via local cortical connections, and to more distant areas via long association pathways such as the corpus callosum.The propagation of bursting activity is normally prevented by intact hyperpolarization and a region of surrounding inhibition created by inhibitory neurons. With sufficient activation there is a recruitment of surrounding neurons via a number of mechanisms. The propagation of activity in neural tissue is generally associated with synaptic transmission, but epileptiform activity in the hippocampus can propagate with or without synaptic transmission . This suggests an underlying common nonsynaptic mechanism for propagation.

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Epileptic Headache , A Rare Painful Seizure

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Introduction: epileptic headache (EH) is a rare combination of epilepsy and headache.
Result: EH may occur at any age, affects both sexes equally .in some patients it has features of migraine, or as a tension-type headache, while in others is indefinable. The kind of pain and its location may also vary. It may last for seconds to days, in which case it is a headache/status epilepticus.A shorter duration seems to be more frequent in the case of temporal and anterior foci.Minor accompanying symptoms in about half of the cases include phono/photophobia, vomiting, pallor, difficulty in talking, agitation. Ictal EEG

recordings show abnormalities compatible with an epileptic seizure that begin and stop at the same time as the headache. In some cases, the abnormalities can only be detected by deep electrodes.Interictal EEG abnormalities may be present or not, and the patient may also experience other kinds of epileptic seizure.The brain diseases detected include genetic encephalopathies,trauma, malformations/dysplasias, neoplasms and chronic encephalitis; idiopathic epilepsy has only been reported in two cases. Lesions may be occipital, parietal, temporal or frontal, and the variable features of the headache do not always correlate with the site of the lesion or EEG focus.

Conclusions: EH must be diagnosed on the basis of the presence of EEG epileptic activity coinciding with the duration of the pain. The positive effect of the acute administration of an anti-epileptic drug on the headache episode suggests the possibility of EH and the appropriateness of making an ictal EEG recording.

Keyword: epilepsy,heaedache

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Is Rituximab Effective in Refractory Status Epilepticus?

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Background: Refractory status epilepticus (RSE) is a life-threatening conditions that lasting more than 60 min and do not respond to first and second-line anticonvulsant drug therapy. How often RSE occurs, the effect of rituximab to control seizure on clinical outcome is poorly defined (1).

Methods: In this review, a general search in Medline, Science Direct and Springer databases were done during years of 2004 to 2019. We evaluated human studies of NCS and NCSE in critically ill patients and the results are presented here. Chen JW and et al studies during self-sustaining status epilepticus showed that a depletion occurs in hippocampus of the predominantly inhibitory peptides dynorphin, galanin, somatostatin, and neuropeptide Y,

whereas the expression of the proconvulsant substance P and neurokinin B is increased, in cells that do not normally express them at detectable concentrations (2).The recent discovery by Shorvon S and et al showed that Super-refractory status epilepticus can be due to anti-NMDA-receptor antibodies and the recognition that this is a common condition has stimulated interest in the possibility that other, as yet undiscovered, antibodies may be playing a part in the pathogenesis of SE (3).

Findings: Many of the most refractory cases of SE seem to occur in young adults who present with new-onset refractory SE which often appears to have an inflammatory or autoimmune etiology. NMDA-receptor (N-methyl-D-aspart) and Voltage-gated potassium channels (VGKCs)-antibody receptor can cause encephalitis (4). During the refractory SE cytokine levels include interleukin (IL)-1β, IL-2, IL-4, IL-5, IL-6, IL-10, IL12 is raised (5). Rituximab is an anti-CD20 chimeric monoclonal antibody that results in B-cell depletion and decreased IL-10 level with anti-NMDA effect. The mechanisms of rituximab include not only delayed antibody depleting effects but also direct B cell modulating effects, and it is possible that the reconstitution of B cells after one dose of rituximab generates long lasting changes to the circulating B cell population (6). Rituximab with dose of 1g two weeks apart, with 1 g repeated six and twelve months later (and planned re-treatment at 18 months) abated seizure after 2 weeks of initiation (6).Thus it can help to improve clinical and cognitive impairment in refractory SE.

Conclusion: Despite the retrospective nature of this study, our findings support an off-label use of rituximab, with the consideration risk of infectious complications, we suggest that rituximab could be used to reduce significant morbidity and mortality in RSE.

Key words: refractory status epilepticus, interlukines, VGKCs, NMDA

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Newer AEDs and Drug-Resistant Epilepsy

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Approximately 20-30% of patients with epilepsy have a form of refractory or drug-resistant epilepsy (DRE), that is defined as failure of adequate trials of two tolerated, appropriately chosen antiepileptic drugs (whether as monotherapies or in combination) to achieve sustained seizure freedom.
All patients with DRE should be referred to multi-disciplinary or comprehensive epilepsy center. The first step of evaluation in such center is determination whether there is a true refractory epilepsy, i.e., ruling out the differential diagnoses of DRE. In the second step, seizure focus and type of seizures and/or syndromes as well as surgically remediable epilepsies (those with known pathophysiology, predictable natural history, and progressive features, e.g., developmental delay or interictal behavioral disorder) and surgically non-remediable cases are accurately defined.
Patients who are not candidate for surgery, for example those with epileptogenic zone (EZ) in motor cortex or language areas, patients whose EZ overlaps with eloquent cortex, multifocal seizures and who are unwilling to surgery are managed by therapeutic options other than surgery including: trial of previously untried newer AEDs with lesser interactions, better efficacy and tolerability, with mechanism of action other than those of traditional antiepileptic drugs, corticosteroids, ketogenic diet and even trial of drugs in clinical development (experimental antiseizures) such as

Cannabinoids, Everolimus and Ganaxolone. Tiziana G and coworkers (2019) reported that 12%-17 % of DREs became seizure free with the addition of a previously untried new AED. Complementary alternative medicine (CAM), such as behavioral therapy and Ayurvedic medicine are also the matters of concern. We herein, will review some of the newer AEDs such as zonisamide, lacosamide, rufinamide, stirioentol, eslicarbazepine, perampanel and retigabine.

Keywords: Newer AED, Drug-resistance Epilepsy; Surgically non-remediable Epilepsies.

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Comparison of Serum Zinc Levels in Children with Epilepsy and Febrile Convulsions

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Objective: Epilepsy is one of the most common and chronic neurological diseases in children. The prevalence of this disease among children in Iran is estimated at 5%, which is higher than the average prevalence in other countries. Several studies have been done on the role of trace elements in serum and its role in the pathogenesis of epilepsy, but there is still little information on the role of zinc and its serum level in children with epilepsy compared to fever-induced seizures.

Methods & Materials: patients with febrile convulsion and epileptic patients younger than 6 years old and admitted to pediatric neurology ward of Ghaem hospital were divided into two groups of 22 each with parental consent. The third group was selected as the control group with 22 patients in the same age range from febrile patients without pediatric seizure. The amount of 2 ml of blood was collected within the first 6 hours of admission and measured in the biochemical laboratory of Ghaem Hospital by a dedicated serum zinc expert. At the end the results were compared and then analyzed.

Results: A total of 22 epileptic children, 22 children with febrile seizure and 22 children with no seizure as control group were enrolled. The mean age of

the patients in the study was 3.00 ±1.84. The results showed that the serum zinc level in the group of children with epilepsy was 84.53±29.42 mg.L, in the febrile seizure group was 82.14±27.61 mg.L and in the control group was 83.02±28.25 mg.L. Results of statistical analysis showed that there was no significant difference between the three groups (p = 0.96). Statistical analysis also showed no significant difference between each two groups.
Conclusion: The results of this study show that there is no difference between serum zinc level between patients with febrile convulsion and those with epilepsy. However, according to the results of other studies, further studies with larger sample sizes are needed to obtain stronger evidence in this topic.
Key words: Epilepsy, serum zinc , pediatric.

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Sport Comorbidities in Children with Epilepsy

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Pubmed physical exercise comorbidities in epilepsy

Children with epilepsy are often advised against Participation in sports and exercises .mostly because of fear , over protections ,and ignorance about its nature .A major cause for a reduced quality of life in people with epilepsy is the prejudice that comes with the disease. people with epilepsy are often discriminated against at school, in the work place, and they may be denied basic rights, including the ability to be actively engaged in sports. Thus schools and institutions need to plan educational programs for children with epilepsy. Exercise has been shown to provide some benefits such as reduce the frequency of seizures, improvement of self-confidence, reduction of anxiety, depression, obesity and make better in bone density and coronary heart disease.no studies were found in providing a correlation between seizures and exercises but one supportive hypothesis proposes that beta-endorphins released during exercise has inhibited epileptic discharges.
Material and Methods: Between 10 children at ages 5-16 years old , referred to the Khatam Hospital in the city of Tehran (2017-2018) five of

them(2 girls,3boys) have history of neonate convulsion, no major motor or sensory impairment has reported. After participating in sports, seizures occurred again at school in form of GTC.

Discussion : This study has claimed that children and teenagers who suffer from epilepsy may experience prolonged seizures while exercising or practicing any sport .people with epilepsy are at higher risk of injury and sudden death rather than healthy people. Participation in sport/exercise in rare cases can trigger seizures. But a regular exercise program increases serotonin, noradrenaline, dopamine synthesis and regulates Neurotrophin, reduces stress and seizures.

Finding: Five of the 10 children with epilepsy have showed seizures during exercises at school in form of GTC. They reported history of neonatal febrile convulsion. Their attacks controlled with AEDs partially. They experienced some CPS during LTM .Brain MRI showed normal. dehydration can cause body stress which would see lower the seizure threshold and cause seizures .They had signs of headache, Fatigue ,nausea ,dizziness, hunger during exercise, due to electrolyte imbalance that are triggers.some medication such as Topamax may overheat their body during sport and cause confusion and seizures.,

Results: According to this study, Children with CPS with or without secondary generalization, seizures occurred during strenuous exercises. Such as ball games, jogging and hiking. Whereas, patients with TLE in exhaustive sports showed none experienced seizures during or after exercises. Finally hypoxia, dehydration, hyponatremia, hyperthermia, hyperventilation and hypoglycemia during exercise appears to deter seizure onset. Drinking plenty of fluids (water, juice) during and soon after exercise, we will see upper the seizure threshold. Therefore, they stay well-hydrated. Encourage them to do the activities during the coolest parts of the day in hot weather, or try activity for shorter periods of time and rest frequently, play with a buddy if possible. The amount or intensity of exercise may be gradually increased if the child tolerates it without any problems.

Conclusion: participation in sports and physical activity is an important way to maintain both physical and psychological health.preventive care education for children with epilepsy during exercises at school is important. The majority of sports are safe for epileptics to participate in (Running, bike, gymnastics, aerobic, yoga, ...)and will potentially reduce seizure frequency and improve quality of life .sports at heights, motor, shooting, scuba diving not recommended. Swimming and horseback riding, permitted if under

supervision proper protection such as helmet, knee-elbow pads and life vest. So, regular physical exercise had led to better seizure control. Suggesting that increased attention and vigilance during physical activity may reduce the occurrence of injury for children with epilepsy.
Children with CPS are higher risk of hurt rather than TLE.

