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Inhalt

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Ligue Suisse contre l'Epilepsie
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Swiss League Against Epilepsy

Richtlinien für die Autoren

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Was ist an die Redaktion einzureichen?

Alle Manuskripte sind inklusive Abbildungen und Tabellen in dreifacher Ausführung einzureichen. Bevorzugt wird eine elektronische Manuskripteinreichung per e-mail (Textverarbeitung: MS Word), alternativ die Zusendung von drei Ausdrucken und einer CD (für Abb. und Tab. ist das verwendete Programm anzugeben).

Prof. Dr méd. Serge Vulliémoz

Chères et chers collègues,

Pourquoi est-ce arrivé ?
Qu'est-ce que ça change pour moi ?
Est-ce que ça va revenir ?
Que faire pour l'éviter ?

Une première crise d'épilepsie constitue un évènement extrêmement marquant dans la vie d'une personne avec potentiellement de nombreuses conséquences médicales et psychosociales, tant privées que professionnelles, notamment en lien avec l'hygiène de vie, la conduite de véhicule à moteur et certaines activités à risque. L'enjeu le plus important est bien sûr le diagnostic correct, la prédiction du risque de récidive et ainsi le diagnostic éventuel d'épilepsie et son traitement. Toutes ces étapes constituent souvent des défis diagnostiques et pronostiques pour les cliniciens.

Dans ce numéro d'Epileptologie, quatre articles présentent les évidences et les recommandations actuelles tant sur le plan sémiologique, électroencéphalographique, radiologique et thérapeutique, avec des cas illustratifs. L'importance de la recherche clinique et du développement de nouveaux outils diagnostiques et pronostiques est également soulignée.

L'application d'une prise en charge optimisée et moderne ainsi qu'une remise en question répétée des cas difficiles est cruciale pour réduire à la fois les sous-diagnostics et les sur-diagnostics. En effet, la surinterprétation de facteurs favorisant plus que provoquants, la sémiologie non-objective décrite par les témoins, la présence de grapho-éléments inhabituels non-pathologiques à l'EEG et la découverte de lésions fortuites à l'imagerie sont des pièges classiques dont l'impact peut être réduit par une confrontation entre les différents éléments sémiologiques, l'EEG et l'imagerie. Sur le plan thérapeutique, on ne peut qu'insister sur l'importance du choix le plus rationnel du traitement en fonction du contexte clinique en cas de diagnostic d'épilepsie.

Excellente lecture !
Bien cordialement

Serge Vulliémoz

Prof. Dr. med. Serge Vulliémoz

Why did it happen?
What does it change for me?
Will it come again?
What can I do against it?

A first epileptic seizure represents an extremely marking event in the life of a person, with several potential medical and psychosocial consequences both in the private and professional life, notably with respect to lifestyle, driving and avoidance of certain activities. The most important challenge is of course the correct diagnosis, the prediction of recurrence risk and therefore, the diagnosis of epilepsy and its treatment. All these steps often constitute diagnostic and prognostic challenges for the clinicians.

In this issue of Epileptologie, four articles present the evidence and current recommendations for the clinical evaluation, EEG recording and imaging procedures with illustrative cases. The importance of clinical research and the development of new diagnostic and prognostic markers is also stressed.

The application of an optimised and modern management and the repeated questioning in difficult cases is crucial to reduce both under- and over-diagnosis. Indeed, the overinterpretation of favoring rather than triggering factors, the non-objective semiology described by eye-witnesses, the presence of non-pathologic EEG variants and the discovery of incidental lesions on imaging are classical traps. Their impact can be reduced by a careful confrontation between the various elements of semiology, EEG and imaging. From a therapeutic perspective, we can only insist on the importance of a most rational choice of anti-epileptic drug in each specific clinical situation, in case a diagnosis of epilepsy is made.

I wish you an excellent reading!
Sincerely,

Serge Vulliémoz

Prof. Dr. med. Serge Vulliémoz

Liebe Kolleginnen und Kollegen

Warum ist es passiert?
Was ändert das für mich?
Wird es wieder vorkommen?
Was kann ich dagegen tun?

Ein erster epileptischer Anfall ist ein sehr einschneidendes Ereignis im Leben eines Menschen, mit zahlreichen möglichen medizinischen und psychosozialen Konsequenzen für den privaten und beruflichen Alltag. Er kann die Lebensführung beeinträchtigen, zum Beispiel im Hinblick auf das Autofahren oder das Ausüben bestimmter Sportarten. Die wichtigsten Herausforderungen bestehen dabei in der korrekten Diagnosestellung, dem Abschätzen des Wiederholungsrisikos, der Einordnung des Anfalls als epileptisch oder nicht-epileptisch und dem Einleiten der entsprechenden Behandlung. Alle diese diagnostischen und prognostischen Überlegungen beinhalten für den Kliniker anspruchsvolle Entscheidungen.

In dieser Ausgabe der Epileptologie befassen sich vier Artikel mit den Erkenntnissen und aktuellen Empfehlungen für die klinische Untersuchung, EEG-Ableitungen und Bildgebungstechniken, auch mittels anschaulicher Fallbeispiele. Dabei wird die Wichtigkeit der klinischen Forschung und der Entwicklung von neuen diagnostischen und prognostischen Mitteln betont.

Die Anwendung eines optimierten und modernen Fallmanagements und das wiederholte Infragestellen getroffener Massnahmen ist entscheidend, um ein Unter- oder Überdiagnostizieren zu vermeiden. Tatsächlich sind eine Überinterpretation von anfallsbegünstigenden statt anfallsprovozierenden Faktoren, eine nicht objektive Beschreibung des Anfalls durch einen Zeugen, das Auftreten von ungewöhnlichen nicht pathologischen Zeichen im EEG und die Entdeckung von zufälligen Läsionen bei der Bildgebung klassische Fallstricke. Wenn man diese Faktoren sorgfältig mit den verschiedenen Elementen der Semiologie in Verbindung setzt, können Fehlinterpretationen vermieden werden. Wird die Diagnose einer Epilepsie gestellt, ist die Wahl des für diesen klinischen Kontext geeignetsten Antiepileptikums von grosser Bedeutung.

Serge Vulliémoz

First Seizure – is it Really Epilepsy?

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Summary

Seizures are among the most common neurologic conditions leading to an emergency room admission. However, there are a number of paroxysmal events that can mimic epileptic seizures. On the one hand, it is important to delineate isolated seizures from epilepsy, on the other hand, there is a number of non-epileptic paroxysmal disorders that might mimic epileptic seizures. As the diagnosis of epilepsy has long-term social, medical, and prognostic implications, it is crucial to determine the correct diagnosis as early as possible.

A careful history is essential to determine the correct workup, which usually includes routine-EEG, MRI, in some cases video-EEG-monitoring or cardiologic workup. This article will summarize the most important aspects that help to make the correct diagnosis.

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Key words: First seizure, syncope, psychogenic non-epileptic seizure, differential diagnosis

Erster Anfall – ist es wirklich Epilepsie?

Epileptische Anfälle gehören zu den häufigsten neurologischen Ursachen einer Zuweisung auf die Notfallstation. Allerdings gibt es eine grosse Zahl von Ereignissen, die epileptischen Anfällen ähneln. Einerseits ist es von Bedeutung, einzelne provozierte Anfällle von einer eigentlichen Epilepsie abzugrenzen, andererseits gibt es paroxysmale Ereignisse nicht-epileptischer Genese. Da die Diagnose Epilepsie erhebliche langfristige soziale, medizinische und prognostische Konsequenzen mit sich bringt, ist es äusserst wichtig, so früh wie möglich eine korrekte Diagnose zu stellen.

Eine sorgfältige Anamneseerhebung ist die Grundlage des weiteren diagnostischen Vorgehens. Dieses beinhaltet üblicherweise Routine-EEG und MRI, in speziellen Fällen Video-EEG-Monitoring oder kardiologische Abklärungen. Dieser Artikel soll die wesentlichen Aspekte zusammenfassen, die dabei helfen, eine korrekte Diagnose zu stellen.

Schlüsselwörter: Erster Anfall, Synkope, psychogene nicht-epileptische Anfälle, Differenzialdiagnose

Première crise – est-ce que c'est vraiment épilepsie ?

Les crises d'épilepsie sont une des présentations neurologiques les plus fréquentes dans les services d'urgence. Toutefois, il y a un certain nombre de phénomènes paroxystiques qui peuvent mimer des crises d'épilepsie. D'une part il est important de distinguer une crise isolée d'une épilepsie. D'autre part, il y a de nombreux troubles neurologiques paroxystiques non-épileptiques qui peuvent mimer des crises d'épilepsie. Comme un diagnostic d'épilepsie a des implications pronostiques médicales sociales à long terme, il est crucial de déterminer le diagnostic correct aussi tôt que possible. Une anamnèse soignée est essentielle pour déterminer le bilan diagnostique adéquat qui comprend habituellement un EEG standard, une IRM et dans certains cas un enregistrement video-EEG prolongé ou un bilan cardiologique. Cet article résume les aspects principaux qui aident à poser un diagnostic correct.

Mots clés : Première crise, syncope, crise psychogène non-épileptique, diagnostic différentiel

Introduction

All over Europe, the number of patients with neurological diseases in the emergency room increases, both due to demographic changes and the development of the specialty [1 - 3]. Among those patients, seizures rank within the top three most common diagnoses [4]. Since the percentage of misdiagnosis of epilepsy can be as high as up to 30% [5], every referral with suspected seizure should be critically challenged. This is especially of relevance as current criteria allow establishing the diagnosis of epilepsy already after one or two seizures. Hence, it is even more important to rule out other conditions mimicking epilepsy at the first appearances of seizures [6].

The most important differential diagnoses can be divided into three groups: 1. provoked seizures, 2. (physiologic) non-epileptic paroxysmal disorders including syncope, and 3. psychogenic non-epileptic seizures. This article summarizes important aspects that need consideration when taking the history and planning further investigations including EEG, CCT/MRI, and cardiologic workup including tilt table test or video-EEG-monitoring.

Epileptic seizures

Case report 1

A 24-year-old woman is admitted to the emergency room after a first generalized tonic-clonic seizure. At arrival 45 min after the seizure she is awake and reports no symptoms beside sore muscles. Physical examination reveals a lateral tongue bite but no other abnormalities. Her husband who has witnessed the event reports no behavioral abnormalities preceding the incident and a sudden start with loss of consciousness, a tonic phase followed by generalized shaking of all extremities for about a minute. Afterwards the patient was agitated and disoriented for 20 minutes.

MRI showed no abnormalities but EEG revealed generalized polyspike and spike-wave complexes.

On repeated history the patient reported that for some years she experienced short twitching movement sometimes in the morning that led to some broken tableware but did not alarm her.

Taking the history

Detailed history is the mainstay for an accurate classification of any paroxysmal event [7]. It is crucial not to rely solely on the information given by the patient himself but to seek actively for eyewitnesses of the event and interview them directly and as soon as possible. A precise documentation of seizure semiology

Table 1: Distinguishing features among common paroxysmal disorders adapted from Reuber M et al. [8].

	Epileptic seizure	Syncope	PNES
Trigger	unexpected	long standing, pain	emotional stress, surrounded by others
Prodromal symptoms	epileptic aura, i.e. • epigastric • psychic • visual/acoustic	nausea, sweating dizziness tunnel vision impaired hearing	emotional stress
Time course	sudden, rapid crescendo to maximal severity	sudden, rapid crescendo to maximal severity	waxing and waning
Falls	tonic/atonic falls	slumping	protective movements, no relevant trauma
Eyes	open	Half open	closed
Movements	tonic, clonic, atonic, complex	atonic, myoclonic	asymmetric/asynchronous movements, head rolling
Appearance	cyanosis	pallor	variable
Vital signs	tachycardia	orthostatic	mild tachycardia
Tongue biting	lateral tongue bite	variable	bite at tip of tongue
Breathing	postictal stertorous	shallow	normal
Duration	<3 min	seconds to minutes	minutes to hours
Reorientation	minutes to hours	prompt	fluctuations for hours

– especially the initial phase – gives precious hints for localizing the epileptogenic focus and relation to imaging results. Fifty percent of patients with an apparent "first seizure" have had minor seizures before the event, so their diagnosis is epilepsy [9] with the exception of multiple events within 24 hours that do not lead to the diagnosis of epilepsy and are not associated with an increased risk of recurrent events [10]. Also it is well known that nocturnal seizures pose a higher risk of recurrence [11], so documentation of the time of the event is important.

Based on history and clinical findings it is possible to diagnose an epilepsy syndrome in about half of the patients presenting with a first epileptic seizure [12]. It has to be emphasized that there are rarely single clinical signs or symptoms that definitely prove or rule out the diagnosis of an epileptic seizure. Usually it is rather the combination of signs that makes one or the other diagnosis likely. **Table 1** is summarizing the relevant signs of the most important differential diagnosis for paroxysmal spells.

Yet, even a given diagnosis of an epileptic seizure does not prove epilepsy. It is always important to rule out provocative factors, as even recurrent provoked seizures do not justify the diagnosis of epilepsy (**Table 2**).

Table 2: Examples of provocation factors

Alcohol withdrawal
Benzodiazepine or barbiturate withdrawal
Medication (tramadol, imipenem, theophylline, bupropion and others)
Metabolic disorders (uremia, hypoglycemia, hyponatremia and others)
Drugs (cocaine, amphetamines and others) Infection – CNS or systemic
Acute brain injury • Trauma • Stroke • Brain surgery
Severe sleep deprivation

Particular attention should be paid to detailed description of the epileptic event as this leads to valuable hints to localization or leads to the diagnosis of primary generalized epilepsy syndrome. Epileptic aura can give localizing hints too (**Table 3**). In the revised classification, aura is defined as a focal seizure without impairment of consciousness involving subjective sensory or psychic phenomena only [13]. On the other hand, complex hallucinations like such as seeing formed objects or hearing words or sentences are very unlikely epileptic [8].

Table 3: Focal signs in epilepsy

Region of Onset	Characteristic focal signs
Frontal	Focal clonic motor
	Hypermotor behavior
Temporal	
Mesial	Autonomic (epigastric) Amnestic/Dysmnesic Déjà vu, Jamais vu
Gustatory/Olfactory	
Lateral/posterior	Auditory
Neocortical	Complex visual Dysphasic
Parietal	Sensory
Occipital	Simple visual

Laboratory testing

The main objective of laboratory testing in the setting of first seizure is the exclusion of provoked seizures.

Creatinkinase is often elevated after generalized tonic-clonic seizures. Yet any trauma in the context of spells can also cause an elevation of CK, so this does not distinguish epileptic vs. non-epileptic events.

Elevated postictal prolactin levels can support the diagnosis of an epileptic seizure vs. psychogenic non-epileptic seizures [14, 15]. However, prolactin is also elevated after syncope and trauma, so in this context it does not help to discriminate epilepsies and other disorders.

Genetic testing is appropriate only in rare cases of a known genetic epileptic syndrome in the family.

Imaging

Every patient with a first epileptic seizure should undergo imaging to detect underlying diseases and structural abnormalities. In most instances MRI is the appropriate method, but in emergency setting and patients not eligible for MRI, e.g. with pace-makers, computed tomography (CT) will be the method of choice [16 - 18], but reveals an epileptogenic lesion in just 30% percent of patients with refractory epilepsy [19]. MRI showed epileptogenic lesions in 38 of 141 patients presenting with a first epileptic seizure, including 17 tumors [11]. A more recent study showed 29% of abnormal imaging in patients with a single seizure episode [18].

No lesion was revealed in patients with a generalized epilepsy syndrome [11]. So in very typical cases of primary generalized epilepsies (e.g. childhood absence, juvenile myoclonic epilepsy) with typical EEG-changes and adequate response to antiepileptic drugs imaging may not be necessary [13, 17]. Imaging should be performed on a 3T machine using a standardized protocol [20, 21].

Other imaging techniques such as SPECT and PET are not routinely necessary in the setting of first epileptic seizures.

Electroencephalography (EEG)

EEG is the most specific technique in diagnosing epilepsy. Epileptiform discharges are seen very rarely in adults and children without epilepsy (0.2 - 3%) [22, 23]. Also during the interpretation, benign epileptiform variants as well as changes due to toxic or metabolic disorders have to be recognized [24] to avoid false positive findings.

Routine EEG more than 48 hours after the event is non-diagnostic in up to 70% in patients with epilepsy. So a normal interictal EEG does not rule out the diagnosis of epilepsy. The yield may be increased to more than 50% by recording within 12 h of the event [25] repeated recordings [26], sleep deprived-EEG [27] and especially by performing ictal or post-ictal recordings [11, 28, 29].

Recognition of an ictal EEG pattern confirms the diagnosis of an epileptic event and helps to classify the seizure type. Also, it is of relevance to evaluate the risk of seizure recurrence: Within two years the risk of recurrence in patients with epileptiform discharges is 83%; in patients with non-epileptiform abnormalities 41%; and in patients with normal EEG 12% [30]. In some patients this information is not mandatory, otherwise it is advisable to perform video-EEG monitoring [31].

Case report 1 – diagnosis

The patient's seizures can be classified as generalized tonic-clonic seizure and myoclonic seizures. The history and the patient's age are strongly suggestive of genetic epilepsy, most likely of juvenile myoclonic epilepsy. This diagnosis is supported both by the findings of her EEG and the absence of irregular findings on MRI.

Epileptiform mimics of somatic origin

Case report 2

A 33-year-old male was admitted to our EEG-Monitoring-Unit after presentation in the emergency room due to a first generalized seizure. Eyewitnesses described the event to last for up to 3 minutes, with open eyes, jaws pressed together, jerky movements. Afterwards the patient felt tired, but was oriented rapidly. On further questioning, he mentioned that similar, though less severe events had occurred before, mostly associated with pain or emotional stimuli. Routine-EEG, ECG, bedside orthostatic testing and MRI were normal.

After 24 hours of video-EEG-monitoring without any specific findings provocation was performed by drawing blood. Prior to the puncture the patient was informed about the painful and traumatic nature of the procedure. Shortly after needle insertion a short loss of tone was seen with loss of consciousness followed by irregular cloni of all extremities, and then another atonic phase occurred with a generalized tonic phase afterwards. After a total duration of 40 seconds the patient regained consciousness without any postictal phenomena.

Monitoring revealed a habitual heart rate of approximately 56 bpm, which raised up to 92 bpm shortly before needle insertion and fell to 40 bpm for 8 seconds starting in the moment of insertion and followed by an asystole of 32 s duration. Afterwards sinus rhythm restarted spontaneously. Electroencephalographically 6 s after onset of the asystole a theta-slowing was observed, after further 5 s EEG was dominated by diffuse suppression. Normal EEG-activity was seen 5 s after return of normocardic sinus rhythm (**Figure 1**).

Syncope:

Syncope is characterized by a transient and rapidly reversible loss of consciousness accompanied by a loss of postural tone [32]. There are several causes for syncope (**Table 3**).

