

SPECIAL REPORT

Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009

*†Anne T. Berg, ‡Samuel F. Berkovic, §Martin J. Brodie, ¶Jeffrey Buchhalter, ##J. Helen Cross, ††Walter van Emde Boas, ‡‡Jerome Engel, §§Jacqueline French, ¶¶Tracy A. Glauser, ###Gary W. Mathern, ***Solomon L. Moshé, †††Douglas Nordli, ††††Perrine Plouin, and ‡Ingrid E. Scheffer

*Department of Biology, Northern Illinois University, DeKalb, Illinois, U.S.A.; †Department of Neurology, Epilepsy Center, Northwestern Children's Memorial Hospital, Chicago, Illinois, U.S.A.; ‡Epilepsy Research Centre, University of Melbourne (Austin Health), West Heidelberg, Victoria, Australia; §Epilepsy Unit, Western Infirmary, Glasgow, Scotland; ¶Department of Neurology, Phoenix Children's Hospital, Phoenix, Arizona, U.S.A.; #Neurosciences Unit, UCL-Institute of Child Health, Great Ormond Street Hospital, London, United Kingdom; **National Centre for Young People with Epilepsy, Lingfield, United Kingdom; ††Department of EEG/EMU, Epilepsy Clinic "Meer & Bosch," Heemstede; Stichting Epilepsie Instellingen Nederland, Hoofddorp, The Netherlands; ‡‡Department of Neurology, UCLA, Los Angeles, California, U.S.A.; §§Department of Neurology, New York University, New York, New York, U.S.A.; ¶¶Department of Neurology, Cincinnati Children's Hospital, Cincinnati, Ohio, U.S.A.; ###Department of Neurosurgery, UCLA, Los Angeles, California, U.S.A.; ***Department of Neurology, Albert Einstein College of Medicine, Bronx, New York, U.S.A.; and†††Department of Neurology, Hôpital Necker Enfant Malades, Paris, France

SUMMARY

The International League Against Epilepsy (ILAE) Commission on Classification and Terminology has revised concepts, terminology, and approaches for classifying seizures and forms of epilepsy. Generalized and focal are redefined for seizures as occurring in and rapidly engaging bilaterally distributed networks (generalized) and within networks limited to one hemisphere and either discretely localized or more widely distributed (focal). Classification of generalized seizures is simplified. No natural classification for focal seizures exists; focal seizures should be described according to their manifestations (e.g., dyscognitive, focal motor). The concepts of generalized and focal do not apply to electroclinical syndromes. Genetic, structural–metabolic, and unknown

represent modified concepts to replace idiopathic, symptomatic, and cryptogenic. Not all epilepsies are recognized as electroclinical syndromes. Organization of forms of epilepsy is first by specificity: electroclinical syndromes, nonsyndromic epilepsies with structural–metabolic causes, and epilepsies of unknown cause. Further organization within these divisions can be accomplished in a flexible manner depending on purpose. Natural classes (e.g., specific underlying cause, age at onset, associated seizure type), or pragmatic groupings (e.g., epileptic encephalopathies, self-limited electroclinical syndromes) may serve as the basis for organizing knowledge about recognized forms of epilepsy and facilitate identification of new forms.

KEY WORDS: Epilepsy, Classification, Syndrome, Seizure, Organization.

The history of classification has rested largely upon astute observations and expert opinions. First published in 1960 and last updated officially in 1981 for seizures (Commission on Classification and Terminology of the International League Against Epilepsy [ILAE], 1981) and 1989 for epilepsies (Commission on Classification and Terminology of the

International League Against Epilepsy, 1989), the ILAE classifications are based on concepts that, for the most part, predate modern neuroimaging, genomic technologies, and concepts in molecular biology. The original authors foresaw that changes to the classification would be needed as new information was acquired and as new investigative technologies were developed. This is no simple task. Attempts have been made to update the 1989 and 1981 documents (Engel, 2001, 2006); however, no new proposal has been forthcoming.

A primary motivation for revising the classification in the 2005–2009 Commission term and to continue revising it in the future is to bring epilepsy out of the

Accepted December 22, 2009; Early View publication February 26, 2010.

Address correspondence to Anne T. Berg, Department of Biology, Northern Illinois University, DeKalb, IL 60115, U.S.A. E-mail: atberg@niu.edu

Wiley Periodicals, Inc.

© 2010 International League Against Epilepsy

shadows of expert opinion and assertion-dominated arguments so that the classification of the epilepsies fully reflects and profits from all of the other advances being made in basic and clinical neurosciences and so that those advances can be incorporated into clinical practice. In the following report we present the main findings and recommendations of the Commission's deliberations during the 2005–2009 term accompanied by comments interleaved with the main text. The comments provide background, explanations, and justifications for these decisions and provide some insight into the variety of considerations that were addressed and why specific decisions were made.

Although changes have been made to terminology and concepts, we emphasize that no changes (other than to nomenclature) are being made to the list of epilepsy entities ("syndromes") already recognized and updated in the 2006 Task force report (Engel, 2006). Furthermore, the revisions made to terminology and concepts in epilepsy do not have any tangible impact on how clinicians use the electroclinical syndromes that have been internationally recognized and that are applied to people with epilepsy around the world every day.

TERMINOLOGY AND CONCEPTS FOR CLASSIFICATION OF SEIZURES AND EPILEPSIES

Mode of seizure onset and classification of seizures

Generalized epileptic seizures are conceptualized as originating at some point within, and rapidly engaging, bilaterally distributed networks. Such bilateral networks can include cortical and subcortical structures, but do not necessarily include the entire cortex. Although individual seizure onsets can appear localized, the location and lateralization are not consistent from one seizure to another. Generalized seizures can be asymmetric.