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Speech and Language Disorders After Rolandic Epilepsy in Children

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Background: Among the types of childhood epilepsy, Rolandic epilepsy is a benign disorder with very good prognosis that accounts for 15% of childhood epilepsy. The most common age for Rolandic epilepsy is 6 to 10 years, usually at bedtime. Symptoms of Rolandic epilepsy included tonic and colonic facial muscular contractions, burning sensation, itching, numbness, loss of consciousness, difficulty speaking, and salivation from the mouth due to the lack of facial muscle control. One of the most common problems that occur after childhood epilepsy is speech and language disorders. Therefore, the purpose of the present study is to review speech and language problems after Rolandic epilepsy in children.
Methods: In this review, studies were conducted from 2011 to 2019 from PubMed, Science Direct, Google Scholar databases were investigated using "Epilepsy, Rolondic epilepsy, Seizure, Speech and Language Disorder, Children and Child" key words. Studies that examined the relationship between speech and language disorders and benign Rolandic epilepsy were included in the present study.
Findings: Of the 23 articles, 7 related articles, all of which were available in full text and were in English language, were evaluated. There was a large difference between the articles in terms of the indices studied, sample number, method of implementation, and so on. A review of studies showed that seizure freedom and prolonged life without seizure was associated with

higher scores on all language tasks during the follow-up period after epilepsy. Higher age at the onset of epilepsy, higher IQ, and higher baseline scores were associated with higher follow-up scores across all language tasks. Chronic seizure-induced brain damage is associated with decreased language skills in affected children and limits the intra-syllabic, syllabic, and phonemic levels. There are also deficits in the cognitive, phonological, and verbal working memory of these children. Changes in semantic skills were also the most common problem in the reviewed studies, and these children also exhibited morpho-syntactic language disorders. Children with Rolandic epilepsy also have difficulty understanding sentences and show deficits in short-term auditory memory and central auditory processing that can be effective in language deficits in these children.

Conclusion: The results of the reviewed studies indicate a high likelihood of occurrence of speech and language disorders in children with benign Rolandic epilepsy. However, longitudinal studies with long-term follow-up are needed to better comment in this regard. However, children with benign epilepsy appear to need speech therapy services to assess and treat speech and language disorders in addition to receiving treatment to manage their epilepsy.

Key Words: Speech and Language Disorders, Seizure, Rolandic Epilepsy, Children

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Hepatocyte Growth Factorattenuatesthe severity of Status Epilepticus in Kainic Acid-induced Model of temporal Lobe Epilepsy by Targeting Apoptosis and Astrogliosis

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Objectives: Although drug therapy is the most common treatment for epilepsy, proper seizure control is not achieved with current medications. The present study was conducted to evaluate the protective effects of hepatocyte growth factor(HGF) in a rat model of temporal lobe epilepsy (TLE) and explore possible molecular mechanisms.

Materials and Methods: A rat model of temporal lobe epilepsy was established using intra-hippocampal injection of kainic acid(4µg).Intra-cerebrovascular injectionof HGF(6 µg)was performed 30 min before injection of kainic acid. Learning and memory impairment were investigated by behavioral tests.ELISA assay was used to determine astrogliosis and DNA fragmentation.Changes in neuronal density and mossy fiber sprouting were evaluated by Nissl and Timm staining,respectively.
Results: Behavioral assessments indicated that kainate treated rats showed spontaneous seizure and their alternation percentage scores in Y-Maze test were lower ($P<0.001$). Likewise,the passive avoidance test confirmed learning disability in Kainate treated rats($P<0.001$). HGF administration reduced the number of spontaneous seizures, alternation percentage score ($P<0.001$), and cognitive disturbances ($P<0.001$).The histopathological results also showed that HGF administration protected contributed to reduction of neuronal loss in the CA3 subregion of hippocampus and inhibited formation of aberrant mossy fiber sprouting (MFS) ($P<0.01$). Also, 2ELISA assay showed a significant decrease in GFAP ($P <0.01$), and DNA fragmentation ($P<0.05$) following HGF administration.
Conclusion: Our findings demonstrate the validity of HGF in protection against progression of the kainate-induced TLE in rats by improvement of learning, cognitive disturbances and inhibiting of apoptosis and astrogliosis.
Keywords: Hepatocyte growth factor; Temporal lobe epilepsy; Astrogliosis; Apoptosis; memory impairment.

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Epilepsy and Quality Of Life in Iranian Epileptic Patients

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Introduction: Epilepsy is one of the common neurological disorders with physical, emotional and social consequences. Epilepsy affects the quality of life more than any other chronic disease, and occasionally stigma is more than the disease itself affects a patients' life. The aim of the present study

was to investigate different dimensions of the quality of life of epileptic patients in Khorasan Razavi province, Iran.
Method: In this cross-sectional study, 100 patients were randomly selected on the basis of their national code numbers. After confirmation of the diagnosis of epilepsy by the neurologists and having the criteria for entering the study, they completed the QOLIE-31 questionnaire. Finally, data was analyzed statistically by SPSS software.
Results: The study sample comprised 100 PWEs, aged 18-74 years (34 ± 13), of whom 58 (58%) were females. Tonic-colonic seizure was the most common (60%) type of seizure. The obtained score of each sub scale and the range of overall score of qolie-31 was 16.40- 79.18 with the mean of 49.7± 16. The overall score obtained in this study was not significantly different from the global score of the region. For the sub scales, the lowest mean score was 14.3 ± 30.9, and the highest mean score was 25.2 ± 57.4, to subscales of overall quality of life and cognitive functioning, respectively.
Discussion: In fact, the ultimate and preferred outcome of all treatments and care interventions is patient's quality of life. Thus, improvement of the quality of life in patients with epilepsy should be one of main goals in their treatment.
Keywords: Epilepsy, QOLIE-31 questionnaire, quality of life

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The Antiepileptic and Neuroprotective Effect of the *Thymus Vulgaris* Against the Pentylentetrazol Kindled Model of the Seizures in the Male Rats

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Background: In traditional medicine, a large number of plants have been used to cure neurodegenerative diseases such as seizure and other memory-related disorders. In the present study, the effect of *Thymus vulgaris* extract (TVE) on the epileptic animal model was studied.
Methods: In this experimental study, twenty-four male Wistar rats were randomly selected and were divided into experimental and control groups.

The experimental groups were treated by the intraperitoneal (i.p.) injection of 50 and 100, mg/kg of TVE. The control negative group received normal saline and the control positive group received phenobarbital (30 mg/kg,i.p.). Kindling was successfully induced by repeated administration of a sub-convulsant dose of pentylenetetrazol (PTZ) (35 mg/kg; i.p.) at an interval of each 48 h in 30 days. In addition, after the end of the experiment, the rats were put to death and their brains were removed for the histological study.
Findings: The ANOVA demonstrated that compared to the control group, the TVE delayed the initiation and duration of the tonic, clonic and tonic-clonic seizures and significantly reduced the tonic and clonic seizures. Furthermore, the administration of the TVE significantly prevented the production of the dark neurons in different areas of the hippocampus compared to PTZ group.
Conclusion: It is concluded that the TVE possess beneficial effects on learning and memory impairments in repeated seizures model which is accompanied by antioxidant effects in the brain.
Key words: Thymus vulgaris, Antiepileptogenic, Kindling development, Hippocampus, pentylenetetrazol

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Basic of EEG Machine

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Electroencephalography continues to be an essential diagnostic test in clinical practice and its use has evolved over nearly 90 years since its invention (by Hans Berger in 1929).
Approaching EEG interpretation for the first time requires some understanding of EEG's basis, recording technology, and general capabilities and limitations. With understanding of these facets, the EEG activity is more clearly interpreted and the diagnostic questions can be more readily addressed. Therefore, we need to know about electricity and electronics as they relate to EEG.

The basic systems of an EEG machine include data collection, storage, and display. The components of these systems include electrodes, connecting wires, amplifiers, a computer control module, and a display device.
The EEG amplifiers convert the weak signals from the brain into a more discernable signal for the output device. They are differential amplifiers that are useful when measuring relatively low-level signals.
A variety of output printers and monitors are available for EEG machines.
Since the data collected is analog, it must be converted to a digital signal so electronic output devices can be used. Therefore, the primary circuitry of the EEG typically has a built-in analog to digital converter section.

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Management of Status Epilepticus

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Status epilepticus is a medical emergency that requires rapid and vigorous treatment to prevent neuronal damage and systemic complications.
Failure to diagnose and treat status epilepticus accurately and effectively results in significant morbidity and mortality. The most common subtype is generalized tonic-clonic status epilepticus.
Nonconvulsive forms include petit mal status and complex partial status, which may manifest as behavioral disturbances. Simple partial status epilepticus consists of persistent motor, sensory, or autonomic seizures that do not impair cognition. Subclinical status epilepticus generally refers to seizures occurring in an unresponsive or comatose individual in the absence of overt signs of seizure activity.
Therapy should proceed simultaneously on four fronts: termination of seizures; prevention of seizure recurrence once status is controlled; management of precipitating causes of status epilepticus; management of the complications
Refractory and super-refractory status epilepticus (SE) are serious illnesses with a high risk of morbidity and even fatality. In the setting of refractory generalized convulsive SE (GCSE), there is ample justification to use continuous infusions of highly sedating medications.
Forms of SE other than GCSE (and its continuation in a "subtle" or nonconvulsive form) should usually be treated far less aggressively, often with non-

sedating anti-seizure drugs (ASDs). Management of "non-classic" NCSE in ICUs is very complicated and controversial, and some cases may require aggressive treatment.
Continuous EEG monitoring is crucial in guiding the management of these critically ill patients: in diagnosis, in detecting relapse, and in adjusting medications.
The morbidity and mortality of RSE is substantial, but many patients survive and even return to normal function, so RSE should be treated promptly and as aggressively as the individual patient and type of SE indicate.
Keywords: Status epilepticus, Refractory and super-refractory status epilepticus

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Depression in Epilepsy: Prevalence and Treatment

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The prevalence of depression in patients with yet active epilepsy ranges from 20% to 55%, while that in those with controlled epilepsy ranges from 3% to 9%. As compared to the general population of adults, the rate of depression in epilepsy patients is 4- to 5-fold greater. In addition, the prevalence for a depressive-like state in patients with epilepsy has been shown to be higher as compared to healthy control subjects. Suicide attempts as well occur 10 times more frequently in affected patients than the general population, with the risk considered to be particularly high in those with temporal lobe epilepsy, up to 25-fold greater than in the general population.
Two important clinical questions must be answered before prescribing antidepressants to a patient with epilepsy. First, a decision must be made regarding prioritization when considering the most appropriate treatment, replacement of an antiepileptic drug with a negative psychotropic property or administration of antidepressant agents. Second, is the antidepressant being considered universally effective for different types of depression seen in epilepsy patients? Unfortunately, while these issues are decisively important

for clinical practice, there is only insufficient evidence available, thus some expert opinion will be presented as a substitute.
Only inconclusive findings have been provided in view of the efficacy of antidepressant drugs for patients with epilepsy, with only 2 randomized controlled trials (RCTs) conducted thus far. Results obtained in one of those failed to confirm differences between placebo and tricyclic antidepressant administrations, and the other failed to provide sufficient descriptions to consider the findings trustworthy. Although safety has been confirmed for some classes of selective serotonin reuptake inhibitor (SSRI) and serotonin and norepinephrine reuptake inhibitor (SNRI) medications over a short term, a slight but definite proconvulsant property has been found in nearly all antidepressants, including tricyclic antidepressants, SSRIs, SNRIs, and noradrenergic and specific serotonergic antidepressants over a long ter. Lamotrigine is also available for patients with epilepsy and depression, with 2 RCTs presented, of which 1 demonstrated efficacy in comparison with a placebo.

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Behavioral Disorders in Epilepsy Patients with Intellectual Disability

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The following five topics will be discussed.
A) Prevalence: It is considered that 20-50% of individuals with intellectual disability (ID) show behavioral problems, while 30-40% of individuals affected by ID also have epilepsy. Thus, obviously, many epilepsy patients are also complicated with ID.
B) Epilepsy-specific behavioral disorders in patients with ID and epilepsy: Previous findings are controversial and strong arguments have been provided, both those showing no difference between ID patients with and without epilepsy (Deb & Joyce 1999; Espie et al. 2003), and that the alleged association, if any, may actually be due to the contribution of autistic spectrum disorder (Smith & Matson 2010), as well as those showing lower rates of psycho-symptoms in this subgroup, possibly because of the psychotropic

effects of AEDs (Arshad et al. 2011), with a 7-fold increase in the rate of behavioral disorders reported (Turkey et al. 2011).
C) Standard medical treatment for behavioral problems in epilepsy patients with ID. It is challenging to establish a standard medical treatment regimen for this specific group. Although it is important to be well aware of related difficulties and lack of unanimously approved results, there are some helpful suggestions to be noted. Specifically, the following 2 questions will be discussed along with presentation of 4 relevant case vignettes.
D) Is antipsychotic medication truly helpful to control disruptive behavior in epilepsy patients with ID?
E) Will discontinuation of benzodiazepines help to decrease behavioral problems in epilepsy patients with ID?