Due to the observation of myoclonic movements (in up to 90% of syncopes) during the phase of unconsciousness, syncopes are often be mistaken for seizures. In convulsive syncopes, the myoclonic movements fol-

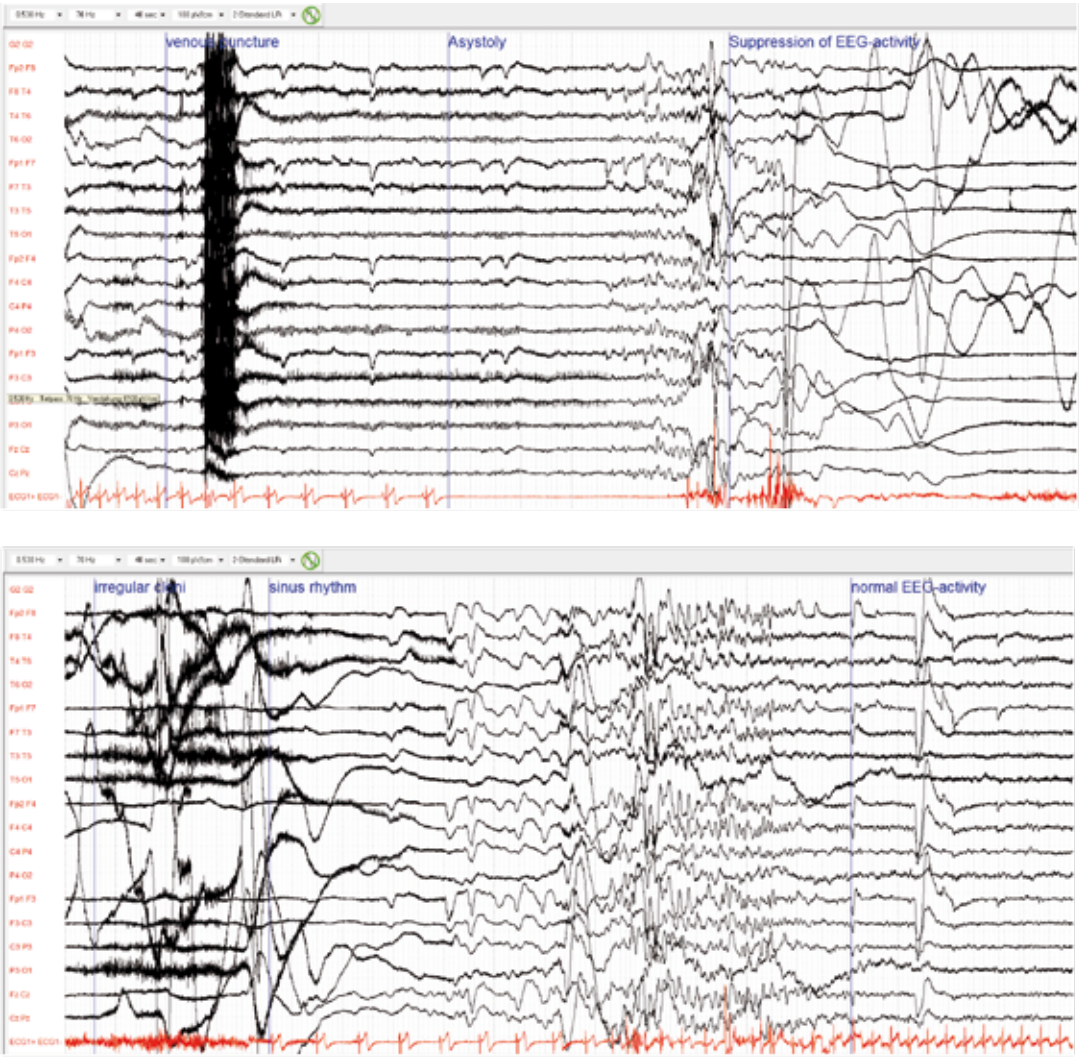

Figure 1: EEG during asystoly

low an initial loss of tone, whereas during a seizure cloni emerge from an initial tonic phase. Additionally, the lack of postictal confusion can help to distinguish between generalized seizures and convulsive syncopes, whereas a loss of urine or tongue bites can occur in both, seizures and syncopes. In syncopes caused by orthostatic hypotension or vasovagal reflex the duration usually is shorter than in epileptic seizures, mostly lasting a few seconds after reaching the horizontal position. In patients with cardiogenic syncopes, the duration may be longer, thus up to 20 - 30% of patients with cardiogenic syncopes are misdiagnosed as epileptic seizures. In order not to miss a potentially life threatening cardiac disease with arrhythmias (e.g. Brugada-Syndrome) in patients with recurrent convulsive events, careful cardiac workup up to the implantation of loop-recorders is sometimes needed besides taking up a detailed medical history [33].

Apart from the above mentioned cardiogenic syncopes, the remaining categories are mostly provoked by clear triggers like standing, raising from the supine position, increase of abdominal pressure, pain or maneuvers which increase vagal tone – so history helps in most cases to distinguish between a syncope and an epileptic event.

Table 4: Forms of syncope

Vasovagal	dumping syndrome pain syncope miction syncope pressoric syncope (defecation, cough, sneeze)
Orthostatic	
Cardiogenic	myocardial infarction primary rhythmogenic valvular/obstructive

Case report 2 – diagnosis

The patient's history with paroxysmal events triggered by pain or emotion was suggestive of vasovagal syncope and was supported by the absence of any abnormal findings on EEG, standard-ECG and MRI. It was proven by triggering a typical episode with a combination of fear and pain, resulting in syncope with asystole.

Transitory ischemic attack (TIA):

TIA is defined as transient neurologic dysfunction of sudden onset due to a disturbance of perfusion with duration of less than one hour and is also characterized by the lack of persisting structural brain damage [34]. Since both seizures and TIA can cause focal neurological symptoms like aphasia, palsy or sensory phenomena, both differential diagnoses have to be taken into account when confronted with such complaints in the emergency department.

A rare condition mimicking a focal seizure is a limb-shaking TIA, associated with carotid artery stenosis, often provoked by orthostatic or certain neck movements leading to reduced perfusion of the territory of the affected vessel. The observed jerking however resembles rather choreatic movements or tremor and can also be accompanied by a dystonic limb posturing or an ataxic component. Usually the face is spared and in contrast to focal motor seizures there is no march of convulsion observed. The latency between the provoking action and the onset of dyskinesia is usually only a few seconds [35].

A life threatening neurovascular condition that can be mistaken as focal dyscognitive epileptic seizure or status is an occlusion of the top of the basilar artery. Due to infarction of the rostral and dorsal parts of the midbrain, it can lack lateralizing signs like palsy and is characterized by altered consciousness/apathy or hypersomnolence in combination with abnormal eye and pupil movements, sometimes even associated with hallucinations [36]. In most of these patients a careful neurologic examination reveals signs of a brainstem lesion. In doubt CT-angiography is a mandatory examination.

Transient global amnesia (TGA):

Isolated memory loss (anterograde, but also retrograde for the last hours or days before symptom onset) is the main characteristic of TGA. Headaches and dizziness are common accompanying symptoms, however, there are no focal neurological deficits other than memory impairment [37].

Since most seizures of temporal origin are accompanied by staring, oral or manual automatisms and a loss of responsiveness, the absence of these features corroborates the diagnosis of TGA [38]. The most important distinguishing feature of TGA however is its duration: while seizures with amnestic episodes last less than 15 minutes, an episode of TGA has a duration of mostly 4 - 8 hours, never lasting longer than 24 hours [37].

Migraine aura:

A migraine aura can mimic epilepsy due to its similarity in the evoked clinical symptoms like visual phenomena, which also can occur in occipital lobe epilepsy or sensory disturbances that can have their origin in parietal lobe epilepsy.

One of the most important features helping in the differentiation between a migraine aura and epileptic seizures is the speed of the „march" of the symptoms. In epileptic seizures, a march of symptoms takes only a few seconds, whereas migraine-auras develop within minutes – similarly the all-over duration of migraine-aura is longer (up to 60 minutes, commonly 15 - 20 minutes vs. mainly 1 - 2 minutes for example in occipital lobe epilepsy). Fortifications and photopsia are frequent signs in visual auras and are usually very bright and often (not always!) colorless, wandering towards the periphery, and are often followed by a scotoma [38, 39]. In epileptic seizures, the visual phenomena are mostly colored, of circular shape, and multiply during the attack. They often start in the peripheral temporal hemifield and move horizontally toward the contralateral side.

The occurrence of headache afterwards is not very helpful for the differential diagnosis especially in patients with visual phenomena, because postictal headaches (often undistinguishable of migraine-headache) are a common finding in occipital lobe epilepsy [39].

Additionally, in migraine with visual auras cases with focal occipital slowing in EEG have been described, even more in hemiplegic migraine [40].

Others:

For the sake of completeness, drop attacks, which are idiopathic in 60%, and cataplectic attacks should be named in the list of differential diagnosis of seizures. Both share the feature of sudden loss of tone without alteration of consciousness, discriminating from atonic seizures or syncopes, which are accompanied by a loss of consciousness [41, 42].

However, some atonic seizures similar to drop attacks last only a few seconds with full orientation after the fall. The age of the fallen patient is indicative, since astatic seizures occur in patients with specific epileptic syndromes with onset in the childhood [38], while drop attacks usually occur in the elderly. To differentiate atonic seizures from cataplectic events the duration of the spells (minutes in cataplexy) and the history (provoking emotional triggers and excessive daytime sleepiness in cataplexy) can be of avail.

Last but not least, movement disorders in some cases can be hard to distinguish from epileptic phenomena, e.g. in paroxysmal dyskinesia or myoclonic jerks. The former can be preceded by dizziness or sensory phenomena that can be mistaken for a „seizure-aura" [32]. Non-epileptic myoclonic jerks (besides of physiologic myocloni in drowsiness, on awakening or after a syncope) are usually symptom of either neurodegenerative disorders, metabolic, infectious or paraneoplastic diseases with mostly concomitant other symptoms and signs [38].

Patients with myoclonic jerks after resuscitation represent a difficult diagnostic entity on the ICU, since the distinction of Lance-Adams-Syndrome (LAS) in sedated patients from myoclonic status epilepticus (MSE) can be challenging, as there are no distinctive EEG-features. But a clear diagnosis in these cases is crucial, since the former has a fairly good prognosis and the latter a devastating one. The most important hints are given on the one hand by the response after stopping the sedation (awakening in LAS, persisting coma in MSE) and on the other hand by the time of onset (MSE presents within 12 - 24 hours after return of spontaneous circulation (ROSC), LAS evolves later and has a chronic course after discharge from hospital with intention- or action-myoclonus) [43].

Psychogenic non epileptic seizures

Case report

A 22-year-old female patient was announced to arrive at the emergency room by ambulance for treatment of status epilepticus for more than 20 minutes; GCS was reported to be 6. On arrival of the patient the neurologist on call and the anesthesiologists were summoned, the latter ready to intubate the patient.

The ambulance staff reports that the patients' mother called them because the young woman had a seizure. By the time the ambulance arrived the seizure was ongoing for 20 minutes. The patient did not respond to questions, had her eyes closed, and had jerky movements of all four limbs. 5 mg midazolam were injected. In the ambulance the seizure stopped, the patient opened her eyes and was responsive, though slightly drowsy. However, on arrival at the emergency room the symptoms started again.

On neurologic examination the patient's eyes were closed. When trying to check the pupillary responses the eyes were screwed tightly. She had asynchronous movements of all four extremities with inconsistent withdrawal to pain stimuli; her head was rolling from side to side.

The anesthesiologists point out that the GCS is 6 at most and urge the neurologist on call to make a decision for intubation to protect airways in a formally comatose patient and to go on with diagnostics and therapy...

Psychogenic non-epileptic seizures (PNES) are a challenge especially for young neurologists on call for two reasons: First of all it is often not easy to differentiate the clinical signs from those of epileptic seizures. Furthermore there sometimes is time pressure to perform an extensive emergency workup as the patient appears to suffer from a serious acute organic disease. Yet it is crucial to make the correct diagnosis as soon as possible, as a misdiagnosis has severe consequences for the patients' further treatment and the prognosis of the disease – the longer the delay of the diagnosis, the poorer the prognosis [44]. Presently, diagnostic delay is 7 - 10 years [45], and 80% of patients with PNES receive antiepileptic drugs before the correct diagnosis is made [46].

Clinical signs

There are some features that have been shown helpful in distinguishing epileptic from psychogenic non-epileptic features. Some of the most relevant signs that are easy to evaluate are summarized in **Figure 2** and **Table 1**. They are also helpful to make the diagnosis of PNES in the case described above.

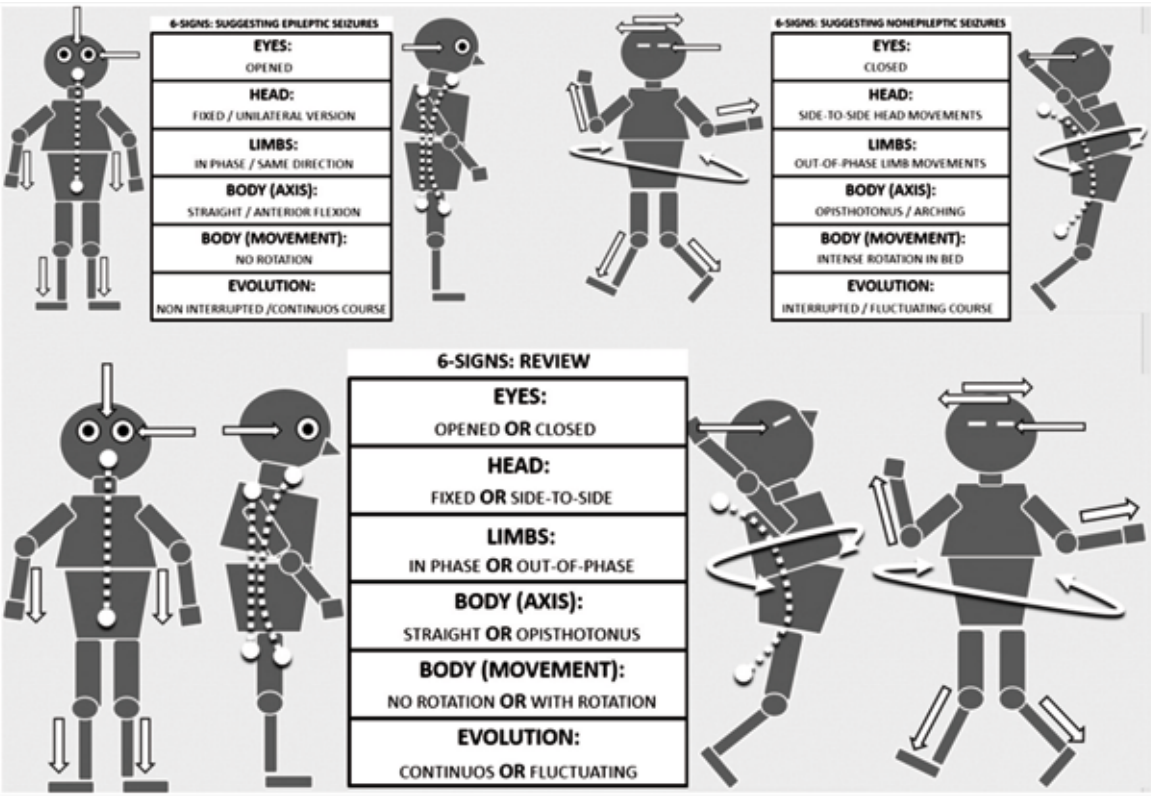

Figure 2: 6-sign bedside test for discrimination for epilepsy vs. PNES, from De Paola et al. [47] with permission

Other signs might be helpful in making the correct diagnosis of PNES:

- the circumstance of the occurrence of the attack (intensified or alleviated by bystanders)
- ictal crying/weeping [48]
- duration of more than 10 minutes [49]
- history of pain or fibromyalgia [50]
- history of physical, emotional or sexual abuse [51]

However, signs commonly attributed to epilepsy such as urinary incontinence or injuries do not discriminate PNES from epileptic seizures [12]. It has to be kept in mind that there is no single sign which specifies a 100% for epileptic seizures, rather it is essential to find a set of clues pointing to PNES [52].

Diagnostics

Even in cases that appear obvious at first glance, EEG and cerebral imaging (usually MRI) are usually performed to rule out abnormalities that point to epileptic seizures in spite of the clinical impression of PNES. This is especially important as about 15 - 20% of patients with PNES also have epileptic seizures [53, 54].

Video-EEG-Monitoring is considered as gold standard to differentiate PNES from epileptic seizures – however, this is rarely applied after a first seizure.

Therapy

Early in the course of the disease it has been shown to be effective to simply communicate the diagnosis to the patient [55]. Still in most patients a professional psychiatric evaluation is required, and especially cognitive behavioral therapy has been shown to be effective. Yet, a neurologist should also accompany the patients' therapy at least for some time as a somatic frame for psychiatric treatment is often required [56].

Case report 3 – diagnosis

In this patient several typical signs of PNES could be documented: The long duration, the effect of the surroundings on the consciousness, the closed eyes and her movements (asynchronous movements and head rolling). On further examinations EEG and MRI were normal, while a history of physical abuse was obtained.

Conclusion

There are a number of paroxysmal disorders resembling epileptic seizures, and it might be difficult to get to correct diagnosis when confronted with a patient with or after a first event. Yet the correct diagnosis is of utmost importance to avoid medical complications, social consequences and unnecessary costs for the healthcare system.

Even in 2016 the most important clues are still obtained by taking a thorough history and a careful physical examination. Further technical investigations are usually required to confirm the diagnosis. Among them of most importance are early EEG, cerebral imaging and cardiac evaluations and in some cases video-EEG-monitoring.

References

1. *Casado V. Neurological patient care in emergency departments. A review of the current situation in Spain. Neurologia 2011; 26: 233-238*
2. *Rizos T, Jüttler E, Sykora M et al. Common disorders in the neurological emergency room – experience at a tertiary care hospital. Eur J Neurol 2011; 18: 430-435*
3. *Lange MC, Braatz VL, Tomiyoshi C et al. Neurological diagnoses in the emergency room: differences between younger and older patients. Arq Neuropsiquiatr 2011; 69: 212-216*
4. *De Falco FA, Sterzi R, Toso V et al. The neurologist in the emergency department. An Italian nationwide epidemiological survey. Neurol Sci 2008; 29: 67-75*
5. *Benabis SR, O'Neill E, Tatum WO, Heriaud L. Outcome of prolonged video-EEG-monitoring at a typical referral epilepsy center. Epilepsia 2004; 45: 1150-1153*
6. *Fisher RS, Acevedo C, Arzimanoglou A et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia 2014; 55: 475-482*
7. *Angus-Leppan H. Diagnosing epilepsy in neurology clinics: a prospective study. Seizure 2008; 17: 431-436*
8. *Reuber M, Elger CE. Psychogenic nonepileptic seizures: review and update. Epilepsy Behav 2003; 4: 205-216*
9. *Angus-Leppan H. First seizures in adults. BMJ 2014; 348: g2470*
10. *Kho L, Lawn ND, Dunne JW, Linto J. First seizure presentation: do multiple seizures within 24 hours predict recurrence? Neurology 2006; 67: 1047-1049*
11. *Krumholz A, Wiebe S, Gronseth GS et al. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2015; 84: 1705-1713*
12. *King MA, Newton MR, Jackson GD et al. Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients. Lancet 1998; 352: 1007-1011*
13. *Berg AT, Berkovic SF, Brodie MJ et al. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia 2010; 51: 676-685*
14. *Abubakr A, Wambacq I. Diagnostic value of serum prolactin in PNES in the epilepsy monitoring unit. Neur Clin Pract 2016; 6: 116-119*
15. *Chen DK, So YT, Fisher RS. Use of serum prolactin in diagnosing epileptic seizures: report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology 2005; 65: 668-675*
16. *Cendes F. Neuroimaging in investigation of patients with epilepsy. Continuum 2013; 19: 623-642*
17. *Recommendations for neuroimaging of patients with epilepsy. Commission on Neuroimaging of the International League Against Epilepsy. Epilepsia 1997; 38: 1255-1256*
18. *Ho K, Lawn N, Bynefelt M et al. Neuroimaging of first-ever seizure: Contribution of MRI if CT is normal. Neur Clin Pract 2013; 3: 398-403*
19. *Bronen RA, Fulbright RK, Spencer DD et al. Refractory epilepsy: comparison of MR imaging, CT, and histopathologic findings in 117 patients. Radiology 1996; 201: 97-105*
20. *Bernasconi A, Bernasconi N, Bernhardt BC, Schrader D. Advances in MRI for 'cryptogenic' epilepsies. Nat Rev Neurol 2011; 7: 99-108*
21. *Cascino GD. Neuroimaging in epilepsy: diagnostic strategies in partial epilepsy. Semin Neurol 2008; 28: 523-532*
22. *Cavazzuti GB, Cappella L, Nalin A. Longitudinal study of epileptiform EEG patterns in normal children. Epilepsia 1980; 21: 43-55*
23. *Hendriksen IJ, Elderson A. The use of EEG in aircrew selection. Aviat Space Environ Med 2001; 72: 1025-1033*
24. *Santoshkumar B, Chong JJ, Blume WT et al. Prevalence of benign epileptiform variants. Clin Neurophysiol 2009; 120: 856-861*
25. *Sofat P, Teter B, Kavak KS et al. Time interval providing highest yield for initial EEG in patients with new onset seizures. Epilepsy Res 2016; 127: 229-232*
26. *Salinsky M, Kanter R, Dasheiff RM. Effectiveness of multiple EEGs in supporting the diagnosis of epilepsy: an operational curve. Epilepsia 1987; 28: 331-334*
27. *Fountain NB, Kim JS, Lee SI. Sleep deprivation activates epileptiform discharges independent of the activating effects of sleep. J Clin Neurophysiol 1998; 15: 69-75*
28. *Baldin E, Hauser WA, Buchhalter JR et al. Yield of epileptiform electroencephalogram abnormalities in incident unprovoked seizures: a population-based study. Epilepsia 2014; 55: 1389-1398*
29. *Flink R, Pedersen B, Guekht AB et al. Guidelines for the use of EEG methodology in the diagnosis of epilepsy. International League Against Epilepsy: commission report. Commission on European Affairs: Subcommission on European Guidelines. Acta Neurol Scand 2002; 106: 1-7*
30. *Commission on Epidemiology and Prognosis, International League Against Epilepsy. Guidelines for epidemiologic studies on epilepsy. Epilepsia 1993; 34: 592-596*
31. *Ghougassian DF, d'Souza W, Cook MJ, O'Brien TJ. Evaluating the utility of inpatient video-EEG monitoring. Epilepsia 2004; 45: 928-932*
32. *Cornes SC, Shih T. Evaluation of the patient with spells. Continuum Lifelong Learning Neurol 2011; 17: 984-1009*
33. *Kanjwal K, Karabin B, Kanjwal Y, Grubb BP. Differentiation of convulsive syncope from epilepsy with an implantable loop recorder. Int J Med Sci 2009; 6: 296-300*
34. *Hermann DM, Steiner T, Dienster HC et al. Vaskuläre Neurologie, zerebrale Ischämien, Hämorrhagien, Gefässmissbildungen, Vaskulitiden und vaskuläre Demenz. Stuttgart: Georg Thieme Verlag, 2010: 191*
35. *Ali S, Khan MA, Khealani B. Limb-shaking transient ischemic attacks: case report and review of literature. BMC Neurology 2006; 6: 5*

