

A proposal for a five-dimensional patient-oriented epilepsy classification

Tobias Loddenkemper^{1,2*}, Christoph Kellinghaus^{1*}, Elaine Wyllie¹, Imad M. Najm¹, Ajay Gupta¹, Felix Rosenow³, Hans O. Lüders¹

¹ Department of Neurology, The Cleveland Clinic Foundation, Cleveland, OH, USA

² Department of Pediatrics, The Cleveland Clinic Foundation, Cleveland, OH, USA

³ Department of Neurology, Philipps-University Marburg, Marburg, Germany

* Both authors contributed equally to the work

Received August 10, 2005; Accepted September 2, 2005

ABSTRACT – The recent proposal by the ILAE Task Force for Epilepsy Classification consists of a multi-axial syndrome-oriented approach. Epilepsy syndromes, as defined by the ILAE, group patients according to various, poorly defined parameters. The resulting syndromes have frequently no biological significance, with overlap among different syndromes and syndromes changing with age. Additionally, only a minority of patients can be classified syndromatically, and the axes of this classification system convey redundant information. We propose a five-dimensional, patient-oriented approach to classifying epilepsies. This approach shifts from the syndrome-oriented approach to a standard, neurological, methodological, patient-oriented approach, using independent criteria in each of the five dimensions. Similar to general neurology, the first step in each patient-physician encounter in epileptology is to take a history of the presenting symptoms and generate a hypothesis regarding the localization and etiology of the symptom within the nervous system. Therefore, the main dimensions of this classification consist of: 1) localization of the epileptogenic zone, 2) seizure semiology classified according to the semiological seizure classification, 3) etiology, 4) seizure frequency, and 5) related medical conditions. These dimensions characterize all of the information necessary for patient management, are independent parameters, and include more pertinent information with regards to patient management than the ILAE axes. All patients can be classified according to this five-dimensional system even at the initial patient encounter when no detailed test results are available. Information from clinical tests, such as MRI and EEG, are translated into the best possible working hypothesis at the time of classification, allowing for increasing precision of the classification as additional information becomes available. This patient-oriented classification envisions an epileptic seizure as an independent symptom of a central nervous system dysfunction due to different causes, with various cortical localizations, occurring at various frequencies, and in conjunction with other diseases and clinical symptoms.

Key words: epilepsy classification, semiological seizure classification, ILAE, patient-oriented

Correspondence:

T. Loddenkemper, MD
Department of Neurology,
The Cleveland Clinic Foundation,
9500 Euclid Avenue, S 51,
Cleveland, Ohio, 44195
USA
Tel.: (+00 1) 216 444 2200 (#27698)
Fax: (+00 1) 216 444 0230
<loddent@ccf.org>

Introduction

History of epilepsy classification

The first ILAE epilepsy classification provided a standard system that eventually was accepted worldwide (Gastaut 1969, Merlis 1970). A major dichotomy between generalized and focal (“partial”) epilepsies, based on clinical characteristics of each seizure type linked with EEG features, anatomical substrate, etiology and age of manifestation, was established (Merlis 1970). The first revision, in 1985, led to the listing of multiple syndromes defined primarily as a cluster of semiological seizure types, EEG patterns etiologies, age at onset, and seizure frequency (*Proposal for classification of epilepsies and epileptic syndromes*, 1985). The dichotomy of localization-related versus generalized epilepsies was complemented by a second etiological dichotomy (idiopathic and symptomatic). Four years later, the expression “cryptogenic” was introduced to classify epilepsies that were presumed to be symptomatic, but without definite proof (*Proposal for revised classification of epilepsies and epileptic syndromes*, 1989). This revision also stressed the syndromic approach.

Current syndrome-oriented proposal by the ILAE

The most recent proposal by the ILAE (Engel 2001), is again based on epilepsy syndromes and presents a multi-axial approach: 1) seizure description, 2) seizure type, 3) epilepsy syndrome, 4) etiology, and 5) impairment. We feel that the view that epilepsies are diseases and that the “epileptic syndromes” are their phenotypic expression is an oversimplification. Almost invariably, epileptic seizures: 1) are the consequence of multiple etiologies (see detailed discussion below), 2) any given phenotypic expression (“epileptic syndrome”) can be the consequence of different etiologies, and 3) any given etiology can produce different phenotypic patterns (“epileptic syndromes”). We certainly recognize that identification of clusters of phenotypic patterns in patients with epileptic seizures may be a useful research tool, particularly for identification of genes that are etiologically related to the epileptic seizures. However, a more practical approach is to simply assume that seizures are an expression of cortical pathology of different etiology (etiologies) affecting different locations of the brain. An epilepsy classification would then define, with precision, the location of the cortical pathology, the symptomatology of the seizures, and the etiology (or frequently etiologies) that led to the epileptic seizures.