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The experiences of Iranian patients with epilepsy from their disease: A content analysis

Mansoureh Karimollahi, Parviz Molavi, Saeed Sadeghieh-Ahary, Ghasem Fattahzadeh-Ardalani, Solmaz Almasi

This qualitative study investigated experiences of patients with epilepsy in Iran regarding stigma. Twenty-two participants were chosen by purposive sampling method. After getting informed consent, we conducted and recorded interviews and then transcribed them verbatim. After that, all the researchers read the texts thoroughly, and the data were analyzed using conventional content analysis method. Seven categories emerged from the analysis including need for support, defense mechanisms, superstitious beliefs, and negative feelings, negative reactions of others, imposed deprivations, and spirituality. These results will increase healthcare professionals' knowledge about the problems of Iranian patients with epilepsy and improve the design of healthcare models that can promote successful coping strategies for them.

Interleukin-35; as a Novel Immuno-biomarker in Epilepsy

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Background: The occurrence of the recurrent seizures is termed as epilepsy. The neurobiology mechanisms of epilepsy is inflammation and alteration in permeability of the blood-brain barrier. Inflammation can lead to synaptic changes and neuronal hyper-excitability.
Besides pro-inflammatory cytokines, anti-inflammatory cytokines exist in epileptogenic microenvironment. Interleukin-35 (IL-35) is one of the latest anti-inflammatory cytokines in immunology field. The purpose of this study was to perform systematic review to determine the role of IL-35 in epilepsy development.
Methods: This systematic review was performed to identify studies that were published in Pubmed, ScienceDirect, Scopus databases and Google Scholar search engine, in 2010 - October 2019 time interval by using 4 keywords (Epilepsy, Immuno-biomarker, Interleukin-35, and Inflammation). Of the 96 articles initially identified based on inclusion criteria, 35 were selected based on our exclusion criteria.
Findings: Documents have revealed the high levels of pro-inflammatory cytokines such as IL-1B, IL-6 in neuronal epileptogenic brain tissue. It is better to say that if the condition led toward anti-inflammatory state, severity of the epilepsy, and patient prognosis would be more desirable. According to accumulative data, the levels of IL-35 in epileptogenic environment has a negative correlation with the severity of the epilepsy.
Conclusion: In attention to the inflammation in epileptogenic environment, high expression of IL-35 may cause less neuronal damage following seizure and improve the prognosis. Also, IL-35 could be as an immunological target in the treatment of the refractory epileptic patients.
Key words: Epilepsy, Immuno-biomarker, Interleukin-35, Inflammation.

The relationship between epilepsy, rubella and smallpox in autism in children in West Azarbaijan province: a case-control study

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Background & Aims: Autism is a brain disorder that limits one's ability to communicate with others. Differences in the nervous and brain systems cause the person to act differently and may have difficulty communicating with others, with interest in limited activities, repetition of specific behavior patterns, or behavior patterns in social interactions.
Materials & Methods: This is a case-control study in which the case group is composed of individuals with autism and the control group or the same control group includes healthy individuals who were compared in the two groups. The population used in this study is all children who have been diagnosed with autism in West Azarbaijan health centers in 2016.
Results: According to the results of the present study, there was no significant difference between the groups in terms of rubella and chickenpox ($p > 0.05$), but the distribution of epilepsy was statistically significant ($p = 0.002$). Conclusion: Although autism spectrum disorders are becoming more and more prevalent in scientific societies today, issues such as more accurate and efficient diagnostic methods, prevalence rates and the best treatments are some of the ambiguities.
Key words: Autism, Epilepsy, Rubella, Chickenpox

Seizures Associated with Nonneurologic Medical Conditions

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Seizures frequently arise during the course of medical illnesses that do not primarily affect the central nervous system (CNS). A patient's history, including a review of medications and physical examination, should be informed by a consideration of the seizures as a symptom of CNS dysfunction. The urgency to pursue a diagnosis is related to the time of presentation following the seizure. In a neurologically intact patient without progressive symptoms, quick (within days), but not emergent (within hours), evaluation may be appropriate. Within the first 24 hours, vital signs, level of consciousness, and focality on examination determine urgency. The need for emergent neuroimaging studies and lumbar puncture depends on the likelihood of intracranial lesion, CNS or systemic infection, a patient's metabolic state, and the possibility of drug or alcohol intoxication. In a patient who presents more than 1 week after an initial seizure, recurrent attacks establish the diagnosis of epilepsy. Several factors predispose a patient to seizures, including (i) changes in blood-brain barrier permeability as a result of infection, hypoxia, dysautoregulation of cerebral blood flow, or microdeposition of hemorrhage or edema secondary to vascular endothelial damage; (ii) alteration of neuronal excitability by exogenous or endogenous substances, such as excitatory and inhibitory neurotransmitters; (iii) inability of glial cells to regulate the neuronal extracellular environment; (iv) electrolyte imbalances; (v) hypoxia–ischemia; and (vi) direct and remote effects of neoplasm. Some patients without epilepsy may be genetically prone to seizures secondary to systemic factors. Understanding the interaction of other organ systems is necessary for the appropriate management of seizures. In patients with hepatic or renal dysfunction, changes in pharmacokinetics induced by metabolic dysfunction alter treatment with antiepileptic drugs (AEDs). In cases of hepatic dysfunction, plasma concentrations must be correlated with serum albumin and protein levels and, if possible, free (unbound) levels. Patients with hepatic and renal failure may have normal serum albumin levels, but altered protein binding, resulting in elevated concentrations of free drug .

Key words: seizure, medical condition

In Vivo Models of Status Epilepticus

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Background: Experimental studies have been done in animal models because doing experiments at the cellular level in humans is clearly limited. Here, we focused on chemical methods as in vivo models of SE.
Methods: This literature review is based on English-language articles sourced from PubMed without date limitation for using the following terms. Chemical method, In vivo, Status epilepticus.
Findings: The most seizure-prone in both in vivo and in vitro preparations are done in limbic structures. In this regard, limbic and paralimbic structures include the hippocampus, entorhinal cortex, and amygdala and nonlimbic regions can be induced to produce SE models. In chemical methods, using different compounds, either systemically, directly to the brain parenchyma, or into the ventricular system. Rats have been the most commonly considered model. Other species include the mouse, rabbit, piglet, baboon, and other species have been used as well. Chemicals can be separated into promoters of excitatory neurotransmission (e.g., kainic acid, domoic acid) and those that oppose inhibitory neurotransmission (e.g, bicuculline, penicillin).
Conclusion: Although chemical models of status epilepticus are moderately easy to generate, the nature of this kind of model makes it challenging to differentiate between properties produced by SE and direct neurotoxic properties of a precise medication.
Keywords: Chemical method, In vivo, Status epilepticus

"ESES is it a pretty rare condition in Iranian children with epilepsy?!"

Mahmoud Mohammadi, MD

ESES (Electrical Status Epilepticus in Sleep) is one of the topics with many debates on it! Most debates are on definition and terminology. Many consider "ESES" as a synonymous for "CSWS" (Continuous Spike and Wave during Sleep), but some authors indicate that the "ESES" defines the EEG pattern seen during sleep, mainly in two clinical conditions (i.e., "CSWS" vs. "LKS" or Landau Kleffner Syndrome). In one survey done in a group of Iranian Neurologists, 56% of respondents agreed that these two terms are not synonymous (in American neurologist this figure was 31%).
The other matter of debate is that; many people think that "ESES" is a rare condition in pediatric epilepsy age group. In a busy pediatric epilepsy clinic in Tehran among 876 pediatric patients firstly visited because of epilepsy there was 10 patients with ESES (near 1%), who were not diagnosed as having it previously!! It's also noteworthy to state that majority of them were not "CSWS" and "LKS". The main cause for their ESES was "drug induced ESES".In my talk, I will address on "ESES", definition, debates on it and its nature and outcome in our patients at our EMU and pediatric epilepsy clinic.
Keywords: Pediatric epilepsy, ESES, CSWS, EMU, drug induced ESES, pediatric epilepsy clinic

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Evaluation of anticonvulsant activity of Lactuca sativa seeds and Asperugoprocumbensleaves

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Background: Epilepsy is a chronic disorder which is accompanied by reparative and self-limiting convulsion. In Iranian traditional medicine, many herbal drugs have been used for treatment of epilepsy. Nowadays many cases of epilepsies are controlled by using the current official antiepileptic medications but these drugs have various side effects on the

other hand. There are also drug resistant convulsions which are refractive to these drugs. Therefore herbal medicines have been considered as a source of new anticonvulsants.
Methods: In this Study anticonvulsant activity of methanolic (80%) extract of leaves of Asperugoprocumbensand seeds of Lactuca sativa were evaluated in male NMRI mice, using pentylentetrazole (PTZ) and maximal electroshock (MES) models. **Findings:** The results showed that total methanolic extract of Asperugoprocumbenshave significant anticonvulsant activity at dose of 20-320mg/kg in MES model (ED_{50}= 173.9mg/kg with 95% confidence interval of 56.204-1869.203mg/kg), but at doses up to 320 mg/kg has no effect in PTZ model. Total methanolic extract of Lactuca sativa has no any significant anticonvulsive activity in both PTZ and MES models.
Conclusion: Then, total methanolic extract of Asperugo procumbensleaves fractionate with 3 solvents including etherdepetrol, chloroform and ethylacetate and anticonvulsant activity of them was considered. Chloroform fraction showed anticonvulsant activity in MES model (ED_{50}= 202.92 mg/kg with 95% confidence interval 66.034-2723.197 mg/kg).
Keywords: Asperugo procumbens, Lactuca sativa, anticonvulsant, PTZ, MES

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Study of Speech Disorders in children with Epilepsy

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Background: Epilepsy is one of the most common neurological disorders that occurs during childhood. It usually along with other disorders including cerebral palsy, mental retardation, attention-deficit-hyperactivity disorder, etc. Children with epilepsy are at more high risk for speech disorders, language disorders, school-age learning disabilities, behavioral and emotional problems. Although speech and language problems occur frequently in children with epilepsy, they are often overlooked. These speech disorders lead to impaired quality of Social and Communication Life of children with epilepsy. so we aimed to investigate the speech disorders in children with epilepsy.

Methods: The present study was conducted using articles published from 2000 to 2019 by searching databases such as "PubMed", "Science direct", "Scopus", "Google scholar" and "Library Resources". Initial search was done with the keywords "epilepsy", "speech", "speech disorders" and "communication disorders" and then the relevant articles were selected and used.
Findings: Studies show that a high percentage of children with epilepsy have speech disorders such as dysarthria, phonological disorders, dysfluencies and extraneous vocalizations, but a small number of children receiving speech therapy. It should be noted that the incidence of each disorder varies depending on the severity of the epilepsy and the brain regions affected.
Conclusion: speech is the richest means of communication and people can convey their needs, desires, beliefs and thought with this. any dysfunction in it leads to damage to the quality of life. So that children are the future makers of any society, recognizing any damage to children's speech subsystems is necessary. Also, early treatment and awareness of other professionals associated with these children is important.
Keywords: epilepsy, speech, speech disorders

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Juvenile Myoclonic Epilepsy

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Introduction: Juvenile myoclonic epilepsy (JME) is often regarded as a common epilepsy syndrome in which seizures are relatively easy to control and drug resistance should raise the suspicion about incorrect diagnosis, inappropriate lifestyle, noncompliance or inadequate/insufficient treatment; Nevertheless, true resistance to adequate drugs is not uncommon and is found in 15.5-37% of JME series of tertiary epilepsy centers.
Prognostic factors for refractoriness: JME is a heterogeneous condition. Age of onset is slightly higher in the group with easy to control seizures. Non - classic JME phenotypes are more prevalent in drug resistant cases. A recent meta - analysis suggested six variables as prognostic factory for refractoriness including, having three seizure types, non - classic clinical presentation,

childhood absence epilepsy / absence in general evolving to JME, psychiatric comorbidities, earlier age at seizure onset and praxis - induced seizures.
Treatment options: at the present time Valproate (VPA) is the first choice antiepileptic drug (AED) in men with JME. The next AED choices if VPA fails to control the seizures or is poorly tolerated will be VPA and Lamotrigine (LTG)in combination, Levetriacetam (LEV)LTG or Topiramate. If all mentioned AEDs fail to control the seizures Zonisamide either as monotherapy or add on drug may be an effective option.
Evidence suggests that VPA should not be given to women of childbearing age. The safest AEDs in terms of teratogenicity are probably LEV and LTG respectively.
When dealing with refractory JME it may be well to remember the possible benefits of older therapies such a Primidon, phenobrbital, Colobazam and Clonazepam. Acetazolamide and Prampanel are other alterative choices in pharmacoresistant JME patients. It is important to mention that some AEDs may aggravates seizures in these patients.Vagal nerve stimulation may be considered as a last resort in pharmacoresistant cases,
Conclusion: JME is a heterogeneous epilepsy syndrome incorporating different subtypes; as a result, it will be characterized by different outcomes. Future prospective studies will be needed in this challenging population to optimize the management of intractable cases and to test the reliability and genealizability of above mentioned prognostic factors.