36. Louis RC. „Top of the basilar" syndrome. Neurology 1980; 30: 72-79
37. Quinette P, Guillery-Girard B, Dayan J et al. What does transient global amnesia really mean? Review of the literature and thorough study of 142 cases. Brain 2006; 129: 1640-1658
38. Schmitz B, Tettenborn B. Paroxysmale Störungen in der Neurologie. Heidelberg: Springer Medizin Verlag, 2005: 221
39. Sances G, Guaschino E, Perucca P et al. Migralepsy: A call for a revision of the definition. Epilepsia 2009; 50: 2487-2496
40. Chastan N, Lebas A, Legoff F et al. Clinical and electroencephalographic abnormalities during the full duration of a sporadic hemiplegic migraine attack. Neurophysiol Clin 2016; May 4
41. Höllinger P, Sturzenegger M. Kurzdauernde Bewusstlosigkeit (Synkopen) Teil III: Neurologische Aspekte von Synkopen. Schweiz Med Forum 2002;19: 467-472
42. Burgess CR, Scammell TE. Narcolepsy: neural mechanisms of sleepiness and cataplexy. J Neurosci 2012; 32: 12305-12311
43. English WA, Giffin NJ, Nolan JP. Myoclonus after cardiac arrest: pitfalls in diagnosis and prognosis. Anaesthesia 2009; 64: 908-911
44. Carton S, Thompson PJ, Duncan JS. Non-epileptic seizures: patients' understanding and reaction to the diagnosis and impact on outcome. Seizure 2003; 12: 287-294
45. Reuber M, Fernández G, Bauer J et al. Diagnostic delay in psychogenic nonepileptic seizures. Neurology 2002; 58: 493-495
46. Smolowitz JL, Hopkins SC, Perrine T et al. Diagnostic utility of an epilepsy monitoring unit. Am J Med Qual 2007; 22: 117-122
47. De Paola L, Terra VC, Silvado CE et al. Improving first responders' psychogenic nonepileptic seizures diagnosis accuracy: Development and validation of a 6-item bedside diagnostic tool. Epilepsy Behav 2016; 54: 40-46
48. Bergen D, Ristanovic R. Weeping as a common element of pseudoseizures. Arch Neurol 1993; 50: 1059-1060
49. Dworetzky BA, Mortati KA, Rossetti AO et al. Clinical characteristics of psychogenic nonepileptic seizure status in the long-term monitoring unit. Epilepsy Behav 2006; 9: 335-338
50. Benbadis SR. A spell in the epilepsy clinic and a history of "chronic pain" or "fibromyalgia" independently predict a diagnosis of psychogenic seizures. Epilepsy Behav 2005; 6: 264-265
51. Duncan R, Oto M. Predictors of antecedent factors in psychogenic nonepileptic attacks: multivariate analysis. Neurology 2008; 71: 1000-1005
52. Avbersek A, Sisodiya S. Does the primary literature provide support for clinical signs used to distinguish psychogenic nonepileptic seizures from epileptic seizures? J Neurol Neurosurg Psychiatry 2010; 81: 719-725
53. Benabis SR, Agrawal V, Tatum WO 4th. How many patients with psychogenic nonepileptic seizures also suffer from epilepsy? Neurology 2001; 57: 915-917
54. Bettini L, Croquelois A, Maeder-Ingvar M, Rossetti AO. Diagnostic yield of short-term video-EEG-monitoring for epilepsy and PNES: a European assessment. Epilepsy Behav 2014; 39: 55-58
55. Duncan R, Razvi S, Mulhern S. Newly presenting psychogenic nonepileptic seizures: incidence, population characteristics, and early outcome from a prospective audit of a first seizure clinic. Epilepsy Behav 2011; 20: 308-311
56. LaFrance WC Jr, Reuber M, Goldstein LH. Management of psychogenic nonepileptic seizures. Epilepsia 2013; 54(Suppl 1): 53-67

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Summary

New diagnostic criteria define epilepsy as a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures. Two factors are associated with an increased risk of relapse: the presence of a cerebral lesion and epileptiform abnormalities (EA) in the electroencephalogram (EEG). In this paper we focus on the risk of relapse after a first unprovoked seizure; we review the yield of standard and sleep EEG to identify EA and/or abnormal but unspecific slowing. Sensitivity is defined as the percentage of EEG with EA, when epilepsy is present; specificity as the percentage of presence of epilepsy, when EEG shows EA. Main findings are: 1) Sensitivity and specificity of interictal EA are: 17% and 95% for adults, and 58% and 70% for children. An adult presenting with a first unprovoked seizure has a 77% post-test probability of relapse if routine EEG includes EA and 47% if it does not (focal and generalized discharges confounded). Percentages for children are slightly lower than adults (66% and 38%). 2) There is an increased yield if routine EEG is performed within 24 hours after seizure (51% in a mixed population of children and adults). 3) Identification of EA after the third normal standard wake EEG is extremely low. Sleep EEG increases significantly the likelihood to detect EA, i.e. with up to 50%. Standard EEG carries valuable information with respect to the underlying syndrome and risk of relapse. If negative, we propose to obtain a sleep recording, including the first 2 hours after awakening.

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Key words: First seizure, relapse risk, drug treatment, MRI

EEG nach erstem unprovoziertem Anfall – welche Zusatzinformation können wir erwarten?

Die neuen diagnostischen Kriterien für Epilepsie definieren diese Erkrankung als eine andauernde Prädisposition, Anfälle zu generieren. Zwei Faktoren sind mit einem Rückfallrisiko assoziiert: das Vorhandensein einer zerebralen Läsion und epileptogene Anomalien (EA) im Elektroenzephalogramm (EEG). In diesem Artikel diskutieren wir das Risiko eines Rückfalls nach einem ersten nicht-provozierten Anfall und den Ertrag von Standard- und Schlaf-EEG zur Identifizierung von EA und/oder unspezifischen EEG-Verlangsamungen. Sensitivität ist definiert als die Fähigkeit des EEGs, EA zu entdecken, wenn eine Epilepsie vorhanden ist; Spezifizität bezieht sich auf die Wahrscheinlichkeit, Epilepsie zu diagnostizieren, wenn das EEG EA zeigt. Hauptergebnisse: 1) Sensitivität und Spezifizität von EA sind 17 % und 95 % für Erwachsene sowie 58 % und 70 % für Kinder. Ein Erwachsener hat eine Rückfallwahrscheinlichkeit von 77 %, wenn das EEG EA zeigt, und 47 %, wenn das nicht der Fall ist. Die Zahlen für Kinder sind etwas niedriger (66 % und 38 %). 2) Der Gewinn eines Standard-EEGs ist höher, wenn es innerhalb von 24 h nach dem Anfall durchgeführt wird (51 % in einer gemischten Patientenpopulation von Kindern und Erwachsenen). 3) Die Wahrscheinlichkeit, doch noch EA zu finden, wenn das 3. Standard-EEG normal ist, ist extrem niedrig. Die Ausbeute kann deutlich erhöht werden durch ein Schlaf-EEG, d.h. bei 23 - 50 % mehr Patienten kann eine Epilepsie diagnostiziert werden. Das Standard-EEG enthält wertvolle Informationen bezüglich des zugrundeliegenden Syndroms und Rückfallrisikos. Falls negativ, empfehlen wir, ein Schlaf-EEG durchzuführen, welches alle Schlafstadien sowie die ersten 2 Stunden nach dem Erwachen umfasst.

Schlüsselwörter: Erstanfall, Rückfallrisiko, medikamentöse Behandlung, MRT

Contribution de l'EEG au diagnostic épileptique après une première crise non provoquée

L'épilepsie est une affection cérébrale caractérisée par une prédisposition durable à générer des crises d'épilepsie. Deux facteurs sont associés à une augmentation des récidives : la présence d'une lésion cérébrale et une anomalie épileptiforme (AE) à l'électroencéphalogramme (EEG). Dans ce papier, nous mettons l'accent sur le risque de récidive après une crise non provoquée et revoyons la place de l'EEG standard et de l'EEG de sommeil dans l'identification des AE et/

ou autres anomalies non spécifiques. La sensibilité est définie comme la capacité de l'EEG à détecter les AE lorsque la maladie est présente; la spécificité est définie comme le risque d'avoir la maladie lorsque l'EEG révèle une AE. Voici nos conclusions principales: 1) la sensibilité et la spécificité d'une AE interictale sont : 17% et 95% pour les adultes, 58% et 70% pour les enfants. Un adulte se présentant avec une première crise non-provoquée a une probabilité post-test de récidive de 77% lorsque l'EEG montre une AE et de 47% en l'absence d'AE (décharges focales et généralisées confondues). Le pourcentage chez les enfants est discrètement plus bas (66% et 38%). 2) L'EEG de routine est de meilleur rendement lorsqu'il est réalisé dans les 24 heures après la crise (51% d'anomalies dans une population mixte d'adultes et d'enfants). 3) L'identification d'une AE après le troisième EEG est extrêmement faible. L'EEG de sommeil augmente significativement la probabilité de détecter une AE et ceci jusqu'à 50%. L'EEG standard nous informe surtout sur la présence d'un syndrome épileptique et du risque de récidive. Si ce dernier est négatif, un EEG de sommeil, incluant les premières heures après l'éveil, est de mise.

Mots clés : Première crise, risque de récidive, traitement médicamenteux, IRM

1. First seizure and epilepsy: current definition and epidemiology

Epilepsy is one of the most frequent neurological diseases, affecting between 0.5 - 1% of the population, i.e, approximately 50 Mio people worldwide [1]. In 2005, a task force directed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy defined epilepsy as "A disorder characterized by an enduring predisposition of the brain to generate epileptic seizures and by the neurobiologic, cognitive, psychological and social consequences of this condition" [2]. A commonly used operational definition employed for epidemiological purposes considers a diagnosis of epilepsy after 2 unprovoked seizures occurring at least 24 hours apart [3]. Studies showed that after 2 unprovoked non-febrile seizures, the probability of having another seizure was 73% [3] at 5 years (95% CI is 59 - 87%) versus 40 - 52% after a single unprovoked seizure [1].

Nowadays, the "two unprovoked seizures" definition appears to be inadequate in several clinical circumstances. In 2009, Hesdorffer showed that a patient who presented with a single unprovoked seizure after a remote brain insult, such as stroke, tumor, central nervous system infection or trauma is at high risk of a second unprovoked seizure. This risk is comparable to the risk for further seizures after 2 unprovoked seizures [4]. The same is true for distinct epileptic syndromes (like juvenile myoclonic epilepsy), reflex epilepsy or a single symptomatic seizure of a focal cortical dysplasia [5].

Regarding these considerations, in 2014, the task force of the ILAE re-considered the diagnosis of epilepsy by any of the following conditions [6]:

- At least two unprovoked seizures occurring more than 24 hours apart
- One unprovoked seizure and a probability for further seizures similar to the general recurrence risk after two unprovoked seizures (at least 60%)
- At least two seizures in a setting of reflex epilepsy

The threshold of 60% is considered as estimation and not as strict cut-off. This number is based on the risk of relapse after two unprovoked seizures, which is about 60% at 2 years and 70 - 75% at 5 years of follow-up. It requests a workup to calculate the individual risk of predisposition for further seizures.

As we will discuss below ("Risk of relapse"), two factors are consistently associated with an increased risk of relapse: the presence of cerebral lesion and epileptiform abnormalities in the EEG. Seizures clustering within 24 hours confer approximately the same risk for later seizure as a single seizure [7]. Thus, two or more seizures occurring in a 24-hour period are considered to be a single unprovoked seizure.

High risk for recurrence after a single seizure should lead to the consideration of starting an antiepileptic treatment already after the first seizure. In that case, the risk of recurrent seizures, at least during the first 2 years, is significantly reduced by an average of 34% [8]. However, the long-term prognosis is not changed; for this reason, when a lesion is present, the possibility of surgery should be brought up already during the first consultation.

2. Routine EEG in first seizure

Routine EEG should be performed within 24 hours of the first seizure. Indeed a prospective study on 300 consecutive patients showed that interictal epileptiform abnormalities (EA) were present in 51% of patients who underwent an EEG within the first 24 hours, compared to 34% of the patients who had a later EEG [9]. However, it is of note that this study included many children, which differ from adults in terms of occurrence likelihood of discharges. Several studies have shown that interictal EA are more frequent after seizures (postictal activation) [10, 11]. Although these studies were performed on chronic epilepsy, it seems that this increased frequency also applies to new-onset epilepsies [9]. Unfortunately in many cases, scheduling of early EEG is not feasible. On the other hand, very early EEG may show transient, less specific abnormalities, like postictal slowing, which must be interpreted cau-

tiously, as they can also result from the presence of a lesion and are not necessarily a sign of epileptogenicity [12]. An exception are rhythmic delta, extratemporal or temporal, which usually indicates the presence of seizures [13].

Routine EEG should be performed with at least 21 electrodes, placed according to the standard 10 - 20 system and last at least 20 minutes. It is recommended that hyperventilation of 3 minutes and intermittent photic-stimulation at 1 - 50 Hz with the eyes open and closed at each frequency are carried out. The placement of additional inferior temporal electrodes (F9, T9, P9 and F10, T10, P10) is of extreme importance in particular if temporal seizures are searched, a frequent constellation in adults.

Accurate classification of seizure type will help clinicians in diagnostic and therapeutic decisions. Clinical history is fundamental, but unfortunately, after a first episode, this is fraught with limitations due to the lack of witnesses, or peri-ictal amnesia. King et colleagues [9], on a population of 300 patients (20% below 16 years, range 5 - 83 years), were able to classify seizures into focal versus generalized in just 47% of cases after considering medical history and physical examination findings alone. When EEG findings were also taken into account, correct classification was possible in an additional 30%; thus, in their study group, only 23% of seizures remained unclassified. Specific syndromes also influence the likelihood of seeing EA on EEG, with higher rates in patients with absence seizures (92%) and atonic or myoclonic seizures (85%) compared with focal seizures (59%) [14].

What is the relevance of non-epileptiform abnormalities, such as focal slow activity, regional attenuation, or abnormalities of background cerebral rhythms? They are much less specific risk predictors than EA, although they can imply localized structural pathology underlying the seizure disorder, or diffuse cortical dysfunction as in symptomatic generalized epilepsies [15]. Non-epileptiform abnormalities are more common in symptomatic cases (25%) than in idiopathic epilepsy syndromes (7%) [14, 16]. As stated above, rhythmic focal delta usually indicate active epileptogenicity.

What happens if the first routine EEG is normal? A retrospective study on 619 patients reveals that the cumulative yield of EA is 39% after the first EEG study and 68% after the third. Beyond the 3rd EEG, the probability to find epileptiform abnormalities is very low. Thus, at this point a sleep EEG should be requested if this was not yet done before [17].

3. Sleep EEG

The yield of EEG can be significantly increased in all age groups by the use of sleep recording. Indeed sleep states influence the presence of interictal and ictal epileptic activity. Particularly, non-rapid eye movement (NREM) sleep has been characterized as a state of relative "neuronal synchronization". Such coordinated synaptic activity allows the recruitment of a critical mass of neurons, necessary to initiate and sustain epileptic activity [18]. This is why interictal (mainly focal) EA are more common in NREM sleep than in awake recordings. Carpay et al. [14] reported that 60 of 177 (34%) children with normal findings during a standard recording showed EA after sleep deprivation (mostly during sleep). Similarly, King et al. [9] reported that 35% of adults and children whose initial EEG findings were normal, showed EA in a subsequent study performed during sleep. Overall, the literature suggests that sleep EEG increases the yield of significant EEG abnormalities by 30 - 35%.

Whereas NREM sleep may "unmask" the EA that are not present on awake state, REM sleep is reported to show fewer EA. However, REM recordings show a more limited electric field of EA, i.e. corresponding to the true irritative region and thus contributing to localization of the epileptogenic focus [19, 20]. Shinnar et al. [16] described 148 children with unprovoked first seizure who had both sleep and wakefulness recorded on a single EEG. EA were identified either only while awake or only while asleep in 30% of subjects, and in both states in 70% of subjects. While generalized discharges are more common during the awake state, focal discharges are more easily detected during the sleep state.

Sleep recording can be also useful to detect epileptic seizures, of which patients can be unaware. NREM sleep activates frontal lobe seizures more than temporal lobe seizures, and temporal lobe seizures are more likely to secondarily generalize during sleep than during wakefulness [21, 22]. A variety of epilepsy syndromes occur predominantly or exclusively during NREM sleep, or during awaking phases. For example, EEG in patients suffering from "grand mal on awakening" may have a completely normal routine EEG, but very active and frequent EA just before awakening (**Figures 1** and **2**). Other striking examples are the syndrome of continuous spike-wave activity during slow-wave sleep, defined by an EEG pattern consisting of generalized slow-spike-wave discharges present for 85 - 90% of slow-wave sleep and relatively suppressed during REM sleep and wakefulness, and the Landau-Kleffner syndrome. These syndromes, characterised by a continuous spike-wave in slow sleep, start in early to mid-childhood and lead to cognitive regression and seizures. Early, appropriate treatment is indicated to attempt to ameliorate the electrical status and improve the child's cognitive function.

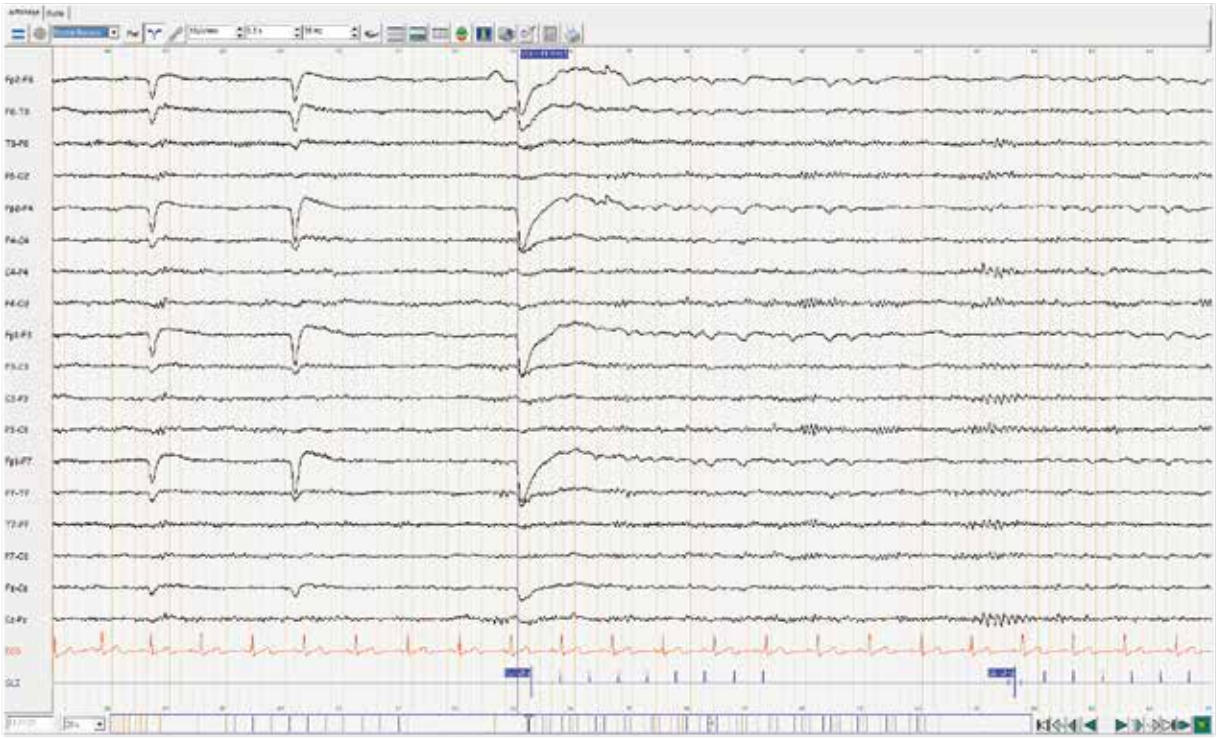

Figure 1. 19 y.o. patient with a first unprovoked generalized seizure during wakefulness. Routine EEG was performed <24 hours of the episode. It showed a posterior background activity at 8Hz, bilateral, symmetric, reactive. Bipolar montage.