Focal epileptic seizures are conceptualized as originating within networks limited to one hemisphere. They may be discretely localized or more widely distributed. Focal seizures may originate in subcortical structures. For each seizure type, ictal onset is consistent from one seizure to another, with preferential propagation patterns that can involve the contralateral hemisphere. In some cases, however, there is more than one network, and more than one seizure type, but each individual seizure type has a consistent site of onset. Focal seizures do not fall into any

Comments: Introduction

Within the context of epilepsies and seizures, the word "classification" has been used to refer to at least three concepts:

1. The list of entities that are recognized as distinct forms of epilepsy: Nothing has changed in the elements of this list for specific types of electroclinical syndromes, although the list of seizures has been simplified from previous versions.
2. The concepts and structure underlying the organization and presentation of that list: The 1989 classification (Commission, 1989) was an organization built on concepts that no longer correspond to or accurately describe our increasing knowledge of seizures and the epilepsies. Consequently, the current organization and the concepts on which it is based are abandoned or revised. The dimensions by which we characterize seizures and epilepsies should represent useful, natural classes. Furthermore, the order and organization of the list of recognized syndromes need not be singular, constrained, or rigid but should be flexible to reflect our best current understanding of the neurobiology, the clinical features, prognostic implications, and any other features relevant to clinical practice or research.
3. The methods and process that determine which entities are recognized and those features by which those entities are organized: The expert-opinion review process for "admitting" a syndrome to the list will need to be replaced by a system based upon objective analysis and assessment of relevant evidence. This will be required to provide leads for new potential syndromes and some guidance into the natural classes and dimensions by which a scientific classification could be constructed (Berg & Blackstone, 2006). We intend to initiate such a process in the future.

In reviewing the current classifications, such as they are, and in modifying terminology and concepts, the Commission's work was aided by proceedings of the Monreale workshop (Capovilla et al., 2009). Although we set forth a revised, simplified classification for seizures, we did not find that there was an adequate knowledge base currently to propose a new classification (in the sense of organization) of epilepsies. Rather we have provided new terminology and concepts that better reflect the current understanding of these issues. A guiding principle has been to strive for clarity and simplicity so that terms refer to single qualities and are not a mixture of different concepts and dimensions. Another guiding principle has been, to the greatest extent possible, not to accept assumptions and assertions as the basis for classification and to acknowledge areas for which we do not have good information for making decisions. We present new concepts, but acknowledge them as concepts in need of further development and evidence (e.g., for generalized and focal seizures).

Comments: Classification and terminology as it relates to seizures:

The Commission accepted the ILAE definition of epileptic seizure (Fisher et al., 2005): “a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.” Therefore, the comments are limited to describing epileptic seizures and are not designed to assist the clinician in distinguishing epileptic seizures from nonepileptic events. This will be treated separately in a diagnostic manual.

The terms “focal” and “generalized” have been used to express a dichotomous classification for both seizures and the epilepsies. In fact in the late 1800s, Hughlings-Jackson wrote that focal discharging lesions caused both focal and generalized seizures (see York & Steinberg, 2009). For seizures, based on current electroclinical evidence, the Commission felt that it was still of some pragmatic utility to maintain the terminology, although it was generally acknowledged that these terms likely did not represent a clear dichotomy.

The conceptualization of generalized seizures as arising in and rapidly engaging bilaterally distributed networks was, in part, an attempt to address the apparently generalized nature of spasms in the context of a focal lesion. This could represent a paradigmatic breakthrough in thinking about manifestations versus underlying pathology. There was much lively discussion and at times bitter disagreement over how best to classify spasms, as generalized or focal or both. In the end, the considerable collective knowledge of spasms represented by the various Commission members was still not up to the task of resolving this issue precisely because of inadequate information. Spasms are thus left on their own.

The 1981 seizure document used the terms simple partial, complex partial, and partial seizures secondarily generalized (Commission, 1981). This terminology was imprecise, as the terms “simple” and “complex” were often misused or misunderstood. Moreover, the distinction based on impairment of consciousness or awareness, although of great pragmatic social importance (e.g., for driving), was impossible to define precisely (Gloor, 1986). The term “secondarily” generalized is poorly understood and inconsistently used. Currently, we have inadequate information to create a *scientific classification* within focal seizures. Instead, we recommend that focal seizure be described according to features that are the most useful for a given specific purpose. For example, in many circumstances such as the differential diagnosis of epileptic versus nonepileptic events or in presurgical evaluation it is often useful to describe the specific elemental features of seizures and their sequence of occurrence (Luders et al., 1993). Others may wish to recognize terms to describe degree of disability caused by the seizures. We encourage those interested to consult the Glossary of Ictal Semiology (Blume et al., 2001) for well-defined descriptive terms.

recognized set of natural classes based on any current understanding of the mechanisms involved.

The following specific changes to the 1981 classification of seizures have been made.

1. Neonatal seizures are no longer regarded as a separate entity. Seizures in neonates can be classified within the proposed scheme.

2. The previous subclassification of absence seizures has been simplified and altered. Myoclonic absence seizures and eyelid myoclonia are now recognized.

3. Spasms were not explicitly acknowledged in the 1981 classification of seizures. They are now included. The term “epileptic spasms,” which includes infantile spasms, was recognized previously (Blume et al., 2001). Because spasms may continue past or even occur de novo after infancy (Camfield et al., 2003, Goldstein & Slomski, 2008), the more general term “epileptic spasms” is used. There was inadequate knowledge to make a firm decision regarding whether spasms should be classified as focal, generalized, or both; consequently, they have been placed in their own group as unknown.