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Reproductive Issues In Women With Epilepsy

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Hormones affect seizures, and seizures affect hormonal regulation and secretion. Subtle manifestations of hormonal influences on seizures and vice versa may easily be overlooked because they are not usually emphasized In the training of neurologists. Awareness of how different hormones relieve or exacerbate seizures may lead to improvement in the treatment of seizures with the use of adjunctive hormonal therapy.

Gender-based differences in AED pharmacokinetics, sex steroid hormones, and reproductive life events raise special issues for women with epilepsy. A prominent precipitation of seizures in association with the menstrual cycle has been termed catamenial epilepsy. This is reported in approximately 55% of women with epilepsy. The most common pattern of clustering of seizures is perimenstrual, typically in the 3 days before and 3 days after onset of the period. Less common patterns are periovulatory (occurring around ovulation) and luteal, in association with inadequate luteal phase cycles. The mechanism of catamenial epilepsy is thought to be related to the opposite effects of estradiol and progesterone on seizure threshold.Estradiol is a proconvulsant, whereas progesterone has an anticonvulsant effect. Progesterone therapy has been suggested as a treatment when catamenial epilepsy is not responsive to standard AEDs.

Reproductive issues are also an important concern of epileptic patients and their families. Both men and women with epilepsy have lower birth rates than the general population and adults with active epilepsy have lower birth rates in comparison to those who no longer have seizures after childhood. Infertility is the failure to conceive after regular intercourse in women who are not using contraception for a duration of 1 year for women <35 years and 6 months for those >35 years . Signs of infertility may include menstrual irregularity, obesity, hirsutism, an Galactorrhea.Infertility in Women With Epilepsy is likely multifactorial attributed to psychosocial factors, decreased libido, and neuroendocrine alterations secondary to seizures and antiepileptic drugs (AEDs).The hypothalamic-pituitary-gonadal axis (HPG-axis) and feedback inhibitory mechanisms play a key part in infertility among Women With Epilepsy. Reversible/treatable causes of infertility should be identified and addressed if Women With Epilepsy wish to conceive. Understanding the implications of epilepsy and the primary treatment, antiepileptic drugs (AEDs), on reproductive health is necessary and integral in particular to the care of women with epilepsy.

Key words : Epilepsy, Infertility, Catamenial Epilepsy

Study of Speech and Language Disorders in Adults with Epilepsy

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Background: Epilepsy is a chronic illness in which one experiences repeated epileptic seizures due to a chronic underlying process. According to this definition, people who have only one epileptic seizure or are attacked by modifiable and preventable conditions are not considered legitimate. The prevalence of the disease is estimated to be about 5-10 per 100,000 people. The classification of epileptic seizures includes focal epileptic seizures, primary epileptic seizures, and unclassified operations. Complications from epileptic seizures include memory loss, learning disabilities and speech disorders, psychological problems, especially depression and anxiety, suffocation, head trauma, sudden death, and so on. Speech and language disorders in adults with epilepsy.
Methods: In this systematic review, studies from the years 2010-2015 were searched from library, sience direct and pubmed databases using the keywords Epilepsy, Speech and languagedisorder, Adults, and in the process, studies of speech and language disorders in Adults with epilepsy were examined.
Finding: Of the 22 articles, 6 articles were available for access to full text and free libraries, possible database databases. You can print between material provided by visitor feedback, sample study, teaching method, and so on. Using specific and special resources and situations in the brain, the signs and inventions of the conversation and the text of the text and the text in the face of the person who can easily express the quality in words and sentences, methods, models of the treasury Vocabulary, translational disorders, and speech and language disorders are understood.
Conclusion: The results indicate that speech and language disorders are a result of epilepsy in adults. So adults with epilepsy who suffer from speech and language disorders can refer to speech therapists and try to reduce their speech and language disorders with the help and support of speech therapists and receiving rehabilitation services.
Key words: Epilepsy,Speech and language disorder,Adults

The Efficacy of Vitamin D3 as Adjuvant Therapy in Control of Drug Resistant Epilepsy

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Background: Drug-resistant epilepsy (DRE), also known as refractory epilepsy (consist of 25% of epileptic patients), is defined as failure of trials of two antiepileptic drugs (AED schedules) to achieve sustained seizure freedom. Vitamin D3 is the form of vitamin D called cholecalciferol. Calcitriol is a synthetic physiologically-active analog of vitamin D, specifically the vitamin D3 form. The aim of this study was to assess the efficacy of Vitamin D3 as an adjuvant therapy in reducing the seizure frequency of patients with drug resistant epilepsy.
Method: On hundred and fourteen patients (18-70 years old age) with drug resistant epilepsy were assessed for this double blind-clinical trial study between 2018-2019. First, Serum level of vitamin D3 were measured and those Patients with normal serum level of Vitamin D3 were excluded from study. Those with low serum level were enrolled in the study and divided randomize in two groups. First group were received anti-epileptic drugs (AEDs) and oral Vitamin D3 (6000 IU/day for 8 weeks and then 3000 IU/day as a maintenance dose) and the second group were followed as a control group and just received AEDs. Patients were followed for 3 months and seizure frequency before and after this trial were compared between two groups. Kolmogorov –Smirnov method was used for statistical analyzing of the data. As the data distribution was normal, independent T-test was used.
Result: Forty-four patients (22 males & 22 females) had low serum vitamin D3. The average age was 33.5 years. The frequency and duration of seizures reduced in those patients received vitamin D3 more than those patients received placebo but this comparison was not significant (P= 0.123). There was a significant difference between two groups and seizure frequency were reduced more than 50% in patients received vitamin D3 as an adjuvant therapy.

Discussion: This case –controlled study was done on forty-four adult uncontrolled epileptic patients. Epileptic patients randomize divided two groups. The case group received AEDs with vitamin D3 and the controlled group placebo with AEDs. These patients followed three months for frequency of seizure relapse. Although epileptic attacks is reduced with vitamin D3 as adjunct therapy but not significant.
Conclusion: In our study the frequency and duration of epileptic attacks were reduced in patients received AEDs with vitamin D3 in compare only AEDs but it was not significant.
Key Words: Drug resistant epilepsy- Adjunct therapy- Vitamin D3

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Drug-Resistant epilepsy: Mechanisms, Pathogenesis

Dr. Dariush Nasabi Tehrani
Neurologist

Despite the development of new antiepileptic drugs (AEDs),~ 20%_30% of people with epilepsy remain refractory to treatment and are said to have drug resistant epilepsy (DRE).
This multifaceted condition comprises
*intractable seizures ,
*neuro biochemical changes ,
*cognitive decline ,
*psychosocial dysfunction ,
DRE management is complicated by the heterogeneity among this patient group.
The underlying mechanism of DRE is not completely understood.
Relate to both the intrinsic characteristics of the particular epilepsy (associated syndrome, lesion initial response to AED and the number and type of seizure prion to diagnosis) and other pharmacological mechanism of resistance is important.
The four current hypotheses behind pharmacological resistance are the "transporter","target", "network" and "intrinsic severity.
We have challenge in managing patients with DRE and this requires a multidisciplinary approach.

Physicians, surgeons, psychiatrists, neuropsychologists, pharmacists, dietitians, and specialist nurses.
Attention to comorbid psychiatric and other diseases in paramount.
Attention to seizure threshold and psychoactive drugs.
Attention to risk factors drugs and patients.
Attention to psychopathology and epilepsy.
Attention to excitatory/inhibitory mechanisms.
Attention to pseudo pharmacoresistance.
Attention to AEO compliance and tolerability.
Some of the reasons for drug resistance lie in the way physicians treat this issue.
The last word is treat the causes drug resistant epilepsy must be highlight.

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When to Start and When to Stop AEDs

Mahyar Noorbakhsh,MD
Epileptologist

A large body of evidence has developed in recent years, allowing a more accurate estimate for seizure recurrence risk after occurring of new-onset seizure, and for stopping antiepileptic drugs therapy (AEDs) when the seizures have been controlled. In decision making for the start of AED treatment after a first seizure, a neurologist should respond to many questions, including: Is the seizure provoked or unprovoked? Is the seizure associated with an epileptic syndrome or not? Therefore, it is necessary to know the definitions, such as acute symptomatic seizures, remote symptomatic seizures, progressive symptomatic seizures, and more.
It is evident that about 10% of the population will have a seizure at some time in their lives, but less than half of these patients will have multiple seizures. When deciding whether to start AEDs, the parameters like the recurrence rate estimation, consequences of having a second seizure, the efficacy of medications in preventing future seizures, the potential toxicity of antiepileptic drugs, and patient values and preferences should be considered. According to previous data, the risk of seizure recurrence after

an unprovoked seizure increases in a specific clinical and electrophysiological setting such as prior brain lesions, EEG with epileptiform abnormalities, significant brain imaging abnormalities, and nocturnal seizures. It seems that when the patient has these items, it is necessary to start the AED treatment.
For the AED discontinuation, we know that about 70% of patients with recent-onset epilepsy achieve seizure freedom with adequate antiepileptic drug treatment. For these patients, the questions are that whether, when, and how the therapy can be discontinued. The Italian League against Epilepsy has issued evidence-based guidelines to help physicians in their decision to withdraw or withhold antiepileptic drugs in patients with a prolonged period of seizure freedom. For this purpose, the following items should be considered: the duration of the seizure remission period before starting AED discontinuation, the presence of specific risk factors of relapse, the specific types of epileptic syndromes, the evaluation of the general conditions of life of a given patient (emotional state, job, driving, and other daily activities), and the possible age-related differences. It seems that some situations increase the chance for recurrence seizures after AED withdrawal such as abnormal EEG, documented brain insults (focal brain abnormalities and intellectual decline), focal seizures, older age at epilepsy onset, positive FH of epilepsy, history of FC,and known epilepsy syndrome. Some of these factors look stronger than others and nevertheless, patients should not be encouraged to withhold treatment unless a combination of two or more of these factors is present.
It seems that the start and withdrawal of AED are still challenging conditions, and some of the situations are vague and should be evaluated in future researches.