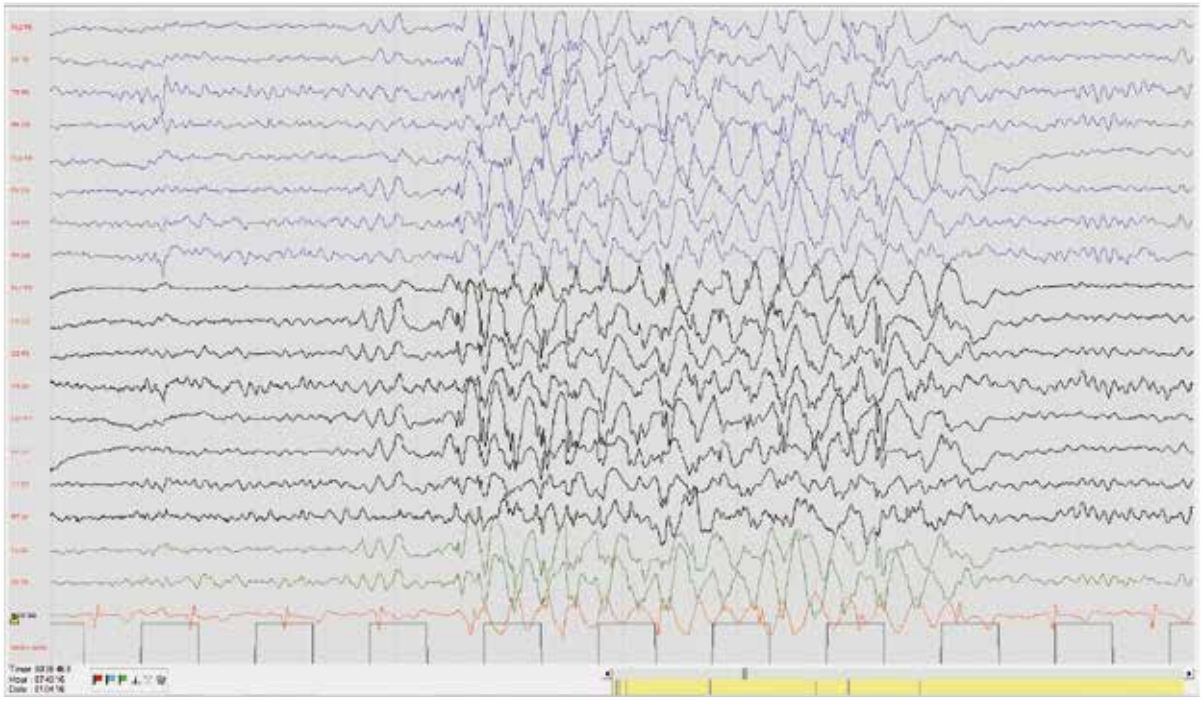

Figure 2. Same patient. Light sleep on awaking showed frequent bursts of 4 Hz generalized spike-poly-spike wave-complexes, of variable length, without clinical correlates. Bipolar montage.

4. Relevance of ictal recordings in the 1st EEG

It is possible that the first seizure which comes to medical attention, is not the patient's true first seizure [9, 23]. Patients presenting at emergency often have a history of more subtle seizures (e.g., absence seizures or myoclonic or simple partial seizures) that were not identified by the patient or its entourage. These types of seizures could be observed already during the first routine EEG. For this reason the facilitating techniques are fundamental during EEG: for instance, hyperventilation can trigger absences in children with untreated childhood or juvenile absence epilepsy; photic stimulation can induce myoclonic jerks in patients with juvenile myoclonic epilepsy. Focal seizures occur more rarely during standard EEG, and if they do, they are rather an alarming sign for a very active epileptic condition and hospitalisation should be considered. In any case, individualized and specialized care and appropriate antiepileptic medication should be initiated. If the routine EEG shows an electrical, or non-convulsive, status epilepticus, injection of antiepileptic drugs under EEG control and hospitalisation is strongly recommended.

5. Risk of relapse

In 2014, a meta-analysis estimated the risk of relapse after the first event in patients who were treated immediately or with delay and showed a risk of 15%, 8%, 6% and 7% of relapses after 6, 12, 18 and 24 months in patients who were treated immediately. If an observational attitude was chosen and treatment postponed, these numbers increased to 18%, 10%, 9% and 7%. The risk of relapse was higher in patients with an abnormal EEG than with an abnormal imaging, given that not all epilepsy syndromes are related to cerebral lesions [24]. Several studies with long follow-up showed that 80 to 90% of individuals recur within two years of the initial seizure [25].

However, while early antiepileptic treatment decreased the number of further seizures, it did not change relapse rate beyond 2 years disease duration. Indeed the two multi-centre randomized trials (FirST, MESS) failed to show any change in long-term prognosis in patients with early treatment versus delayed treatment after further seizures [26].

EEG and brain imaging are considered essential as part of the neuro-diagnostic evaluation of adults presenting with an apparently unprovoked first seizure, as suggested by the practice parameter from the American Academy of Neurology [27]. A prospective study on 208 consecutive patients with first seizure followed for 5 years [28], showed that an EEG with epileptiform abnormalities was associated with a relative increase for seizure recurrence at 1 to 5 years of 2.16 (95% CI 1.07 - 4.38) as compared to patients without such EEG abnormalities. It is important to remember that the EA presence in healthy subjects is extremely rare, with an incidence of 0.5% [29].

Although interictal EA have been associated with a higher risk of relapse [1, 30 - 32] their diagnostic value has been unclear for a long time. Indeed a meta-analysis of 2003 [32] showed that sensitivity and specificity of interictal EA for seizure relapse after a first seizure varies widely among published studies, with a range from 20% to 80% for sensitivity, and 41% to 99% for specificity. Just recently, a Cochrane [33] systematic review and meta-analysis about diagnostic accuracy of routine EEG on 1799 patients with first seizure and 1 year of follow-up was published [34]. In adults, sensitivity (defined as the percentage of EEG with EA, when epilepsy is present) is 17.3% (range 7.9 - 33.8) and specificity (percentage of presence of epilepsy, when EEG shows EA) is on average 94.7% (range 73.7 - 99.1). In children, a sensitivity value of 58 % (range 49.7 - 65.6) and a specificity of 70% (range 57.5 - 79.5) were identified. The same study revealed that an adult presenting with a first unprovoked seizure has a 77% post-test probability of relapse if routine EEG includes EA (positive likelihood ratio) and 47% if it does not (negative likelihood ratio). Similary, a child has a 66% post-test probability of relapse if routine EEG includes EA and 38% if it does not. These observations are extremely important, considering that a patient with a first unprovoked seizure should be treated if the probability of relapse is >60% at 10 years [6].

Other factors carry important information regarding the overall prognosis, as the underlying syndrome. Idiopathic generalized (or genetic generalized, as it is named in the new classification) epilepsy achieves remission in 80 to 85% compared to focal epilepsy in 40 - 65% [3]. Multiple seizure types in the same patient are associated with higher seizure recurrence [26]. Younger age at onset has also been described as predictor of worse outcome. Onset of epilepsy before the age of 12 months is a poor prognostic factor. Best prognosis is noted if onset occurs after the age of three years [25]. A prospective observational study of over 1000 adults presenting with a first unprovoked seizure showed a similar likelihood of seizure recurrence in older (> 65 years) compared with younger adults (53 versus 48 percent). However, by five years, the cumulative risk of recurrence was higher in older adults (75 versus 61 percent). This relates to a greater likelihood of a remote symptomatic etiology rather than age itself [35]. Another powerful predictor of the long-term prognosis is the early response to treatment. Several studies found that the response to the first antiepileptic drug showed to be the strongest predictor of good long-term outcome in adults and children. Along the same line, patients who are not seizure-free after ≥ 2 antiepileptic drugs should be referred to specialized centre to determine the reasons for lack of response and/or search for the possibility of epilepsy surgery [36].

Recently, Fisch et al. showed that patients with installed medical follow-up are significantly more likely to receive a precise diagnosis and increased delay to the next unprovoked seizure in comparison with patients without organized medical care (p=0.008). The study emphasized the need of specialized care starting already in the emergency room, provided by epileptologists. After a first evaluation, important exams such as EEG and MRI are rapidly and reliably scheduled and results can be discussed at the next appointment. Early-specialized improved not only the diagnostic accuracy, but also adherence to follow-up consultations, probably because patients better understood their condition and the importance of compliance and lifestyle adjustments [37].

Psychiatric and neuropsychological comorbidities are associated with a lower response to drug treatment and higher risk of failure of remission. In these cases, specialized consultations, relevant non-epileptic treatment and/or increased frequency of follow-up appointments should be scheduled, at least initially [38, 39].

To conclude, EEG is a fundamental test to diagnose the presence or absence of epilepsy after a first seizure. Ideally, it should be performed as fast as possible after the event, if possible within 24 hours. Proper and correct diagnosis of the type of epilepsy is fundamental in order to offer optimal treatment and prognostic information regarding seizure relapse. It is self-evident that such information is of utmost importance for the medical and socio-professional wellbeing of each patient. It should not be forgotten that with each initiation of treatment the possibility and timing of withdrawal of antiepileptic medication should be discussed with the patient, if possible early in the course of the disease to avoid "autonomous" withdrawals which end in the emergency room.

References

1. *Berg AT, Shinnar S. The risk of seizure recurrence following a first unprovoked seizure: a quantitative review. Neurology 1991; 41: 965-972*
2. *Fischer MJ, Scheler G, Stefan H. Utilization of magnetoencephalography results to obtain favourable outcomes in epilepsy surgery. Brain 2005; 128: 153-157*
3. *Hauser WA, Rich SS, Lee JR et al. Risk of recurrent seizures after two unprovoked seizures. N Engl J Med 1998; 338: 429-434*
4. *Hesdorffer DC, Benn EK, Cascino GD, Hauser WA. Is a first acute symptomatic seizure epilepsy? Mortality and risk for recurrent seizure. Epilepsia 2009; 50: 1102-1108*
5. *Fauser S, Huppertz HJ, Bast T et al. Clinical characteristics in focal cortical dysplasia: a retrospective evaluation in a series of 120 patients. Brain 2006; 129: 1907-1916*
6. *Fisher RS, Acevedo C, Arzimanoglou A et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia 2014; 55: 475-482*
7. *Neligan A, Bell GS, Giavasi C et al. Long-term risk of developing epilepsy after febrile seizures: a prospective cohort study. Neurology 2012; 78: 1166-1170*
8. *Wiebe S, Tellez-Zenteno JF, Shapiro M. An evidence-based approach to the first seizure. Epilepsia 2008; 49(Suppl 1): 50-57*
9. *King MA, Newton MR, Jackson GD et al. Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients. Lancet 1998; 352: 1007-1011*
10. *Marsan CA, Zivin LS. Factors related to the occurrence of typical paroxysmal abnormalities in the EEG records of epileptic patients. Epilepsia 1970; 11: 361-381*
11. *Gotman J, Marciani MG. Electroencephalographic spiking activity, drug levels, and seizure occurrence in epileptic patients. Ann Neurol 1985; 17: 597-603*
12. *Wirrell EC. Prognostic significance of interictal epileptiform discharges in newly diagnosed seizure disorders. J Clin Neurophysiol 2010; 27: 239-248*
13. *Trinka E, Leitinger M. Which EEG patterns in coma are nonconvulsive status epilepticus? Epilepsy Behav 2015; 49: 203-222*
14. *Carpay JA, de Weerd AW, Schimsheimer RJ et al. The diagnostic yield of a second EEG after partial sleep deprivation: a prospective study in children with newly diagnosed seizures. Epilepsia 1997; 38: 595-599*
15. *Smith SJ. EEG in the diagnosis, classification, and management of patients with epilepsy. J Neurol Neurosurg Psychiatry 2005; 76(Suppl 2): ii2-7*
16. *Shinnar S, Kang H, Berg AT et al. EEG abnormalities in children with a first unprovoked seizure. Epilepsia 1994; 35: 471-476*
17. *Baldin E, Hauser WA, Buchhalter JR et al. Yield of epileptiform electroencephalogram abnormalities in incident unprovoked seizures: a population-based study. Epilepsia 2014; 55: 1389-1398*
18. *Steriade M, Contreras D, Amzica F. Synchronized sleep oscillations and their paroxysmal developments. Trends Neurosci 1994; 17: 199-208*
19. *Sammaritano M, Gigli GL, Gotman J. Interictal spiking during wakefulness and sleep and the localization of foci in temporal lobe epilepsy. Neurology 1991; 41: 290-297*
20. *Adachi N, Alarcon G, Binnie CD et al. Predictive value of interictal epileptiform discharges during non-REM sleep on scalp EEG recordings for the lateralization of epileptogenesis. Epilepsia 1998; 39: 628-632*
21. *Bazil CW, Walczak TS. Effects of sleep and sleep stage on epileptic and nonepileptic seizures. Epilepsia 1997; 38: 56-62*
22. *Crespel A, Coubes P, Baldy-Moulinier M. Sleep influence on seizures and epilepsy effects on sleep in partial frontal and temporal lobe epilepsies. Clin Neurophysiol 2000; 111(Suppl 2): S54-59*
23. *Hamiwka LD, Singh N, Niosi J, Wirrell EC. Diagnostic inaccuracy in children referred with "first seizure": role for a first seizure clinic. Epilepsia 2007; 48: 1062-1066*
24. *Bonnett LJ, Marson AG, Johnson A et al. External validation of a prognostic model for seizure recurrence following a first unprovoked seizure and implications for driving. PLoS One 2014; 9: e99063*
25. *Shinnar S, Berg AT, Moshe SL et al. The risk of seizure recurrence after a first unprovoked afebrile seizure in childhood: an extended follow-up. Pediatrics 1996; 98: 216-225*
26. *Su L, Di Q, Kwan P et al. Prediction for relapse and prognosis of newly diagnosed epilepsy. Acta Neurol Scand 2013; 127: 141-147*
27. *Krumholz A, Wiebe S, Gronseth G et al. Practice Parameter: evaluating an apparent unprovoked first seizure in adults (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2007; 69: 1996-2007*

28. Hauser WA, Rich SS, Annegers JF, Anderson VE. Seizure recurrence after a 1st unprovoked seizure: an extended follow-up. Neurology 1990; 40: 1163-1170
29. Gregory RP, Oates T, Merry RT. Electroencephalogram epileptiform abnormalities in candidates for aircrew training. Electroencephalogr Clin Neurophysiol 1993; 86: 75-77
30. Camfield PR, Cramfield CS, Dooley JM et al. Epilepsy after a first unprovoked seizure in childhood. Neurology 1985; 35: 1657-1660
31. Berg AT. Risk of recurrence after a first unprovoked seizure. Epilepsia 2008; 49(Suppl 1): 13-18
32. Gilbert DL, Sethuraman G, Kotagal U, Buncher CR. Meta-analysis of EEG test performance shows wide variation among studies. Neurology 2003; 60: 564-570
33. Leeflang MM, Deeks JJ, Gatsonis C et al. Systematic reviews of diagnostic test accuracy. Ann Intern Med 2008; 149: 889-897
34. Bouma HK, Labos C, Gore GC et al. The diagnostic accuracy of routine electroencephalography after a first unprovoked seizure. Eur J Neurol 2016; 23: 455-463
35. Lawn N, Kelly A, Dunne J et al. First seizure in the older patient: clinical features and prognosis. Epilepsy Res 2013; 107: 109-114
36. Mohanraj R, Brodie MJ. Early predictors of outcome in newly diagnosed epilepsy. Seizure 2013; 22: 333-344
37. Fisch L, Lascano AM, Vernaz Hegi N et al. Early specialized care after a first unprovoked epileptic seizure. J Neurol 2016; Sept 7 Epub ahead of print
38. Hitiris N, Mohanrai R, Norrie J et al. Predictors of pharmacoresistant epilepsy. Epilepsy Res 2007; 75: 192-196
39. Petrovski S, Sczoeke CE, Jones NC et al. Neuropsychiatric symptomatology predicts seizure recurrence in newly treated patients. Neurology 2010; 75: 1015-1021

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Brain Imaging After a First Seizure

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Summary

Neuroimaging is one of the main pillars of diagnostic workup in epilepsy. After a first seizure neuroimaging is indicated in all patients but those presenting with a typical genetic generalized epilepsy. Emergency imaging is warranted if the seizures may be the symptom of an acute brain pathology. If the patient returns "back to baseline" at the time of clinical examination, MR imaging may be performed electively using a dedicated epilepsy protocol. Data on seizure recurrence rates over 10 years are still lacking for many classical brain pathologies associated with epilepsy. Novel imaging techniques may be helpful in detecting prolonged seizures and mimics in the emergency setting.

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Key words: Epilepsy, guidelines, neuroradiology

Zerebrale Bildgebung nach einem ersten Anfall

Die zerebrale Bildgebung ist ein zentrales Element der diagnostischen Beurteilung von Epilepsien. Nach einem ersten Anfall ist eine zerebrale Bildgebung bei allen Patienten indiziert, ausser bei Patienten mit einem typischen Bild einer genetisch generalisierten Epilepsie. Eine notfallmässige Bildgebung ist dann notwendig, wenn der Anfall Zeichen einer zugrundeliegenden akuten Hirnerkrankung sein kann. Bei Patienten, die zur Zeit der Untersuchung bereits wieder ihren Normalzustand erreicht haben, kann die MR-Bildgebung elektiv und nach einem speziellen Epilepsieprotokoll durchgeführt werden. Daten zur Wahrscheinlichkeit eines Anfallsrezidivs innerhalb von 10 Jahren, wie in der aktuellen Definition der Epilepsie gefordert, liegen für viele Gehirnpathologien, die mit Epilepsie einhergehen, nicht vor. Neue bildgebende Techniken können hilfreich sein, insbesondere, um in Notfallsituationen prolongierte Anfälle und Epilepsie-Mimikers zu erfassen.

Schlüsselwörter: Bildgebung, erster epileptischer Anfall, Epilepsie, Leitlinien

L'imagerie cérébrale après une première crise

L'imagerie cérébrale représente un important pilier du processus diagnostique en cas d'épilepsie. Après la première crise épileptique une imagerie cérébrale est indiquée chez tous les patients sauf en cas d'épilepsie génétique typique. Une imagerie cérébrale en urgence est nécessaire si la crise peut être signe d'une affection cérébrale aigue sous-jacente. Si le patient est à nouveau dans son « état habituel » lors de la consultation, une imagerie résonance magnétique peut être effectuée électivement de préférence selon un protocole d'épilepsie spécialisé. Données sur la fréquence de récidive de crises épileptiques sur 10 ans, comme revendiqué pour la nouvelle définition d'épilepsie, ne sont pas disponibles pour une grande partie de pathologies cérébrales associées à l'épilepsie. Des techniques d'imagerie cérébrale nouvelles peuvent être utilisées notamment en cas d'urgence pour détecter des crises épileptiques prolongées et des mimiqueurs.

Mots clés : Imagerie cérébrale, crise épileptique, épilepsie

Introduction

Neuroimaging constitutes one of the three main pillars in the diagnosis of epilepsy following a first seizure. MR imaging as well as computed tomography allow to screen for pathological conditions and alterations of brain anatomy that promote the development of epilepsy after a first seizure [1]. Epilepsy is characterized as a disorder substantiated by an "enduring predisposition to generate epileptic seizures". While this condition is fulfilled after two unprovoked seizures (i.e.: i) of unknown etiology or ii) in relation to a demonstrated preexisting brain lesion or progressive CNS disorder), the International League Against Epilepsy (ILAE) has

integrated risk profiles that allow the diagnosis of epilepsy after a first seizure, given an equal risk of > 60% to develop epilepsy (a second unprovoked seizure) within the next 10 years or by the established diagnosis of an epilepsy syndrome [2]. These profiles encompass clinical, neurophysiological and neuroimaging features that predispose to epilepsy [3]:

i. a prior brain insult; increased relative rate for seizure recurrence at 1 to 5 years 2.55 (95% confidence interval [CI] 1.44 - 4.51)
ii. an EEG with epileptiform abnormalities; increased relative rate for seizure recurrence at 1 to 5 years of 2.16 (95% CI 1.07 - 4.38)
iii. a nocturnal seizure; increased relative rate for seizure recurrence at 1 to 4 years of 2.1(95% CI 1.0 - 4.3)
iv. abnormal brain imaging; increased relative rate for seizure recurrence at 1 to 4 years of 2.44 (95% CI 1.09 - 5.44)

There is converging evidence from class II and class III studies that "abnormal brain imaging" related to a prior ischemic brain insult, previous brain infection or head trauma equal the risk of a 2nd seizure to predispose to epilepsy [4 - 6]. However, data on the 10 years' risk of seizure recurrence are lacking for other brain lesions, as e. g. long term epilepsy associated tumors (as e. g. ganglioglioma and dysembryoblastic neuroepithelial tumors or hippocampal sclerosis) [1]. From a health economics point of view, consequences arise since a plain CT in those patients to confirm a remote brain lesion by identifying damage associated with one of the above mentioned lesions would be enough to diagnose epilepsy, however at the risk to overlook other structural lesions that may necessitate intervention.

This short review aims to extend the discussion beyond this current state of evidence towards decision making in clinical practice, where particularly the following questions have to be addressed with priority:

a. Is the underlying imaging finding of the patient related to a seizure or a mimicking condition (i.e. a seizure like episode)?
b. Does the underlying imaging finding confirm an underlying acute neurological disorder that has to be immediately treated (i.e. may point towards a symptomatic or provoked seizure)?
c. Is there a substantial lesion of the brain that explains the first seizure and influences the prognosis – or is it just a coincidental finding?
d. Are newer imaging techniques available which are promising to increase the diagnostic yield?