4. For focal seizures, the distinction between the different types (e.g., complex partial and simple partial) is eliminated. It is important, however, to recognize that impair-

Table 1. Classification of seizures^a

Generalized seizures
Tonic-clonic (in any combination)
Absence
Typical
Atypical
Absence with special features
Myoclonic absence
Eyelid myoclonia
Myoclonic
Myoclonic
Myoclonic atonic
Myoclonic tonic
Clonic
Tonic
Atonic
Focal seizures
Unknown
Epileptic spasms

^aSeizure that cannot be clearly diagnosed into one of the preceding categories should be considered unclassified until further information allows their accurate diagnosis. This is not considered a classification category, however.

ment of consciousness/awareness or other dyscognitive features, localization, and progression of ictal events can be of primary importance in the evaluation of individual

Comments: Terminology and concepts for underlying cause:

The terms idiopathic, symptomatic, and cryptogenic have taken on a variety of meanings and connotations laden with presumptions which, at times, conflate multiple concepts into a single word. This has resulted in considerable contradiction and confusion. The term idiopathic was defined in the 1989 document: “There is no underlying cause other than a possible hereditary predisposition. Idiopathic epilepsies are defined by age-related onset, clinical and electrographic characteristics, and a presumed genetic etiology.” We now state a minimum threshold for presuming a form of epilepsy does in fact have a genetic basis. Undocumented assertions are not accepted. Examples of epilepsy syndromes that would be classified as genetic epilepsies include childhood absence epilepsy, autosomal dominant nocturnal frontal lobe epilepsy, and Dravet syndrome. Note that in the 1989 classification, Dravet syndrome was not classified as idiopathic epilepsy. Dravet is now considered as a genetic epilepsy.

The term “idiopathic” was also used to convey the idea of a highly pharmaco-responsive form of epilepsy. Many, although not all, of the traditional “idiopathic” epilepsies also spontaneously remit during a predictable age range (a separate quality or dimension) and were generally thought to be unaccompanied by other consequences or disabilities, although this is clearly not the case, as a variety of subtle cognitive and behavioral disorders are seen in association with these epilepsies.

The new terminology and concepts require that the concept of cause contain only one dimension and not be used to imply others. Cause is no longer equated with prognosis, and the implication that “idiopathic” confers the quality of “benign” is intentionally discarded. It is possible that the genetic defect may have other effects in addition to the seizures but, as best we can tell, these other effects are not interposed between the genetic effect and the seizures.

The term “symptomatic” is a truism; all epilepsy is symptomatic of something. It is often substituted for the concept of a poor prognosis. The term “structural and metabolic” is intended to highlight that there is a separate disorder the relationship of which to epilepsy is not as direct. The grouping of structural and metabolic disorders together is only to distinguish this concept from that of genetic (i.e., genetic vs. all else). Depending on the purposes, it will be necessary to subdivide these heterogeneous causes further starting with separate groups for structural and for metabolic. Within each of these subdivisions, further taxa will be elaborated (e.g., for malformations, gliomas, and mitochondrial disorders). Other ILAE Commissions and other groups around the world are tackling these very issues.

“Cryptogenic” was defined in 1989 as “presumed symptomatic,” apparently meaning “lesional.” It is, however, from among these “cryptogenic” epilepsies that genetic electroclinical syndromes such as autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) and autosomal dominant epilepsy with auditory features (ADEAF) have been discovered (Scheffer et al., 1995; Ottman et al., 1999). In replacing the term “Cryptogenic” with “unknown,” the Commission discarded the notion that a clinical hunch should be the basis of a scientific classification.

Examples of syndromes that would be classified as “of unknown cause” include epilepsy of infancy with migrating focal seizures and myoclonic epilepsy in infancy [formerly benign myoclonic epilepsy of infancy, (Engel, 2006)]. At the present time, it might be reasonable to include some of the traditional electroclinical syndromes previously classified as “idiopathic” in the unknown category as well. These include benign rolandic epilepsy (Vadlamudi et al., 2006), Panayiotopoulos syndrome, and benign occipital epilepsy of the Gastaut type (Taylor et al., 2008). It is likely that genetic factors are involved in these syndromes. Current *evidence* (e.g., low or absent concordance in siblings) does not suggest that genetic factors are paramount. This issue will be revisited if high quality evidence supporting the hypothesis of a genetic contribution comes to light.

As new genetic contributions to epilepsy are recognized, it may often be difficult to know how best to characterize them with respect to the preceding distinctions. For example, *ARX*, a homeobox gene, is associated with phenotypic heterogeneity including West syndrome and lissencephaly (Stromme et al., 2002). *STXBPI* encodes a protein involved in synaptic vesicle release and is associated with Ohtahara syndrome (Saito et al., 2008). Both syndromes involve severe encephalopathic forms of epilepsy. In the first case, one might consider the *ARX* mutation in the structural/metabolic category. In the case of *STXBPI*, because of the function of the protein product, one might associate this with the concept of genetic epilepsy. No determination has been made in either case at this time. Instead the role of the specific genetic error should be recognized, but it is not necessary to pigeon-hole the cause of the disorder further unless there is an adequate basis for doing so. We advocate a focus on mechanisms. This focus should ultimately reveal the natural classes. The overly simplistic designation of “genetic” versus “structural-metabolic” will then be replaced by a more precise characterization of the underlying cause.

patients and for specific purposes (e.g., differential diagnosis of nonepileptic events from epileptic seizures, randomized trials, surgery). Nothing in this recommendation precludes describing focal seizures according to these or other features.

5. Myoclonic atonic (previously called “myoclonic astatic”) seizures are now recognized.

Table 1 presents the list of recognized seizure types.

Descriptors of focal seizures

For pragmatic reasons and 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. We have listed *examples* chosen to facilitate continuity with the 1981 seizure document and which have been drawn from the glossary of ictal semiology (Blume et al., 2001) (Table 2).

The classification of status epilepticus will be the subject of a separate report in the future.