Investigating the Relationship Between Spiritual Attitude and Coping with Stressful Conditions in Mothers of Children with Epilepsy in Selected Hospitals of Mashhad University of Medical Sciences in 2019

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Background: Epilepsy is often associated with permanent stress due to being chronic.Therefore, mothers need to know strategies for reducing or coping with stress and its associated factors. Spiritual attitude is one of the strategies to deal with stress.The purpose of this study was to investigate the relationship between spiritual attitude and coping strategies in mothers of children with epilepsy in Mashhad.
Methods: A cross-sectional descriptive study was performed on 100 mothers of children with epilepsy admitted to Imam Reza Hospital, Dr. Sheikh Hospital and Akbar Hospital. Data collection was done through a three-part questionnaire(demographic characteristics,spiritual attitudes of God,and Endler and Parker stress coping strategies. The questionnaires were completed by families. Data were analyzed by SPSS 20 software and descriptive statistics).Chart, frequency distribution tables, and descriptive and inferential indices(chi-square, independent t-test,paired t-test) were analyzed.
Findings: The results showed that mothers who had better spiritual beliefs were significantly (P=0/004) than mothers who had spiritual beliefs, spiritual behaviors and those who had social pretensions. And mothers who made social pretensions showed the least effort to cope with stress. The results also showed that 45% of mothers choose avoidance or avoidance in stressful situations, 40% choose emotion-focused coping,and 15% choose problem-focused coping.Spearman correlation coefficient showed that there was no significant relationship between spiritual attitude score and its domains in mothers with child birth rate and family economic status. As well as the age of children with maternal emotion-focused coping (P<0/001).And avoidance (P<0/01). There was a significant inverse relationship.The number of children in the family was not significantly correlated with any of the different coping strategies.

Conclusion: There is a significant relationship between spiritual attitude and strategies for coping with stress and it can be influenced by choosing the appropriate strategy for coping with stress and increasing mothers' attitude toward epilepsy and increasing their positive attitude toward epilepsy. The process of treating the patients has changed.
Key word: Epilepsy,stress,spiritual attitudes,parents

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Attitude to Epilepsy in Iranian

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Introduction: Epilepsy is one of the most common neurology problems. That is a brain disorder that has neurobiological, cognitive, psychological, and social consequences for affected patients. Despite advances in medical science and modern technology, epilepsy remains as a stigmatized condition and negative public attitude toward epilepsy is a common phenomenon especially in developing countries such as Iran. Purpose of this study was determine the attitude to epilepsy in Iranian.
Method: This review study was carried out with investigation of scientific and research sites such as (Google scholar, SID, ….) without time limit.
Results: Reviewed study indicated that there was different attitudes about epilepsy in Iranian but some of them can be destroy. They are such as: most people believed that epilepsy caused by brain damage but some of them believed that is an inherited disease, due to fever or stress, evil spirits is the cause.
Most people believed that epilepsy and seizure are different and children with epilepsy could go to school and have normal education and they believe pregnancy to be appropriate for epileptics but a few number of thoes would not allow their children to marry a person with epilepsy. Results indicated

that there was positive and significant correlation between education and positive attitude to epilepsy.
Conclusion: According to this survey, In spite of having positive attitudes in some aspects, there was not adequate knowledge about this disease. It is suggested that additional efforts must be made to increase the knowledge of the general population through education programs especially among school children. Community education can have positive effects on increasing correct information and decreasing epilepsy stigma.
Keywords: Attitude, Epilepsy, Iranian

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Evaluating Performance of Polymeric Biosensor by a Single Multichannel Micro Electrode Array in a Portable Monitoring System for Preventing Drug Resistance Epilepsy Defects

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Introduction: There are several proven methods to investigating neural activities of electro genic cells in different points of human's body. Within these methods, performing electronic tools such as biosensors for monitoring different signals of brain, heart and other pulses such as breath simultaneously during daily routines in different balance of cautions can improve the choice of treatment progress in some neuro disorders such as drug resistance epilepsy. Therefore, in this research attach to technical science of production a polymeric biosensor with a multichannel micro electrode array (MEA) with capability of touch the brain signals on scale, it was attempt to make a portable monitoring system to record and investigating signals by navigating them into a smart cellphone. Through this method by detecting critical signals on threshold of seizures in aura state can prevent most defects even SUDEP with release an alert on cellphone rather start recording the seizure activities through interictal spikes to post investigations.

However, localizing electrode on the specific point close to seizure prediction horizon (SPH) with no need to electrolyte gel can obtain a non-invasive method with suitable accuracy to touch and scanning brain signals on scale.

Modelling and methods: The set-up which contains a 64-channel MEA with capability of infrastructural electromagnetic waves amplification and an interface circuit with four main parts i.e. Power supply, Opamp, (HPF/LPF) Filters and Voltage convertor for external wave amplification and noise cancelation are used to convert brain signals to a single analysable signal for processing unit within cellphone. Wave navigation was followed by 3.5(mm) stereo jack that more than two signals further main brain signal can navigated with this as mentioned earlier. The accuracy of MEA can be improved by thin layering a biocompatible conductive polymer such as PEDOT: PSS on a flexible substrate to increase touch surface area of electrode with skin. Now, after calculating a parameter known as signal to noise ratio (SNR) with detection probability of signal and noise (P_i):

$SNR = (P_{signal}/P_{noise}) = \mu/\sigma$ (Eq.1)

if SNR~N, then according to wave law:

$\lambda = (1/N)\ln(X_n/X_{n+1}) \rightarrow \lambda_n = \ln(X_1/X_{n+1})$ (Eq.2)

Therefore, by defining distinct value for landa as $\lambda_{n,crit}$ then seizure possibility index (SPI) to release a command by processor after detecting this critical point by signal analysis is:

$SPI = \lambda_{n.crit} \times SNR$ (Eq.3)

Results and discussion:

Brain activity with 10-20 (mV) amplitude by 100 (μV) oscillating and frequency bellow 30 (Hz) can be sensed by conventional electrodes and electrolyte gel beneath the contact surface, but this amplitude could increase up to 1 (V) with dry MEA with own of symmetric shape of electrode. On the other hand, using an Opamp this value can be increased more by signal amplification between each channel with other ones. whereas the mentioned MEA has 4 main sites with 16 channels in each site, after oscillography and detecting the reference channel, output signal of each site should be amplified with each other too that results showed that wave amplification between two cross sites was better than two adjacent sites. However, by eliminating artifacts and strong signals after weak signals respectively by HPF and LPF can attach a suitable signal that using mathematic methods

such as FFT algorithm can detect seizure critical peaks on it even on amplitude vs. time area in 3D mode.

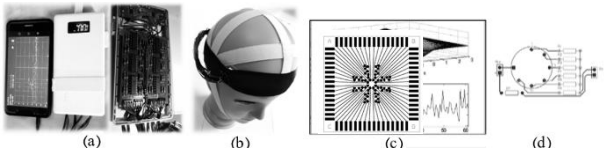

Figure1. (a) the final set up; (b) the electrode localization; (c) The signal in two and three dimensional modes; (d) Electrode structure with four main 16-channel sites.

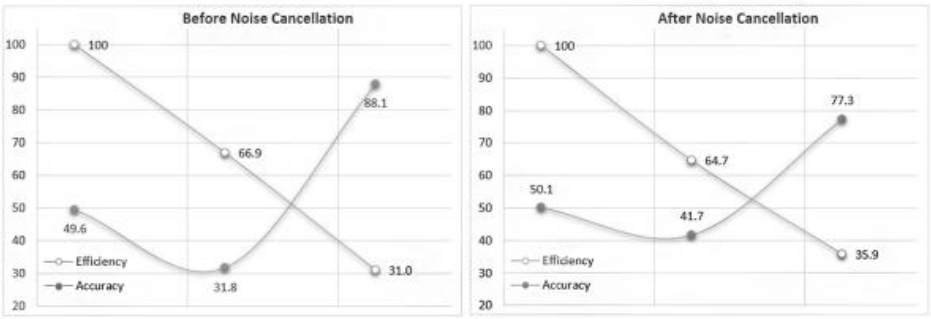

Fig2. Comparison of efficiency and accuracy coefficients, for MEA, amplified signal between cross-sites, and conventional electrodes whether before and after noise cancelation.

Conclusion: Though, comparing the efficiency of MEA with conventional wet electrodes showed perfect value for MEA, but accuracy vice versa. Nevertheless, close accuracy whether after and before noise cancellation during repeated experiments showed good performance of this biosensor for brain signals scanning.

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Epilepsy & Sexual Dysfunction

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Epilepsy, AEDs and reproductive hormonal system have complex interactions. Hormones can affect seizure frequency.on the other hand, both epilepsy and/or AEDs can compromise The reproductive hormonal and sexual functions.reproductive and sexual dysfunction in people with epilepsy are not gender specific,both men and women are affected. Use of AEDs seems to be associated with frequent occurrence of reproductive and sexual problems including diminished potency,polyclystic overian changes hyperandrogenism, menstrual disorders, and reduced fertility. Psychosocial complications associated with epilepsy can also affect reproductive health and sexuality. Regular multidisciplinary evaluation including neurologist, endocrinologist,urologist,gynecologist and psychiatrist is needed while managing patients with epilepsy. Large sample sized longitudinal designed studies and longer lengths of exposure to AEDs may be helpful in characterizing the impact of length and time of exposure effect of AEDs on reproductive function. These studies should include the new AEDs. Furthermore,better understanding of the molecular properties of endocring effects on seizures over a lifetime seems to have a promising therapeutic profile for treatment of epilepsy.

HORMONES AND SEIZURES

ESTROGEN: The relationship between estrogen and seizures is complex and controversial. A few studies suggest that estrogen has the potential to enhance neuronal excitability and increase seizures. An epileptogenic effect was found when conjugated equine estrogen where applied to the cerebral cortex. Acuted administration of estrogen was found to have a proconvulsant effect in pentylenetetrazole-induced seizures. Elevation of estrogen–to-progesterone ratio has been suggested as a cause of seizure exacerbation during perimentopause and the decrease in seizure frequency. However, many recent studies indicated that estrogen has little beneficial effect on seizure activity. At either physiological or supraphysiological levels. In contrary, other studies showed that estrogens may decrease seizures. In ovarectomized famele rats, B-estradiol can reduce seizures inducted by N-methyl- d-aspartate (NMDA)or kainic acid (KA). A decline in seizure frequency was reposted in some

women with primary generalized seizures around the time ovulation and in postmenopausal epileptic women utilizing estrogen as replacement hormonal therapy. On the other hand, strogen has showen a neuroprotective effect from seizure-inducted brain damage. Estrogen has showen to protect hippocampal cells in ka model of epilepsy from glutamate - induced excitotoxicity. pretreatment with B-estradiol was found to prevent cell loss in the dentate gyrus after atatus epilepticus period. Briellmann et al in their study utilizing quantitative magnetic resonance imaging to measure the hemicranial and hippocampal volumes of patients with temporal lobe epilepsy(TLE) reported that females are less vulnerable to seizure-essociated brain damage.the neuroprotective effect has been attributed to its antiapoptosis, antioxidant, and cerebral vasodilator effect with improvement of cerebral blood flow and increasing cerebral glucose utilization. Estrogen directly inhibits NMDA receptors. It upregulates different neurotrophins as neuropeptide Y (NPY). It also activates growth factor signaling pathways in neurons such as mitogen-activated protein kinases and cyclic adenosine monophosphate (AMP)response element binding protein.
These controversial data about estrogen effects cloud be related to various variables such as the different species (humans vs animals)the used animal model,sex (males vs famales), hormonal status (naïve vs gonadectomized/ agedanimals), specific region of the brain tested, estrogenic substance (ie,conjugated estrogens have more convulsant effect than B- estradiol) estrogen dose (low vs high dose)and treatment duration and the latency prior to seizure testing (acute vs chronic)

Study of Language Disorders in Children with Epilepsy

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Background: One of the most important indicators of children development is the acquisition of language skills that is closely related to the communication components. Unfortunately, language skills can be affected by a variety of diseases, including epilepsy, cerebral palsy, head trauma, mental retardation, autism, and so on. Since epilepsy is the most common chronic disease of the nervous system in childhood, accurate identification of damaged skills is necessary for early identification and treatment. Since language is the basis of verbal communication, this study aimed to investigate the language skills of children with epilepsy in order to help in drawing a language profile and increase awareness of these disorders.

Methods: For this purpose, scientific databases such as Science Direct, PubMed, Scopus and SID were reviewed to identify articles between 2000 and 2019 and that related to epilepsy, its nature, characteristics of those affected, communication and language disorders, the nature of these disorders, and epilepsy-related communication and language disorders were identified. The search was initially conducted with the keywords of epilepsy, language and communication. Then, articles about language disorders result from epilepsy in children were used.