For discussion we refer to the guidelines of the German Society of Neurology (DGN) 2012 [7], the British National Institute for Health and Care Excellence (NICE) guidelines [8] and to the American Academy of Neurology (AAN) guidelines on imaging (2015) [3].

a. Is it a seizure or a seizure-like episode?

Here, two different scenarios must be taken into account. First, under given emergency conditions, without clear confirmation of a witnessed seizure, the principal role of neuroimaging is to rule out potential other causes of persisting neurological deficits not related to a seizure. This may be related to an ischemic stroke with persisting motor deficits and/or aphasia, migraine with aura, a stroke-like episode related to an acute infection (e. g. brain abscess), mitochondrial encephalopathies, malignancies, venous thrombosis or hemorrhage [1, 3]. These conditions may also initially present with a symptomatic (i. e. a provoked) seizure, and special consideration must be given to the precise nosological definition of the underlying condition.

Under such conditions, neuroimaging should be performed immediately in the emergency setting to initiate appropriate treatment as soon as achievable. Computed tomography including contrast administration or – if available – MR imaging should be timely requested. Considering the high numbers of stroke mimickers and chameleons of up to 14% of cases presenting in the ER with stroke-like episodes, appropriate diagnosis may avoid persisting damage due to misinterpretation [9]. Thus, a clear cut clinical description of the condition, the reporting of persisting deficits and the suspected diagnosis is mandatory to guide the neuroradiologist in selecting the appropriate imaging technique [10, 11].

Secondly, patients presenting with a seizure that may be of non-epileptic origin as e. g. syncope, conversion disorders or otherwise not explained mental impairment, and having returned to their baseline clinical status can be scheduled for elective further evaluation that is mainly based on patients history, clinical examination, interictal EEG findings, laboratory results (i. e. creatine kinase evaluation, potentially serum prolactine level changes) and testing of the cardiovascular regulation. For the mimicker, neuroimaging plays a minor role in the etiological workup, yet should be taken into consideration if a vascular or metabolic brain disorder is suspected.

b. Is the seizure a symptom of an underlying acute neurological disorder that has to be further investigated without delay?

Urgent brain imaging is mandatory after a first seizure, as a seizure may be the first symptom of an acute underlying neurologic disease. It is particularly important in patients who present with a history of a recent head trauma, focal seizure onset, lateralized symptoms on clinical examinations or focal EEG changes [1]. Further consideration should be given to prevalent systemic disorders that may affect the brain, as HIV infection, immunocompromised, anticoagulation, alcoholism or

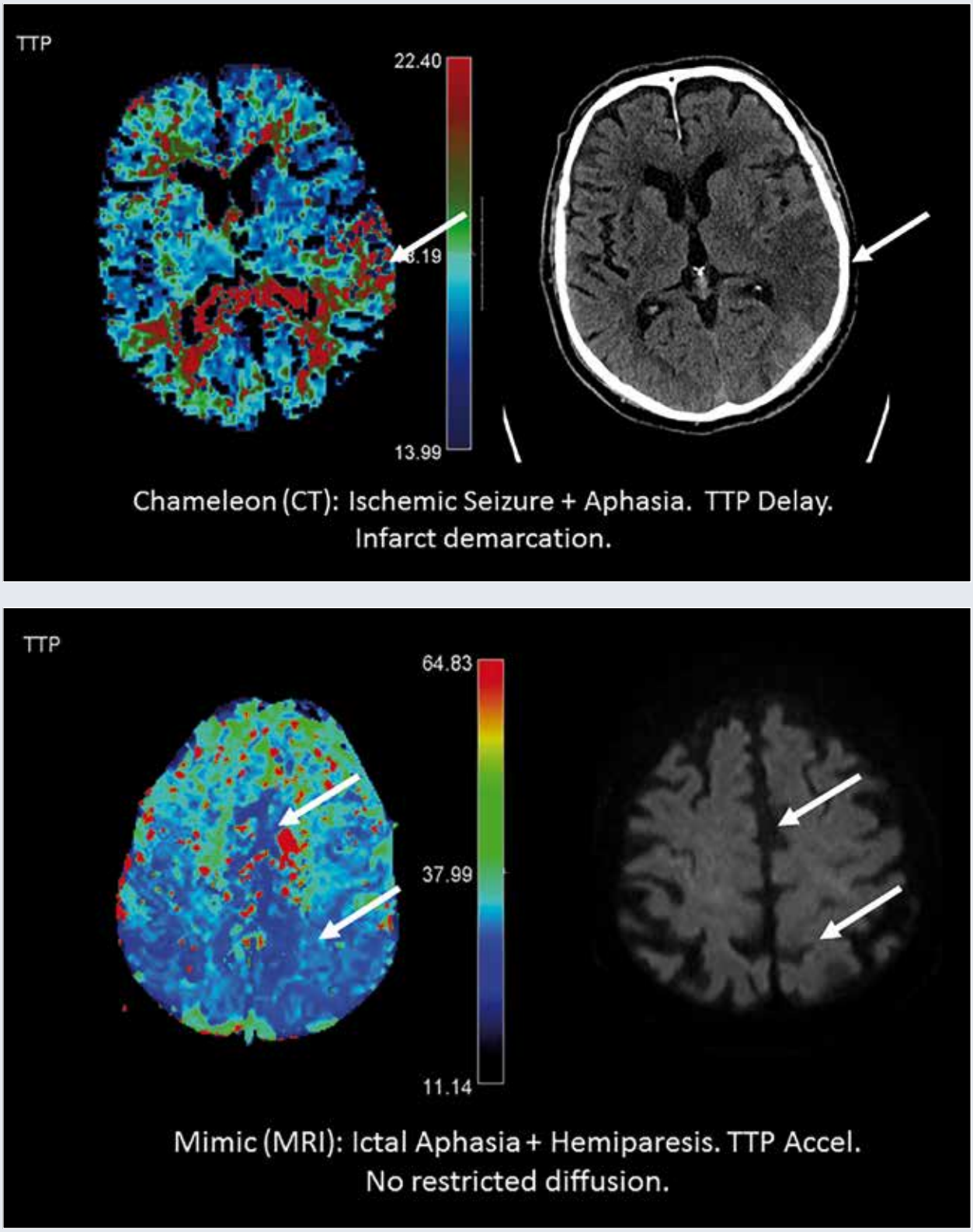

Figure 1 a and 1 b: Stroke presenting with a seizure – Seizure presenting with hemiparesis and aphasia

bleeding diathesis. If there is no direct relationship to an CNS insult, brain imaging may be carried out electively and should directly encompass a dedicated MR epilepsy imaging protocol, as recently proposed by Wellmer and colleagues, preferably using MRI at higher field strengths (3 T) instead of standard protocols [12].

The detection rate of abnormalities detected with neuroimaging lies – dependent on inclusion criteria – between 1 and 48% of all MRI and CT, with recent study of Hakami and coworkers reporting 28% of potentially structural epileptogenic lesions in patients having had an unprovoked epileptic seizure and 53% if the seizures

had a focal onset [13]. While encephalomalacia due to stroke, encephalitis and head trauma is the most frequent abnormality detected in series that included remote symptomatic seizures, it must be emphasized that more than 50% of pathologies others than stroke, hemorrhage, calcifications, encephalomalacia and brain tumors may be obscured by plain CT [14]. Clinically important examples of pathological imaging findings are resumed in **Figures 2 - 4**.

c. Is there a substantial lesion of the brain that explains the first seizure and influences the prognosis – or is just a coincidental finding?

There is evidence from 2 class II and one class III studies that structural brain lesions may generate an enduring predisposition for unprovoked seizures [3]. However, the evidence for the prediction of ≥ 60% probability of seizure recurrence in 10 years – accord-

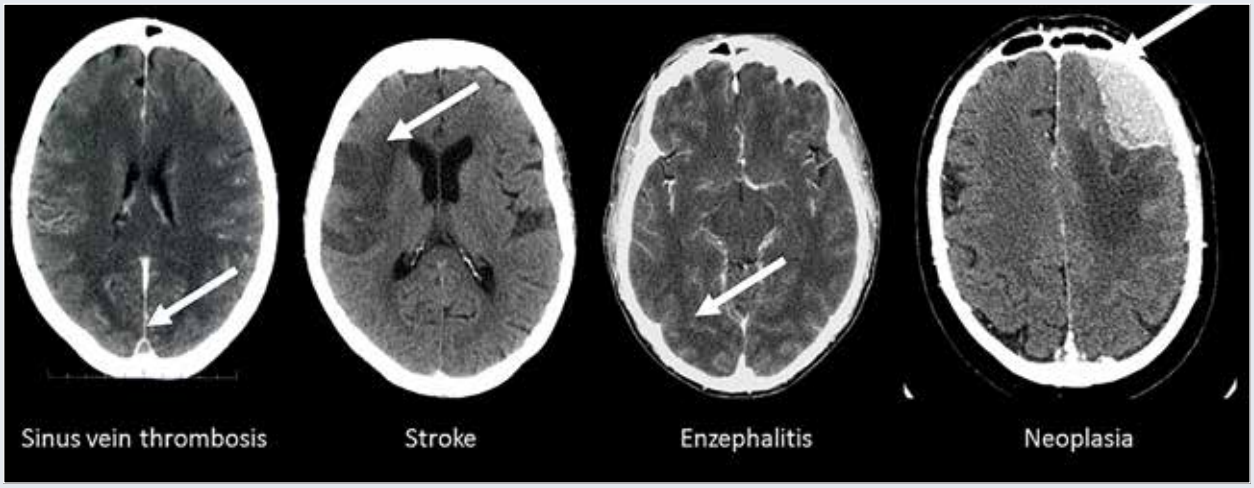

Figure 2: Causes of acute symptomatic seizure, Left: Contrast-enhanced CT-image depicting a thrombus within the superior sagittal sinus. 2nd image left: Acute stroke in the media territory of the right side visualised by hypodense demarcation of parenchyma on unenhanced CT. 3rd image left: Contrast enhanced CT with extravasion of contrast agent in the subarachnoidal space as correlate of blood-brain-barrier dysfunction in meningoencephalitis. Right: Right frontal contrast-enhancing extraaxial tumor suggesting meningioma.

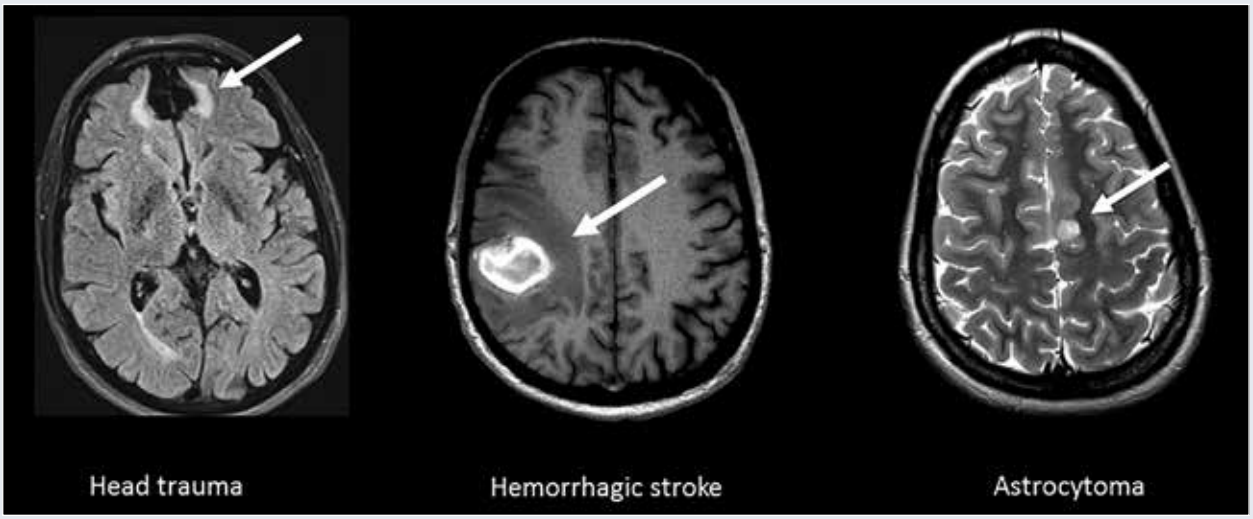

Figure 3: Typical imaging findings in patients with first seizure, Left: FLAIR image with bilateral fronto-polar/fronto-mesial chronic lesions after head trauma. Middle: Right cortico-subcortical subacute haemorrhage on T1-weighted image.
Right: T2-weighted image showing a T2-hyperintense tumor adjacent to cortical tissue of the left SMA. Cortical involvement of the lesion indicates epileptogenic potential.

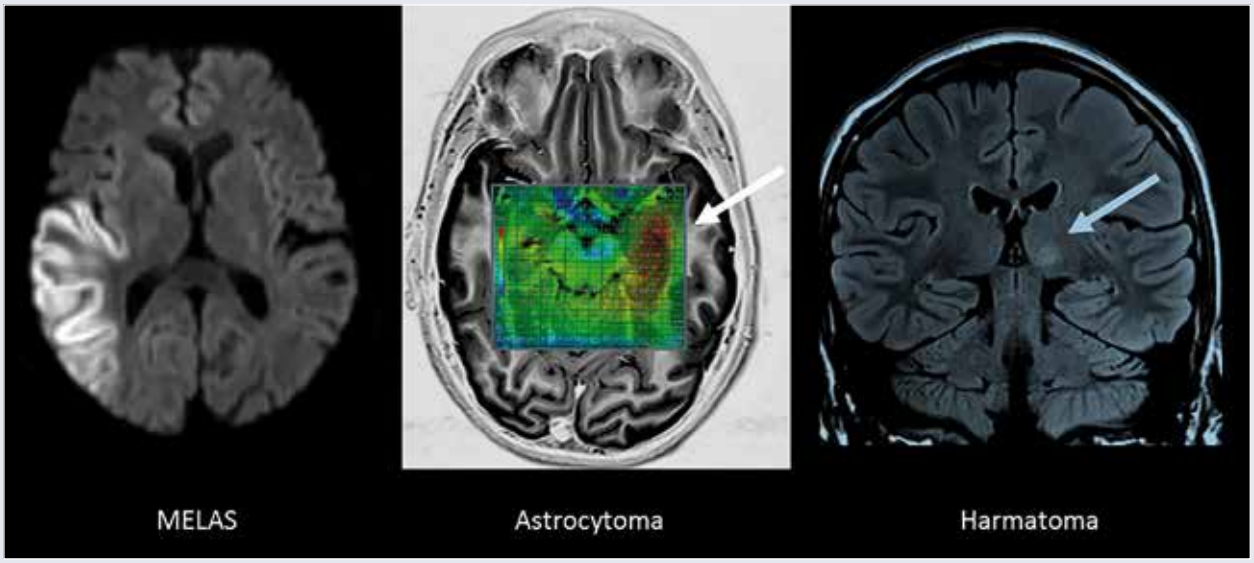

Figure 4: Typical imaging findings in patients with first seizure (cont.) Left: Diffusion restriction on DWI in the right temporal lobe in a patient with MELAS. Middle: MR-Spectroscopy unveiling a astrocytoma in the left mesiotemporal structures by documenting increased cholin concentrations within the tumoral tissue. Right: Diencephalic harmatoma on FLAIR image.

ing to the new epilepsy definition requirements – is currently restricted to lesions that are sequelae of an insult to the brain. For brain lesions such as low grade gliomas, cavernomas and AVMs, mesiotemporal sclerosis and malformations of cortical development the 10 years seizure recurrence rates have not yet been specifically studied. Hence, the presence of these brain lesions does not fulfill the requirements of the current criteria to replace a second unprovoked seizure [1] (see **Figure 5** for illustrative cases). Clearly, more epidemiological data are required to further translate the current imaging definitions from a "potentially epileptogenic structural brain lesion" into a "predictive brain lesion for recurrent seizures". Notably, almost 50% of the brain lesions detected during the workup of a first seizure may nowadays be considered as incidental. Thus, the imaging result has to be always balanced towards the personal situation of the patient and the type of lesion in the discussion if an antiepileptic treatment has to be started of a single seizure. A growing low-grade CNS tumor may be resected for neuro-oncological reasons, yet not due to its epileptogenicity. A diagnosis of epilepsy carries severe consequences for the individual patients and may be difficult to be reversed. Hence, even in case of "potential epileptogenic lesion" on neuroimaging, waiting for seizure recurrence prior to making a diagnosis of epilepsy may still be appropriate. Neuroimaging under emergency conditions is required to inform the epileptologist about potentially treatable conditions related to the seizure and to decide whether a presumably unprovoked seizure may turn into a provoked one (which alters the prognosis). Further, elective neuroimaging should be performed in every patient with focal abnormalities on EEG, focal neurological deficits and focal seizure onset. MRI can be omitted in clear cut cases of genetic generalized epilepsies. If MRI is requested, the qualitative requirements should be targeted toward the detection of epileptogenic lesions, thus following epilepsy protocol standards that warrant further postprocessing and lesion analysis.

d. Are newer imaging techniques available which are promising to increase the diagnostic yield?

As discussed above the application of the new definition of epilepsy requires epidemiological data on seizure recurrence rates in 10 years that are not available for a large portion of clinic situations after a first seizure. In parallel new imaging techniques emerged in recent years, for example brain perfusion measurements, susceptibility weighed imaging (SWI), simultaneous EEG/fMRI recordings and neuronal current imaging (NCI) or various nuclear medicine techniques e. g. PET measurements. All these new techniques have been applied to epilepsy. Currently, knowledge of the diagnostic benefit of these techniques are based on case studies. In the following we will give illustrative examples of different imaging approaches and discuss the potential of these techniques that could be selectively used in patients.

Brain perfusion measurements on CT or MRI are part of the emergence imaging protocols in the majority of hospitals in Switzerland. In cases of unwitnessed episodes of seizures, persisting altered mental state or focal deficits, acute stroke has to be ruled out during the emergency situation. Epileptic brain activity induces hemodynamic changes which can be detected on perfusion measurements. A hyperperfusion can be identified in the majority of cases during nonconvulsive status epilepticus [10] (**Figure 6**). The "epileptic" hyperperfusion has a cortical distribution, is not related to

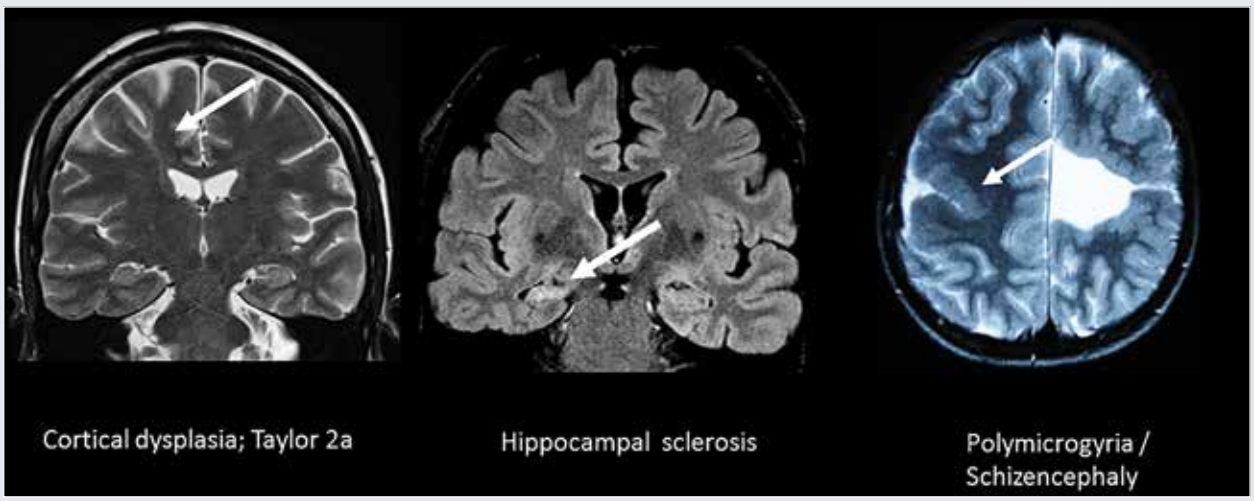

Figure 5: Imaging findings in specific epilepsy syndromes, Left: Juxta-cortical T2 hyperintense lesion (transmantle sign) in the cortical dysplasia Type Taylor 2a. Middle: FLAIR hyperintense and atrophic hippocampal formation in hippocampal sclerosis in mesiotemporal epilepsy (MTLE). Right: Inborn polymicrogyria / schizencephaly in Lennox-Gastaut syndrome.

vascular territories and should motivate an immediate electro-clinical evaluation. In the postictal state, especially during a Todd's paresis or aphasia, brain hypoperfusion can be visualized. The distribution of the "epileptic" hypoperfusion of postictal state is unrelated to the vascular territories and in general covers the whole hemisphere. In emergency setting epilepsy-related perfusion alterations may guide diagnostic workup. Data on treatment decisions and outcome are not available.

