Classifying Epilepsy: What’s New?

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Introduction

A clear understanding of the classification of seizures and epilepsies is essential for their diagnosis, treatment, and prognostication. The management of a patient with seizures begins with an understanding of his/her seizure type based on semiology and, if pertinent, epilepsysyndrome. Specific seizure types or syndromes often respond better to specific medications or surgical approaches. Some electroclinical syndromes carry a benign prognosis or high likelihood of seizure remission by a certain predictable age. Other seizure syndromes may carry a generally poorer prognosis, and fore-knowledge allows focused treatment and lifestyle modifications for patients and families.

The classification of epileptic seizures has largely evolved with clinical observation, EEG findings and expert opinions. The International League Against Epilepsy (ILAE) first published a classification system in 1960. The last official update for seizures was published in 1981, and the last official update for the epilepsies was published in 1989. However, over the last two to three decades, we have come to know much more about epilepsies due to the advances in neuroimaging, genomics and molecular biology. This “knowing much more” has changed our concepts towards the causation and phenomenology of seizures. These aspects need to be incorporated in epilepsy classification so as not just to reflect current scientific understanding but also to make the management and clinical decision-making easier for even the non-specialized clinician.

To this effect, the ILAE commission, in its 2005-2009 term had sought to revise the terminology and concepts for classification of both seizures as well as epilepsies so as to reflect the advances being made in basic and clinical neurosciences. Input was sought from experts in fields of genetics, neuroimaging, therapeutics, pediatric and adult epileptology, as well as statistics and research design. A report on these inputs was subsequently submitted but is yet to be officially endorsed. These proposals are not meant to be permanent but form “part of a transition to a system that will ultimately allow for meaningful translation of scientific understanding into the classification of the epilepsies for clinical and other purposes”.

New Terminologies and concepts

Mode of seizure onset

It is now recognized that generalized seizures do not necessarily involve the entire cerebral cortex. They can be originating at some point within one or more of bilaterally distributed networks. In patients with generalized seizures, including those with known generalized electroclinical syndromes, at times ictal onsets have been noted to be localized and seizure semiologies to be asymmetric. However, unlike focal seizures, the location and lateralization of such seizures are usually not consistent from one event to another.

Focal seizures originate within networks limited to one cerebral hemisphere, which may include subcortical structures. For each seizure type, ictal onset is consistent from one seizure to another. These may consistently propagate along preferred network(s) involving the contralateral hemisphere.

While emphasizing this conceptual shift, certain specific changes have been suggested to the 1981 classification of seizures.

1. Neonatal seizures are classified within the classification scheme and not separately.
2. The sub-classification of absence seizures has been simplified. Myoclonic absence seizures and eyelid myoclonia are now recognized as subtypes of absence seizures.
3. It is now known that the so-called “infantile” spasms may continue past or even occur de novo after infancy. Therefore, the more generic term “epileptic spasms” is recommended for use. It is still not possible to classify these as focal or generalized and so they have been placed in their own group as “unknown” mode of onset.
4. The traditional classification used the terms simple partial, complex partial, and partial seizures-secondarily generalized. However, the terms “simple” and “complex” are often misused or misunderstood. In addition, this distinction, based on impairment of consciousness or awareness, may not always be precise and well defined and has therefore been recommended for discontinuation.

The mode of onset of seizure is usually of greater practical importance than the mode of spread. The term “secondarily generalized” usually does not add to the management of focal seizures, makes them liable to be confused with generalized seizures and has therefore been eliminated. Since the information required to scientifically classify focal seizures is still inadequate, the ILAE Commission recommends that focal seizures be described according to features that are most useful for a given specific purpose. This may include detailed description of semiology for the purpose of differentiation between epileptic and nonepileptic events and for presurgical evaluation.

5. The myoclonic atonic seizures are now re-classified as myoclonic atonic seizures.

Descriptors of focal seizures

Even as the commission report discourages the terms simple and complex partial seizures, in order to facilitate continuity with the 1981 classification of seizures, descriptors of focal seizures may be used, individually or in combination with other features depending on the purpose. Chiefly, these include:

- With observable motor or autonomic components. This corresponds to the concept of “simple partial seizure”.