Findings: Children with epilepsy are delayed in developing language skills such as comprehension and production of words, comprehension and production of simple and complex sentences, and grammatical structure of sentences relative to their normal peers. These children also show deficits in word retrieval, and school-based learning skills, which can vary depending on the type of epilepsy, the severity of the lesion, sex, age at onset of epilepsy, verbal IQ, and the presence of co morbid disorders.

Conclusion: Given the high prevalence of language disorders and subsequent communication disorders in children with epilepsy, the impact of these disorders on their future performance, including their academic performance and quality of life, and the high prevalence of epilepsy in this population, appropriate referral, careful assessment of language skills, and early

intervention are essential and could prevent many of the following potential problems.

Keywords: Communication Components, Language, Language Skills, Epilepsy

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Legal Review of the Use of the Sina Robot in Practice Surgery for Epilepsy Patients

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When brain cells transmit signal to one another, there are some problems that people find as epileptic seizures. Sometimes during a seizure, the patient falls and the floor going out. Some seizures are diagnosed with the process of fragmentation of the brain, even if its severity is different, the injuries caused by these seizures are the same. Because some of the brain cells disappear during any seizure. Recurrent seizures, especially during childhood, can also lead to mental retardation. Therefore, treatment should start without waste of time. While most patients are treated with medication, some of them have to use surgical procedures. Surgical procedures are divided into three parts: a) removal of the defective area; b) cutting the transmission paths between the common areas; c) placing the battery. The surgeon's robots, with enhanced precision and surgical control, and the use of optical equipment and displays, have been employed to monitor the quality of surgical care for human health. The Sina's Robot Surgery, who won the Best China Entrepreneurship Award in 2018, has been instrumental in reducing patient recovery, reducing surgical complications, less injuries to the patient, and reducing the cost of surgery. The Sina's Robot, made up of two parts, was first unveiled at the 2014 inotex exhibition. The first part of the device sends orders to the robot under the supervision of the doctor and his control. The special advantage of this robot is that the control center or surgical console can be far from the site of the second part of the robot, which is the operator's part, and thus a remote operation is realized. The second part is located next to the robot's patient, who acts on the surgical site by performing a low-invasive operation through small incisions in the patient with high precision and control. The degree of freedom of the

surgical instrument and the accuracy of this robot are monitored by a surgeon. According to the legal provisions 272, 290, 496, 501, 503, 677 of the Islamic Penal Code, the scope of criminal liability of this robot, the user and its controller, taking into account its use in surgical operations of epilepsy patients by descriptive-analytical method Dedication.
Keywords: Epilepsy, Sina Robot, Criminal Responsibility, Surgery

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Acute Symptomatic Seizures: to Treat or Not to Treat?

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Purpose of review: Acute symptomatic and provoked seizures by definition occur in close proximity to an event and are considered to be situational. A number of population studies, including some classic reports, have identified the relative risk factors for subsequent seizure recurrence. In this article, the authors review the literature on acute symptomatic and provoked seizures with regard to therapeutic approach and risk of recurrence.
Methods: Systematic review of the literature and of epidemiologic studies.
Result: Multiple seizures in a given 24-hour period do not increase the risk of seizure recurrence. Remote symptomatic seizures, an epileptiform EEG, a significant brain imaging abnormality, and nocturnal seizures are risk factors for seizure recurrence. Patients with acute symptomatic seizures in the setting of certain conditions including subdural hemorrhage, traumatic penetrating injuries, cortical strokes, neurocysticercosis, venous sinus thrombosis, and viral encephalitis have a higher rate of seizure recurrence although the rate of recurrence of seizures is less than that of patients with unprovoked seizures.
Conclusion: In patients with acute symptomatic and provoked seizures, short-term treatment with anti-seizure medications is appropriate. In patients with acute symptomatic seizures with persistent epileptiform activity on EEG and structural changes on imaging, longer-term treatment (i.e., a few months as opposed to 1week) with anti-seizure medications can be considered due to high risk of seizure recurrence. If a patient subsequently has an unprovoked seizure, there is yet a higher risk of

recurrence of seizures and likelihood of the development of epilepsy. In these patients, long-term seizure treatment can be considered, keeping in mind that although anti-seizure treatment may reduce risk of seizure recurrence in the short-term, it does not appear to influence long-term seizure remission rates.

Key words: Acute symptomatic seizure, treatment, seizure recurrence risk

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Diffuse Hemispheric Disturbances and Epilepsy

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Sturge-weber syndrome, Rasmussen's encephalitis, Hemimegalencephaly, Vascular malformations and Large congenital porencephalic cysts as some examples of pathologies with diffuse hemispheric disturbances properties in the pediatric patients group, may be concomitant with some frequent motor seizures which can be generalized or unilateral in their nature.

In this study we will have a brief review on some of the pathologies with diffuse hemispheric disturbances properties and their concomitance with some specific seizure types and will point to some important clinical notes about them.

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Autoimmune Epilepsy

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Autoimmune epilepsy has been one of the fastest growing topics in the last few decades after the discovery of neural autoantibodies. Autoimmune epilepsy is characterized by new-onset refractory seizures along with subacute progressive cognitive decline, behavioral and psychiatric dysfunction. Neural specific antibodies are commonly associated with autoimmune

epilepsy including autoantibodies against neuronal intracellular (ANNA-1, CRMP-5, GAD65, Ma/Ta) or surface cell (NMDAR, LGI-1, AMPAR, GABAR, CASPR2, DPPX) proteins. An autoimmune mediated epilepsy is suspected when medically intractable seizures encountered in the presence of at least one neural antibody, and inflammatory changes found in CSF or MRI or presence of family history of autoimmune disease. Predictive models (Antibody Prevalence in Epilepsy and Encephalopathy [APE2] and Response to Immunotherapy in Epilepsy and Encephalopathy [RITE2] scores) consisting clinical features and initial neurological assessment could be utilized for cases selection, evaluation and management in autoimmune epilepsy. Currently there is no level one data regarding the treatment of autoimmune epilepsy from randomized controlled trials. Practically, first line of treatment is intravenous methylprednisolone (1g/day for 3 to 5 days) and/or intravenous immunoglobulin (IVIG) (0.4 g/kg/day for 3-5 days). If no response is observed it is essential to try the second line immunosuppressant, Rituximab or Cyclophosphamide. It is certain that early diagnosis and appropriate treatment could improve the clinical course and the prognosis in these patients.

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Non-convulsive Status Epilepticus and Non-Convulsive Seizures in Critically Ill Patients

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Background: Non-convulsive seizures (NCS) or non-convulsive status epilepticus (NCSE) is a common problem in critically ill patients. They have been reported in 8–20 % of critically ill patient populations, and delayed diagnosis and treatment of NCSE may lead to increased mortality. Diagnosis of seizures in this particular population of patients can be challenging as clinical manifestations are often subtle or absent. On the other hand, delayed diagnosis and treatment of NCSE has been associated with higher patient morbidity and mortality.

Methods: In this review, a general search in Medline, Science Direct and springer databases were done during years of 2010 to 2019. We evaluated human studies of NCS and NCSE in critically ill patients and the results are presented here in short.
Findings: Identifying patients at higher risk of developing NCSE/NCS help prioritize cEEG monitoring when resources are limited. A past history of epilepsy, meningitis/encephalitis, CNS tumor, acute brain insults such as intracerebral hemorrhage (ICH), subarachnoid hemorrhage (SAH), traumatic brain injury (TBI), and ischemic stroke are independent risk factor for developing NCSE/NCS.
Conclusion: This review discusses specific clinical features along with history and potential risk factors to identify patients at high risk of NCSE/NCS in the critical care unit and highlights the therapeutic options for early management of NCSE/NCS.
Keywords: Status Non-Convulsive Seizures, Non-Convulsive Status Epilepticus, Critically Care, Altered mental State, cEEG Monitoring

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Status Epilepticus: an Epilepsy Emergency and the Response to Immunotherapy

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Background: Epilepsy emergencies include acute repetitive seizures and status epilepticus. Their prognosis depends on the etiology of the seizures and the time spent in status epilepticus. Status epilepticus (SE) is a condition in which patients suddenly experience a prolonged seizure or a flurry of very frequent seizures. Status epilepticus that persists despite at least 2 standard anticonvulsant medications is termed refractory status epilepticus (RSE). New-onset refractory status epilepticus (NORSE) is defined as a condition, not a specific diagnosis, with new onset of refractory status epilepticus without a clear acute or active structural, toxic or metabolic cause in a patient without active epilepsyMost of the common causes of RSE can be identified within 24-72 hours of presentation. In up to

half of the cases of NORSE, a possible or probable cause is ultimately found, most often autoimmune or paraneoplastic encephalitis, with infectious causes less common. In the remaining half, no cause is identified despite an extensive work-up.

Summary: Autoimmune epilepsy is an underrecognized condition, and its true incidence is unknown. Identifying patients with an underlying autoimmune origin is critical because these patients' condition may remain refractory to conventional antiseizure medications but may respond to immunotherapy. EEG seems as a limited diagnostic tool in differentiating epilepsy and/or encephalopathy patients with a possible autoimmune etiology from those without. However, antineuronal Abs associated with encephalitis should be considered in the etiology of status epilepticus forms. A possible autoimmune etiology for seizures may be considered in the presence of continuous slow waves, FIRDA, and delta brush pattern in the EEG.

In two-thirds of NORSE cases, the course of the syndrome begins with a mild febrile illness, associated with malaise, fatigue and symptoms of upper respiratory tract or gastro-intestinal tract infection. Symptoms of meningeal inflammation, such as headache and photophobia, are uncommon. Behavioral and cognitive symptoms, such as apathy or agitation, amnesia, and sometimes hallucinations can be observed. The presence of hallucinations may suggest an autoimmune etiology, especially anti-NMDA receptor encephalitis. This initial phase lasts a few days to a week or two and is followed by the progressive onset of seizures. Both focal seizures with impaired awareness (previously known as complex partial seizures, and typically described as staring episodes) and bilateral tonic-clonic seizures can occur. They are initially intermittent but become increasingly more frequent and the patient's consciousness declines as he/she transitions into status epilepticus. The most common causes of NORSE and FIRES are autoimmune/paraneoplastic disorders, such as encephalitis associated with anti-neuronal antibodies (anti-NMDA
receptor, anti-voltage-gated potassium channel complex, etc.), followed by viral encephalitis. The treatment of SE initially consists of benzodiazepines (lorazepam, diazepam, or clonazepam), followed by a standard anticonvulsant medication, as in most cases of SE. Preference is given to drugs that are available in IV form (valproic acid, phenytoin, levetiracetam, phenobarbital and lacosamide).

By definition, NORSE do not respond to these first two lines of treatment, and additional drugs are required. The two options are either to try additional anticonvulsant medications and/or to induce pharmacological coma with an anesthetic drug.Medications available in an IV formulation are often favored but others (e.g., topiramate, pregabalin) are sometimes used later as add-on therapy. Of the three, midazolam has the best safety profile but may be associated with a higher risk of recurrent seizures. Barbiturates are associated with more prolonged coma and need for mechanical ventilation, with a higher rate of complications. Propofol carries a small risk of propofol infusion related syndrome (PRIS), a potentially lethal syndrome of acidosis, kidney and heart failure.
When an underlying cause is identified it should be appropriately treated.it is common to use approaches that modulate the immune system. These options include IV steroids, IV immunoglobulins, plasma exchange therapy (plasmapheresis) and some monoclonal antibodies against inflammatory cells (e.g., rituximab). The efficacy of these strategies is suggested by small case series, though never investigated in controlled trials.
Conclusion: Status Epilepticus is an epilepsy emergency and neurologists try to treat it emergency to reduce the morbidity and mortality of this grave disease recently one of the refractory causes of status epilepticus is autoimmune encephalitis and Response to Immunotherapy has been reported satisfactory in some cases. But more investigation must be performed.