Another recently established imaging technique is the susceptibility weighted imaging (SWI). This technique is sensitive to the paramagnetic effect of the imaged tissue. Hemosiderin and calcifications are the main target of SWI but changes in deoxygenated blood content in veins are as well visible. In a recent study, our group reported the potential to detect focal and generalised hyperperfusion in status epilepticus by SWI [11]. The presence of hypointense veins as potential correlate to nonconvulsive status epilepticus (NCSE) may – like perfusion measurements detecting a hyperperfu-

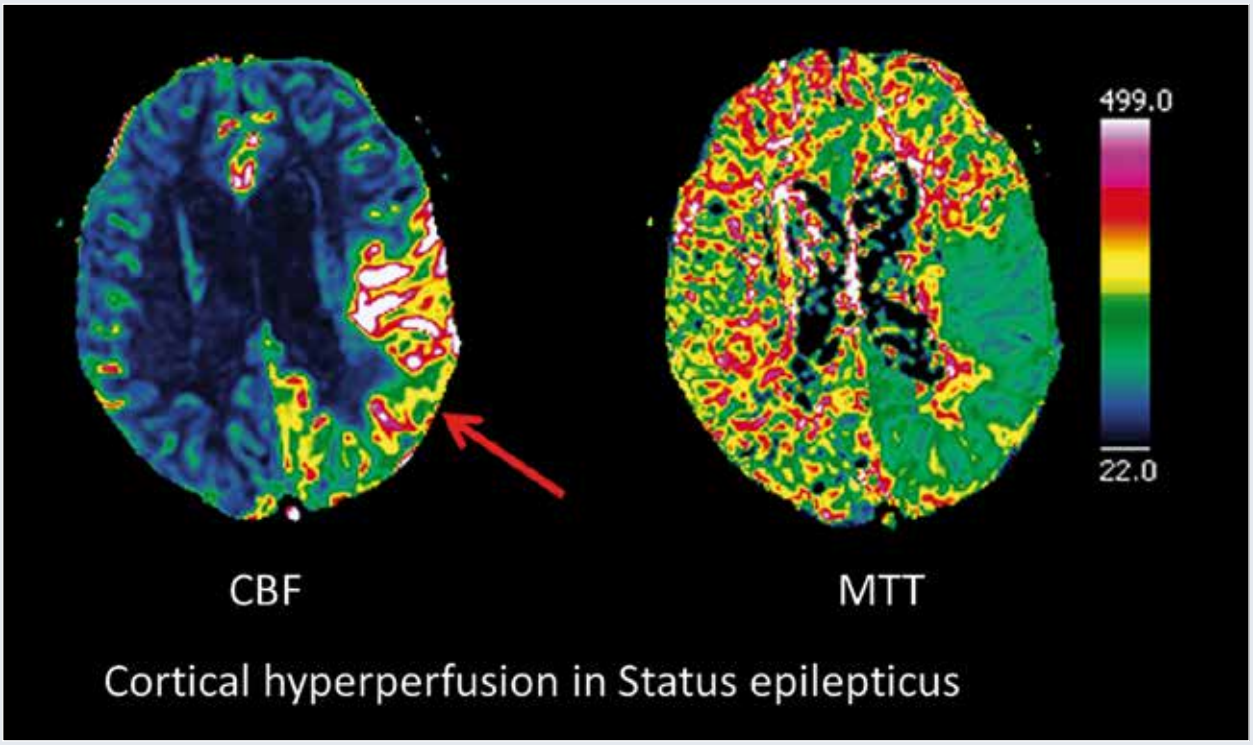

Figure 6: Perfusion measurement during NCSE, Hyperperfusion (red arrow) in NCSE visualized by increased cerebral blood flow (CBF) left side and reduced mean transit time (MTT) right side.

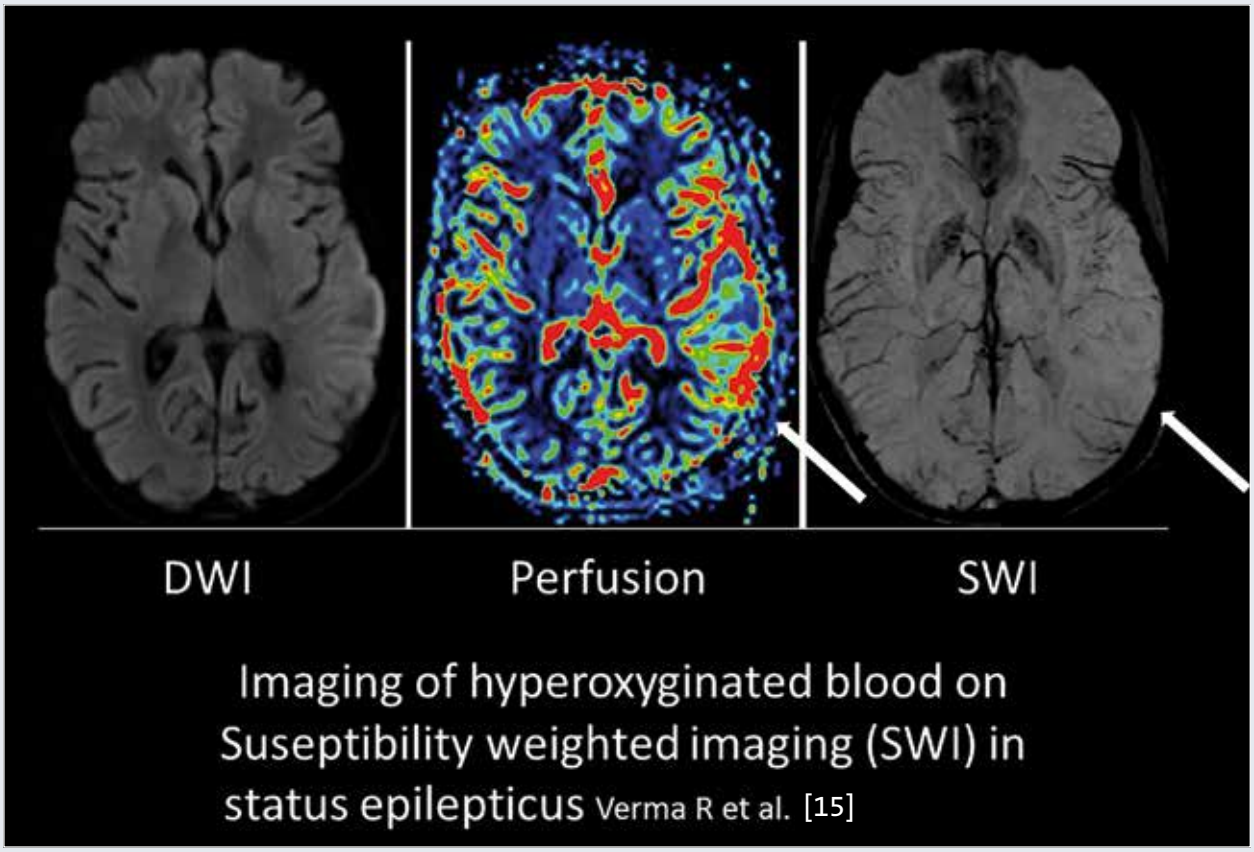

Figure 7: SWI showing on the right side disappearance of hypointensive signal in cortical veins in the region of ongoing hyperperfusion (middle image) during non-convulsive status epilepticus. The diffusion weighted imaging (DWI) (left image) detects a diffusion restriction within the symptomatogenic zone as defined by the perfusion imaging of the current status epilepticus.

sion – lead to an immediate EEG recording to establish the diagnosis of NCSE. The diffusion weighted imaging (DWI) changes do most likely indicate parenchymal damage, however the prognostic role of epilepsy related diffusion changes in respect to seizure recurrence and cognitive outcome has to be established (see **Figure 7**).

Recording EEG signals inside the MR scanner during BOLD measurements is called simultaneous EEG/fMRI. Analysis correlates hemodynamic changes to epileptiform EEG activity and is an established tool in epilepsy research and progressively gaining importance in the presurgical epilepsy workup [16]. The examples given here, highlight additional information from EEG/fMRI in two patients with similar clinical and EEG findings consisting in generalized seizures and diffuse interictal epileptic spike-wave activity on surface EEG after first seizure. In the first patient simultaneous EEG/fMRI recording shows a focal hemodynamic change in frontal operculum as correlate to a frontal lobe epilepsy with rapid generalisation (image on the left side). In the second patient (image on the right side) a generalized pattern of hemodynamic changes with positive BOLD correlate in the thalamus point to an underlying generalized genetic epilepsy (**Figure 8**).

The imaging techniques based on perfusion changes in the brain as perfusion measurements itself, SWI or EEG/fMRI rely on measuring indirect effects of the epileptic neuronal activity. The Neuronal Current Imaging (NCI) has been developed in our group aiming at visualising neuronal activity directly on MR images [17]. The underlying principle is that the distortion of the magnetic field as induced by electric currents arising from high frequency neuronal activity is depicted by an MRI sequence adapted from magnetisation transfer imaging protocols. A first study shows encouraging results in lateralising of the epileptic activity. In most of the cases the seizure onset zone was located in the lobe of activation in the NCI. Interestingly, in patients with drug-resistant epilepsy with a favourable outcome after surgery NCI activity has disappeared on the postoperative MRI. The example given here, shows the spatial concordance of the distribution of the amplitude mapping of interictal spikes and the localisation of the NCI measurement (**Figure 9**). Clinical relevance of NCI needs to be established by consecutive studies and experiences.

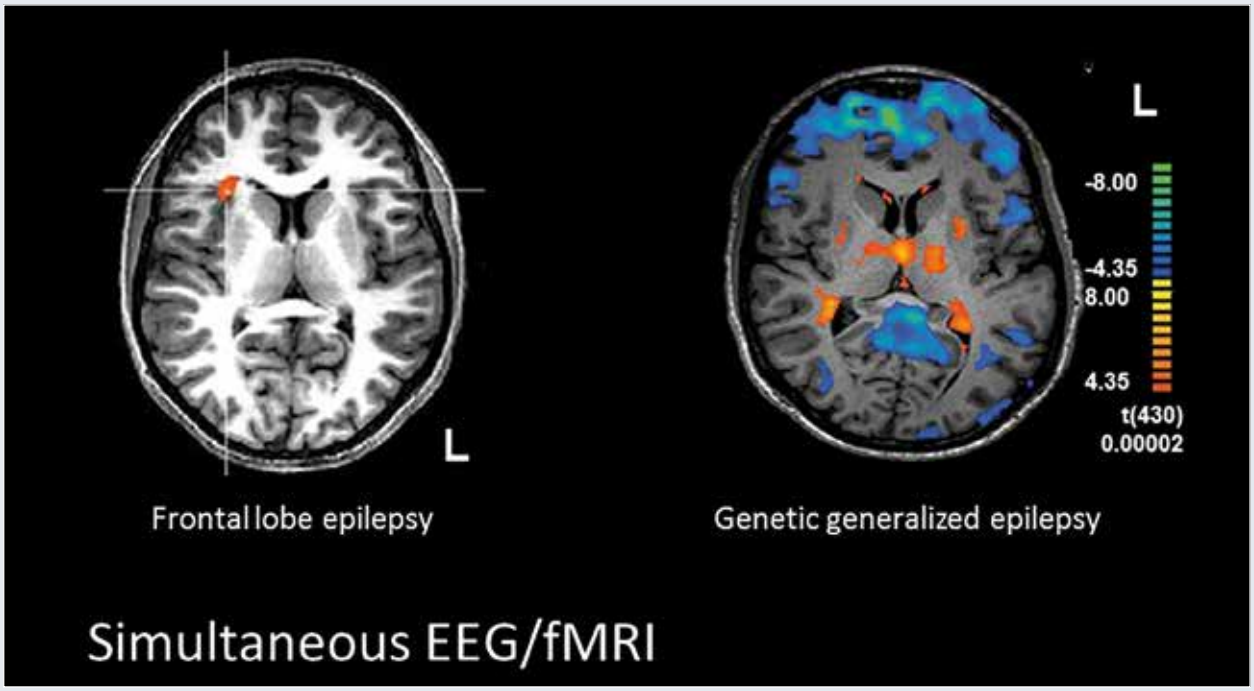

Figure 8: Simultaneous EEG/fMRI with different findings in focal epilepsy and genetic generalized epilepsy (for details see text).

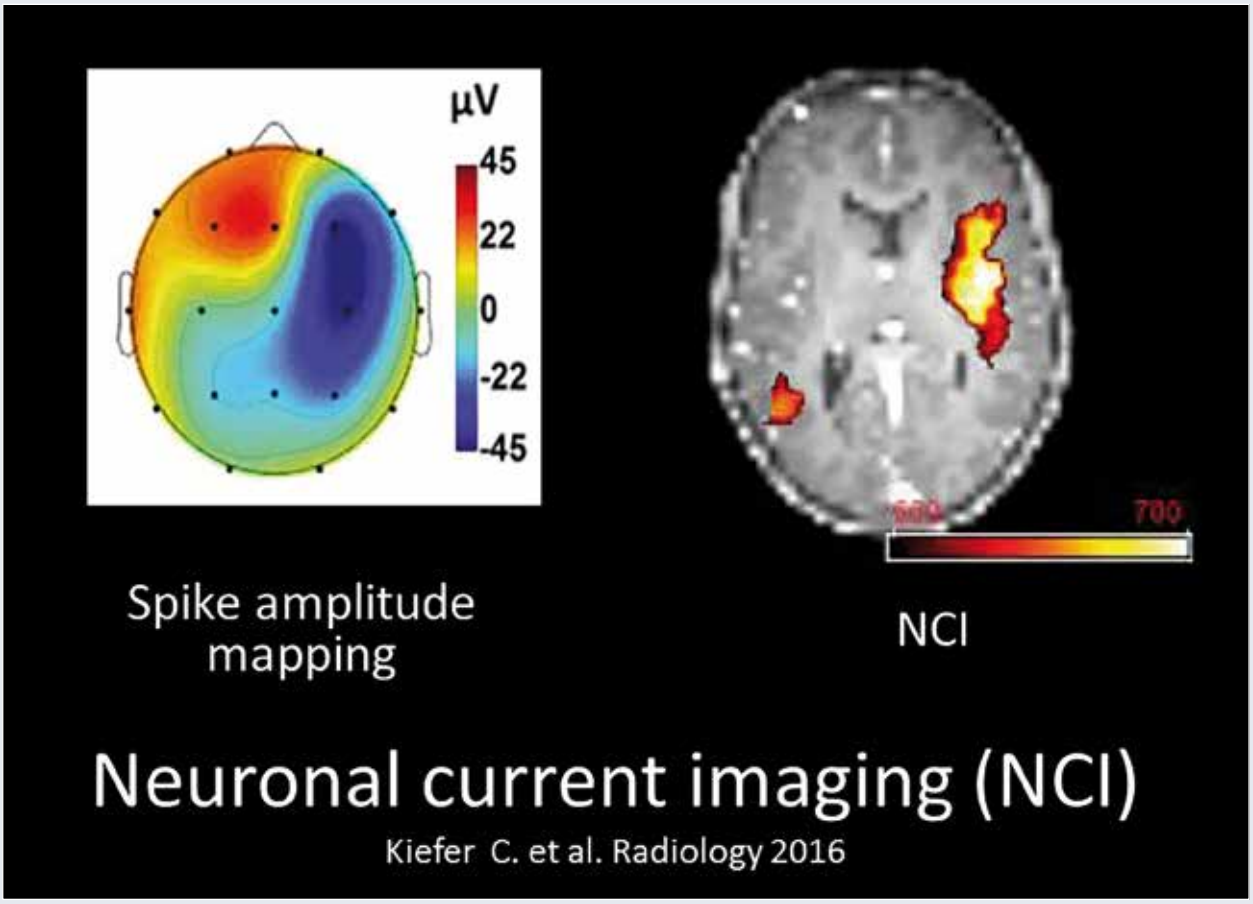

Figure 9: Neuronal current imaging (NCI) as first imaging technique directly related to neuronal activity shows activity in the accordance to epileptic EEG signals.

Summary

Neuroimaging is one of the main pillars of diagnostic workup in epilepsy. After a first seizure neuroimaging is indicated in all patients but those presenting with a typical genetic generalized epilepsy. Emergency imaging is warranted if the seizures may be the symptom of an acute brain pathology. If the patient returns "back to baseline" at the time of clinical examination, MR imaging may be performed electively using a dedicated epilepsy protocol. Data on seizure recurrence rates over 10 years is still lacking for many classical brain pathologies associated with epilepsy. Novel imaging techniques may be helpful in detecting prolonged seizures and mimics in the emergency setting.

References

1. *Crocker CE, Pohlmann-Eden B, Schmidt MH. Role of neuroimaging in first seizure diagnosis. Seizure 2016; Jun 1 Epub ahead of print*
2. *Fisher RS, Acevedo C, Arzimanoglou A et al. ILAE official report: a practical clinical definition of epilepsy. Epilepsia 2014; 55: 475-482*
3. *Krumholz A, Wiebe S, Gronseth S et al. Evidence-based guideline: Management of an unprovoked first seizure in adults: Report of the Guideline Development Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2015; 84: 1705-1713*
4. *Hui AC, Tang A, Wong KS et al. Recurrence after a first untreated seizure in the Hong Kong Chinese population. Epilepsia 2001; 42: 94-97*
5. *Hopkins A, Garman A, Clarke C. The first seizure in adult life. Value of clinical features, electroencephalography, and computerised tomographic scanning in prediction of seizure recurrence. Lancet 1988; 1: 721-726*
6. *Kho LK, Lawn ND, Dunne JW, Linto J. First seizure presentation: do multiple seizures within 24 hours predict recurrence? Neurology 2006; 67: 1047-1049*
7. *Erster epileptischer Anfall und Epilepsien im Erwachsenenalter. Hans-Christoph Diener, Christian Weimar (Hrsg): Leitlinien für Diagnostik und Therapie in der Neurologie. Berlin: DGN, 2012*
8. *Epilepsies: Diagnosis and Management. National Institute for Health and Clinical Excellence 2011. London: NICE, 2016*
9. *Tsivgoulis G, Alexandrov AV, Chang J et al. Safety and outcomes of intravenous thrombolysis in stroke mimics: a 6-year, single-care center study and a pooled analysis of reported series. Stroke 2011; 42: 1771-1774*
10. *Hauf M, Slotboom J, Nirkko A et al. Cortical regional hyperperfusion in nonconvulsive status epilepticus measured by dynamic brain perfusion CT. AJNR Am J Neuroradiol 2009; 30: 693-698*
11. *Verma RK, Abela E, Schindler K et al. Focal and generalized patterns of cerebral cortical veins due to non-convulsive status epilepticus or prolonged seizure episode after convulsive status epilepticus – A MRI study using susceptibility weighted imaging. PLoS One 2016; 11: e0160495*
12. *Wellmer J, Quesada CM, Elger CE et al. Proposal for a magnetic resonance imaging protocol for the detection of epileptogenic lesions at early outpatient stages. Epilepsia 2013; 54: 1977-1987*
13. *Hakami T, McIntosh A, Todaro M et al. MRI-identified pathology in adults with new-onset seizures. Neurology 2013; 81: 920-927*
14. *King MA, Newton MR, Jackson GD et al. Epileptology of the first-seizure presentation: a clinical, electroencephalographic, and magnetic resonance imaging study of 300 consecutive patients. Lancet 1998; 352: 1007-1011*
15. *Verma RK, Abela E, Schindler K et al. Focal and generalized patterns of cerebral cortical veins due to non-convulsive status epilepticus or prolonged seizure episode after convulsive status epilepticus – A MRI Study using susceptibility weighted imaging. PLoS One 2016; 11: e0160495. doi: 10.1371/journal.pone.0160495*
16. *Hauf M, Jann K, Schindler K et al. Localizing seizure-onset zones in presurgical evaluation of drug-resistant epilepsy by electroencephalography/fMRI: Effectiveness of alternative thresholding strategies. AJNR Am J Neuroradiol 2012; 33: 1818-1824*
17. *Kiefer C, Abela E, Schindler K, Wiest R. Focal epilepsy: MR imaging of nonhemodynamic field effects by using a phase-cycled stimulus-induced rotary saturation approach with spin-lock preparation. Radiology 2016; 280: 237-243*

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Summary

We review in this article the relevant points in the choice and introduction of a first antiepileptic drug (AED). We will present three important aspects regarding that choice: first the guidelines, then the AED characteristics and third some common patient profiles. Although the available guidelines evaluate evidences and provide invaluable information on best tolerated and most efficacious treatments in general scenarios, they have limitations. Given the intensive work they require, they are often not fully up-to-date. Furthermore, they are limited to the inclusion criteria of the corresponding studies, which rarely include patients with significant somatic or psychiatric comorbidities. From a review of the guidelines, we will present the individual characteristics of the AED and how they differ one from the other. We will then discuss frequent and particular clinical situations and emphasize the peculiarities that determine the choice of an AED.