Epilepsy classification for any given patient should be a patient-oriented, continuously changing dynamic process that becomes more precise as we obtain additional information.

Patient-oriented epilepsy classification

We developed a five-dimensional epilepsy classification (1. epileptogenic zone, 2. seizure semiology, 3. etiology,

4. seizure frequency, and 5. related medical information). This proposal follows the approach established in clinical neurology, characterizing diseases based on the CNS location of the lesion (dimension 1), the clinical symptoms (seizure semiology, dimension 2), and the etiology (dimension 3).

These essential cornerstones are complemented by the severity of the disease (seizure frequency, dimension 4) and related clinical information (dimension 5) (*table 1*).

Table 1. The patient-oriented epilepsy classification. A multi-dimensional approach derived from general, neurological, diagnostic principles.

<p>1. Epilepsy-localization Where is the lesion?</p> <p>2. Seizure Semiology What are the symptoms?</p> <p>3. Etiology What is causing the epilepsy?</p> <p>4. Seizure frequency How frequent are the symptoms?</p> <p>5. Related medical conditions, if applicable Additional related findings in the history, examination and diagnostic procedures?</p>

Dimension 1 - epileptogenic zone (EZ)

Dimension one is based on the concept of the EZ, which is defined as “the area of cortex that is indispensable for the generation of epileptic seizures” (Rosenow and Luders 2001). The extent and location of the EZ cannot be determined precisely with current techniques. To estimate the extent of the EZ, epileptologists use different techniques, including history taking, seizure semiology (history, observation/video), electrophysiological studies (EEG, MEG), structural neuroimaging (CT, MRI) and functional and metabolic neuroimaging (PET, SPECT, fMRI, MRS), metabolic tests (e.g. prolactin level), (histo)-pathological and genetic studies. The term *focal* is used if there is evidence of an EZ within one cerebral lobe. *Multilobar* refers to one EZ covering two or more contiguous unilateral lobes (e.g. fronto-temporal, temporo-parietal, etc). *Hemispheric* refers to an EZ covering most or all of a hemisphere. *Multifocal* refers to more than one, *independent, non-adjacent EZ*. *The term generalized is used if the cortex is diffusely epileptogenic (figure 1)*. All terms (except for “generalized”) can be attributed by the side of the EZ (e.g.: “left” and/or “right”) (*table 2*). Epilepsy syndromes (e.g. Lennox-Gastaut-syndrome) can be added in parentheses after defining the EZ (see example 1).

The five-dimensional classification applies only to patients with epilepsy (= at least two, spontaneous epileptic seizures). For patients with unclear epileptic or non-epileptic events we recommend the term “paroxysmal event”.