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Drug Resistant Epilepsies: News and Challenges

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A task force of the International League Against Epilepsy (ILAE) proposed that drug-resistant be defined as the failure of adequate trials of two tolerated, appropriately chosen and administered antiseizure drugs (whether as monotherapy or in combination) to achieve seizure freedom.

Approximately ⅓of patients with epilepsy are drug refractory (Between 30 to 40 percent).
This is obviously a very significant challenge in managing a patient with drug-resistant epilepsy. Neurologists try to use combinations of different medications, typically with different mechanisms of action, hopefully to achieve the best effectiveness in terms of seizure control.
An ongoing challenge to both researchers and clinicians alike, DRE management is complicated by the heterogeneity among this patient group.
The underlying mechanism of DRE is not completely understood. Many hypotheses exist, and relate to both the intrinsic characteristics of the particular epilepsy (associated syndrome/lesion, initial response to AED, and the number and type of seizures prior to diagnosis) and other pharmacological mechanisms of resistance. The four current hypotheses behind pharmacological resistance are the "transporter", "target", "network", and "intrinsic severity" hypotheses.
Of equal challenge is managing patients with DRE, and this requires a multidisciplinary approach, involving physicians, surgeons, psychiatrists, neuropsychologists, pharmacists, dietitians, and specialist nurses.Treatment options need to consider the economic burden to the patient and the likelihood of AED compliance and tolerability. Overall, resective surgery offers the best rates of seizure control. It is not an option for all patients, and there is often a significant delay in referring to epilepsy surgery centers. Optimization of AEDs, identification and treatment of comorbidities, patient education to promote adherence to treatment, and avoidance of triggers should be periodically performed. Identifying those individuals who are most at risk of seizure relapse and development of DRE remains a challenge.
"Intrinsic" factors
Certain pediatric epilepsy syndromes, including Lennox–Gastaut syndrome, Rasmussen encephalitis, and early infantile epileptic encephalopathy among others, are almost invariably drug refractory. Similarly, underlying structural abnormalities in non-idiopathic localization-related epilepsies, which account for >50% of adult cases of DRE, must be considered. A common observation is that epilepsy from an underlying vascular lesion is more treatment responsive than that due to mesial temporal sclerosis (MTS), cortical dysplasia, or dual pathology. In fact, it has been observed that up to 80% of individuals with MTS develop DRE and these individuals

are unlikely to benefit from ongoing medication trials alone. Another consistently identified risk factor for DRE is having a high number of seizures prior to diagnosis and treatment. Management of patients with DRE is challenging because the mechanism underlying it is not completely understood nor do we understand why pharmacoresistance develops in some individuals and not others. The pathogenesis underlying DRE is likely to be multifactorial and variable with both genetic and environmental factors implicated and several theories for how DRE develops. The "transporter hypothesis" is based on findings of overexpression of multidrug efflux genes and concomitant proteins in human epileptic brain tissue and in animal models of DRE. the extent that these transporters contribute to drug resistance is still relatively unknown.

In contrast, the alternative "target hypothesis" suggests an epilepsy-induced alteration of cellular targets of AEDs, leading to a reduction in sensitivity. These targets include various receptors and ion channels, but this hypothesis is principally based on studies with carbamazepine (CBZ) on voltage-gated sodium channels in hippocampal neurons. Sodium channels of hippocampal CA1 neurons from patients with MTS were studied and compared with neocortical neurons from patients without MTS. The mechanism of action of CBZ, use-dependent block of voltage-dependent sodium channels, was completely lost in these DRE patients. Similarly, a loss of drug-target sensitivity has also been found in rat models of temporal lobe epilepsy.

Other hypotheses have emerged more recently, born from findings in patients and animal models of DRE. The "network hypothesis" proposes that seizure-induced structural brain alterations such as axonal sprouting, synaptic reorganization, neurogenesis, and gliosis can contribute to the formation of an abnormal neural network.

Traditionally, there are a few options available for people with medically refractory epilepsy. The most common one is epilepsy surgery, which has been performed since the 1940s. It is a very mature procedure, very reliable, but most of the surgical treatment is still open brain surgery. Somewhere between 60 and 70 percent of patients with drug-resistant epilepsy who have surgery become seizure-free, which is the standard of care if the medications were not to work? So, any patient who has drug-resistant epilepsy should be evaluated for surgery. Open brain surgery is effective but also carries higher risk for complications, pain and psychological impacts. Recently, minimally invasive epilepsy brain surgery has advanced quite

significantly, particularly a procedure called laser ablation for patients with epilepsy.
Are there other options besides surgery? Vagus nerve stimulation (VNS) has been shown to decrease the frequency and intensity of seizures, with 30%–40% of patients achieving a >50% reduction in seizure frequency. Another device gaining attention is deep brain stimulation, with open-label and some small controlled studies finding a reduction in seizure frequency by ≥50%.
Diet therapy: The ketogenic diet was proposed as a treatment for seizures prior to introduction of modern AEDs. The There is demonstrated efficacy in children with DRE, with more than one-third experiencing a ≥50% reduction in seizures.
Alternative diets to consider are the modified Atkins diet and low-glycemic-index diet.
Cannabis: Recently, there has been intense interest regarding the potential of medical cannabis to treat seizures, due to mounting anecdotal reports and media coverage of its success.
Conclusion: Management of DRE requires a multidisciplinary and often multitreatment approach with timely referral to specialist epilepsy centers for prompt evaluation. Selection of the patients and treatment modality are the most challengeable facts that must be considered as the first and the most important step in the management.

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Genetic Causes of Pharmacoresistant Epilepsy Syndromes and Drug Repurposing Approaches Using Zebrafish as a Model Organism

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Background: Many patients with neurodevelopmental disorders present with pharmacoresistant epileptic seizures that do not respond to available anti-seizure drugs (ASDs). Most of these diseases are caused by genetic

mutations, such as SCN1A mutations in Dravet syndrome, CHD2 mutations in Lennox-Gasteaux syndrome, and HNRNPU and DHPS mutations in two of the growing number of ultra-rare epileptic encephalopathies. These syndromes are typically characterized by a combination of epileptic seizures, cognitive impairment, and behavioral abnormalities. In this study, we are generating and phenotypically characterizing new animal models for these syndromes, with the goal of using selected models for drug repurposing or drug discovery.

Methods: Zebrafish loss-of-function models were generated using CRISPR mutagenesis, ENU mutagenesis (via the Zebrafish Mutation Project at the Sanger Centre), or by antisense knockdown using morpholino oligomers. Epileptic seizures were characterized in zebrafish larvae (1) by behavioral analysis, using an automated video tracking system to quantify locomotor activity and seizure-like behavior; (2) by electrophysiological analysis, using a single electrode placed in the midbrain to generated open-field recordings; (3) by whole-brain imaging of calcium dynamics using a transgenic line with pan-neuronal expression of gCaMP.

Findings: Drug repurposing screening using our zebrafish epilepsy models identified constituents of the medicinal plant *Curcuma longa* as being able to significantly decrease seizure frequency. These results were obtained using behavioural analysis, and were confirmed by electrophysiological analysis. Ongoing studies into the mechanism of action of these constituents has revealed novel targets and signalling pathways, possibly identifying novel therapeutic entry points for pharmacoresistant epilepsies.

Conclusion: Zebrafish, which are now well-accepted as a model organism for a wide range of human diseases, are an ideal platform for disease modelling and drug discovery, especially for neurodevelopmental syndromes with refractory seizures. We look forward to translating the findings from our zebrafish-based studies into the clinic in the near future.

Keywords: pharmacoresistant epilepsy syndromes, drug repurposing, Zebrafish, genetic mutations

Stimulation Therapy for Epilepsy

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One in three epilepsy patients has insufficient control of their seizures with medicines. Resective or ablative surgery offers an excellent chance of seizure freedom for appropriately-selected patients. However, a substantial number of patients with refractory epilepsy are not candidates for surgery, and some patients who undergo surgery do not attain seizure freedom.
Neurostimulation is a growing field in the treatment of refractory epilepsy.
Vagus Nerve Stimulation (VNS) was FDA-approved in 1997, and is the mostly widely used neurostimulation therapy for epilepsy in the US. VNS provides scheduled therapy to prevent seizures, and on-demand therapy to help abort or shorten seizures when they occur. Newer versions of the VNS device are equipped with seizure detection, based on EKG changes; this enables automated delivery of therapy at the time of a seizure.
Deep brain stimulation (DBS) is effective in the treatment of conditions such as Parkinson's disease, essential tremor, dystonia, and obsessive-compulsive disorder. Numerous targets have been proposed or investigated for the treatment of seizures. The pivotal clinical trial targeting the anterior nucleus of the thalamus showed some promise in some outcome measures, but was not FDA-approved because it did not meet the prespecified primary outcome. The device is approved for use in other countries, and may be re-visited at some point in the US. Responsive neurostimulation (RNS) is unique among neurostimulation therapies in that it targets stimulation directly at the epileptogenic source. RNS was FDAapproved in 2013. The device records electrocorticography and can be programmed to accurately detect seizures, and deliver stimulation to terminate a seizure. An interesting and consistent finding across the various modalities of neurostimulation for epilepsy is that studies have shown increasing efficacy over time. Each modality has been shown to have a favorable safety profile, and may show improved quality life. Neurostimulation is expected to be a growing area for investigation, and for clinically available treatment options for patients with refractory epilepsy. However it is vitally important to note that rates of complete seizure-freedom with neurostimulation are very low compared to resective and ablative surgery. Therefore patients with refractory epilepsy should have a thorough evaluation for surgery before being implanted with a neurostimulator.

Epilepsy Around Puberty

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Background: Epilepsy in adolescence causes significant neurologic burden. Adolescence is a great transition from childhood to adulthood which is associated with physiological changes, emergence of new types of epilepsy and also new social responsibilities. These factors have a complex relation with each other which is worth considering and is the main objective of this paper.
Methods: I have searched the Pubmed, Scopus and Embase databases between 1965 and 2019 with following keywords: seizure, epilepsy, puberty, adolescence and hormone. English articles in form of clinical studies which considered epilepsy in adolescence and around puberty have been included.
Findings: Epilepsy in adolescence commonly consists of childhood onset epilepsy syndromes which persist to adolescence (benign childhood epilepsy with occipital paroxysms(Gastaut type), Lennox–Gastaut syndrome, childhood absence epilepsy, etc.), epilepsy syndromes with onset in adolescence (juvenile absence epilepsy, juvenile myoclonic epilepsy, progressive myoclonic epilepsies, etc.) and also epilepsy due to other acquired etiologies. Hormonal changes during puberty affect the seizure activity and electroencephalographic findings. Both epilepsy and antiepileptic drugs (AEDs) may cause alteration in sexual hormones and consequently play a role in hyposexuality and psychiatric disorders and also derail psychological development at this age. Moreover adverse effects of AEDs might potentially endanger bone health, fertility and general health of this group of patients.
Conclusion: Special consideration of epilepsy in adolescence and comprehensive management of these patients seems necessary to improve quality of life and prevent future complications.
Keywords: seizure, epilepsy, puberty, adolescence.

Quantification of Hippocampus Signal by T2 Relaxometry in Mesial Temporal Lobe Sclerosis

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Background and purpose: In visual assessment of mesial temporal lobe sclerosis MRI study, there are a few pitfalls , sometimes difference between signal of two hippocampus is not possible and sometimes bilateral abnormal signal .Intensity of hippocampus effects our decision making .Our goal is to compare visual assessment and T2 relaxometry for detecting hippocampal sclerosis.
Materials and methods: 50 patient with mesial temporal lobe sclerosis diagnosed by clinic and EEG were analyzed by neuroradiology and then T2 relaxometry study by 16 multiecho images was performed for comparison.
Result: Visual analysis categorized 65% of patient as hippocampus sclerosis and about 35% as normal but T2 relaxometry detected about 80% of patient with visually detected HS and about 30% with visually normal MRI findings, considering together, visual assessment plus T2 relaxometry can detected about 75% of hippocampus sclerosis.
Conclusion: Use of T2 relaxometry, can increase detection of hippocampus sclerosis in about 30% of patient with normal visual MRI findings .