Epileptologie 2016; 33: 232 – 239

Key words: Choice, comorbidity, interaction

Antiepileptika erster Wahl bei Erwachsenen: Von Richtlinien zur personalisierten Medizin

Dieser Artikel stellt die notwendigen Konzepte zur Wahl und Einführung eines ersten antiepileptischen Medikaments auf den Prüfstand. Es stehen zwar „Guidelines“ zur Verfügung, welche Evidenzen bewerten und wichtige Informationen über die Therapien mit bester Toleranz und höchster Wirksamkeit in Standardsituationen bieten. Diese unterliegen jedoch Beschränkungen. Angesichts der erforderlichen Arbeit zu deren Ausarbeitung liegen diese nicht immer aktualisiert vor. Darüber hinaus sind sie durch Einschlusskriterien der entsprechenden Studien limitiert, die selten Patienten mit relevanten psychiatrischen oder somatischen Begleiterkrankungen einbeziehen. Nach einer Zusammenfassung der „Guidelines“ führt dieser Artikel die individuellen Eigenschaften jedes Antiepileptikums sowie häufige und spezielle klinische Anwendungssituationen auf. Der Fokus liegt auf den Besonderheiten, welche Wahl und Einführung der Antiepileptika bestimmen.

Schlüsselwörter: Wahl, Begleiterkrankung, Interaktion

Médicaments antiépileptiques de première ligne: des recommandations à la médecine personnalisée

Cet article passe en revue les différents nécessaires aspects pour choisir et introduire un premier médicament anti-épileptique. Des recommandations sont disponibles. Elles résument la littérature et donnent ainsi une information précieuse sur les traitements les mieux tolérés ou les plus efficaces dans des situations générales, mais elles ont des limitations. Au vu du travail nécessaire à leur rédaction, elles ne sont pas toujours complétement à jour. De plus, elles sont restreintes par les critères d’inclusion des études qu’elles analysent, qui intègrent rarement des patients avec d’importantes comorbidités, psychiatriques ou somatiques. Avec les recommandations comme point de départ, cet article présente ensuite les caractéristiques individuelles de chaque anti-épileptique et les situations cliniques fréquentes ou particulières. Un accent est mis sur les particularités qui détermineront ensuite le choix et l’introduction des antiépileptiques.

Mots clés : Choix, comorbidité, interaction

Introduction

The AEDs are symptomatic treatments for epilepsy. The chance for a patient to be seizure free after a first AED is approximately 50% [1]. There are small efficacy variations between AED but the major differences lie in their adverse events profile and pharmacokinetic properties.

Previously, physicians had the choice between 6 “older” AEDs often with a complex hepatic metabolism and high potential for interactions [2]. After 1990, “newer” AEDs have been commercialized, with much simpler pharmacokinetics and less adverse effects, but

with a higher cost. **Table 1** lists a selection of the AEDs that will be cited in this article, sorted by date of introduction.

Clinicians were traditionally more prone to use older AEDs. The trend is now reversing, as illustrated by a British cohort study on more than 60 000 patients [3]: the use of phenytoin (PHT) has decreased from 39.5% in 1993 to 18.3% in 2008. Meanwhile, older generation AEDs are increasingly being replaced by newer AEDs, with lamotrigine (LTG) and levetiracetam (LEV) prescription rates increasing from 2% to 17% and 0 to 8.6%, respectively in the same interval. For those 2 AEDs prescription rates of as much as 30 - 35%, are now reported [4].

To illustrate this review we will consider a fictive case. Mrs G. is a 22-years-old woman and presents with a first unprovoked generalized tonico-clonic seizure. The neurological examination and brain magnetic resonance imaging are normal. The electroencephalogram shows generalized spike and wave discharges. The patient is professionally active, is married, takes oral contraception and is known for a severe anxiety disorder. Taking in consideration of the situation of this fictive patient, we will discuss what is likely to be the best AEDs in this case.

Table 1: Name, abbreviation and date of introduction of selected AEDs. The double line represents the limit between "older" and "newer" AEDs.

Name	Abbreviation	Year of introduction
Phenobarbital	PB	1912
Phenytoin	PHY	1938
Primidone	PRM	1954
Ethosuximide	ESM	1960
Valproic acid	VPA	1967
Carbamazepine	CBZ	1974
Vigabatrin	VGB	1993
Gabapentin	GBP	1993
Lamotrigine	LTG	1995
Topiramate	TPM	1996
Oxcarbazepine	OXC	1998
Levetiractam	LEV	2000
Pregabalin	PGB	2005
Zonisamide	ZNS	2007
Lacosamide	LCM	2009
Perampanel	PER	2013

Overall, we now benefit from the choice of more than 20 drugs. Not every AED is however a good option to start therapy after a first seizure. Several suggestions were made by various neurology or epileptology societies, based on available studies and are published as guidelines. We will briefly review the most widely used guidelines. We will then try to fill the gap between these guidelines and everyday practice by showing individual AED characteristics and how they fit each patient's profile.

Guidelines and illustrative studies

There are several guidelines published in the treatment and diagnosis of epilepsy. A recent review shows that there were at least 35 of them in 2016 [5]. **Table 2** presents treatment recommendations from four important societies: the International League Against Epilepsy (ILAE), the American Academy of Neurology, together with the American Epilepsy Society (AAN/AES), the National Institute for Health and Care Excellence (NICE) and the Société Française de Neurologie (SFN). The differences between guidelines are due to the date of redaction and methodological differences in rating and the evaluation of the available literature [6]. Overall, the guidelines reflect on the increasing place given to newer AEDs over older AEDs. Traditionally, the two "gold standards" were carbamazepine (CBZ) (especially the extended release form) for focal onset seizure and valproate (VPA) for generalized onset seizure. Recent studies have challenged this view. We will now discuss five of these studies [7 - 11] to illustrate this point and understand the rationale of the published guidelines.

The SANAD arm A [8] was an open label multicentre randomized trial with 1700 patients. For the treatment of epilepsy with focal onset seizure, it compared the "gold-standard" CBZ to four newer AEDs: gabapentin (GBP), lamotrigine (LTG), oxcarbazepine (OXC) and topiramate (TPM). In term of retention time (which is influenced by seizure control as well as adverse events), LTG was superior to all the other drugs. The SANAD arm B [9] had a similar design but included patients with generalized onset seizures. VPA was the "challenged" drug against LTG and TPM. In this latter study, VPA showed better efficacy than LTG and better tolerability than TPM. Regarding these results, the authors considered LTG to be the best drug in focal-onset and VPA the best one in generalized-onset seizure (with the exception of women of childbearing age, as discussed below). Although important and well designed, these studies are limited by their open label design and were thus considered "Class III" by the ILAE. A class III study cannot be used to consider a grade A recommendation and this is why LTG is only ranked grade C for the treatment of focal onset seizure in ILAE guidelines.

Brodie et al. [7] have studied LEV in focal epilepsy. They conducted a randomized, double blind, multi-

Table 2: Comparison between four published guidelines. Levels of evidence are expressed using grade A-D or first and second choice for the NICE guidelines. For abbreviations see **Table 1**.

Association	**ILAE**	**AAN/AES**	**NICE**	**SFN**
Guidelines	International	American	British	French
Date (and publication)	Glauser et al. Epilepsia (2006 and 2013)	French et al. Neurology (2004)	*Society website* (2016)	*Society website* (2014)
Sorted by	Grade (A-D)	Grade (A-B)	First (1) or second (2) choice	Grade (A-B)
Comment	Efficacy review (Do not consider itself as a guideline)	Only reviewed **new** AED		
Focal onset seizure	**Adults** A: CBZ, LEV, PHT, ZNS B: VPA C: GBP, LTG, OXC, PB, TPM, VGB D: CZP, PRM	A/B: GBP, TPM, LTG, OXC	1: CBZ, LTG 2: LEV, OXC, VPA	**General** A/B: CBZ, OXC, LEV, LTG
	Elderly A: GBP, LTG, B: - C: CBZ D: TPM, VPA			**Elderly** A: LTG
Generalised onset	**Adults** A, B: - C: CBZ, LTG, OXC, PB, PHT, TPM, VPA. D: GBP, LEV, VGB	A/B: -	1: VPA 2: LTG Discuss CBZ and OXC	A: - B: VPA, LTG
Absences	**Children** A: ESM, VPA B: - C: LTG D: -	A: - B: LTG	1: ESM, VPA 2: LTG	A: - B: LTG, VPA
Juvenile Myoclonic Epilepsy	A, B, C: - D: TPM, VPA		1: VPA 2: LEV, LTG, TPM	A: - B: LTG, VPA

centre non-inferiority trial on 579 patients. It showed that LEV was non-inferior to extended-release CBZ in monotherapy. This important trial ranked LEV as grade A recommendation in the ILAE and SNF guidelines. The AAN/AES guidelines were published before this study and therefore they could not include it. The NICE guidelines recommended LEV only as second line treatment because it was not considered cost-effective.

LEV has been further studied in the elderly population. A randomised, double blind retention study from 2015 [11] compared extended-release CBZ, LEV and LTG in this population. LEV was superior to extended-release CBZ. LTG did not differ significantly from the other two drugs. This tends to indicate that the newer AEDs are better candidates AEDs in the elderly, probably because of their relative low propensity of cognitive adverse event and the absence of liver enzyme induction, which can lead to interaction with comedications as discussed below. This is an example of a recent study whose conclusions have not been integrated in guidelines yet. There is also an open label randomized trial of LEV in focal epilepsy, compared with LTG showing no significant difference [10].

In conclusion, guidelines can only bring evidence regarding what questions have been asked in clinical trials, mostly efficacy and to a lesser extend safety of AEDs [6]. A clinician may need more knowledge to choose the appropriate drug for each patient.

Table 3: Important theoretical aspect regarding AED use. SIADH: Syndrome of Inappropriate Anti-diuretic Hormone secretion. For interpretation, see the text.

Name and abbreviation	Spectrum	Elimination (adapt doses)	Pharmacokinetic Specificities.	Useful when...	Avoid when...	Specific sides effects
Valproic acid (VPA)	Broad	Hepatic	Potent liver enzyme inhibitor	Depression Anorexia Migraine	Overweight Essential tremor Pregnancy Osteoporosis	Weight gain Ammonium encephalopathy Polycystic ovary The worst for young woman
Carbamazepine (CBZ)	Narrow	Hepatic	Liver enzyme inducer	Depression Trigeminal neuralgia	Overweight oral contraception Osteoporosis	SIADH Severe skin rash ->see genetic testing
Gabapentin (GBP)	Narrow	Renal	Only renal clearance No interaction	Anxiety Insomnia Neuropathic pain Essential tremor	-	Somnolence
Lamotrigine (LTG)	Broad	Hepatic and renal	Metabolism induced by oral contraception and pregnancy	Depression Anorexia oral contraception Pregnancy Older patients	Insomnia (Myoclonus)	Severe skin rash (especially when rapid introduction with VPA
Topiramate (TPM)	Broad	Renal > hepatic	Liver enzyme inducer (high doses) +/- inhibitor	Overweight Migraine Essential tremor	Depression Anorexia Oral contraception (if >200mg/d) (Pregnancy)	Anorexia Nephrolithiasis Paraesthesia Psychiatric and phasic troubles
Oxcarbazepine (OXC)	Narrow	Hepatic	Liver enzyme inducer (high doses) +/- inhibitor	Depression	Oral contraception Osteoporosis	SIADH (more than CBZ)
Levetiracetam (LEV)	Broad	Renal	Clearance increase during pregnancy +/- oral contraception	oral contraception Pregnancy	Depression Anxiety	Psychiatric troubles (anxiety, irritability, psychosis)
Pregabalin (PGB)	Narrow	Renal	Only renal clearance No interaction	Anxiety Insomnia Restless Legs Neuropathic pain	Overweight	Somnolence Oedema
Zonisamide (ZNS)	Broad	Renal > hepatic	Metabolism inducible	Overweight Oral contraception	Anorexia	Similar to TPM but possibly less psychiatric side effects
Lacosamide (LCM)	Narrow	Hepatic and renal	-	-	-	-
Perampanel (PER)	Narrow (Broad?)	Hepatic	Half-life>48h	-	-	Somnolence +/- irritability

Table 4: Practical information regarding AEDs introduction. This table is only indicative and does not substitute for official information and clinician experience. Average price in 2014, adapted from Rossetti 2015 (Rossetti, Epileptologie, 2015)

Name and abbreviation	Initial Dose	Maximal Dose	Points/potential adverse events to be aware of	Average/month in CHF (dosage)
Valproic acid	2x500mg	3000mg/d	-	20.- (1000mg)
Carbamazepine	2x200mg	1600mg/j	Hyponatremia Skin rash Genetic HLA testing for population at risk (before introduction)	20.- (800mg)
Gabapentin	100mg 3x/j aim: 900-1200mg/d	2400mg/j	-	120.-. (1800mg)
Lamotrigine	1x25mg (12.5 if concomitant VPA)	600mg/d	Skin rash	70.- (200mg)
Topiramate	1x25mg (for 1 week)	200mg/d (400mg/d)	-	55.- (100mg)
Oxcarbazepine	2x150mg	2400mg/d	Hyponatremia	90.- (1200mg)
Levetiractam	2x500mg	3000mg/d	Irritability or psychosis	60.- (1000mg)
Pregabalin	2x75mg	600mg/d	-	120.- (300mg)
Zonisamide	1x50mg (for 1 week)	400mg/d	-	115.- (200mg)
Lacosamide	2x50mg (1x50mg)	400mg/d	-	160.- (200mg)
Perampanel	1x2mg	8-12mg/d	-	250.- (6mg)

Beyond guidelines: tailoring the treatment according to the patient's needs

As pointed out above, guidelines reflected on the trials that assessed these medications. People included in trials are chosen in order to demonstrate a difference between the two arms of the studies. The results are difficult to extrapolate to clinical practice as these studies are limited by their short duration, rigid inclusion and exclusion criteria, inability to analyse the effect of concomitant medications, and lack of dosing flexibility. Regulatory AED trials often ignore aetiology and epilepsy syndrome which may affect prognosis, and also include homogenous cohorts with a high seizure frequency, without major comorbidities [12]. In order not to worsen any concomittant condition or to interfere with other treatment, it is important to consider the overall situation of the patient before starting a AED. Furthermore, AEDs can be chosen to help to improve the symptoms of another condition, such as mood disorder, neurogenic pain, or insomnia. **Tables 3** and **4** summarize important aspects in the choice of the first line AED listing 11 of the most common ones. Beyond the most relevant AEDs from the guidelines, this table adds two of the latest AEDs lacosamide (LCM) and perampanel (PER), whose prescription rate is likely to be growing in everyday practice (e. g. LCM has been approved for monotherapy in the USA in 2014). We did not however include retigabine (as its discontinuation was recently announced), nor PHT or phenobarbital (PB) (due to their adverse events and pharmacokinetic, these medications are usually not suitable first-line drugs nowadays). For **Table 3**, each column presents informations with clinical implications. Broad spectrum AED are used in case of generalized onset seizures, although the underlying level of evidence is weak, as underlined in the guidelines. A recent evidence review [13] has supported the use of just 5 AEDs for the treatment of primarily generalized convulsive seizures: LTG, LEV, TPM, VPA, with evidence for ZNS considered low-level. Of these, only LTG, LEV, and TPM have demonstrated efficacy in randomized, double blind, placebo-controlled trials of adjunctive treatment for drug-resistant generalised onset seizures. A recent study also suggests that PER could be used in that context [14]. The next column shows clearance mechanisms and pharmacokinetic properties that have to be taken into consideration in case of renal or hepatic failure. Drugs with pure hepatic metabolism are also more prone to lead to interaction. The three last columns are important for a tailored AED choice regarding each patient. It presents the effects of the different AEDs in conditions other than epilepsy. **Table 4** shows practical data: proposed initial and usually maximal dosage, recommended controls and average monthly prices.

The titration and dosing schema is another important aspect of the choice of first line AEDs. The speed of titration needed is usually dictated by the activity of the disease. A medication whose titration to reach efficient level takes weeks (such as LTG) is inadequate to control an epilepsy with daily disabling seizures. Similarly, the availability of an intravenous formation (such as LEV, LCM) also allows, most often with a loading bolus, to obtain quickly efficient medication levels. On the other side, titration pace is likely to be slowed down in patients reporting frequent medication intolerance. The dosing can also be determinant, for instance to improve compliance with AEDs requiring only one daily dosing (ZNS for instance) [15]. The first-line medication is then titrated according to the response (control of seizure) and tolerance. If the control is insufficient, it has been suggested at times to increase the dosage until signs of intolerance appear. Remission, which is the aim of a first line treatment, is however likely to occur at relatively low dosage [16], making inappropriate an indiscriminate continuous dosage increase if no effect on seizures is observed.

We will now discuss several common situations: elderly patients, patients with neoplasm or HIV infection, women in child bearing age, patients with intellectual disability and CBZ genetic testing.

Specific populations

The most relevant aspects of elderly patients are comorbidities (leading to frequent comedications) and often reduced renal and hepatic functions [11]. Regarding this aspect, drugs with simpler pharmacokinetic and without liver enzyme induction action (non-"inducers") should be preferred, as illustrated in the above-mentioned guidelines. Osteoporosis is often present in older patients and can also be worsened by inducers. Those patients are also more liable to cognitive adverse effects of medication. In this population, LEV, LTG, or PGB, are good candidates AEDs.

Patients with primary brain tumor, metastases or cancer in general are at increased risk of seizure and often need both AED and chemotherapy. Liver enzyme induction is also problematic in this case: CBZ, PHT, PB and primidone (PRM) can decrease the efficacy of the chemotherapy agent. VPA has a possible direct beneficial effect against glial cell tumor but this has not yet been proven in prospective trials [17]. Meanwhile, VPA can also lead to increased chemotherapy serum concentration possibly leading to toxicity, because of its action as liver enzyme inhibitor [18]. The same rule applies for HIV-infected patients taking antiviral agents, as induction by AEDs can lead to failure of antiretroviral treatment. Some antiretroviral treatments can also interfere with metabolism of some AEDs (mostly CBZ). The AAN issued guidelines regarding treatment adjustment in this case [19].

It is the general consensus to continue AEDs during pregnancy because of the potentially severe consequences of recurrent seizures for the mother and the

foetus [20]. Indeed, the consequences of uncontrolled seizures are considered to outweigh the risk of medication. Overall, children of mothers with epilepsy taking AEDs are at increased risk of major foetal malformations (approximately 3 - 7% compared to 2% in the general population) [21, 20], but important differences exist between AEDs [22]. The AEDs with the best profile in this situation are LTG, LEV, CBZ, and OXC. The worst AED in pregnancy is by far VPA. It causes a malformation risk of 6% for doses <700 mg and up to 25% for doses >1500 mg. Beyond this risk, there are also cognitive and developmental complications for the child after its exposition. In child bearing age women, VPA should be reserved to patients not responding to other treatment option. LTG and LEV are safe AEDs in pregnancy, although they undergo a change in their metabolism during pregnancy and their serum level needs to be followed, to adapt the dosage accordingly.

Regarding contraception, liver enzyme inducers AEDs again are better avoided because they can lead to loss of efficacy of contraceptive pills. The alternative is to use highly dosed contraceptive pills. Conversely, the oral contraception can induce the metabolism of LTG which may also justify dosage adaptation.

Epilepsy is more prevalent in people with intellectual disabilities, with prevalence rates of up to 50% in severely disabled institutionalized patients [23]. The seizures are often intractable and the management of adverse events can be complicated by comorbidities and communication difficulties. The aim of the treatment should be not to worsen cognition or motor skills as well as to avoid to induce behavioural difficulties. Among AEDs, the newer ones probably have good efficacy and tolerance, as illustrated by a prospective study showing a high 3-year retention of approximately 70% for LTG [23].

CBZ (more than LTG) is associated with skin hypersensitivity reactions in up to 10% of patients. Most are erythematous maculopapular rash. However, in rarer cases (1-10/10 000) much more severe reactions can happen such as Steven Johnson syndrome or toxic epidermal necrolysis. These complications are potentially very severe and are associated with genetic susceptibility in HLA variants HLA-B*15:02 and HLA-A*31:01, which have different prevalence according to patient's origin. While European Medicines Agency and the American Food and Drug Administration require the search for HLA-B*15:02 before instituting CBZ in people with Asian ancestry (descendant of Chinese, Thai, Indian, Malay, Filipino, Indonesian; level A), they are not taking position on systematic testing for HLA-A*31:01. The level of evidence was recently reviewed [24] with the following recommendation: preventive genetic testing for HLA-B*15:02 for patients at risk of having this variant, but also possibly for general population (level C). Testing of HLA-A*31:01 is recommended for all patients regardless of origin (level B) in this review, although the benefit of testing this HLA variant is less clear. Swissmedic also supports the testing for HLA-A*31:01 in Caucasians. The Swiss League Against Epilepsy issued a statement, currently in press, putting these recommendations in perspective. It is not the point of this article to argue with the regulatory authorities recommendations, but the potential necessity of genetic testing before introducing CBZ led in practice to a decrease of its use.

Conclusion

Back to the treatment of Mrs G. The first aspect is that she has epilepsy with generalized onset seizure, for which, the level of evidence for the choice of treatment is low. Five AEDs have a broad spectrum of action: VPA, LTG, TPM, LEV and ZNS. Although probably the most efficient, VPA is not a good option regarding the fact that this patient is in childbearing age. The often prescribed LEV can worsen the anxiety disorders and should also be avoided. LTG is a good option because it has favourable effect on mood disorders and it is a safe option for pregnancy. It is compatible with contraception or pregnancy although doses have to be adapted.

In conclusion, it is essential to consider the patient globally when choosing the first AED, in order to maximise the chances of achieving remission as quickly as possible without significant adverse events.

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References

1. *Kwan P, Brodie MJ. Early identification of refractory epilepsy. New Engl J Med 2000; 342: 314-319 http://doi.org/10.1056/NEJM199401273300403*
2. *French JA, Kanner AM, Bautista J et al. Efficacy and tolerability of the new antiepileptic drugs I: treatment of new onset epilepsy: report of the Therapeutics and Technology Assessment Subcommittee and Quality Standards Subcommittee of the American Academy of Neurology and the American Epilepsy Society. Neurology 2004; 62: 1252-1260 http://doi.org/10.1212/01.wnl.0000123693.82339.fc*
3. *Nicholas JM, Ridsdale L, Richardson MP et al. Trends in antiepileptic drug utilisation in UK primary care 1993-2008: Cohort study using the General Practice Research Database. Seizure 2012; 21: 466-470 http://doi.org/10.1016/j.seizure.2012.04.014*
4. *Malerba A, Ciampa C, De Fazio S et al. Patterns of prescription of antiepileptic drugs in patients with refractory epilepsy at tertiary referral centres in Italy. Epilepsy Res 2010; 91: 273-282 http://doi.org/10.1016/j.eplepsyres.2010.08.002*
5. *Sauro KM, Wiebe S, Dunkley C et al. The current state of epilepsy guidelines: A systematic review. Epilepsia 2016; 57: 13-23 http://doi.org/10.1111/epi.13273*

6. French JA. Can evidence-based guidelines and clinical trials tell us how to treat patients? Epilepsia 2007; 48: 1264-1267 http://doi.org/10.1111/j.1528-1167.2007.01123.x
7. Brodie MJ, Perucca E, Ryvlin P et al. Comparison of levetiracetam and controlled-release carbamazepine in newly diagnosed epilepsy. Neurology 2007; 68: 402-408
8. Marson AG, Al-Kharusi AM, Alwaidh M et al. The SANAD study of effectiveness of carbamazepine, gabapentin, lamotrigine, oxcarbazepine, or topiramate for treatment of partial epilepsy: an unblinded randomised controlled trial. Lancet 2007; 369; 1000-1015 http://doi.org/10.1016/S0140-6736(07)60460-7
9. Marson AG, Al-Kharusi AM, Alwaidh M et al. The SANAD study of effectiveness of valproate, lamotrigine, or topiramate for generalised and unclassifiable epilepsy: an unblinded randomised controlled trial. Lancet 2007; 369: 1016-1026 http://doi.org/10.1016/S0140-6736(07)60461-9
10. Rosenow F, Schade-Brittinger C, Burchardi N et al. The LaLiMo Trial: lamotrigine compared with levetiracetam in the initial 26 weeks of monotherapy for focal and generalised epilepsy – an open-label, prospective, randomised controlled multicenter study. J Neurol Neurosurg Psychiatry 2012; 83: 1093-1098 http://doi.org/10.1136/jnnp-2011-301999
11. Werhahn KJ, Trinka E, Dobesberger J et al. A randomized, double-blind comparison of antiepileptic drug treatment in the elderly with new-onset focal epilepsy. Epilepsia 2015; 56: 450-459 http://doi.org/10.1111/epi.12926
12. Sander JW. New antiepileptic drugs in practice – How do they perform in the real world? Acta Neurol Scand 2005; 112(Suppl 181): 26-29 http://doi.org/10.1111/j.1600-0404.2005.00505.x
13. Rheims S, Ryvlin P. Pharmacotherapy for tonic-clonic seizures. Expert Opin Pharmacother 2014; 15: 1417-1426 http://doi.org/10.1517/14656566.2014.915029
14. French JA, Krauss GL, Wechsler RT et al. Perampanel for tonic-clonic seizures in idiopathic generalized epilepsy. Neurology 2015; 85: 950-957 http://doi.org/10.1212/WNL.0000000000001930
15. Sander JW. The use of antiepileptic drugs – principles and practice. Epilepsia 2004; 45: 28-34 http://doi.org/10.1111/j.0013-9580.2004.455005.x
16. Kwan P, Brodie MJ. Effectiveness of first antiepileptic drug. Epilepsia 2001; 42: 1255-1260 http://doi.org/10.1046/j.1528-1157.2001.04501.x
17. Rudà R, Pellerino A, Soffietti R. Does valproic acid affect tumor growth and improve survival in glioblastomas? CNS Oncol 2016; 5: 51-53
18. Yap KYL, Chui WK, Chan A. Drug interactions between chemotherapeutic regimens and antiepileptics. Clin Ther 2008; 30: 1385-1407 http://doi.org/10.1016/j.clinthera.2008.08.011
19. Birbeck GL, French JA, Perucca E. Evidence-based guideline: Antiepileptic drug selection for people with HIV/AIDS : Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Ad Hoc Task Force of the Commission on Therapeutic Strategies of the Internation, 2012 http://doi.org/10.1212/WNL.0b013e31823efcf8
20. Tomson T, Battino D. Teratogenic effects of antiepileptic drugs. Lancet Neurol 2012; 11: 803-813 http://doi.org/10.1016/S1474-4422(12)70103-5
21. Meador K, Penovich P, Baker G. Antiepileptic drug use in women of childbearing age. Epilepsy Behav 2009;15: 339-343 http://doi.org/10.1016/j.yebeh.2009.04.026.Antiepileptic
22. Hernandez S, Shen A, Holmes LB. Comparative safety of antiepileptic drugs during pregnancy. Neurology 2012; 78: 1692-1699 http://doi.org/10.1212/WNL.0b013e3182574f39
23. Carpay JA, Aalbers K, Graveland GA, Engelsman M. Retention of new AEDs in institutionalized intellectually disabled patients with epilepsy. Seizure 2009; 18: 119-123 http://doi.org/10.1016/j.seizure.2008.07.007
24. Amstutz U, Shear NH, Rieder MJ et al. Recommendations for HLA-B15:02 and HLA-A31:01 genetic testing to reduce the risk of carbamazepine-induced hypersensitivity reactions. Epilepsia 2014; 55: 496-506 http://doi.org/10.1111/epi.12564

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„Seit meinem 17. Lebensjahr plagten mich immer wiederkehrende Krampfanfälle, und im Alter von 49 Jahren kam endlich die Erlösung. Ich weiss, was ich habe! Ich weiss, warum ich es habe! Und ich weiss, dass es eine Therapie gibt und ich diese Krankheit verstehen und vielleicht auch hinter mir lassen kann.“ (Sonja Casutt, Betroffene psychogener Anfälle)

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« Je souffre de convulsions récurrentes depuis mes 17 ans, mais je n'ai trouvé le salut qu'à 49 ans. Je sais enfin ce que j'ai ! Je sais pourquoi je l'ai ! Et je sais qu'il existe un traitement, que je peux comprendre la maladie et peut-être même la laisser derrière moi. » (Sonja Casutt, patiente atteinte de crises psychogènes)

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Unvollständige Unterlagen werden nicht bearbeitet. Es können sowohl bereits publizierte als auch zum Druck angenommene Arbeiten eingereicht werden. Bei der Einreichung ist mitzuteilen, ob und wo die Arbeit veröffentlicht bzw. zum Druck angenommen wurde.

Die Arbeiten können in deutscher oder englischer Sprache verfasst sein. Dem Kollegium können auch Arbeiten zur Preisvergabe vorgeschlagen werden.

Zusätzlich zu den Arbeiten sind folgende weitere Unterlagen einzureichen:

- ein Lebenslauf
- eine Stellungnahme des Klinik-/Institutsvorstandes zur Bewerbung
- für den Fall von Mehrautorenarbeiten, bei denen nicht alle Autoren am Preis beteiligt werden sollen, eine Aussage über den Anteil der einzelnen Autoren an der publizierten Arbeit. Unter den für den Preis vorgeschlagenen Autoren einer Arbeit muss der korrespondierende Autor der Arbeit sein. Falls dies nicht so ist, ist dies zu begründen.

Über die Preisvergabe entscheidet in geheimer Wahl das Preisrichterkollegium aus Vertretern der Deutschen und der Österreichischen Gesellschaft für Epileptologie sowie der Schweizerischen Epilepsie-Liga: Dr. med. Günter Krämer (Zürich; Vorsitz), Prof. Dr. med. Rudolf Korinthenberg (Freiburg), Prof. Dr. med. vet. Wolfgang Löscher (Hannover), Prof. Dr. med. Günther Sperk (Innsbruck).

Das Kollegium ist in seinen Entscheidungen frei und unabhängig. Seine Entscheidungen sind nicht anfechtbar. Der Rechtsweg ist ausgeschlossen. Die Preisverleihung nimmt der Vorsitzende des Kollegiums auf der Dreiländertagung in Wien (3.-6. Mai 2017) vor.

Mit freundlicher Unterstützung von UCB Pharma GmbH.

Laudatio Research Recognition Award 2016

Since 2004 the Swiss League against Epilepsy (SLAE) grants annually a Research Recognition Award (Forschungsförderungspreis) to foster experimental and clinical research in the field of epileptology. With a price money of CHF 25'000 the Research Recognition Award is the highest Award granted by the SLAE. It aims at fostering scientific projects exploring the causes of epilepsy, thereby also leading to novel treatments.

Projects executed either in Switzerland or abroad during a sabbatical by scientists or clinicians active in Switzerland are considered. The main criteria for granting the Research Recognition Award are outstanding scientific quality, the opportunity to study novel methods and techniques and to establish or consolidate international collaborations, as well as the overall feasibility of the project [1]. The previous awardees are listed in the following Table:

Awardees of the Research Recognition Award of the Swiss League against Epilepsy

Year	Awardees
2015	Christian Rummel, Bern
2014	Christophe Lamy, Fribourg
2013	Jean-Yves Chatton, Lausanne, and Benjamin Stöcklin, Basel
2012	Bernhard Schmitt, Zürich
2011	Johannes Lemke, Bern
2010	Pierre Lavenex, Fribourg
2009	Jean-Marc Fritschy and Michela Zattoni, Zürich
2008	Alexandre Datta, Basel
2007	Anne-Chantal Héritier Barras, Mary Kurian and Margitta Seeck, Genf
2006	Svenja Landweer, Basel, and Andrea Rossetti, Lausanne
2005	Reinhard Ganz and Matthias Schmutz, Zürich
2004	Susanne Müller, Zürich / San Francisco

The Research Commission of the SLAE consisting of Dr. Günter Krämer, Dr. Klaus Meyer, Professor Christoph Michel and Dr. Markus Schmutz granted the Research Recognition Award 2016 unanimously to

Prof. Jean-Marc Fritschy and **Tilo Gschwind** (University of Zürich) for their project

"Using closed-loop optogenetic intervention to investigate the mechanisms of epileptogenesis and its anti-epileptogenic effects in a mouse model of temporal lobe epilepsy"

Prof. Fritschy is one of the brightest shining stars in the field of preclinical epilepsy research in Switzerland

Jean-Marc Fritschy (left) and Tilo Gschwind

and beyond. The project of Prof. Fritschy and his main collaborator, Tilo Gschwind, makes use of a novel technology to investigate top priorities in epilepsy research, namely mechanisms of epileptogenesis, approaches to prevent epilepsy, neuronal networks, and temporal lobe epilepsy.

Several clinical features and neuropathological changes of temporal lobe epilepsy associated with hippocampal sclerosis can be reproduced experimentally upon intrahippocampal injection of kainic acid in adult mice, the animal model used in this project. The effect of kainic acid on hippocampal activity can be divided into three phases, starting with a non-convulsive status epilepticus, followed by a latent period of about 2 weeks, and finally a persistent chronic phase of spontaneously recurring non-convulsive seizures. The latent period is considered to represent the phase of epileptogenesis. It is characterized by the occurrence of low voltage spikes and spike-and-wave discharges. However, it has not been established so far whether such epileptiform activity is a mere manifestation of the functional alterations provoked by kainic acid or indeed the driver of epileptogenesis. The main goal of the awarded project is to investigate how epileptic discharges during the latent phase of the kainic acid model are involved in the formation of an epileptic focus.

This will be done by performing EEG recordings in kainic acid-injected mutant mice expressing light-operated channels, thus by using a novel technology: closed-loop optogenetics, an exciting field which through unprecedented specificity will allow new insights into neuronal networks. The technique applied here makes use of light sensitive proteins called opsins which are expressed in ion channels of specific neuronal populations in the hippocampus. Thus, the activity levels of such neuronal populations can be directly modulated through the delivery of light via implanted electrodes. Thereby light stimulation patterns designed to either mimick or block epileptic activity are used in an on-demand fashion, providing intervention only when needed. Hence, detected epileptic discharges can be modulated with instantaneous feedback. Towards this end Tilo Gschwind, in collaboration with the Stan-

ford University, greatly improved the seizure detection software which now enables detection of epileptic activity within 20 - 40 ms and thus allows immediate closed-loop intervention upon very short epileptogenic events.

By using this technique it will now be possible to perform targeted manipulations of neuronal function on-demand during the phase of epileptogenesis in the kainic acid model, which has never been done so far. This will allow to better understand how epileptic discharges during epileptogenesis are involved in the development of spontaneously recurring seizures and the formation of epileptic foci. In addition, improving online seizure detection will contribute to advance current clinical closed-loop approaches such as interventions using deep brain stimulation.

Prof. Fritschy was born in Geneva. He completed his academic studies with the Diploma and PhD degrees at the Universities of Geneva and Lausanne, respectively. In 1996 he habilitated at the Medical Faculty of the University of Zürich on the topic of $GABA_A$-receptor subtypes in brain and was awarded shortly thereafter with the «Georg Friedrich Götze-Preis». Since 2004 he is Professor of Pharmacology at the Institute of Pharmacology and Toxicology of the University of Zürich and since 2010 Director of the Neuroscience Center Zürich. Since last year Prof. Fritschy is also Deputy Dean of the Faculty of Medicine of the University of Zürich. He was and still is member of many scientific societies and editorial boards and published extensively in major journals.

In the name of the Research Commission and the SLAE I cordially congratulate Prof. Fritschy and Tilo Gschwind, on the Research Recognition Award 2016!

Markus Schmutz

1. *Krämer G, Mühlebach C. Epilepsie. Auszeichnungen und Preise, Stipendien und Stiftungen 2012/2013. Fünfte, aktualisierte und erweiterte Auflage. Bad Honnef: Hippocampus Verlag 2012: 111-113*

Mise au concours – Soutien de la recherche

Promotion de la recherche scientifique dans le domaine de l'épilepsie (surtout sous forme d'aide initiale) par la Ligue Suisse contre l'Epilepsie (Ligue contre l'Epilepsie)

La Ligue contre l'Epilepsie soutient les projets scientifiques dans le domaine de l'épileptologie par un montant total de

CHF 25'000.—

par an, la priorité étant accordée aux projets cherchant à élucider les causes et à mettre au point des traitements de l'épilepsie.

Aucune bourse ne sera octroyée pour la formation de base ou continue ou pour des séjours à l'étranger. En revanche, la prise en charge de frais de voyage et de séjour (sans salaire) est possible pour les séjours de courte durée (quelques semaines au maximum) lorsque ces séjours servent à apprendre des méthodes appliquées dans le cadre d'un projet bénéficiant de soutien en Suisse.

Si le requérant a déjà fait une demande de soutien ailleurs, il faut nous en informer en spécifiant où et avec quel résultat.

Délai de remise des demandes :

31 décembre 2016

Les demandes sont à adresser par voie électronique à strassmann@epi.ch.

Voir instructions : www.epi.ch/soutien_recherche

Ligue Suisse contre l'Epilepsie
Seefeldstrasse 84
8008 Zurich
Tél. 043 488 67 77
Fax 043 488 67 78
info@epi.ch

Mise au concours – Prix de la meilleure thèse

La Ligue Suisse contre l'Epilepsie (Ligue contre l'Epilepsie) décerne tous les 3 ans un prix d'un montant de

CHF 1'000.—

pour la meilleure dissertation dans le domaine de l'épileptologie.

Tous les domaines spécialisés et tous les groupes professionnels couvrant les disciplines fondamentales ou cliniques sont invités à soumettre leur candidature. Aucune limite d'âge n'a été fixée.

Le jury décernant le prix se compose de trois membres du comité directeur de la Ligue contre l'Epilepsie. Il peut être complété au besoin par des experts externes. La décision est prise par vote secret.

Si le requérant a déjà fait une demande de soutien ailleurs, il faut nous en informer en spécifiant où et avec quel résultat.

Le prix est toujours décerné l'année suivante dans le cadre de l'assemblée annuelle ou générale de la Ligue contre l'Epilepsie.

Les dossiers de candidature doivent parvenir au Secrétariat de la Ligue contre l'Epilepsie (Seefeldstrasse 84, 8008 Zurich) jusqu'au

31.12.2018

et comporter les pièces suivantes :

- cinq exemplaires de la dissertation achevée et remise au décanat,
- cinq exemplaires d'une prise de position du directeur de thèse (il peut par exemple s'agir de l'expertise concernant la dissertation).

JAHRESTAGUNG 2017

der Deutschen und Österreichischen Gesellschaften für Epileptologie und der Schweizerischen Epilepsie-Liga

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3.–6. MAI 2017 • Austria Center Vienna

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Riedelgasse 5 • 1130 Wien

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Charité-Universitätsmedizin Berlin
Campus Charité Mitte
Charitéplatz 1 • 10117 Berlin/DE

Tagungsort
Austria Center Vienna
Bruno-Kreisky-Platz 1
1220 Wien

Deadlines
Abstract-Deadline:
30. Oktober 2016

Frühbucherdeadline:
07. März 2017

Online-Anmeldung ab Oktober 2016 unter:
www.epilepsie-tagung.de

21.-28.1.2017 | Grindelwald
56. Fachtagung für Neurophysiologie und angrenzende Gebiete
Information: Prof. Dr. J. Mathis,
Neurologische Univ.-Klinik,
Inselspital, 3010 Bern, Sekretariat: Annemarie Zaugg,
Tel. 0041 / 31 / 6323054, Fax 0041 / 31 / 6329448,
e-mail: annemarie.zaugg@insel.ch,
www.neuro-alpin.net

16.-18.2.2017 | Luxor, Ägypten
4th East Mediterranean Epilepsy Congress
Information: ILAE/IBE Congress Secretariat,
7 Priory Office Park, Stillorgan Road,
Blackrock, Co. Dublin A94 FN26, Ireland,
Tel. 00353 / 1 / 2056720, Fax 00353 / 1 / 2056156,
e-mail: luxor@epilepsycongress.org

23.-26.3.2017 | Athen, Griechenland
11th World Congress on Controversies in Neurology (CONy)
Information: comtecMED, Medical Congresses,
53 Rothschild Boulevard,
PO Box 68, Tel Aviv, 6100001, Israel,
Tel. 00972 / 3 / 5666166, Fax 00972 / 3 / 5666177,
e-mail: Info@comtecmed.com,
www.comtecmed.com/Cony

6.-8.4.2017 | Salzburg, Österreich
6th London-Innsbruck Colloquium on Status Epilepticus and Acute Seizures
Information: pco tyrol congress, Ina Kaehler,
Rennweg 3, A 6020 Innsbruck, Österreich,
Tel. 0043 / 512 / 575600, Fax 0043 / 512 / 575607,
e-mail: se2015@cmi.at, www.statusepilepticus.eu

22.-27.4.2017 | Boston, USA
69th Annual Meeting of the American Academy of Neurology (AAN)
Information: AAN, 201 Chicago Avenue,
Minneapolis, MN 55415, USA,
Tel. 001 / 612 / 9286000,
www.aan.com/conferences/2017-annual-meeting

3.-6.5.2017 | Wien, Österreich
10. Dreiländertagung der Österreichischen und Deutschen Gesellschaften für Epileptologie und der Schweizerischen Epilepsie-Liga
Information: Epilepsie-Liga,
Seefeldstrasse 84, 8008 Zürich,
Tel. 0041 / 43 / 4886777, Fax 0041 / 43 / 4886778,
e-mail: info@epi.ch,
www.epi.ch

5.-7.5. 2017 | Dakar, Senegal
3rd African Epilepsy Congress
Information: ILAE/IBE Congress Secretariat,
7 Priory Office Park, Stillorgan Road,
Blackrock, Co. Dublin A94 FN26, Ireland,
Tel. 00353 / 1 / 2056720,
Fax 00353 / 1 / 2056156

24.-27.06.2017 | Amsterdam, Holland
3rd Congress of the European Academy of Neurology (EAN)
Information: ean Head Office,
Breite Gasse 4/7,
A 1070 Wien, Österreich,
e-mail: amsterdam2017@eaneurology.org,
www.eaneurology.org/amsterdam2017

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Epilepsien im ersten Lebensjahr

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Non-Epileptologic EEG Diagnostics

Nummer 4 – Dezember 2016
First Seizure: What's Next?