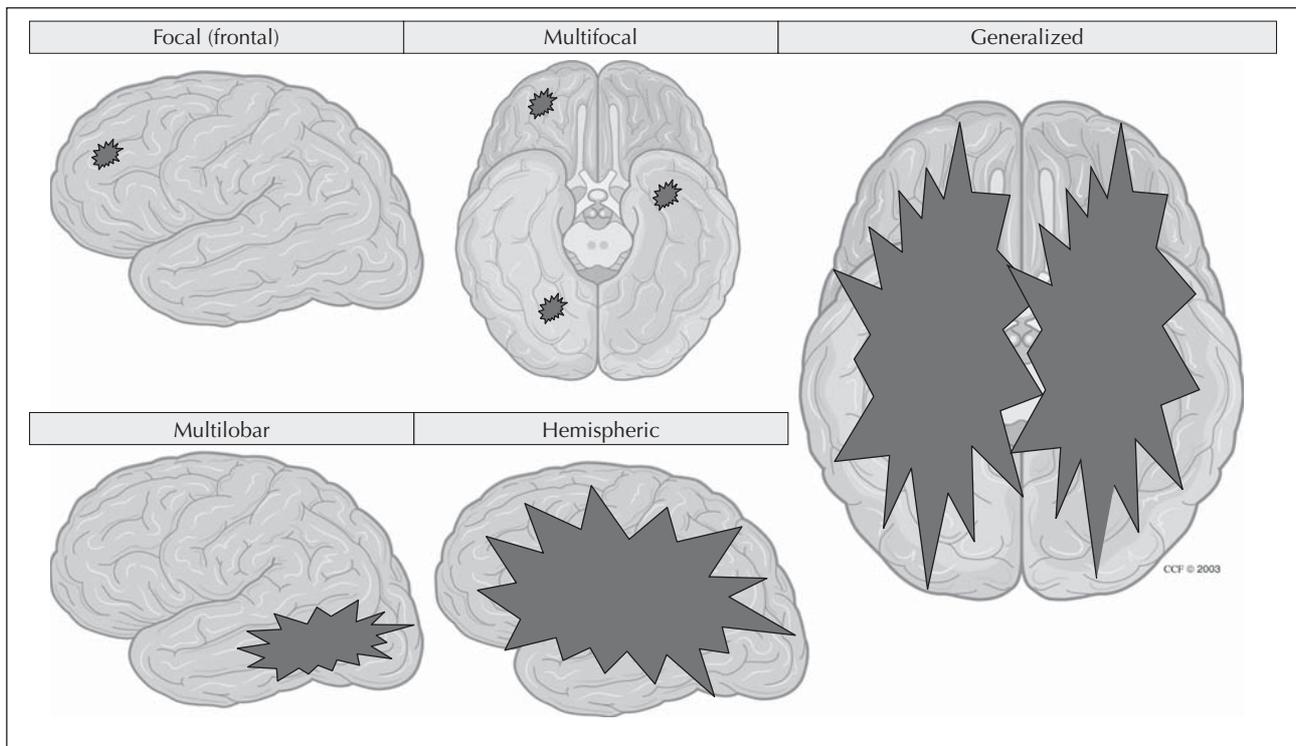


Figure 1. Localization of the epileptogenic zone.

This figure demonstrates possible locations of the epileptogenic zone and illustrates *focal* (circumscribed epileptogenic zone within one lobe of the brain), *multilobar* (a single epileptogenic zone covering two or more contiguous lobes of one hemisphere), *hemispheric* (covering most or all of a hemisphere), and *multifocal* (more than one independent epileptogenic zone, not adjacent to each other). The term *generalized* characterizes *diffuse widespread epileptogenicity that cannot be sorted into one of the above mentioned categories*.

Dimension 2 - seizure classification

Seizures are the main symptoms of patients with epilepsy. A semiological seizure classification, based solely on seizure symptomatology, has been developed at our institution. This semiological seizure classification is independent of any other technique, e.g. EEG or MRI. It has been applied successfully for more than a decade in Cleveland and at other institutions, and has been described in detail elsewhere (Luders *et al.* 1993, Luders *et al.* 1999, Benbadis *et al.* 2001). A seizure is classified based upon its main clinical features, e.g. automatisms, clonic movements, or aphasia. If a seizure consists of several different features evolving in a sequence, these components can be classified independently, linked by arrows in order of occurrence.

Dimension 3 - etiology

Current research indicates that epileptic seizures have multi-factorial etiologies. This includes a combination of genetic factors of different strength that lower the patient's threshold to epileptic seizures. In some patients, this predisposition may be sufficient to actually trigger seizures. In other patients, an additional, predominant genetic factor (such as a channelopathy) or a structural abnormality

(tumor, trauma, etc.) may be essential for the generation of seizures.

These considerations led us to design a classification that allows the choice of multiple etiological factors. With the currently available diagnostic techniques, the pathological etiologies can be documented most objectively. The system allows identification of one or more etiologies and includes many etiologies which are non-pathological (metabolic, genetic, etc.). Concomitant causes can be mentioned in brackets. The etiological classification consists of 12 categories and subcategories (*table 3*).

Classification of etiology is highly dependent on the amount of knowledge, and progress in investigational methods. Therefore, subcategories of etiologies are incomplete and can be supplemented by rare entities not mentioned here.

Dimension 4 - seizure frequency

Combined seizure frequency of all seizure types is classified to provide a guideline for epilepsy severity (*table 4*). In clinical practice, the actual seizure-frequency may be also important. An actual number indicating the total seizure frequency during a given time interval may be included in brackets (e.g.: 3/month).

Table 2. Dimension 1 – epileptogenic zone.

Unclassified	
Focal	frontal perirolandic* temporal neocortical temporal mesial temporal parietal occipital other**
Multilobar	fronto-temporal temporo-parietal fronto-parietal temporo-parieto-occipital other
Hemispheric multifocal	bifrontal bitemporal other***
Generalized	

* The perirolandic area is defined as the precentral gyrus and the postcentral gyrus, lined by the precentral sulcus, the postcentral sulcus, and the sylvian fissure (Kuzniecky *et al.* 1995). This definition derives from developmental and functional bonds between the primary motor and sensory areas. Additionally, epilepsies arising from the primary motor or sensory areas have unique implications and challenges regarding surgical therapy (Brun 1999).

** Other locations such as subcortical regions (e.g. hypothalamus) can be included here.

*** Multifocal epileptogenic zones can include multiple combinations of epilepsy locations (e.g. «left frontal and right parieto-occipital»).

Dimension 5 – related medical information

Dimension 5 consists of free text that allows the entry of important, related, medical information. It provides additional information on important complementary findings in the history (e.g. “head trauma with loss of consciousness 1996”), physical examination (e.g. “left hemiparesis” or “mental retardation”), and additional diagnostic tests that are not an integral part of the classification (e.g. “right centro-temporal, benign focal epileptiform discharges on EEG” in a patient with left temporal lobe epilepsy).

Epileptic syndromes

Epileptologists have defined many epileptic syndromes. Some of these syndromes are useful concepts, summarizing some essential characteristics of patients with epilepsy. The five-dimensional epilepsy classification allows inclusion of a syndromatic classification, which can be listed in parentheses after the EZ.

Table 3. Dimension 3 – etiology

Hippocampal sclerosis
Tumor
Glioma
DNET
Ganglioglioma
Other
Malformation of cortical development
Focal malformation of cortical development
Hemimegalencephaly
Malformation of cortical development with epidermal nevi
Schizencephaly
Lissencephaly
Holoprosencephaly
Heterotopic grey matter
Hypothalamic hamartoma
Hypomelanosis of Ito
Other
Malformation of vascular development
Cavernous angioma
Arterio-venous malformation
Sturge-Weber Syndrome
Other
CNS infection
Meningitis
Encephalitis
Abscess
Other
(Immune-mediated) CNS inflammation
Rasmussen»s encephalitis
Vasculitis
Other
Hypoxic-ischemic brain injury
Focal ischemic infarction
Diffuse hypoxic-ischemic injury
Peri-ventricular leukomalacia
Hemorrhagic infarction
Venous sinus thrombosis
Other
Head trauma
Head trauma with intracranial hemorrhage
Penetrating head injury
Closed head injury
Inheritable conditions#
Tuberous sclerosis
Progressive myoclonic epilepsy
Metabolic syndrome
Channelopathy
Mitochondrial disorder
Chromosomal aberration
Presumed genetic cause
Other
Structural brain abnormality of unknown cause
Other
Unknown - unclear etiology based on the current information

Category «inheritable conditions» includes conditions that are inherited in a mendelian or mitochondrial fashion or are potentially inheritable due to chromosomal aberrations (translocation, deletions, or insertions). The sub-category «presumed genetic cause» can be used in a situation where there is a family of multiple affected family members with epilepsy but without a yet-specified genetic diagnosis.

Table 4. Dimension 4 – seizure frequency

<ul style="list-style-type: none"> • Daily – one or more seizures per day. • Persistent – less than one seizure per day, but at least one seizure in the last six months. A persistent pattern must be recognizable in the period prior to the last 6 months. • Rare or none – less than one seizure per six months. These patients are required to have had more than two documented seizures, with the last seizure occurring more than 6 months ago. • Undefined – the following conditions are classified as undefined seizure frequency, because it is not possible to predict the seizure frequency : unknown seizure frequency ; recent onset of epilepsy ; breakthrough seizures in an otherwise well-controlled patient due to medication change/reduction or other provoking factors (sleep deprivation, alcohol, hypoxia, chemotherapy etc.) ; patients with less than six months follow-up after epilepsy surgery

Example 1: a 3-month-old boy with epileptic spasms

Seizures started on the first day of life, with clusters of epileptic spasms (three to 15 clusters/day). The child was encephalopathic, without developmental progression. Seizures were resistant to multiple antiepileptic medications, including ACTH. Video-EEG revealed epileptic spasms associated with a generalized burst suppression pattern on EEG and no differentiation between ictal and interictal EEG.

1. *Epileptogenic zone*: generalized (Ohtahara syndrome)
2. *Semiology*: epileptic spasms
3. *Etiology*: unknown
4. *Frequency*: daily
5. *Related medical information*: developmental delay epileptic encephalopathy

Epileptic spasms were still present at nine months of age. Neuropsychological testing revealed severe mental retardation, decreased responsiveness and no spontaneous interaction. Repeated video-EEG monitoring showed diffuse, generalized electrodecrement during single epileptic spasms, and interictal hypsarrhythmia. MRI showed diffuse bilateral pachygyria.

1. *Epileptogenic zone*: generalized (West syndrome)
2. *Semiology*: epileptic spasms
3. *Etiology*: bilateral malformation of cortical development
4. *Frequency*: daily
5. *Related medical information*: developmental delay epileptic encephalopathy

On follow-up at age six years, the patient had developed tonic and atonic seizures in the previous three years. Seizures occurred two to four times per day. The patient functioned at the level of an 18-month-old infant. Routine-EEG showed generalized 2.5 Hz slow spike and wave complexes, and multiregional spikes.

1. *Epileptogenic zone*: generalized (Lennox-Gastaut)
2. *Semiology*: atonic seizure ; tonic seizure ; epileptic spasm
3. *Etiology*: bilateral malformation of cortical development
4. *Frequency*: daily
5. *Related medical information*: developmental delay epileptic encephalopathy

Example 2: a 33-year-old patient with left temporal lobe epilepsy due to hippocampal atrophy

This 33-years-old, right-handed man had suffered from several febrile convulsions in infancy. Habitual seizures started at the age of 15 years and were accompanied by a feeling of abdominal discomfort followed by loss of awareness. His wife reported that about once a month he displays lip smacking, fumbling hand movements and occasional right hand posturing. On three occasions within the previous 12 months, evolution into sustained, right-sided head and eye turning followed by stiffening of arms and legs and bilateral symmetric rhythmic arm and leg shaking was witnessed. He failed treatment with several antiepileptic drugs.

1. *Epileptogenic zone*: left temporal
2. *Semiology*: abdominal aura -> automotor seizure -> right versive seizure -> generalized tonic-clonic seizure
3. *Etiology*: unknown (MRI pending)
4. *Frequency*: persistent
5. *Related medical information*: febrile convulsions during infancy

An MRI of the brain revealed left mesial temporal hippocampal atrophy on T1-weighted images, and hyperintensity on flair sequences. Video-EEG monitoring demonstrated left mesial temporal EEG seizures associated with his habitual seizure semiology. Interictal EEG showed left and right temporal sharp waves. The patient declined epilepsy surgery at this point. The classification of the epileptogenic zone and the etiology becomes more precise based on the additional information.

1. *Epileptogenic zone*: left mesial temporal
2. *Semiology*: abdominal aura -> automotor seizure -> right versive seizure -> generalized tonic-clonic seizure
3. *Etiology*: left hippocampal sclerosis
4. *Frequency*: persistent
5. *Related medical information*: febrile convulsions during infancy, predominantly nocturnal seizures

Distribution of the epileptogenicity profile in this patient is illustrated in *figure 2*.

Discussion

Summary

The five-dimensional, patient-oriented epilepsy classification approach discussed here shifts the emphasis from a category-based approach (Engel 2001) to a standard, neurological, patient-oriented approach, using independent criteria in each dimension. Syndromes can be identified in this classification, but are not an essential classification component. The dimensions include more pertinent information with regards to patient management, and are more adaptable to the spectrum of epilepsy patients than the syndrome-oriented approach.

Problems with the ILAE proposal

Poorly defined epilepsy syndromes

Epilepsy syndromes are not strictly defined according to the ILAE. According to the revised ILAE-classification from 1989, an epileptic syndrome is “characterized by a cluster of signs and symptoms customarily occurring together; these include such items as type of seizure, etiology, anatomy, precipitating factors, age of onset, severity, chronicity, diurnal and circadian cycling, and sometimes prognosis” (*Proposal for revised classification of epilepsies and epileptic syndromes*, 1989). The latest revision by the ILAE Task Force is similarly vague and defines an epilepsy

syndrome as “a complex of signs and symptoms that define a unique epilepsy condition” (Engel 2001). “Uniqueness” is not defined. Syndromes group patients according to different parameters. The resulting syndrome frequently has only limited biological significance (Berg *et al.* 1999), and often there is overlap between syndromes.

Certain syndromes specify, at best, two dimensions, and moreover, often the specified information is poorly defined. For example, the term Lennox-Gastaut syndrome is usually associated with generalized or multifocal epilepsy (*Proposal for revised classification of epilepsies and epileptic syndromes*, 1989). In this syndrome tonic seizures, atypical absences, and generalized tonic-clonic seizures are seen most frequently (Goldsmith *et al.* 2000), but no seizure type occurs in all patients and multiple other seizure types have been described (Crumrine 2002). Etiologies are described as “cryptogenic”, symptomatic, or truly unknown (Goldsmith *et al.* 2000). Seizure frequency can vary from seizure-freedom (Goldsmith *et al.* 2000) to status epilepticus (Hoffmann-Riem *et al.* 2000) and “most”, but not all patients may suffer from developmental delay as a related medical condition (Crumrine 2002). Therefore, “Lennox-Gastaut syndrome” does not specify with certainty any of the five dimensions discussed above. In contrast to that, the five-dimensional epilepsy classification defines all these dimensions precisely, and provides most of the information necessary for patient management (example 1).

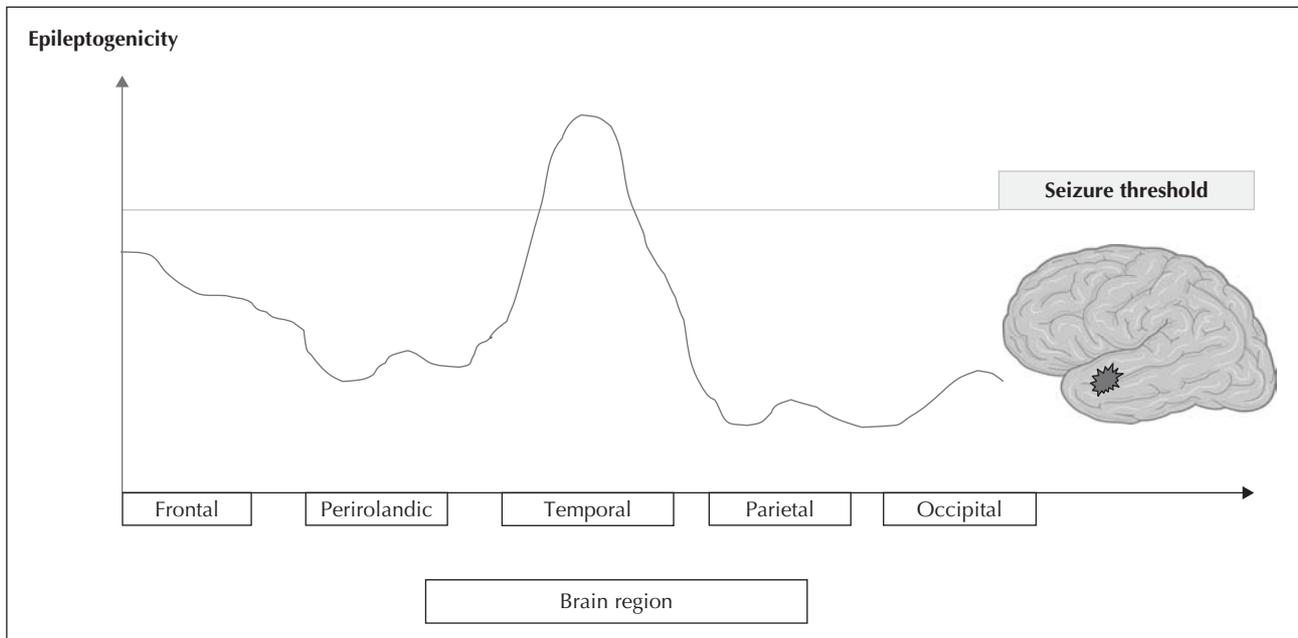


Figure 2. Epileptogenic zone – sample patient with left temporal lobe epilepsy. This diagram depicts different levels of epileptogenicity in different regions of the brain. A rising of the epileptogenicity level in a circumscribed area at a certain time point above the seizure threshold leads to seizures from that area. Individual epilepsy patients have individual epileptogenicity profiles with focal, multilobar, multifocal, hemispheric or generalized epileptogenicity levels.

Epilepsy syndromes are rare

ILAE syndromes may actually only apply to a minority of patients with epileptic seizures. Only 1% with specific localization-related syndromes, and 4% with specific, generalized epilepsy syndromes were found among epilepsy patients in a general family practice setting (Manford *et al.* 1992). In general neurological practice, similar numbers with only 0.7% specific localization-related syndromes and 10% specific generalized epilepsy syndromes were seen (Berg *et al.* 1999). Even in our tertiary epilepsy center, we could only identify 4% of adults and 19% of children with a specific ILAE syndrome (Kellinghaus *et al.* 2004). These studies reveal that the concept of epilepsy syndromes proposed by the ILAE task force is only applicable to a minority of epileptic patients, particularly in general neurological practice.

Most general neurologists have difficulties identifying even the most frequent epileptic syndromes, and, in addition to which, the ILAE classification does not follow the general neurological diagnostic approach (characterization of the symptoms (seizures), localization of the lesion within the nervous system (epileptogenic zone), and determination of its cause (etiology). Therefore, it is unlikely that general neurologists will use a classification system based on the correct identification of syndromes.

Advantages of the five-dimensional epilepsy classification

Independence of dimensions

The dimensions in the five-dimensional, patient-oriented classification system are well defined in order to minimize overlap. There is minimal redundancy of information in the dimensions seizure semiology, etiology, seizure frequency and related medical conditions. The only exception is dimension one: the epileptogenic zone summarizes all available information, including - among many other parameters - seizure semiology and, to a lesser degree, etiology.

Independence from contemporary diagnostic tools

Information from clinical tests, such as MRI and EEG, are translated into the best possible working hypothesis at the time of classification, allowing for increasing precision of the classification as additional information becomes available. However, this relative independence from diagnostic techniques leads to a lack of EEG data in the classification itself. Nevertheless, every patient's EEG is classified according to a separate EEG classification (Lüders *et al.* 2000). The EEG plays a crucial part in the diagnosis of epilepsy, but once the EEG information has been implemented in the diagnosis, there is no need for consideration of the EEG pattern in the classification, as this would only result in redundancy of information. Epilepsy syndromes, such as Lennox-Gastaut syndrome and West syndrome, do not rely on a specific EEG pattern and can or cannot

present with slow-spike and wave complexes, and hypsarhythmia, respectively. The EEG pattern may therefore be helpful in the construction of the classification, but will always be reflected in dimension one.

Based on our experience, only two specific EEG patterns may be both diagnostic and highly sensitive for the diagnosis of a particular epilepsy type: 3 Hz spike and waves, and benign focal epileptiform discharges of childhood.

Information regarding typical absence seizures associated with 3 Hz spike and wave complexes will be reflected in dimension 2, which allows for differentiation between dialeptic seizures with or without 3 Hz spike and wave complexes. The classification for a patient with juvenile absence epilepsy could look like this:

1. *Generalized epilepsy* (juvenile absence epilepsy)
 2. *Semiology*: typical dialeptic seizures
 3. *Etiology*: unknown
 4. *Frequency*: persistent
 5. *Related medical information*: family history of epilepsy
- The information, 3Hz spike and wave complexes, is contained in dimensions 1 and 2.

The other syndrome that can definitely be diagnosed by a unique EEG pattern is benign focal epilepsy of childhood. Although the EEG features are not reflected directly in the classification, they will again be reflected in dimension one. The classification for a BFED patient would read:

1. *Epileptogenic zone*: left perirolandic (benign focal epilepsy of childhood)
2. *Semiology*: right clonic seizures
3. *Etiology*: unknown
4. *Frequency*: rare
5. *Related medical information*: exclusively nocturnal seizures

This could be easily differentiated from a patient with focal epilepsy, e.g. temporal lobe epilepsy:

1. *Epileptogenic zone*: left mesial temporal
2. *Semiology*: abdominal aura -> automotor seizure -> right clonic seizure -> generalized tonic-clonic seizure
3. *Etiology*: left hippocampal sclerosis
4. *Frequency*: rare
5. *Related medical information*: febrile convulsions during infancy

The independence of a specific diagnostic device is an advantage of this classification that makes the proposed classification more likely to better serve future generations as technology advances. Although the EEG is currently one of the best techniques for the diagnosis of the different types of epilepsy, it may be replaced or supplemented by additional electrophysiological or neuroimaging devices and procedures that can estimate the epileptogenic zone even more precisely.

Applicable to all patients

All patients can be classified according to the five-dimensional epilepsy classification. Specification of epilepsy syndromes (e.g. those mentioned in the ILAE-proposal) is not mandatory, but possible if thought to be helpful. Historically important electro-clinical syndromes (e.g. West syndrome) can be included in order to provide key words that convey a cluster of specific information in a single term. However, the syndromes are optional supplemental information.

Patients can be classified in the five-dimensional epilepsy classification independent of the amount of available information. Specialized diagnostic techniques are not necessary for an initial classification. The adaptability of the five-dimensional, patient-oriented epilepsy classification to varying degrees of information makes it suitable for use by physicians in private practice as well as in a tertiary epilepsy center setting, regardless of the availability of diagnostic techniques (e.g. history, EEG, MRI, video-EEG, epilepsy surgery etc.).

The five-dimensional, patient-oriented classification system does not depend on the availability of diagnostic tools and should not change if future diagnostic methods become available.

All essential information is included

All essential information necessary for the management of a patient with epileptic seizures is contained in the five-dimensional patient-oriented epilepsy classification. The five-dimensional classification outlined here provides significant additional information as compared to the syndrome classification.

Follows general neurological principles

The basic approach of the five-dimensional patient-oriented classification is similar to the classification system used by general neurologists, namely the definition of the localization of the lesion (epileptogenic zone), the clinical symptoms (ictal semiology), and the etiology, (table 1). It can be applied to all patients with different degrees of precision depending on the available information. Furthermore, the classification dimensions for the epileptogenic zone, the seizure semiology and the etiology can be easily memorized because these categories mainly use anatomical, descriptive and pathological terms usually well-known to every physician.

Research advantages

The five-dimensional classification is also useful for scientific, taxonomic accuracy and completeness. Each one of the three main dimensions, namely epileptogenic zone, etiology and seizure semiology can serve as an independent scientific grouping variable for research studies, allowing collateral studies according to different parameters, and classification of epilepsies according to different etiologies. This will help to define the phenotype of the

disease that includes epileptic seizures and their symptomatology. Therefore, patient-oriented classification will enable researchers to take a fresh look at clusters of symptoms, and to evaluate these epilepsy entities according to their utilitarian or taxonomic significance. Implications from findings in patients will influence the definition of future epilepsy entities. Similar to the neurological, patient-oriented diagnosis in each patient, the existence and logical grouping of symptoms in an entity can be challenged as further information becomes available.

Limitations of the patient-oriented classification*The construct of the epileptogenic zone*

The gold standard for proof of the extent of the epileptogenic zone can only be determined by resection and subsequent seizure-freedom based on today's technology. However, this gold standard is not applicable to most patients when epilepsy is diagnosed and treatment is initiated. The epileptogenic zone serves as a multifaceted, working hypothesis based on the available clinical and investigational information for each patient, at a certain time point. It can only be the best possible estimation of epileptogenicity, at the time of classification. Further testing can refine the hypothesis, but a margin of error remains. The experience of the classifying physician, and the tests available at the time, may influence the precision of this dimension.

Bias towards focal epilepsy

The five-dimensional classification is oriented towards focal epilepsies. Its telegraphic style provides well-structured, presurgical data at a glance. However, this orientation towards focal epilepsies and presurgical epilepsy evaluation may reduce its practicability as regards generalized epilepsies and childhood epilepsies according to the syndromatic approach in selected cases.

Conclusion

We present a five-dimensional, patient-oriented epilepsy classification in order to spark discussion, and to present a practical alternative to the prevailing syndromatic approach. This proposal is another step on the way towards an epilepsy classification that serves utilitarian and taxonomic needs.

Acknowledgements. Authors TL and CK were supported by Innovative Medizinische Forschung, WWU Münster, Germany (FoeKz. LO 610101 & KE 620201), Author FR was supported by the Ullrich-Foundation Professorship for Neurology/Epileptology. Tables 2, 3 and 4 are reproduced with permission from Wyllie *et al.* 2005. Figure 1 and part of figure 2 reproduced with permission from the Cleveland Clinic Art and Photo Department, Cleveland, Ohio, USA. □

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