- Involving subjective sensory or psychic phenomena only. This corresponds to the concept of an aura.

With impairment of consciousness or awareness. The previously termed complex partial seizure can be referred by this descriptor. The term “Dyscognitive” has been also been proposed for the alteration in awareness.

Evolving to a bilateral, convulsive seizure (involving tonic,
clonic, or tonic and clonic components). This corresponds to the previously used term “secondarily generalized seizure.”

Etiology

The terms idiopathic, symptomatic, and cryptogenic had taken on a variety of meanings and connotations over the years. The commission’s report recommends that the terms idiopathic, symptomatic, and cryptogenic be substituted by genetic, structural/metabolic and “unknown”.2

Genetic

The term idiopathic as defined in the 1989 document implied epilepsies with “no underlying cause other than a possible hereditary predisposition and were defined by age-related onset, clinical and electrographic characteristics, and a presumed genetic etiology.” 2 The current recommendations strongly require irrefutable evidence for genetic basis. Such evidence may derive from specific molecular genetic studies or from appropriately designed family studies1. The genetic designation does not rule out the possibility of contribution of environmental factors in the expression of disease.

Genetic epilepsies would include childhood absence epilepsy, autosomal dominant nocturnal frontal lobe epilepsy, Dravet syndrome, etc. The term “idiopathic” was also used to convey the idea of a highly benign, self-limited, pharmacoresponsive form of epilepsy, occurring and at times remitting in predictable age groups and generally unaccompanied by other neuropsychiatric consequences or disabilities. We now know a variety of subtle cognitive and behavioral disorders to be occurring in association with these epilepsies. In this context, the use of the word “benign” can be misleading for physicians, patients, and families. Therefore, the new report recommended that this term should neither be used nor implied when referring to this group of epilepsies. Instead usage of two new terms has been proposed: self-limited and pharmacoresponsive.

Self-limited: This is a more precise term to denote epilepsies having a high likelihood of spontaneous remission at a predictable age.

Pharmacoresponsive: Designating an epileptic syndrome Idiopathic allowed, within a reasonable certainty, the prediction of rapid seizure control with appropriate medication without significant morbidity. The term pharmacoresponsive may be more meaningful to clinicians as well as families than the term “benign” or “idiopathic”. In general, it was felt that cause should not be equated with prognosis of epilepsy.

However, even “pharmacoresponsive,” may be problematic because: (1) at least one-third of children with benign epilepsies do not need pharmacologic treatment; and (2) patients with the same syndrome may be “pharmacoresponsive” or “pharmacoresistant” and the prediction, almost impossible at the onset of the illness.

Structural/metabolic

The term “symptomatic” as used in the conventional classification is often substituted for the concept of a poor prognosis. The ILAE report recommends the term “structural and metabolic” to highlight that there is a separate disorder, structural or metabolic”, the relationship of which to epilepsy is not as direct as in genetic epilepsies. Structural lesions include acquired disorders such as stroke, trauma, neoplasia and infection, as well as those of genetic origin (e.g., tuberous sclerosis, many malformations of cortical development). Even when associated with genetic defects, there is a separate disorder interposed between such defect and the epilepsy. It may become necessary to subdivide these causes further, starting with separate groups for structural and for metabolic.

Unknown cause

The designation “Cryptogenic” in the previous classification implied an as-yet-unrecognized structural/metabolic defect or “presumed symptomatic”2. The new term “Unknown” is meant to be truly neutral; the epilepsy may have a fundamental genetic defect at its core or it may be the consequence of a separate as-yet unrecognized disorder. It was from among the so-called “cryptogenic” epilepsies that genetic electroclinical syndromes such as autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) and autosomal dominant epilepsy with auditory features (ADEAF) were discovered.9,10 This group would include electroclinical syndromes like epilepsy of infancy with migrain focal seizures and myoclonic epilepsy in infancy [formerly benign myoclonic epilepsy of infancy]11. It might be reasonable to include some of the traditional “idiopathic” electroclinical syndromes as well. These include benign rolandic epilepsy, Panayiotopoulos syndrome, and benign occipital epilepsy of the Gastaut type, in the causation of which genetic factors may be involved but do not appear to be primary12,13.

Diseases, syndromes, and epilepsies

The new report remarks that the 1989 report classification had used the terms “syndromes” and “epilepsies” almost interchangeably and the term “syndrome” took on a broad and very imprecise meaning. Certain highly specific entities such as childhood absence epilepsy and poorly differentiated epilepsies like cryptogenic parietal lobe epilepsies were treated as if they represented the same level of diagnostic precision.

An electroclinical syndrome, however, is a complex of clinical features, signs, and symptoms that together define a distinctive, recognizable clinical disorder with typical age of onset, specific EEG characteristics, seizure types, and other features which, when taken together, permit a specific diagnosis. Syndrome recognition often has implications for treatment, management, and prognosis. The report recommends to restrict the term “syndrome” to a group of clinical entities reliably identified by a cluster of electroclinical characteristics. Patients whose epilepsy does not fulfill the criteria for a specific electroclinical syndrome should be described in terms of a variety of clinically relevant factors like etiology and seizure types.

In clinical practice, one frequently encounters patients who do not fit precise electroclinical syndromes but whose features represent clinically distinctive constellations, based at times on etiology. These are diagnostically meaningful forms of epilepsy and may have implications for clinical management. These include mesial temporal lobe epilepsy, hypothalamic hamartoma with gelastic seizures, epilepsy with hemiconvulsion and hemiplegia, and Rasmussen syndrome. The new report recommends that these constellations are sufficiently distinctive to be recognized as relatively specific diagnostic entities.

In the current classification, many epilepsies with structural or metabolic defects are grouped together as “symptomatic focal epilepsies” and distinguished on the basis of localization. The commission recommended that terms such as “symptomatic temporal lobe epilepsy” be replaced by longer but more precise expressions such as “epilepsy with focal seizures secondary to cortical dysplasia in the temporal lobe.” Localization is not the primary factor of importance for understanding the cause and prognosis of these epilepsies.
The commission decided to discard the terms generalized and focal for modifying the epilepsies themselves3. “Generalized” spasms arising from a focal lesion as occurs in West syndrome and focal seizures arising from a diffuse genetic disorder as occurs in Dravet syndrome were the examples of why and how these terms do not adequately reflect the processes underlying the epilepsies. The term *catastrophic* appears emotionally charged and discouraging and has been rejected in the new recommendations.

The new ILAE report does not appear to fulfill its intent to modernize the classification by incorporating the advances in the neurosciences. In fact it has raked up disagreements and controversies among experts while adding some confusion for the clinician. It is in fact preferable to continue using the previous ILAE classifications, despite their significant incompleteness. Nevertheless, it may be worthwhile for students as well clinicians managing epilepsy to go through these recommendations and the objections thereto in order to develop a better understanding of seizure and epilepsy classification.

**The four dimensional classification**: Luders et al, while urging the commission to abandon a “tentative approach” of finding a smooth transition between the old classification and an incomplete new classification, recommend utilization of all the modern diagnostic technologies in the development of a “really new” classification. The group has been using and teaching a four-dimensional classification of Epilepsies and Epileptic Seizures, the purpose of which has been to classify individual cases to help in the selection of therapeutic approaches and to define prognosis.

1. **Seizures**: The detailed symptomatic description of the seizure along with the frequency and the presence or absence of provocative factors.

2. **Location**: Even though the theoretical differentiation between focal and generalized epilepsies is becoming difficult, when classifying individual cases this may not be as big a problem. Certain simplifying assumptions need to be made considering that the so-called focal seizures, whatever their origin and etiology, tend to respond to similar antiepileptic drugs agents whereas most generalized epilepsies respond to different agents. One also needs to define the epileptogenic zone precisely while considering epilepsy surgery.

3. **Etiology**: The prognosis of epilepsy is often dependent on the etiology. The etiology also often determines the management of epilepsy – both medical as well as surgical.

4. **Related medical conditions**: Specifying the related medical conditions further clarifies the clinical condition and guides treatment.

This four-dimensional approach can be illustrated with examples:

**Case 1 Location**: Left frontal lobe. **Seizures**: Right hand clonic seizure. **Frequency**: 2/month. **Etiology**: Left frontal gliosis. **Related Medical Condition**: Past history of CNS Tuberculosis. Mild left hand paresis.

**Case 2 Location**: Right mesial temporal lobe. **Seizures**: Left hand tonic seizure evolving to bilateral tonic. **Frequency**: 1/month. **Etiology**: Right mesial temporal sclerosis. **Related Medical Condition**: Moderate retardation.

Shorvon felt that despite being a major determinant of prognosis, seizure etiology remains neglected as a dimension in the classification scheme. He has proposed an etiology based classification with four broad categories:

- **Idiopathic**: epilepsy of predominately genetic or presumed genetic origin.

- **Symptomatic**: epilepsy associated with gross anatomic or pathologic abnormalities, and/or clinical features, indicative of underlying disease or condition.

- **Provoked**: epilepsy in which a specific systemic or environmental factor is the predominant cause of the seizures with no gross causative neuroanatomic or neuropathologic changes. This a new category and includes seizures provoked by fever; menstrual cycle and catamenial epilepsy; sleep-wake cycle; metabolic and endocrine-induced seizures; drug-induced seizures, etc. It also includes reflex epilepsies like photosensitive, startle-induced, reading epilepsy, etc.

- **Cryptogenic**: epilepsy of presumed symptomatic nature in which the cause has not been identified.

**Suggested scheme for an etiological classification of epilepsy**

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<tr>
<th><strong>Main category</strong></th>
<th><strong>Subcategory</strong></th>
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<tr>
<td>Idiopathic epilepsy</td>
<td>Pure epilepsies due to single gene disorders</td>
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<td></td>
<td>Pure epilepsies with complex inheritance</td>
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<td>Symptomatic epilepsy</td>
<td>Predominately genetic or developmental causation</td>
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<td></td>
<td>- Childhood epilepsy syndromes</td>
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<td>- Progressive myoclonic epilepsies</td>
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<td>- Neurocutaneous syndromes</td>
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<td>- Other neurologic single gene disorders</td>
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<td>- Disorders of chromosome function</td>
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<td>- Developmental anomalies of cerebral structure</td>
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<tr>
<td>Reflexive epilepsy</td>
<td>Provoking factors</td>
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<td>Cryptogenic epilepsies</td>
<td>Reflex epilepsies</td>
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In Shorvon’s etiologic scheme, the new terms genetic, structural/metabolic and unknown have not been followed. It was felt that some of this change in terminology is cosmetic rather than conceptual. The term genetic for example should not be used unless predominant genetic causation is fully established. Some feel that this category should be in addition to “idiopathic,” “cryptogenic,” and “symptomatic” and not a substitute for “idiopathic”5,16,17,18,19,20. The term structural/metabolic is imprecise and the change from cryptogenic to unknown purely semantic.

**From Books to the consulting rooms**

The nineteenth century scientist John Hughlings Jackson subdivided classification systems into “scientific” and “practical.” The analogy provided was that of a botanist who classified plants according to the evolutionary place and gardeners who grouped plants according to the color of their flowers, shape of their leaves, growth requirements and characteristics.

Thus, for the practicing physician, the classification of epilepsies remains reasonably simple. The first attempt is to differentiate seizures as a symptom of another disease from epilepsy as a disease itself. Further, attention to description
of attacks, age at onset, family history and accompanying disorders will usually lead to accurate practical information. For the treating clinician, the scheme proposed by Luders carries tremendous practical value as all the four dimensions largely direct the symptomatic as well as disease modifying therapy besides determining the prognosis. Classification being the fundamental step towards understanding and therapy of epilepsy, it is important to spend time on this aspect of the disease. Complex classification systems are more for research purposes and the above discussion will help readers to translate the classification systems to fruitfully apply to the patients.

References


17. Guerrini R. Classification concepts and terminology: is clinical description assertive and laboratory testing objective? Epilepsia, 2010; 51:718–720