Underlying type of cause (etiology)

Instead of the terms idiopathic, symptomatic, and cryptogenic, the following three terms and their associated concepts are recommended:

1. Genetic: The concept of genetic epilepsy is that *the epilepsy is, as best as understood, the direct result of a known or presumed genetic defect(s) in which seizures are the core symptom of the disorder. The knowledge regarding the genetic contributions may derive from specific molecular genetic studies that have been well replicated and even become the basis of diagnostic tests (e.g., SCN1A and Dravet syndrome) or the evidence for a central role of a genetic component may come from appropriately designed family*

studies. Designation of the fundamental nature of the disorder as genetic does *not* exclude the possibility that environmental factors (outside the individual) may contribute to the expression of disease. At the present time, there is virtually no knowledge to support specific environmental influences as causes of or contributors to these forms of epilepsy.

2. “Structural/metabolic”: Conceptually, there is a *distinct other structural or metabolic condition or disease* that has been demonstrated to be associated with a substantially increased risk of developing epilepsy in appropriately designed studies. Structural lesions of course include acquired disorders such as stroke, trauma, and infection. They may also be of genetic origin (e.g., tuberous sclerosis, many malformations of cortical development); however, *as we currently understand it*, there is a separate disorder interposed between the genetic defect and the epilepsy.

3. “Unknown cause”: Unknown is meant to be viewed neutrally and to designate that *the nature of the underlying cause is as yet unknown*; it may have a fundamental genetic defect at its core or it may be the consequence of a separate as yet unrecognized disorder.

Diseases, syndromes, and epilepsies

Disease versus syndrome

Although there is reason to distinguish the concepts of disease and syndrome, these terms are not consistently used in medicine. *Ultimately, it was decided not to insist on the disease–syndrome distinction in referring to the epilepsies at this time, although either or both terms have been and will continue to be used depending on the context and custom.* Instead, there are at least three or four groupings that may be invoked in this context and as described below:

Electroclinical syndromes: Henceforth, the use of the term “syndrome” will be restricted to a group of clinical entities that are reliably identified by a cluster of electroclinical characteristics. Patients whose epilepsy does not fit the criteria for a specific electroclinical syndrome can be described with respect to a variety of clinically relevant factors (e.g., known etiology and seizure types). This does not, however, provide a precise (syndromic) diagnosis of their epilepsy.

Constellations: In addition to the electroclinical syndromes with strong developmental and genetic components to them, there are a number of entities that are not exactly electroclinical syndromes *in the same sense* but which represent clinically distinctive *constellations* on the basis of specific lesions or other causes. These are diagnostically meaningful forms of epilepsy and may have implications for clinical treatment, particularly surgery. These include mesial temporal lobe epilepsy (with hippocampal sclerosis), hypothalamic hamartoma with gelastic seizures, epilepsy with hemiclonus and hemiplegia, and Rasmussen “syndrome.” Age at presentation is not a defining feature in these disorders, as we understand them; however, they are

Table 2. Descriptors of focal seizures according to degree of impairment during seizure^a

Without impairment of consciousness or awareness With observable motor or autonomic components. This roughly corresponds to the concept of “simple partial seizure.” “Focal motor” and “autonomic” are terms that may adequately convey this concept depending on the seizure manifestations). Involving subjective sensory or psychic phenomena only. This corresponds to the concept of an aura, a term endorsed in the 2001 Glossary. With impairment of consciousness or awareness. This roughly corresponds to the concept of complex partial seizure. “Dyscognitive” is a term that has been proposed for this concept (Blume et al., 2001). Evolving to a bilateral, convulsive ^b seizure (involving tonic, clonic, or tonic and clonic components). This expression replaces the term “secondarily generalized seizure.”

^aFor more descriptors that have been clearly defined and recommended for use, please see Blume et al., 2001.

^bThe term “convulsive” was considered a lay term in the Glossary; however, we note that it is used throughout medicine in various forms and translates well across many languages. Its use is, therefore, endorsed.

sufficiently distinctive to be recognized as relatively specific diagnostic entities. *Whether or not they are considered “electroclinical syndromes” now or in the future is less important than that they be recognized by clinicians who are treating patients.*

Structural/metabolic epilepsies: The next group includes epilepsies secondary to specific *structural or metabolic lesions or conditions* but which do not, given our current understanding, fit a specific electroclinical pattern, although that may change in the future. Therefore, these entities represent a lower level of specificity than the two previous groups.

Epilepsies of unknown cause: Those epilepsies, which in the past were termed “cryptogenic,” will now be referred to as being of “*unknown*” cause.

Dimensions for classifying epilepsies and organizing information

In referring to syndromes, the dichotomy of focal versus generalized will be abandoned, that is, “the focal or generalized epilepsies.” This is intended to separate the manifestations from the underlying pathology that produced them.

Each syndrome and each patient can be characterized according to a large number of other features, which are often routinely part of any patient’s evaluation and which are essential features in distinguishing among established syndromes. These include the age at onset, cognitive and developmental antecedents and consequences, motor and sensory examinations, EEG features, provoking or triggering factors, and patterns of seizure occurrence with respect to sleep.

Comments: Reestablishing the concept of “electroclinical syndrome” and recognizing the precision or imprecision of diagnosis.

Electroclinical syndromes: The 1989 report used the terms “syndromes” and “epilepsies” almost interchangeably. The result was that the term “syndrome” took on a broad and very imprecise meaning to the point where very specific and highly recognizable entities (such as childhood absence epilepsy) and poorly differentiated and not well-described epilepsies (such as cryptogenic parietal lobe epilepsy) tended to be treated as though they represented the same level of diagnostic precision. The result was a veneer of equivalency bestowed upon all entities identified within that document.

An electroclinical syndrome, however, is a complex of clinical features, signs, and symptoms that together define a distinctive, recognizable clinical disorder. These often become the focus of treatment trials as well as of genetic, neuropsychological, and neuroimaging investigations (e.g., Scheffer et al., 1998, 2008; Guerrini et al., 2007; Ottman et al., 2008). These are distinctive disorders identifiable on the basis of a typical age onset, specific EEG characteristics, seizure types, and often other features which, when taken together, permit a specific diagnosis. The diagnosis in turn often has implications for treatment, management, and prognosis. It would be inappropriate to refer to, for example, epilepsy with a frontal lobe focus and not otherwise specified as a “syndrome.” The currently recognized electroclinical syndromes are presented in the first part of Table 3 organized by typical age at onset, as this is one of the most distinctive and clinically salient dimensions for organizing these entities, but this is just an example of one way to organize them.

Constellations: Whether these entities should be considered syndromes or nonsyndromic epilepsies was the subject of considerable disagreement. Ultimately, these conditions can and should be recognized based on their clinical features. What they are called as a group in no way detracts from their clinical importance.

Epilepsies associated with structural or metabolic conditions: Previously, many such epilepsies were grouped together as “symptomatic focal epilepsies” and distinguished on the basis of localization. We recommend less emphasis be given to localization and more to the underlying structural or metabolic cause. Terms such as “symptomatic temporal lobe epilepsy” are replaced by longer but more precise expressions such as “epilepsy with focal seizures secondary to cortical dysplasia in the temporal lobe.” Localization is not, based on current knowledge, the primary factor of importance for understanding the cause and prognosis of these epilepsies. Further organizations might consider type of lesion, age at onset, localization, seizure type, specific ictal and interictal EEG patterns, or other factors.

Epilepsies of unknown cause: These epilepsies account for one-third or more of all epilepsy, are the most poorly understood, and represent perhaps the most fertile area for future research in imaging and genetics. For such research to be feasible, however, it will require that the simple characterization by localization of interictal focus (e.g., cryptogenic parietal lobe epilepsy) be replaced with a detailed characterization of all relevant features (see next section). Among these poorly differentiated epilepsies are likely to be additional genetic electroclinical syndromes (such as ADNFLE and ADEAF); however, they cannot be recognized until they are adequately characterized. This approach should also facilitate identification of nongenetic determinants of epilepsy.

Table 3. Electroclinical syndromes and other epilepsies

<p>Electroclinical syndromes arranged by age at onset^a</p> <p>Neonatal period</p> <ul style="list-style-type: none"> Benign familial neonatal epilepsy (BFNE) Early myoclonic encephalopathy (EME) Ohtahara syndrome <p>Infancy</p> <ul style="list-style-type: none"> Epilepsy of infancy with migrating focal seizures West syndrome Myoclonic epilepsy in infancy (MEI) Benign infantile epilepsy Benign familial infantile epilepsy Dravet syndrome Myoclonic encephalopathy in nonprogressive disorders <p>Childhood</p> <ul style="list-style-type: none"> Febrile seizures plus (FS+) (can start in infancy) Panayiotopoulos syndrome Epilepsy with myoclonic atonic (previously astatic) seizures Benign epilepsy with centrotemporal spikes (BECTS) Autosomal-dominant nocturnal frontal lobe epilepsy (ADNFLE) Late onset childhood occipital epilepsy (Gastaut type) Epilepsy with myoclonic absences Lennox-Gastaut syndrome Epileptic encephalopathy with continuous spike-and-wave during sleep (CSWS)^b Landau-Kleffner syndrome (LKS) Childhood absence epilepsy (CAE) <p>Adolescence – Adult</p> <ul style="list-style-type: none"> Juvenile absence epilepsy (JAE) Juvenile myoclonic epilepsy (JME) Epilepsy with generalized tonic-clonic seizures alone Progressive myoclonus epilepsies (PME) Autosomal dominant epilepsy with auditory features (ADEAF) Other familial temporal lobe epilepsies <p>Less specific age relationship</p> <ul style="list-style-type: none"> Familial focal epilepsy with variable foci (childhood to adult) Reflex epilepsies <p>Distinctive constellations</p> <ul style="list-style-type: none"> Mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE with HS) Rasmussen syndrome Gelastic seizures with hypothalamic hamartoma Hemiconvulsion-hemiplegia-epilepsy <p>Epilepsies that <i>do not fit</i> into any of these diagnostic categories can be distinguished first on the basis of the presence or absence of a known structural or metabolic condition (presumed cause) and then on the basis of the primary mode of seizure onset (generalized vs. focal)</p> <p>Epilepsies attributed to and organized by structural-metabolic causes</p> <ul style="list-style-type: none"> Malformations of cortical development (hemimegalencephaly, heterotopias, etc.) Neurocutaneous syndromes (tuberous sclerosis complex, Sturge-Weber, etc.) Tumor Infection Trauma <p>Angioma</p> <ul style="list-style-type: none"> Perinatal insults Stroke Etc. <p>Epilepsies of unknown cause</p> <p>Conditions with epileptic seizures that are traditionally not diagnosed as a form of epilepsy per se</p> <ul style="list-style-type: none"> Benign neonatal seizures (BNS) Febrile seizures (FS)
<p>^aThe arrangement of electroclinical syndromes does not reflect etiology.</p> <p>^bSometime referred to as Electrical Status Epilepticus during Slow Sleep (ESES).</p>

Natural evolution of the disorder

Among the many dimensions that may be used for organizing forms of epilepsy, “natural” evolution is highlighted here because of its considerable importance in reflecting our growing understanding of the full nature of the epilepsies.