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The Effects of Domestic Violence on Mental Health of Married Women in Urmia

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Knowing the status of women in different dimensions and planning their status will affect the overall health of the community. The prevalence of

mental illness in women is 2.5 times that of men. One of the major factors affecting the mental health of violence against spouse or partner is living. This includes actions such as physical assault, psychological abuse, marital violence, and so on. The purpose of this study was to investigate the effects of domestic violence on the mental health of married women in Urmia.

Materials and Methods: This descriptive cross-sectional study was performed on 2 women and 3 women in the population of Urmia in year 2 and this study was based on GHQ-28 standard questionnaire for mental disorders and depression. Demographic, Mental Health Violence Records were also classified according to the economic status of the individuals according to their per capita area according to the number of family members and housing infrastructure. Finally, the data were edited with SPSS V.24 software.

Results: The mean age of the subjects in the study group was 41.16 41 1.2 years. 41.7% of the subjects had been subjected to domestic violence, which was 47.11% for physical violence, 31% for psychological violence and 29.89% for violence. It was sexual. 88.7% of physical violence was related to punching, kicking, slapping, 47% throwing objects and 39.19% pushing. Also, bone fractures 7.1% and abortion due to trauma were 3.1%. Psychological abuses and humiliation were 88.1% and 21.7%, respectively. There was also a significant relationship between higher number of children and low economic status and spouse addiction with domestic violence (P = 0.05). 2.14-3.49-OR = 95%) also lucky The prevalence of mental disorder in women who were 3.1 times more violent than other women was significantly correlated with the incidence of violence against women (P = 0.05). (CL = 1.55-5.69-OR = 95%)

Conclusion: Based on the results of violence against women in families with addicted spouses, with high number of children and low economic status, there was also a significant relationship between women who had mental disorders and more chances than others. The women were violent against themselves.

Keywords: Violence, Women's Health, Mental Health

The Relationship Between Selenium and Glutathione Peroxidase in Patients with Epilepsy in West Azarbaijan Province

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Epileptic seizures are a common manifestation of mitochondrial dysfunction in mitochondrial encephalopathies. Selenium is one of the strong antioxidants in the body that interferes with and damages the cell's adverse reactions. Glutathione is also the most abundant intracellular non-enzymatic defense against oxidizing agents in the living organism, especially its brain tissue, and glutathione peroxidase is one of the most important enzymes in the pathway of glutathione metabolism. The purpose of this study was to investigate the association between selenium and glutathione peroxidase in epileptic patients. Be it.

Materials and Method: Our statistical population included 100 infants with epilepsy in West Azarbaijan province in year 1 and 2 healthy children as control group. Demographic information including age, time of onset of disease, history of seizure, family history and medication use as Questionnaires were completed in both groups. Blood samples were obtained from all subjects. Blood samples were collected in tubes containing KEDTA for selenium and heparin for anticoagulation to measure glutathione peroxidase. It was measured by atomic absorption through hydrated ions and not at Data were analyzed with SPSS V.24 software quality.

Results: The mean age of the study group was 9.3 12 12 years, of which 3% were boys and 5% were girls.The mean selenium level in healthy subjects was 91.2 ng and 60.17 ng in healthy subjects, respectively. The most common type of seizure in generalized tonic clonic patients was 41.7% and the lowest type was atonic 6.2%. Imaging results were 21.7% in cerebral atrophy and 4.7% in structural disorders and 37.9% in normal subjects. 72% of patients had lower serum selenium levels than the control group.

Glutathione peroxidase was 85% in the control group and 74% in the control group. The only significant family history and maternal age in pregnancy were related to demographic parameters. (P = 0.005 OR = 3 / 42-9 / 88 OR = 95%)

Conclusion: Based on the results, the level of glutathione peroxidase and selenium in patients with epilepsy is lower than normal, which can be used as one of the previously identified diagnostic factors.

Keywords: glutathione peroxidase, selenium, epilepsy

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SUDEP Update

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Sudden Unexpected Death in Epilepsy (SUDEP) is the major reason for premature death in people with epilepsy and has been an area of intense research over the last decade. The American Academy of Neurology and the American Epilepsy Society recently published a practice guideline based on a systematic review and meta-analysis with emphasis on determining the incidence of SUDEP and the question of whether risk factors for SUDEP have been identified. Subsequent work has established that the SUDEP incidence in the order of 1.1-1.3/1.000 patient years among people with epilepsy, and similar across age groups. The risk, however, varies considerably between people with epilepsy depending on individual risk factors. The systematic review identified generalized tonic-clonic seizures (GTCS; in this context representing focal to bilateral tonic-clonic as well as generalized tonic-clonic seizures) as the major risk factor and concluded that the risk increases with increasing frequency of GTCS. Risk factors identified with moderate confidence were lack of nocturnal supervision, and absence of nocturnal listening device. The latter all based on single studies. The association with GTCS frequency has subsequently been confirmed in a large Swedish population-based case-control study, which also found nocturnal GTCS and living alone as risk factors. Most of the SUDEP victims lived alone and the

combination of living alone and having GTCS increased dramatically the risk of SUDEEP. Current data suggest that the most effective way to prevent SUDEP is to improve control of GTCS, e.g. by epilepsy surgery or by intensified pharmacological treatment. In support for the latter, a meta-analysis of placebo-controlled add-on trials in treatment resistant epilepsy revealed that patients randomized to add-on with active treatment had a substantially lower SUDEP incidence than patients randomized to add-on placebo.

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Impact of Changes in AED Selection on the Risk of Adverse Pregnancy Outcomes

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Prospective studies have provided in recent years new information on the comparative teratogenic risks of antiepileptic drugs (AEDs), enabling a more rational approach to the management of epilepsy in women of childbearing potential. Largely, this information comes from registries initiated some 20 years ago, each enrolling thousands of pregnancies and assessing rates of major congenital malformations (MCMs) following exposure to different AEDs. Smaller scale prospective cohort studies provided comparative data on neurodevelopment of children born from mothers taking AEDs during their pregnancy. Valproate is the drug with the highest risk, whereas prevalence of MCMs is lowest with lamotrigine, levetiracetam and oxcarbazepine. For valproate, phenobarbital, phenytoin, carbamazepine, and lamotrigine, the risk of MCMs is dose-dependent. Prenatal exposure to valproate has also been confirmed to cause an increased risk of cognitive impairments and autistic traits. Based on these emerging data and due to regulatory restrictions on the use of valproate in female patients, there has been a marked shift in AED selection for the treatment during pregnancy over the last years. While the use of valproate, and of carbamazepine has declined substantially, lamotrigine and levetiracetam are prescribed much more often during pregnancy. Prospective pregnancy registries have

attempted to analyse changes in pregnancy outcomes in relation to this shift in treatment strategies. EURAP, the international antiepileptic drugs and pregnancy registry, noted a 27% decline in the prevalence of MCMs over a 14 years period, an improvement that is most likely explained by changes in AED selection.

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Review on Micro RNA as a Potential Biomarker for Diagnosis and Treatment of Epilepsy

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Background: Epilepsy is a CNS neurological disorder in which normal brain activity is jammed resulting in seizures or periods of unusual behavior. Untilnow anti-epileptic drugs are only effective inless than one third of epilepticpatients,and predicting biomarkers are not available when the specific antiepileptic drugs treated.Advanced studieshave showed that miRNA may have akeyrollin the pathogenesis of epilepsy. Several target genes and pathways of miRNA which related to the therapeuticmethods to epilepsy.
Method: We searched PubMed from Jan 1,2014to Jan 1, 2019using the terms "epilepsy ANDmicroRNA AND biomarker" and "seizure AND microRNA AND biomarker".We selected articlesthat featured novel miRNAs in vivo epilepsy models and patients.
Findings: Decrease the expression of has-miR134 could be a potential non-invasive biomarker to usein diagnosis for the epilepsy patients for using hsa-miR-134 also be identified to distinguish patientswithand without epilepsy. miR-181a show significant downregulation in the acute stage, but upregulation in the chronic stage. Other applicable biomarkers for diagnosis of epilepsy are miR-199a,miR124,miR128 etc.
Conclusion: These studies suggest that there can be newdevelopmentsfor diagnosis and treatment ofepilepsy patients. Advanced techniquesand miRNA combination may producemore effective rolesin epilepsy and other

disease. These reports will be available to solve the useof miRNAs asbiomarkers and novel therapy approaches for epilepsy. To summarize all, researcher who focus on miRNAsshould have information onthe causes, treatment, and diagnosis of epilepsy. exploration of anyof these effects on the efficacy of these drugs is worthwhile.

Keywords: Epilepsy,epilepsy biomarkers, microRNA, seizures, diagnosis, temporal lobe epilepsy,status epilepticus, epileptogenesis

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Epilepsy in Systemic Disease

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PURPOSE OF REVIEW: This article addresses the occurrence of acute symptomatic seizures in the setting of many medical illnesses.

RECENT FINDINGS: Many medical illnesses can cause seizures. Metabolic derangements, such as disorders of serum glucose metabolism or renal or hepatic failures can cause seizures, as well as some medications in therapeutic or toxic dosage.

SUMMARY: Acute symptomatic seizures occur most often in illnesses that directly injure the brain. Trauma, stroke, CNS tumors, and CNS infection very commonly cause seizures. However, many medical illnesses do not directly injure the brain but lead to neurologic signs and symptoms, such as seizures. Recognizing these effects, especially in critically ill patients,and appropriate treatment is important for optimizing medical care.

Common Errors in Diagnosis & Management of Status Epilepticus

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Status epilepticus is a serious medical emergency and successful management needs urgent, effective and organized approach. Treatment is largely aimed at stopping seizures in order to avoid brain damage and other morbidities. Common errors frequently seen in the evaluation and management of patients with SE encompasses errors in the following items which are discussed.

1.Misdiagnosis (pseudo-seizure, comatose patient,)
2.Applying inadequate dose of antiepileptic drug or wrong route of administration
3. Missing or not treating underlying cause (Hypoglycemia, CNS Infection)
4.Not correcting Hyperthermia, Electrolyte disturbances (Na, K, Mg), Acidosis, Brain edema
5.Delay in Intubation leading to hypoxic Ischemic Encephalopathy.
6.Excessive delay in switching to second medication or starting anesthetic drugs
7.Delay in initiation of maintenance anti-epileptic drugs following status treatment.

Antiepileptic Drugs Interaction

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Population-based studies of drug utilization demonstrate that 19-24 % of patients with epilepsy use polytherapy with AEDs. In recent studies of children and adults with refractory epilepsy, 64 % used polytherapy with two or more AEDs, and 35 % of the adults suffered from CNS-related co morbid conditions, resulting in a considerable risk of interactions.
Most drug interactions in the past were discovered due to unexpected change in the clinical status of a patient after addition or withdrawal of a drug from existing medication.
Interactions between antiepileptic drugs, or between antiepileptic drugs and other drugs, can be pharmacokinetic or pharmacodynamic in nature. Pharmacokinetic interactions involve changes in absorption, distribution or elimination, whereas pharmacodynamic interactions involve synergism and antagonism at the site of action. Most clinically important interactions of antiepileptic drugs result from induction or inhibition of drug metabolism.
By far the most important pharmacokinetic interactions are those involving cytochrome P450 isoenzymes and glucuronyl transferase (GT) enzymes in hepatic metabolism. Among old generation AEDs, carbamazepine, phenytoin, phenobarbital, and primidone induce the activity of several enzymes involved in drug metabolism, leading to decreased plasma concentration and reduced pharmacological effect of drugs, which are substrates of the same enzymes (lamotrigine, and topiramate).
Practically for preventing antiepetic drugs interaction it is prefer prescribe drugs with different mechanism and their metabolite sites, like the new AEDs such as gabapentin, levetiracetam, tiagabine and vigabatrin do not induce the metabolism of other AEDs.
Key words: Antiepileptic drugs, interactions

Note: