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The importance of semiological information based on epileptic seizure history

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ABSTRACT – Semiology is the backbone of any correct categorization of seizures, as epileptic or not, focal or bilateral, and is fundamental to elucidating how they are anatomically generated in the brain. An anatomical hypothesis derived from seizure history is the precondition for optimally designed ancillary studies. Without understanding seizure semiology, no rational therapy is possible. This article describes the semiological approach using patient history based on full use of patients' self-reports as well as descriptions by witnesses. Auras represent the subjective aspects of seizures and provide important semiological clues as observable signs, sometimes including rather precise direct anatomical information. Methods of extracting, facilitating and analysing self-reports including linguistic conversation analysis are presented in detail. It is highlighted that prodromes, seizure triggers and reflex epileptic mechanisms can provide crucial information for diagnostics and therapy. Special issues considering seizure semiology in children are discussed in a separate section. Other sections are dedicated to the two most important issues of differential diagnosis: how to distinguish (1) focal from "generalized" epilepsies, particularly when focal seizure phenomena appear in a bilateral epilepsy; and (2) epileptic from a series of non-epileptic events.

Key words: subjective seizure symptoms, generalized epilepsy misnomer, conversation analysis, aura, prodrome, seizure triggers

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Semiology is the knowledge of the anatomical significance of signs and symptoms, regarding both onset and development of seizures. This article describes the semiological approach using patient history based on full use of patients' self-reports as well as descriptions by witnesses also addressing several learning objectives (*Box 1*) of the ILAE curriculum (Blümcke *et al.*, 2019).

It is our first clinical approach to finding out if a patient's seizures come from a local lesion or are generated in a bilateral (but not necessarily symmetrical) functional-anatomic system. This knowledge is of paramount importance both for the further diagnostic process and for our therapeutic approaches. On June 22, 1886, Victor Horsley and Hughlings Jackson decided to operate on a patient, for the first time in history, exclusively guided by seizure semiology, and found a tuberculoma at the predicted site. In their report, the term "epileptogenous focus" also appears for the first time (Horsley, 1886). Today, we can fortunately base our surgical interventions upon much more certain and precise procedures but the first step must still be the formulation of an anatomical hypothesis derived from semiological analysis. This starts with the information we can extract from patient history.

There are two different sources of patient history: the patients themselves and witnesses. This highlights one of the fundamental dilemmas of epilepsy, that seizures consist of objective, visible signs and of subjective, invisible symptoms. The visible signs may only be known to witnesses -although some may also be reportable by patients themselves. The invisible symptoms are only known to the patients.

Even if the importance of seizure descriptions in the characterization and management of seizure disorders is widely acknowledged, there has only been little research on how to optimize the process of taking and interpreting the history from patients and witnesses. Especially since the introduction of video-electroencephalographic monitoring into routine care in the 1970s and 1980s, phenomenological research on seizure disorders has predominantly focused on the correlation of observable physiological changes with visible or externally measurable seizure manifestations. In contrast, the subjective symptomatology of seizures has been relatively neglected, although, in terms of seizure semiology, the subjective domain is just as important as the objective one. Some patients are keenly aware of this and insist on being experts on the "inside" of seizures (Wolf, 2020). However, they are not necessarily expert at describing their experiences, and may need help which professional history-taking can provide.

Analysis of patient self-reports

The reasons for the relative dearth of research into subjective seizure experiences may not be limited to the fact that visible seizure manifestations are easier to capture, objectify, analyse and report relative to subjective symptoms, especially when these involve loss of awareness. Other reasons may also be related to the fact that, in order to be available for analysis, symptoms must have been noticed, stored for subsequent recall, remembered, describable and shared with the clinician. Each of these steps can be a significant hurdle, and the fact that many (if not most) seizure symptoms seem to differ from experiences we consider "normal" (and as something that we can therefore easily reference in interaction with others) means that the extraction and interpretation of subjective seizure symptoms for diagnostic categorization and treatment purposes represents a considerable challenge.

Simple questionnaires are a tempting method to elicit subjective data. Brief questionnaires based on $\leq$10 yes/no questions have been shown to differentiate between tonic-clonic seizures and syncope with over 90% accuracy (Hoefnagels *et al.*, 1991; Sheldon *et al.*, 2002). Modelling of a more extensive questionnaire of this nature with over 30 such questions has indicated that it should be possible to differentiate more widely (but with similar levels of accuracy) between patients with syncope on the one hand and those with a wide range of epileptic and (psychogenic) non-epileptic seizure disorders (PNES) on the other (Wardrope *et al.*, in press). However, the distinction between epileptic and non-epileptic seizures on the basis of symptom-based questionnaires has proved much more difficult, typically requiring even more questions and only achieving about 80% accuracy (Syed *et al.*, 2009; Reuber *et al.*, 2016). Recent classification approaches suggest that better classification outcomes may be achievable with machine learning approaches (which can, for instance, take account of the fact that the presence of one particular symptom -*e.g.* "my heart was racing" could point to a diagnosis of syncope or non-epileptic seizure depending on whether it is reported in conjunction with "my vision went blurry" or "I thought I was going to die") (Wardrope *et al.*, in press).

In any case, methods which focus entirely on *which* symptoms patients report do not benefit from an important additional source of diagnostic information, particularly relevant to the distinction between epileptic and non-epileptic seizure disorders and the subdifferentiation of different types of epileptic seizures: *how* patients communicate their experiences. A number of studies used Conversation Analysis to describe the typical communication styles of patients with epilepsy and those with PNES.

Subsequent studies demonstrated that clinicians can use this approach in routine practice and detect diagnostic interactional pointers (Jenkins and Reuber, 2014; Jenkins *et al.,* 2016). Patients with epilepsy have been shown to focus on their subjective seizure symptoms without further prompting. When asked to do so, they elaborate and provide more detailed seizure accounts. Seizure descriptions are characterized by formulation effort (including reformulations, hesitations, restarts). In contrast, patients with PNES tend to focus on the situations in which their seizures have occurred or the consequences of their seizures rather than subjective symptoms. Symptoms are named but not elaborated, even with prompting. Patients resist a focus on seizure symptoms or on particularly memorable individual seizure episodes. Studies with German, English, Italian and Chinese speaking patients have yielded very similar findings, suggesting that the interactional and linguistic phenomena described are not culture-bound but related to the differences in the underlying seizure experiences and pathology (Schwabe *et al.,* 2008; Reuber *et al.,* 2009; Cornaggia *et al.,* 2012; Yuan *et al.,* 2017). Importantly, patients' diagnostically useful communication behaviour is only observable if patients are given enough conversational space to display it. This means that clinicians wishing to use these diagnostic pointers will need to adopt an unusually passive conversational style, especially in the first half of their history taking procedure. They should use open questions giving patients a wide range of response options and let patients respond without early interruption. It has been demonstrated that the mode of questioning required differs significantly from that in routine practice for many clinicians (Ekberg and Reuber, 2015), however, clinicians can learn to change their habits and use open questions in routine practice without extending the length of the history taking procedure (Jenkins *et al.,* 2015).

While open questions are essential to allow patients to highlight those issues most relevant to them and to elicit diagnostically relevant information on patients' conversational styles, there is some evidence that further prompting with a range of possible subjective symptoms can be useful -for instance by asking patients to think about fleeting subjective phenomena which they may not have considered relevant but which could make the difference between a diagnosis of focal versus generalized or unclassifiable epilepsy (Devinsky *et al.,* 1991).

As mentioned above, in order to achieve an optimal interpretational yield of data obtainable by history taking, clinicians will need to combine factual information about seizure symptoms provided by the patient and features of the patient's interactional behaviour with additional data provided by witnesses, especially when seizures involve possible impairment of consciousness. The differential diagnostic accuracy of series of symptom-based questions increases significantly when responses to additional questions about seizure observations are available from witnesses (Chen *et al.,* 2019). Conversely, failure to question witnesses has been identified as one of the key causes of misdiagnoses (Smith *et al.,* 1999). However, in health services in which appointment times are limited, the contributions of witnesses to the history-taking process is likely to reduce the conversation space available to patients, potentially diminishing the opportunity for patients to fully communicate their subjective seizure experiences (Robson *et al.,* 2013). This means that, during the history-taking process, clinicians have to strike a careful balance; while actively managing the contributions from third parties (for instance, the clinician explains at the outset that he/she is very keen to hear from the accompanying person but that it is important to find out what exactly the patient him/herself can say about their seizure first), it is important to seek additional information from seizure witnesses whenever available. Witnesses may, for instance, be aware of behavioural changes prior to seizures that patients had not associated with their seizures, but that may allow the formulation of a more precise seizure diagnosis.

Aura

The aura is at the centre of the subjective domain - *i.e.* within the patient's field of expertise. This term is one of the oldest used in epilepsy and other paroxysmal disorders (*e.g.* migraine, dissociative seizures) and refers to subjective perceptions at seizure onset. Sometimes understood as a "warning" preceding a seizure, epileptic auras in fact represent the first seizure symptoms. Isolated auras not followed by other signs and symptoms are synonymous with "simple partial seizures" (Commission on Classification and Terminology of the International League Against Epilepsy, 1981) or "focal aware seizures" (Fisher *et al.,* 2017a, 2017b). However, the detailed subdifferentiation of subjective ictal experiences of 1981 was, in 2017, reduced to a simplistic distinction between cognitive, emotional or sensory phenomena. This gives rather insufficient weight to their great semiological significance as indicators of the anatomical seizure onset. This information must not be lost but carefully established in cooperation with the patients who usually know that their seizure symptoms occur "with military precision" in an order that does not change (Wolf, 2020) The associations, however, are by no means always immediately obvious. Whereas the striking violent activity

of a patient's hypermotor seizures, as experienced by patients, witnesses and health personnel, may point to the frontal lobe, this may be the result of seizure spread derived from a brief, unimpressive visual aura indicating an occipital focus as the true anatomical origin.

Detailed accounts of auras are meaningful for diagnostic purposes (epileptic vs non-epileptic, focal vs. generalized, anatomical site of seizure onset) as well as patient-oriented therapeutic approaches such as non-pharmacological treatment strategies. However, it should be remembered that seizures may originate in non-eloquent areas and that auras may occur not only with focal but also with generalized seizures (see below).

Auras are, by definition, personal phenomena which may conjure fear due to their bizarre nature. Patients may become afraid that they could be developing a psychiatric condition and relieved when their symptoms are recognized as epileptic. In addition, the recognition of an aura may provide opportunities to counteract perceptions of helplessness as they allow patients to prepare for a seizure by making themselves safe or seeking assistance. Some are able to apply interventions to arrest the emerging seizure activity, in other words, stop seizure propagation. In the course of treatment, symptoms reflecting seizure spread may disappear while subtle initial symptoms persist and become more noticeable. However, patients may still be unaware of their significance and fail to report them. Consequently, if termination of treatment is attempted in the belief that they have long been seizure-free, they are likely to suffer a relapse.

The following techniques can help to obtain a detailed and comprehensive aura description from patients with epilepsy:Start with open-ended questions, be empathic and patient. Early interruptions of the patient should be avoided and pauses tolerated. The patients' choice of initial focus and the way in which they describe their symptoms can be diagnostically important and allow patients to try and formulate experiences which the doctor would be unlikely to ask about. Interruptions may undermine the patient's confidence that these experiences can be shared with the doctor.

– Use lay terms. If patients start to use technical terms, inquire what exactly they mean by them.

– Patients may refer to their typical aura experience using general expressions like "dizziness" or some personal terms which may be misleading. Always encourage patients to describe their experience as precisely as possible. Difficulty with this description is a diagnostic clue by itself because indescribability is a characteristic feature of many epileptic auras. Nonetheless, when properly guided, patients with epilepsy tend to provide coherent accounts of individual seizures (Schwabe *et al*., 2008).

– Sometimes, patients report losing consciousness without an aura. However, they may remember that they somehow unconsciously prepared themselves for a seizure. Listen out for statements such as "how lucky that I had sat down just before the seizure started" or "how lucky that I had taken off my glasses". Such preparations may indicate that patients had a premonition that they cannot recall after the seizure and are therefore as yet unaware of.

– Auras may be rather complex. In terms of providing anatomical insight into the seizure onset zone, the first part of the sequence of perceptions is the most important, but the patient may be more impressed by another symptom and report this in the first place. Explain why the sequence is diagnostically important and insist on a focus on the very first perception in order to counter this tendency. However, even when a fully cooperative patient is fully aware of the importance of the sequence of symptoms, the first intimation of the aura may be so subtle that it remains unnoticed and unreportable for a long time.

– Guide patients towards a specific memory of a seizure that is particularly vivid and well-remembered. This could, for instance, be the first, worst or the most recent seizure.

– Focus on this specific memory. The exploration of immediate circumstances (*e.g.* time of day, previous activity, body position, *etc*.) may prompt patients to re-experience this specific memory and therefore help to elicit additional details. A particular interview technique to help patients elicit memories has been elaborated by Petitmengin *et al*. (2006).

– Once patients vividly remember an aura (indicated by use of present tense and gestures), closed questions can be used to elicit more detailed descriptions of the memory.

– Probe sensory perceptions, *e.g.* sense of smell, taste or hearing *etc*. (see *table 1* for a list of the anatomical meanings for certain aura symptoms).

– Then zoom in on perceived sensations, *e.g.* somatosensory: where does it begin (*e.g.* distally? proximally?), where to and how fast does it spread?

– If patients use gestures rather than words, ask them to try and put into words which re-lived sensation prompted them to use these gestures.

– Patients may use colours to describe non-visual sensations or quite bizarre metaphors to describe feeling states. In contrast, a patient reporting to be "beside himself" may not be using a metaphor but describing a phenomenon of autoscopy and may be able to tell on which side his "double" is standing (usually on the left) which would be unexpected if the phrase was intended metaphorically.

– Inquire whether seizures always progress to impaired awareness or not. Did a patient do something differently when a seizure did not progress?

Table 1. Certain auras and their neuroanatomical localization (modified from Blume *et al*., 2001).

Aura phenomenon	Probable localization of epileptic activity
Affective, *e.g*. fear, depression, joy Anxiety (sudden, brief, intense, without contents)	Temporal Amygdala
Auditory, *e.g*. sounds, noises or single tones Music	Heschl's gyrus, if directed lateralizing to opposite side Temporal
Autoscopy, *i.e*. perceiving a double of oneself	Parietal, probably right
Cephalic, *i.e*. sensation in the head, *e.g*. light-headedness	Frontal
Dyscognitive, *i.e*. disturbance of components of cognition, *e.g*. impaired understanding, scattered thinking, dream-like states	Temporal
Epigastric, *i.e*. abdominal sensation that may rise to the chest or throat	Temporal (mesial)
Experiental (recall of certain old memories) Forced thinking	Temporal Frontal, probably left
Gustatory, *e.g*. bitter, acidic or metallic taste	Temporal
Hallucinatory, *i.e*. composite perceptions, *e.g*. "hearing" and/or "seeing" people Hemineglect	Depends on involved perceptions Opposite parietal lobe
Limb pain Mnemonic, *i.e*. ictal dysmnesia, *e.g*. *déjà-vu* (familiarity) or *jamais-vu* (unfamiliarity)	Opposite postcentral gyrus, parietal operculum Temporal
Olfactory, usually disagreeable odour	Temporal
Somatosensory	Parietal, lateralizing to opposite side
Visual, *e.g*. flickering lights or amaurosis	Occipital, lateralizing if directed

Bringing up this question may make patients aware of spontaneous seizure interruption techniques and one may be able to help patients develop this as a non-pharmacological treatment strategy. Seizure interruption should not necessarily be seen as an alternative treatment (unless patients insist that they do not wish to take medication) but as part of a comprehensive therapeutic approach. This might lead to an increased sense of control and self-efficacy in those able to apply these techniques successfully (Lohse *et al*., 2015; Michaelis *et al*., 2018).

Prodromes: symptoms habitually preceding a seizure by more than a few minutes are called prodromes (Alving and Beniczky, 2013). Their pathology often remains unclear but they may represent minor epileptic activity, focal (aura continua) or generalized (series of absences or "phantom absences"). Their correct identification may provide the key to a successful therapy as in our Case 1 (*appendix 1*).

Reflex epileptic mechanisms

Occasionally, patients may mistake auras for seizure precipitants and vice versa. Among precipitating factors, reflex epileptic mechanisms may contribute significantly to the semiological analysis of seizures.

Patients with juvenile myoclonic epilepsy (JME) often report myocloni in one hand, usually the dominant hand or the one which is active during an often complex task. These praxis-induced local reflex myoclonias (Yacubian and Wolf, 2014) are often misinterpreted as signs of focal epilepsy. Movement-induced focal reflex seizures also exist but they are fully developed focal motor or sensorimotor, usually tonic seizures in the active limb rather than local myocloni. The triggering movements may be rather simple; they are specific and uniform. Similar seizures can be precipitated by touch of a trigger zone (Mameniškienė and Wolf, 2018).

Seizures precipitated by music (certain styles, composers or pieces) are prima vista seizures of the temporal lobe, most likely the right.
Seizures in the presence of environmental flickering lights such as a glittering water surface, stroboscopic lights in a disco or on television indicate photosensitivity which is closely related to idiopathic generalized epilepsies (IGEs). Patients exclusively experiencing provoked seizures may be treated by stimulus avoidance or attenuation alone, without recourse to drugs.

Descriptions by witnesses

While patients may present following an unequivocal epileptic seizure, frequently, the event could more accurately be described as a "spell" of uncertain nature in which a seizure is one of many possibilities. Physicians seldom witness a seizure, and their diagnosis relies heavily on the description of its subjective symptoms by the patient and of its objective signs by a witness. The physician carries the responsibility of taking the appropriate history to extract useful information (Muayqil *et al*., 2018). A brief explanation of the semiology of the main paroxysmal events may facilitate patient and witness descriptions. When questioning them, imprecise terms such as "convulsion" must be clarified, with attention paid to specific features such as body stiffening, limb jerking, the order in which they occurred, and their duration. The objective manifestations of focal seizures, highly predicted by the region of the cortex involved, are more clearly described by a witness than by patients themselves (Nowacki and Jirsch, 2017). Non-specialists and trainees may be more concrete in their history taking technique, which creates a challenge in obtaining diagnostic information given the wide variability in how witnesses report their experiences (Muayqil *et al*., 2018). An accurate interpretation of history is the most critical step in evaluation of paroxysmal events, and it takes years of experience for a physician to acquire the skills and knowledge to differentiate between relevant and non-relevant information.
A reliable witness account is essential to define event semiology since a patient suspected of having suffered a seizure is frequently unreliable due to impairment of awareness or even unconsciousness during the event (Nowacki and Jirsch, 2017). Witnesses describe the first seizure as frightening, disturbing, and bizarre (Aydemir *et al*., 2009). The task of reporting the details of semiology usually falls on the shoulders of a bewildered bystander, and when it involves a first-time seizure victim, the witness is likely to be a first-timer as well (Muayqil *et al*., 2018). While information from witnesses (especially those who have seen several of the patient's episodes) can be important for the diagnostic process, a number of studies have demonstrated that bystanders are often only able to make a relatively modest contribution to the description of the semiology of events. They have also been shown to be more fallible in providing information about the event semiology than patients self-reporting symptoms, signs, and historical data (Bianchi *et al*., 2019).
Due to the inaccuracy and incomplete manner in which the witness may describe the events leading to errors in diagnosis and subsequent treatment, video-recorded seizures have been considered a valuable tool to improve diagnostic accuracy and reduce mistakes (Rugg-Gunn *et al*., 2001). While some considered that semiology of video-recorded events in epilepsy monitoring units (EMU), such as reflex syncope and generalized tonic-clonic seizures (GTCS), should be interpreted with caution because salient features are frequently overlooked or inaccurately recalled even by psychology students (Thijs *et al*., 2008), others considered that first-time witnesses of seizures, independent of gender and educational level, are able to identify important semiological elements more frequently than would be expected by chance alone, and are more likely to associate generalized semiology with seizures or epilepsy than focal signs (Muayqil *et al*., 2018).
On the other hand, almost every patient today owns half an epilepsy monitoring unit in the shape of a cell phone, and their increasing use has allowed clinicians to analyse informal video recordings of seizures. Their diagnostic value cannot be directly compared with video recordings from the EMU as the seizure onset is rarely captured, and important aspects of the seizure semiology may not have been recorded. The diagnostic value of other (potentially helpful) clues in informal recordings, such as interactions between the patient and caregivers, has not been studied yet (Kunze and Reuber, 2018). However, studies using home videos on smartphones have shown sensitivity as high as 95.4% (95% CI: 87.2% to 99.1%), specificity of 97.5 % (95% CI: 94.3% to 99.2%) with positive and negative predictive values of 92.65% (95% CI: 84.1% to 96.8%) and 98.5 % (95% CI: 95.6% to 99.5%), respectively, in differentiating psychogenic non-epileptic seizures from epileptic seizures and other physiological events (Ramanujam *et al*., 2018). Hopefully, soon, at least for patients with recurrent events, standardization of a testing protocol to be applied in real life will greatly help the contribution of witnesses in clinical diagnosis.

Special issues in children

Seizures in children are semiologically different when compared with adults, especially in infancy and early

childhood (Fogarasi *et al*., 2001, 2002). Multiple factors might contribute to this. The developing brain is only able to express a more limited repertoire of signs and symptoms due to its peculiar neurobiology. The movements are usually very simple and proximal in infancy and may not exhibit the classic pattern of evolution seen in later life. In addition, semiological expression in children might dynamically change according to age and developmental status, even in the case of a well-defined focal structural lesion.

Many childhood epileptic syndromes have highly characteristic semiological features. West syndrome is defined by the presence of epileptic spams. Further semiological characterization of spasms into flexor, extensor or mixed is usually erratic and does not have any management or prognostic implications. However, asymmetric spasms may point towards a focal structural aetiology. Clustering of spasms during the sleep-awake transition phase is a highly characteristic finding in West syndrome (Fusco *et al*., 2019).

Many other epileptic encephalopathies may show multiple seizure types, however, there might be a defining seizure type for each syndrome. Tonic seizures in Lennox-Gastaut syndrome is a typical example. Panayiotopoulos syndrome may present with autonomic seizures, and in benign childhood epilepsy with centrotemporal spikes, nocturnal oromotor seizures are typical. In absence epilepsies, special care should be emphasized to elicit the history of other coexistent seizure types, which might have implications for management and prognosis. Some of the associated clinical features, such as neck myoclonia, may point towards treatment resistance and prolonged clinical course.

Semiological characterization of seizures may also have etiological and prognostic implications in children. Myoclonic seizures may usually indicate metabolic/genetic aetiology and may be an initial symptom of a neuroregressive syndrome (Michelucci *et al*., 2019). A prolonged hemiclonic seizure is the defining seizure type of Dravet syndrome. Tonic seizures in early infancy are usually seen in diffuse structural malformations or in certain genetic syndromes. Migrating focal seizures in infancy may indicate an underlying genetic aetiology, classically *KCNT1* mutation. Tay-Sachs disease usually presents with startle myoclonus and developmental regression in infancy. In the neonates, focal clonic seizures may be highly suggestive of a structural brain lesion of vascular origin.

Extraction of semiological information in children is very challenging, especially in infancy and early childhood. Many factors might contribute to this difficulty. A proper history from the parents or caregivers is the most important variable which affects both the ascertainment of the epileptic nature of the event and further characterization of the seizure type and syndrome.

Young children may not be able to verbally express the exact character of the sensory aura. Even older children may find it difficult to describe them. Often, anxious parents may not be able to exactly recollect the semiological details, especially ictal evolution. This might lead to both under- and over-diagnosis of seizures. In small children with severe developmental disabilities, dyskinesias are most often confused with epileptic seizures by families and primary caregivers. There is a real risk for inappropriate usage of AEDs in this clinical scenario. History taking becomes much more complicated in children with cognitive difficulties, ADHD or autistic behaviours, especially if they are institutionalized. It becomes almost impossible to historically differentiate episodic motor stereotypies in children with developmental, cognitive and behavioural difficulties from epileptic seizures, especially if they have pre-existing epilepsy or abnormalities on their interictal EEG. On the other hand, negative motor phenomena and subtle spasms in infancy and young children are most often missed by parents as a manifestation of epileptic seizures. Atonic seizures will be apparent only when the child is erect in the sitting or standing position. In the supine state, these events may be missed or at best regarded as a motor arrest. There are several reports of children with absence seizures misdiagnosed as an inattentive type of ADHD (Auvin *et al*., 2018). In such cases, an ictal EEG recording for confirmation of the diagnosis is therefore worthwhile.

Distinguishing focal from "generalized" seizures and epilepsies

One of the most important tasks in epilepsy diagnosis is to distinguish focal from "generalized" epilepsies (GE), especially because they are treated differently. Sodium channel blockers are drugs of first choice for focal epilepsies but may cause seizure exacerbation in some IGEs whereas resective neurosurgery is only an option in pharmacoresistant focal epilepsies but never in "generalized" epilepsies. The distinction is often a complex task in which the seizure type is only one of several aspects. It is true that generalized seizures defined by a quasi-simultaneous bihemispheric onset do not occur in focal epilepsies, but it is by no means always easy to tell from the history if the seizure onset is bilaterally simultaneous. This is especially true for bilateral tonic-clonic seizures (BTCS) occurring in sleep where an aura may be experienced as a dream, and even a clear focal onset may remain unobserved by either patient or any witnesses. However, the very fact that the seizure occurs in sleep may raise

the suspicion of a focal onset whereas BTCS in the awakening phase are predominantly "generalized".

In contrast, features suggestive of local epileptic activity are by no means uncommon in GE. GEs are system disorders of the brain (Avanzini *et al.*, 2012) in which local epileptic responses of an upregulated system may, *e.g.* occur as reflex seizures, especially in response to sensory and proprioceptive stimulation (Wolf *et al.*, 2015; Baykan and Wolf, 2017).

Various focal symptoms in presumably generalized seizures have been described including: focal tonic stiffening; focal clonic or myoclonic jerks/twitches; focal weakness; oroalimentary, manual and pedalling automatisms (gestural or hyperkinetic/circling), lateralized or not; eye version, *etc.*, usually regarded as characteristic for focal seizures (Seneviratne *et al.*, 2015). Somatosensory, specific sensory (auditory, visual, olfactory, gustatory symptoms), and autonomic or psychic symptoms, usually as aura, were reported by more than 50% patients with "idiopathic generalized epilepsies" in two recent studies (Dugan *et al.*, 2014; Seneviratne *et al.*, 2015). However, the aura defined as the earliest subjective ictal experience, is, like the above-mentioned lateralized clinical features, conventionally considered an indication of focal seizure onset (Dugan *et al.*, 2014). Symptoms suggestive of receptive or expressive aphasia indicating clearly lateralized, *i.e.* dominant, hemispheric origin, were the most frequent aura symptom reported in association with both GTCS or absence and myoclonic seizures in two of the best defined IGE syndromes -juvenile absence and myoclonic epilepsies (Dugan *et al.*, 2014; Seneviratne *et al.*, 2015).

Even if these reports lack a critical evaluation of the origin of such symptoms, some of which may be produced by unobserved absences or myocloni heralding BTCS, there is little doubt that local seizure activity can occur in "generalized" seizures. Other semiological, presumably focal onset features, such as the figure 4 sign, hemiconvulsions, fencing posture, unilateral dystonia, postictal nose wiping, and asymmetric ending of GTCS have also been reported in IGE (Seneviratne *et al.*, 2015). Occasionally, seizures with bilateral onset in genetic as well as structural/metabolic forms of epilepsy may present focal evolution with semiology suggestive of focal seizures, thus presenting an additional pitfall in the diagnosis and treatment of patients with (usually refractory) IGE (Linane *et al.*, 2016).

Certainly, there are key symptoms and signs that are known to be associated with common seizure types, but obviously they cannot be matched in one-to-one relationships with a particular seizure type, because some symptoms appear in more than one seizure type. Behavioural arrest, for example, occurs in both absence seizures and what is now termed "focal impaired awareness seizures" (Fisher *et al.*, 2017a, 2017b). An alternatively suggested term "dialeptic" was coined to describe ictal alteration of consciousness, independent of the correlating ictal EEG and the syndromic context (Lüders *et al.*, 1998; 2019). Other semiological and clinical features are needed to help to differentiate between focal and generalized seizures consisting mainly of alteration of consciousness when the epilepsy diagnosis is established, though again they are not invariably consistent (*e.g.* blinking being more frequent in "generalized" seizures and longer seizure duration in focal seizures) (Baykan *et al.*, 2011).

To decide whether a seizure starting with some focal features indicates a focal epilepsy, its further development as well as its context need to be considered and can to some extent be extracted from history. The development of a seizure in focal epilepsy is likely to express its individual propagation through the brain, whereas in "generalized" epilepsy, any local onset will be followed by the generic semiology characteristic of the respective syndrome. Likewise, if initial deviation of eyes and head, or a photome in one visual hemifield, alternates between sides, a focal epilepsy is unlikely. A child who suffers focal motor seizures of the face and arm with onset in sleep, on alternating sides, does not have an epileptogenic focus and will never be a surgical candidate.

A patient who experiences a series of arrhythmic bilateral myoclonic jerks in the arms in the morning after nights with insufficient sleep is highly likely to have juvenile myoclonic epilepsy. A child of school age from a family in which some members have absence epilepsy and whose school performance is below expectation because their attention keeps slipping during lessons, most probably has childhood absence epilepsy. A young woman who reports seizures in which the fingers of her right hand become numb and start twitching, followed by a spread up the right arm and sometimes involving the right half of the body certainly has no generalized epilepsy but an epileptic focus in the hand field of the left pericentral cortex. It follows that the radiologist who performs her MRI brain scan needs to be told to look at this region attentively in order not to miss any pathological signs.

More recent research has substantially changed our views on the pathophysiological mechanisms of epilepsy by showing that all epilepsies are, probably, network diseases (Fisher *et al.*, 2017a, 2017b). Therefore, some authors consider the dichotomy of focal versus generalized outdated and believe in a "continuum" between focal and "generalized" epilepsies (Rodin, 2009; Lüders *et al.*, 2009). However, not all ictogenic networks necessarily belong to the same type, and the distinction between focal and generalized is of major practical value because of the direct impact on diagnostic and management decisions

Table 2. Important differential diagnoses of epileptic seizures.

Psychogenic events
Syncope
Migraines
Hypoglycaemia
Panic/anxiety attacks
Paroxysmal movement disorders
Acute dystonic reactions, oculogyric crisis
Hemifacial spasms
Parasomnias (REM and non-REM)
Hypnic jerks (sleep starts)
Transient ischaemic attacks (TIA)
Transient global amnesia (TGA) vs transient epileptic amnesia

(Lüders *et al.,* 2009). At the beginning of evaluation and management of every epilepsy patient, we still start with analysis and description of seizure semiology, considering both onset and evolution. Considering, in addition, all syndromic features apparent from history, we will end up, in the majority of cases, with at least an educated guess of whether we are dealing with a "generalized" or focal epilepsy. In the latter case, it is our task to form an anatomical hypothesis and direct the subsequent ancillary investigations to ensure an optimal result (Case 2, *appendix 1*).

Differentiating epileptic and non-epileptic events

The differential diagnosis of seizures (*table 2*) is broad (Benbadis, 2007, 2009), and detailed description of the events, by both the patient and the witnesses, is key. Does the patient have a warning? Is the patient aware during the event? How long is the event? Are there triggers? To some extent, this has already been discussed in the first section of this article, however, further details are outlined below.

Psychogenic non-epileptic seizures (PNES)

A number of "red flags" can raise a suspicion that seizures may be psychogenic rather than epileptic. The circumstances in which attacks occur can be very helpful. PNES tend to occur in the presence of an audience, and occurrence in the physician's office or waiting room is particularly suggestive (Benbadis, 2005). Triggers that would be highly unusual in epilepsy such as getting upset, certain foods, a full moon, pain medication and others are suggestive of PNES rather than epilepsy. PNES tend not to occur in sleep. A history of "fashionable" (likely psychogenic) diagnoses, such as fibromyalgia, unexplained "chronic pain", or chronic fatigue syndrome, is strongly associated with PNES (Benbadis, 2005). Similarly, a florid review of systems (especially written lists of symptoms or diagnoses) suggests somatization (Benbadis, 2005). The psychosocial history, including associated psychiatric diagnoses, may also raise a suspicion of PNES. The examination, paying particular attention to mental status evaluation, including the general demeanor, appropriate level of concern, overdramatization, or histrionic features, can be very telling. Lastly, the examination may uncover demonstrative behaviours such as give-way weakness or tight roping. Performing the examination can itself act as an inducer in suggestible patients, making a spell more likely to occur during the history taking or examination.

Other symptoms when present argue in favour of epileptic seizures. These include significant postictal confusion, incontinence, occurrence out of sleep, and most important, significant injury, although injuries may be reported by patients with PNES. In particular, tongue biting when present is highly specific for GTCS (Benbadis *et al.,* 1995) but only if it is lateral (Brigo *et al.,* 2012). Signs and symptoms that make perfect anatomical sense indicate epilepsy.

Syncope

Syncope is another important condition misdiagnosed as epilepsy. One reason is the frequency with which syncopal events are "convulsive". While conventional teaching states that syncopal episodes are limp, motionless events, they in fact frequently involve brief body jerks (Lempert *et al.,* 1994). Motor symptoms associated with syncope are clonic- or myoclonic-like, tend to last only a few seconds, and terminate once the patient is horizontal, in sharp contrast to the typical GTCS duration of 30 to 90 seconds. Based on history alone, without an accurate description, the distinction between syncope and seizures can, at times, be difficult. A helpful feature is the circumstance of attacks, since the most common mechanism for syncope (vasovagal response) is often triggered by readily identifiable precipitants (*e.g.* pain such as inflicted by medical procedures, emotions, cough, micturition, hot environment, and prolonged standing, exercise). Other historical features that favour syncope include presyncopal prodromes (vertigo, dizziness, light-headedness, nausea, and chest pain) as well as age and a history of cardiovascular disease. Historical features that favour epilepsy include biting, head turning, posturing, urinary incontinence, cyanosis, *déjà-vu* aura, and postictal confusion (Sheldon *et al.,* 2002).

Migraines

Complicated migraines and migraine auras can cause positive focal symptoms in all five senses and as such may mimic focal aware seizures or epileptic auras. In addition, both migraine and seizure focal symptoms "march." The key differentiating factor is the time course: migraine symptoms tend to evolve in minutes while seizure symptoms evolve in seconds. Usually associated symptoms (migrainous headache or more obvious seizure symptoms) will make the diagnosis easy.

Other conditions

Hypoglycaemia rarely causes complete loss of consciousness. When it does, it is most likely to resemble syncope and is preceded by florid prodromes of hunger, weakness, tremulousness, malaise, and abnormal behaviours. Hypoglycaemia typically occurs in reasonably obvious settings (*e.g.* diabetic patients on insulin or oral antihyperglycemics). Symptomatic hypoglycaemica can also trigger convulsive seizures although this is -admittedly- rare (but overdiagnosed!).

Panic attacks are paroxysmal manifestations of anxiety or panic disorder and may be mistaken for seizures (Merritt, 2000). Panic attacks include intense autonomic, especially cardiovascular and respiratory, symptoms. Abrupt and intense fear is accompanied by at least four of the following symptoms: palpitations, diaphoresis, tremulousness or shaking, shortness of breath or sensation of choking, chest discomfort, nausea or abdominal discomfort, dizziness or lightheadedness, derealization or depersonalization, fear of losing control, fear of dying, paraesthesias, and chills or hot flashes. The symptoms typically peak within 10 minutes. Panic disorder often coexists with other manifestations of anxiety such as agoraphobia and social phobia.

Some ***paroxysmal movement disorders*** such as paroxysmal choreoathetosis can mimic seizures.

Acute dystonic reactions, including oculogyric crises, are caused by dopamine receptor blockers such as antipsychotics (neuroleptics including atypical ones) and antiemetics, although other drugs can be involved. They typically occur within one to four days of beginning the medication and are characterized by torsion/twisting movements affecting the cranial, pharyngeal, and cervical muscles. The typical attack lasts for one to two hours, during which the abnormal movement occurs repetitively for seconds to minutes.

Hemifacial spasms (HFS) may superficially resemble a facial clonic seizure, but are a chronic progressive (rather than paroxysmal) disorder. While facial motor seizures typically involve the perioral area, the unilateral facial twitching associated with HFS typically affects the periorbital muscles first and then spreads to other (ipsilateral) facial muscles over a period of months to years. Over time or with exacerbations, the clonic movements can result in a sustained tonic contraction causing forceful (unilateral) eyelid closure.

Parasomnias are the most likely sleep disorders to present a diagnostic challenge since they are, by definition, short-lived paroxysmal behaviours that occur out of sleep. In particular, the non-REM parasomnias (night terrors, sleepwalking, and confusional arousals) can resemble seizures since they include complex behaviours and some degree of unresponsiveness and amnesia for the event. The non-REM parasomnias are most common between ages four and 12 years, and night terrors are particularly common. They are often familial and may be worsened by stress, sleep deprivation, and intercurrent illnesses. Similarly, rhythmic movement disorders such as head banging, is a parasomnia typically seen at transition or Stage 1 sleep, which can also resemble partial seizures. Among REM sleep parasomnias, nightmares rarely present a diagnostic challenge, but REM behaviour disorder may occur with violent and injurious behaviours during REM sleep. The diagnosis of REM behaviour disorder is usually easy as it affects older men and the description of acting out a dream is quite typical. Several historical features can help in differentiating parasomnias from seizures (Derry *et al.*, 2006), but occasionally EEG-video may be necessary, provided that the episodes are frequent enough.

Hypnic jerks or sleep starts are benign myoclonic jerks that everyone has experienced on occasion. While they resemble the jerks of myoclonic seizures, their occurrence, only upon falling asleep, stamps them as benign non-epileptic phenomena. They occur at all ages and can lead to evaluations for seizures, especially when the jerks are unusually violent.

Transient ischemic attacks (TIAs) rarely present a diagnostic challenge, because symptoms of TIAs are typically negative (involving an absence of movement or sensation), and symptoms of seizures are typically positive (involving involuntary movements or sensory hallucinations). In addition, focal symptoms in TIA are stroke-like, *i.e.* maximal acutely, whereas focal seizure symptoms tend to "march" or evolve over seconds. The confusion between TIA and seizures may be more likely when the seizure is unwitnessed and the patient appears with a focal deficit (*e.g.* Todd paralysis or aphasia), especially since both will improve over time (minutes). Contrary to a common misconception, TIA is a rare (if ever) cause of LOC.

Transient global amnesia (TGA) consists of dramatic episodes of anterograde amnesia. Patients are alert and otherwise cognitively intact but cannot form new memories and ask repetitive questions about

Key points

- Subjective and objective symptoms and signs are equally important
- Information on subjective symptoms can only be obtained from patients
- Analysis of their language may distinguish epileptic from non-epileptic events
- An anatomical hypothesis derived from seizure history is a precondition for optimally designed ancillary studies
- Both onset and evolution of seizures need to be considered
- In addition to seizures, the patient history may provide syndromic features helpful for the epilepsy diagnosis
- Patient and witness reports should be converged whenever possible
- Auras and other focal features may occur in bilateral epilepsies
- "Generalized" seizures do not involve the entire cortex but distributed thalamo-cortical networks
- Seizures in children are semiologically different from adults

their environment. This lasts several hours and then resolves. It occurs once in a lifetime, rarely twice. The differential diagnosis is ***transient epileptic amnesia***, which tends to recur and often differs from TGA by involving additional speech disorders and more general confusion rather than isolated amnesia (Lanzone *et al*., 2018).

Conclusions

Semiology is the backbone of any correct categorization of seizures, as epileptic or not, focal or bilateral, and is fundamental to elucidating how they are anatomically generated in the brain. An anatomical hypothesis derived from the seizure history is the precondition for optimally designed ancillary studies which may confirm or refute the hypothesis, or provide further details. Without interpretation of the semiology, no rational therapy is possible.

In the seizure history, the patients' subjective experiences with auras, triggering factors and beyond are of paramount importance and should be collected in an open approach supplemented by structured questioning and interpretation. Whenever possible, the history from the patient should be combined with the reports of witnesses. The fact that seizures with focal signs and symptoms occur not only in focal epilepsies but also in bilateral system disorders, which are misleadingly termed "generalized" epilepsies, draws attention to differences between various focal features and the context in which they occur. In typical cases, however, the distinction is rather straightforward. Particular attention needs to be paid to distinguishing epileptic from a variety of paroxysmal non-epileptic conditions. □

Supplementary data.
Summary didactic slides are available on the www.epilepticdisorders.com website.

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TEST YOURSELF

(1) A 55-year-old woman had an episode of loss of consciousness. She reports that she was vomiting all morning and was feeling poorly for several minutes, to the point that she had to sit down. She then stood up and felt dizzy and "clammy", and then she recalls coming to with people around her. Witnesses describe that she was out for about 30 seconds and had some jerking movements. What is the most likely diagnosis?

A. Seizure
B. TIA
C. Syncope
D. Cataplexy
E. Hypoglycaemia

(2) A 50-year-old woman is brought in by an ambulance after she "lost consciousness". She does not recall anything about the episode and is still lethargic. Her co-worker saw the episode and is in the waiting room. The most important tool to make the diagnosis is:

A. PET scan of the brain
B. MRI of the brain
C. Lab work
D. EEG
E. Obtain history from the eyewitness

(3) A state of altered behaviour and decreased attention habitually preceding a patient's seizures by 1-2 hours ("prodrome"):
A. Indicates subtle focal epileptic activity
B. Indicates subtle generalized epileptic activity
C. Is non-specific
D. Indicates a hangover following a party the preceding evening
E. All four possibilities exist

(4) To date, what is the evidence that video recordings of seizures on smartphones are beneficial:
A. May offer useful information, especially for psychogenic non-epileptic seizures
B. May offer useful information, especially for physiological events
C. May offer useful information, especially for epileptic seizures
D. May offer useful information, especially for focal impaired awareness seizures
E. May offer useful information, especially for lateralizing clinical signs

(5) Behavioural arrest:
A. Is characteristic only of mesial temporal lobe seizures
B. Requires consideration of the EEG and other semiological features to determine the seizure type
C. Is due to secondary bilateral synchronization in all focal seizures types
D. Is characteristic of absence seizures in childhood and adolescence only

(6) Which of the following statements is incorrect regarding seizures in children?
A. Seizures in children may have distinct semiological features compared to adults
B. Semiolgical features may change according to the age of the child
C. Parental description of the semiolgical features is almost always highly reliable
D. Semiolgical characteristics may depend upon the developmental status of the child
E. Semiological features may have prognostic implications

(7) Which of the following statements is true?
A. Classification of epileptic spasms into flexor, extensor and mixed has great clinical significance
B. The presence of migrating focal seizures is always suggestive of an underlying *KCNT1* mutation
C. Focal cortical dysplasia may clinically manifest as epileptic spasms in infancy
D. Patients with Dravet syndrome usually have nocturnal tonic seizures
E. E Visual aura is almost always noted in children with occipital epilepsies.

(8) Which of the following features in the history would point most clearly to a diagnosis of epilepsy rather than psychogenic non-epileptic seizures?
A. A history of tongue biting
B. A history of eye closure during convulsive seizures
C. A history of ictal incontinence of urine
D. Seizure descriptions characterised by formulation effort (*e.g.* hesitations, reformulations, restarts)
E. A history of nocturnal seizures

(9) Which of the following features in the history would point most clearly to a diagnosis of a psychogenic non-epileptic seizure?
A. Patient focusses on the consequences of different seizure events rather than subjective seizure symptoms.
B. Seizures only occurring during daytime
C. Seizures never involving incontinence
D. Seizures never causing injury
E. Seizures involving partial awareness

(10) Precipitation of focal myoclonias in an active hand involved in complex tasks with decision-making ("praxis induction") is highly suggestive of:
A. Focal cortical dysplasia in the contralateral motor strip
B. Focal epilepsy of any aetiology
C. Non-epileptic cortical myoclonus
D. Juvenile myoclonic epilepsy
E. Startle epilepsy

Note: Reading the manuscript provides an answer to all questions. Correct answers may be accessed on the website, www.epilepticdisorders.com, under the section "The EpiCentre".

Box 1. Competencies and learning objectives from the ILAE curriculum (Blümcke *et al.,* 2019) that are addressed in this article

Competency 1.0 Diagnosis

1.3.2 Extract semiology information from patient history
- Emphasis on the equal importance of subjective and objective symptoms and signs
- Subjective symptoms are only known to the patients
- The analysis of their reports can be challenging and needs careful but non-directive structuring
- Significance of auras
- Significance of prodromes
- Significance of factors facilitating seizures (including sleep)
- Both onset and evolution of seizures need to be considered
- Importance of converging patient and witness reports

1.3.4 Interpret semiological signs and symptoms allowing hypotheses on the localization of focal seizures
- Focal seizures have a unilateral onset
- Their spread may be bilateral
- To derive direct anatomical information from auras
- A list of typical auras is provided including their anatomical significance

1.3.5 Interpret semiological signs and symptoms suggesting focal vs "generalized" onset
- A bilateral ("generalized") onset is not necessarily symmetrical
- Auras do not necessarily prove a focal seizure
- Emphasis on the possible occurrence of local signs and symptoms in bilateral epilepsies
- Pathophysiology of local features in bilateral epilepsies
- The role of reflex epileptic mechanisms
- Understanding that in "generalized" seizures, the entire cortex is not involved
- Bilateral seizures involve distributed selective thalamo-cortical networks

1.7.2 Correctly distinguish between focal and generalized epilepsies and recognize epileptic encephalopathies
- See 1.3.5
- Understanding that seizure generation in "generalized" epilepsies involves an upregulation of physiological functional-anatomical systems
- The networks of focal and bilateral epilepsies are categorically different
- Focal features alternating between sides do not indicate a focal epilepsy
- The term "generalized" epilepsies is misleading

1.7.3 Correctly diagnose and classify focal epilepsies
- Diagnosis and classification of a focal epilepsy starts with an anatomical hypothesis derived from seizure semiology
- Subjective symptoms are particularly important
- This hypothesis guides the ancillary investigations which may confirm or refute the hypothesis, or provide further details.

1.7.4 Correctly diagnose and classify "generalized" epilepsies
- Diagnosis and classification of "generalized" epilepsies starts with a hypothesis based on seizure descriptions by patients and witnesses
- "Generalized" epilepsies consist of a limited number of seizure types occurring alone or in typical combinations
- Syndrome features like biorhythmicity and facilitating mechanisms are common
- Reflex epileptic mechanisms are frequent in "generalized" epilepsies
- The tentative diagnosis derived from history needs confirmation or further precision from EEG

1.7.5 Correctly diagnose and classify combined focal and generalized epilepsies including epileptic encephalopathy
- Diagnosis and identification of common epileptic encephalopathies of childhood based on history
- Identification of the defining seizure types of common epileptic encephalopathies and syndromes
- Emphasis on the evolution of seizure types with a neurodevelopmental basis
- Need for a holistic approach to diagnosis, stressing the age at onset, semiological features, and developmental comorbidities

• Identification of certain seizure types may have major diagnostic, management and prognostic implications
• Presence of myoclonic seizures in early childhood generally point towards genetic/metabolic aetiology
1.8 Recognize common non-epileptic paroxysmal events (*e.g*. PNES, syncope, parasomnia)
1.8.2 Recognize the semiology of PNES and suggestion techniques in the diagnosis of suspected PNES
• The style of communication of patients is particularly relevant to the distinction between epileptic and non-epileptic events
• The required mode of history taking differs significantly from that in routine practice for many clinicians (*e.g*. use of open questions, providing conversational space without early interruption)
1.8.3 Describe the formulation of diagnosis of PNES at different levels, as suggested by the ILAE PNES task force
• The process of history taking from the patient and a seizure witness is a cornerstone in the diagnosis of PNES
1.8.4 Recognize the typical semiology and risk profile associated with syncope
1.8.5 (new) Recognize other non-epileptic paroxysmal events
• Migraine
• Hypoglycaemia
• Panic attacks
• Acute dystonic reactions
• Hemifacial spasm
• Parasomnias
• Hypnic jerks (sleep starts)
• Transient ischemic attacks
• Transient global amnesia (distinct from transient epileptic amnesia)

Competency 3.0 Pharmacological treatment

3.2.8 (new) Recognize indications for intermittent treatment with rapidly-acting drugs
3.4 Drug discontinuation
• Emphasis on overlooked minimal isolated auras as a cause of relapse
3.8 (new) Indications, limitations and risks for other non-pharmacological treatments
• Seizure interruption techniques
• Sensory protection to prevent reflex seizures

Competence 4.0 Epilepsy surgery

None of the learning objectives apply since the point "Working knowledge of fundamental techniques for pre-surgical evaluation" is missing in the curriculum.

Appendix 1: Cases

Case 1

Female aged 37, with a brother with CAE and GTCS, fully controlled with VPA.

Her first seizure occurred at age 26 on the morning after return from a transatlantic holiday. A witness description indicated a GTCS without focal onset. She never had absences, myoclonic or focal seizures. The EEG demonstrated rare generalized SW in the awakening phase.

She suffered in the following four years another 10 GTCS, all provoked by parties with a lack of sleep and some alcohol. She declined AED treatment and preferred to try and control her trigger mechanism. Eventually she accepted lamotrigine at age 32 with the prospect that treatment after three seizure-free years might possibly be discontinued without relapse. She became seizure-free with 400 mg LTG. At age 36, she had been seizure-free for three years, however, after the start of a stepwise taper, seizure relapse occurred after dose reduction to 100 mg. She asked about treatment alternatives.

Detailed questioning revealed that all seizures had a prodrome with a lack of concentration which was noticed immediately after awakening. She could not collect her thoughts and all intentions were interrupted after a few seconds, thereafter she needed to start from fresh. This was fully corroborated by her husband: she is clearly "not herself". If she succeeded in falling asleep again, the prodrome did not resume after her second awakening, otherwise, after between 10 minutes and two hours, the event would end in a GTCS.

This prodrome, strongly suggestive of a series of absences, can be considered for acute seizure prevention using a rapidly acting benzodiazepine (Wolf, 2011).

The patient was followed for seven years and became completely seizure-free with acute administration of 10 mg rectal diazepam at perceived risk, in spite of discontinuation of LTG. She uses the rescue medication between 6 and 10 times per year.

Conclusion: Familial idiopathic generalized epilepsy presenting as GTCS only with prodromal absence series. A more precise history provides a successful new strategy based on rescue medication.

Case 2

A 38-year-old communal clerk was transferred from her neurologist with a history of seizures since age 18, with consistently identical semiology: paraesthesias of the left angle of her mouth with spreading over the left cheek, occasionally accompanied by very slight twitches of the corner of the mouth. On only one occasion in 20 years, these developed into a well-described bilateral TCS. She had up to 20 seizures daily, rarely a day without. She was in competent neurological care and proved resistant to all AEDs including the newest as they became available; she was never considered a surgical candidate because the seizures fundamentally were only subjective, so she could live with them. The patient, however, experienced her seizures as extremely unpleasant and irritating, interfering with her work with clients by disabling her speech. She spontaneously accepted presurgical evaluation when rationale and procedures were explained to her in detail.

Anatomical conclusion from self-report: epileptic focus in face field of right postcentral gyrus.

No etiological clues from history and physical examination. EEG with video including ictal tracing was normal. 3 Tesla MRI with epilepsy protocol and special attention to right parietal was unrevealing. Interictal/ictal SPECT and SISCOM, and FDG-PET were normal. PNES was suspected because there were no visible symptoms and advanced ancillary investigations showed nothing abnormal. PNES, however, were unlikely because the seizures were subtle, made anatomical sense and never changed in 20 years. Finally, magnetencephalography confirmed right parietal sharp wave focus. During the long diagnostic process, the patient became seizure-free with lacosamide, therefore no further surgical work-up was required.

Conclusions: (1) careful semiological analysis of patients' self-reports can be diagnostically superior to video-EEG and even sophisticated imaging.

(2) Whether a patient can live with a certain kind of seizure is not up to the doctor to decide, but the patient.