Epileptic encephalopathy. The concept of epileptic encephalopathy has grown in acceptance and use. It was formally recognized in the 2006 report and is now defined within this document. Epileptic encephalopathy embodies the notion that *the epileptic activity itself may contribute to severe cognitive and behavioral impairments above and beyond what might be expected from the underlying pathology alone (e.g., cortical malformation), and that these can worsen over time.* These impairments may be global or more selective and they may occur along a spectrum of severity. Although certain syndromes are often referred to as epileptic encephalopathies, the encephalopathic effects of seizures and epilepsy may potentially occur in association with any form of epilepsy.

Other concepts and terms. The terms catastrophic and benign *are not* recommended. The first has strong emotional overtones and thus is not considered an appropriate term for a diagnostic label or category. The second belies the growing understanding of the relationship between the epilepsies and a wide variety of brain disorders including cognitive, behavioral, and psychiatric illnesses as well as sudden death and suicide. “Benign” can be misleading and leave physicians, patients, and families unaware of and unprepared to address these associated disorders. That said, names of syndromes have not, at this time, been changed.

An interim organization (“classification”) of the epilepsies

In a departure from the 1989 classification of the epilepsies, there is no one specific organization proposed for the revised classification. Instead, the various forms of epilepsy (at all levels of specificity) will be organized according to those dimensions that are most relevant to a specific purpose. These may be comparable to those in the 1989 classification (seizure onset, “etiology,” and age at onset), a different hierarchical arrangement of these same dimensions, a more detailed version of these dimensions, or by entirely different dimensions as needed. For example, Table 3 provides a list of epilepsies from the Task Force on Classification and Terminology (Engel, 2006) according to level of specificity and within those designations, by age where meaningful.

ACKNOWLEDGMENTS

During the Commission’s 2005–2009 term, input was sought from experts in the genetics of epilepsy, neuroimaging, therapeutics, pediatric and adult epileptology, as well as statistics and research design. The results

Comments: Other dimensions for classifying epilepsies and organizing information:

The commission decided to discard the terms generalized and focal for modifying the epilepsies themselves. “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 some of the prime examples of why and how these terms do not adequately reflect the processes underlying the epilepsies.

In addition to the traditional dimensions and features, each syndrome and each patient can be characterized according to a large number of other features, which are often routine parts of any patient’s evaluation and essential features in distinguishing among established syndromes. These include the cognitive and developmental antecedents and consequences, motor and sensory examinations, EEG features, provoking or triggering factors, and patterns of seizure occurrence with respect to sleep. There is also an important traditional cluster of syndromes that might be convenient to maintain, the “idiopathic generalized epilepsies;” however, we recommend that they be called the “genetic generalized epilepsies.”

Natural evolution: Epileptic Encephalopathy. The term “epileptic encephalopathy” can be used to characterize syndromes and also be applied to individuals. As a *domain for clustering and describing syndromes*, an epileptic encephalopathy is an electroclinical syndrome associated with a high probability of encephalopathic features that present or worsen after the onset of epilepsy. Separately but important to note, as a group, they tend to be pharmacoresistant, but this is another quality or dimension. Inclusion of a specific syndrome in the domain of “epileptic encephalopathy” does not imply that all individuals with these disorders will appear encephalopathic; however, the risk is often quite high. *Diagnosing an individual* as having an *encephalopathic course* requires demonstration of a failure to develop as expected relative to same-aged peers or to regress in abilities. Note that it is not necessary for an individual to have a syndrome identified as being one of the “epileptic encephalopathies” (e.g., West, Dravet) in order to have an encephalopathic course. Epileptic encephalopathy can present along a continuum of severity and may occur at any age. The phenomenon is most common and severe in infancy and early childhood, where global and profound cognitive impairment may occur. Adults, however, can also experience cognitive losses over time from uncontrolled seizures (Hermann et al., 2006). Whether these involve similar or different mechanisms as those early in development remains to be seen, but the phenomenon should be recognized.

Inherent in the concept of epileptic encephalopathy is the notion that suppression of epileptic activity may improve cognition and behavior. Early effective intervention may in fact improve seizure control and developmental outcome in some cases (Jonas et al., 2004; Freitag & Tuxhorn, 2005; Jonas et al., 2005; Lux et al., 2005).

“Epileptic encephalopathy” should be viewed as a concept and a description of what is observed clinically with the recognition that, we are rapidly approaching a clearer understanding of the effects of epilepsy on brain function and the potential for lasting deleterious impact in the developing brain. We must, however, recognize that the source of an apparent encephalopathy is usually unknown. It may be the product of the underlying cause, the result of epileptic process, or a combination of both.

The argument against the term, “Benign”: One of the new research Benchmarks of the National Institutes of Health for epilepsy research is to understand the various comorbidities of epilepsy including cognitive, behavioral, and psychiatric disorders as well as mortality (Kelly et al., 2009). There are international efforts underway to understand the mechanisms of sudden death and to educate patients and families of this risk and how it may be mitigated. Increasingly, basic science and clinical studies are illuminating the shared mechanisms between epilepsy and these various other disorders.

Self-limited: The terms “idiopathic” and “benign” captured important features of clinical relevance. We recommend that, instead of designating a group of syndromes as “benign,” we recognize the different qualities that make up the concept of benign and apply them specifically and consistently to individual forms of epilepsy. One of these features is predictable spontaneous remission. Instead of benign, we recommend the descriptive term “self-limited” to mean having a high likelihood of spontaneously remitting at a predictable age. If a better term is devised, that can be considered in the future.

Pharmacoresponsive: In syndromes designated as idiopathic, most cases tend to be pharmacoresponsive. Diagnosis of one of these syndromes allows, within a reasonable certainty, the prediction that the seizures will rapidly come under control with appropriate medication. As yet, we do not have perfect prediction, so some patients diagnosed with a particular syndrome may not be pharmacoresponsive; however, clinical prognostication was never an exact science. Labeling these syndromes as pharmacoresponsive may be more meaningful to clinicians and provide anticipatory guidance to families better than the term “idiopathic,” which requires explanation.

Of note, the inclusion of features that are descriptive of the natural evolution of a form of epilepsy is not, strictly speaking, based upon natural classes but rather on repeated observations and impressions. *They are included for pragmatic purposes.*

Age at onset: For grouping syndromes or individuals, age at onset categories are recommended as per standard use: neonate (<44 weeks of gestational age), infant (<1 year), child (1–12 years), adolescent (12–18 years), and adult (>18 years). For some purposes, it may be helpful to distinguish a category for elderly (>60 or >65). The age ranges are approximate and meant to be used only for convenience in describing already characterized forms of epilepsy. For individual patients, the exact age at onset or best approximation should be used, and greater precision for electroclinical syndromes is encouraged when possible.

Other features: Many other dimensions and features will ultimately be used in describing, classifying, and grouping the different forms of epilepsies and may prove to be more useful for organizing the epilepsies than those used in the 1989 Classification. We may ultimately classify by specific cause, for example, ion channelopathies and by specific ion channel genes, as is being done with prolonged QT syndrome (Johnsons et al., 2009). Alternatively, one could organize a subgroup of epilepsies by age at onset and association with *specific* types of cortical malformations (Lerner et al., 2009). Other dimensions would include but are not limited to detailed aspects of ictal and interictal EEG, structural neuroimaging findings, neurologic examination, and cognitive and psychiatric status.

A syndrome is characterized with respect to many factors. Knowing a given patient's syndromic diagnosis, provides key information about that patient's epilepsy, for example, likely age at onset, EEG patterns, likely responses to medications, and cognitive and developmental status. We can organize our information about these syndromes along the many dimensions by which they are characterized. The benefits of this approach for developing a diagnostic manual are considerable.

For epilepsies that do not fall into clear electroclinical syndromes and which are associated with structural–metabolic causes, the most natural and rational primary approach to organizing them seems to be by specific underlying cause or lesion. For epilepsies of unknown cause and predominately characterized by seizure onset, there is no natural class that validly sorts them into more homogeneous groups. The revised recommended approach explicitly acknowledges this. Forcing these partially or poorly characterized epilepsies into a system of classification for which they are not yet ready suggests greater knowledge than we currently have and impedes progress. Much greater effort should be invested in characterizing individual patients sufficiently to facilitate objective research into identifying previously unrecognized entities. This information can then be used as the basis for objective analyses to identify potential new “syndromes” (Berg & Blackstone, 2006). It will also greatly facilitate the use of the planned diagnostic manual, which will provide a guide with specific definitions and examples that will encourage clinicians to make the necessary, precise observations on all patients in order to make or exclude specific diagnoses.

Comments: Classification in the future:

The previous “classifications” of seizures and epilepsies were often treated as rigid doctrine. Epilepsy classification was dominated by expert opinion and assertion. Advances in all areas of investigation (epidemiology, electrophysiology, imaging, developmental neurobiology, genomics, computational neuroscience, and neurochemistry) have made it clear that such a simple and often autocratic approach does not do justice to the complexity of the underlying developmental and physiologic processes. Therefore, any classifications put forth by this Commission should be viewed as a guide to summarize our current understanding about seizures and epilepsies in a useful manner, one that is responsive to the needs to which it is put and flexible enough to incorporate new information as it develops.

Unfortunately, this remains an area where long-held beliefs and ignorance often clash with reason and evidence. For example, an overly melodramatic comment posted on the website stated that the Commission's rejection of the term “benign” to characterize epilepsy was “... a stone of death to all of us, who have campaigned for year that on evidence, a significant number of patients and mainly children have some forms of epilepsies ... that are entirely benign with little or no detrimental consequences as documented with long term prospective studies over the last 50 years (...). The main consequences ... are psychosocial resulting from equating them with epilepsy.” Such emotional assertions actively ignore the last several years of very productive research in the neurosciences and represent the kind of arguments that are no longer acceptable.

In the future, the Classification of the Epilepsies will essentially be a database. The features discussed earlier and other essential pieces of information will form the basis for a diagnostic manual. In the interim, we encourage people to conceptualize a future classification as a flexible, multidimensional catalog of features for organizing information about different epilepsies (or seizures) as appropriate for purposes of drug development, clinical and basic research, and of course, clinical practice.

of those deliberations were presented at the ICE in Budapest, 2009. Following comments received at the meeting, a written report was disseminated to the many ILAE chapters with an invitation to respond with feedback. The report was also posted on the ILAE website, again with an invitation to comment, and comments were posted on the website. We owe a special debt of gratitude to the many colleagues around the world who took the time to consider our proposals and convey their thoughts, suggestions, and critiques to us throughout this process. We also thank our colleagues Pawel Matykiewicz, Ruth Ottman, Philippe Ryvlin, and Peter Wolf for their input into some of our meetings. The process for approving this report followed that outlined in the Commission Operations Manual of the ILAE, 2009.

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

DISCLOSURE

None of the authors has any conflict of interest to disclose.

REFERENCES

- Berg AT, Blackstone NW. (2006) Concepts in classification and their relevance to epilepsy. *Epilepsy Res* 70:11–19.
- Blume WT, Luders HO, Mizrahi E, Tassinari C, van Emde Boas W, Engel J. (2001) Glossary of ictal semiology. *Epilepsia* 42:1212–1218.
- Camfield P, Camfield C, Lortie A, Darwish H. (2003) Infantile spasms in remission may reemerge as intractable epileptic spasms. *Epilepsia* 44:1592–1595.
- Capovilla G, Berg AT, Cross JH, Moshe SL, Vigevano F, Wolf P, Avanzini G. (2009) Conceptual dichotomies in classifying epilepsies: partial versus generalized and idiopathic versus symptomatic (April 18–20, 2008, Monreale, Italy). *Epilepsia* 50:1645–1649.
- Commission on Classification and Terminology of the International League Against Epilepsy. (1981) Proposal for revised clinical and electrographic classification of epileptic seizures. *Epilepsia* 22:489–501.
- Commission on Classification and Terminology of the International League Against Epilepsy. (1989) Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 30:389–399.
- Engel J. (2001) A proposed diagnostic scheme for people with epileptic seizures and with epilepsy: report of the ILAE Task Force on Classification and Terminology. *Epilepsia* 42:796–803.
- Engel J. (2006) Report of the ILAE Classification Core Group. *Epilepsia* 47:1558–1568.
- Fisher RS, Boas WVE, Blume W, Elger C, Genton P, Lee P, Engel J. (2005) Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia* 46:470–472.
- Freitag H, Tuxhorn I. (2005) Cognitive function in preschool children after epilepsy surgery: rationale for early intervention. *Epilepsia* 46:561–567.
- Gloor P. (1986) Consciousness as a neurological concept in epileptology: a critical review. *Epilepsia* 27(suppl 2):S14–S26.
- Goldstein J, Slomski J. (2008) Epileptic spasms: a variety of etiologies and associated syndromes. *J Child Neurol* 23:407–414.
- Guerrini R, Moro F, Kato M, Barkovich AJ, Shiihara T, McShane MA, Hurst J, Loi M, Tohyama J, Norci V, Hayasaka K, Kang UJ, Das S, Dobyns WB. (2007) Expansion of the first PolyA tract of ARX causes infantile spasms and status dystonicus. *Neurology* 69:427–433.
- Hermann BP, Seidenberg M, Dow C, Jones J, Rutecki P, Bhattacharya A, Bell B. (2006) Cognitive prognosis in chronic temporal lobe epilepsy. *Ann Neurol* 60:80–87.
- Johnsons JN, Hofman N, Haglund CM, Cascino GD, Wilde AAM, Ackerman MJ. (2009) Identification of a possible pathogenic link between congenital long QT syndrome and epilepsy. *Neurology* 72:224–231.
- Jonas R, Nguyen S, Hu B, Asarnow RF, LoPresti C, Curtiss S, de Bode S, Yudovin S, Shields WD, Vinters HV, Mathern GW. (2004) Cerebral hemispherectomy: hospital course, seizure, developmental, language, and motor outcomes. *Neurology* 62:1712–1721.
- Jonas R, Asarnow RF, LoPresti C, Yudovin S, Koh S, Wu JY, Sankar R, Shields WD, Vinters HV, Mathern GW. (2005) Surgery for symptomatic infant-onset epileptic encephalopathy with and without infantile spasms. *Neurology* 64:746–750.
- Kelly MS, Jacobs MP, Lowenstein DH. (2009) The NINDS epilepsy research benchmarks. *Epilepsia* 50:579–582.
- Lerner JT, Salamon N, Hauptman JS, Velasco TR, Hemb M, Wu JY, Sankar R, Shields WD, Engel J, Fried I, Cepeda C, Andre VM, Levine MS, Miyata H, Yong WH, Vinters HV, Mathern GW. (2009) Assessment of surgical outcomes for mild type I and severe type II cortical dysplasia: a critical review and the UCLA experience. *Epilepsia* 50:1310–1335.
- Luders HO, Burgess R, Noachtar S. (1993) Expanding the international classification of seizures to provide localization information. *Neurology* 43:1650–1655.
- Lux AL, Edwards SW, Hancock E, Johnson AL, Kennedy CR, Newton RW, O'Callaghan FJ, Verity CM, Osborne JP. (2005) The United Kingdom Infantile Spasms Study (UKISS) comparing hormone treatment with vigabatrin on developmental and epilepsy outcomes to age 14 months: a multicentre randomised trial. *Lancet Neurol* 4:712–717.
- Ottman R, Barker-Cummings C, Lee JH, Ranta S. (1999) Genetics of autosomal dominant partial epilepsy with auditory features. In Berkovic SF, Genton P, Hirsch E, Picard F (Eds) *Genetics of focal epilepsies*. John Libbey & Co Ltd, London, pp. 95–102.
- Ottman R, Rosenberger L, Bagic A, Kamberakis K, Ritzl EK, Wohlschlagger AM, Shamim S, Sato S, Liew C, Gaillard WD, Wiggs E, Berl MM, Reeves-Tyer P, Baker EH, Butman JA, Theodore WH. (2008) Altered language processing in autosomal dominant partial epilepsy with auditory features. *Neurology* 71:1973–1980.
- Saito H, Kato M, Mizuguchi T, Hamada K, Osaka H, Tohyama J, Urano K, Kumada S, Nishiyama K, Nishimura A, Okada I, Yoshimura Y, Hirai S, Kumada T, Hayasaka K, Fukuda A, Ogata K, Matsumoto N. (2008) De novo mutations in the gene encoding STXBP1 (MUNC18-1) cause early infantile epileptic encephalopathy. *Nat Genet* 40:782–788.
- Scheffer IE, Bhatia KP, Lopes-Cendes I, Fish DR, Marsden CD, Andermann E, Andermann F, Desbiens R, Keene D, Cendes F, Manson JI, Constantinou JEC, McIntosh A, Berkovic SF. (1995) Autosomal dominant nocturnal frontal lobe epilepsy: a distinctive clinical disorder. *Brain* 118:61–73.
- Scheffer IE, Phillips HA, O'Brien CE, Saling MM, Wrennall JA, Wallace RH, Mulley JC, Berkovic SF. (1998) Familial partial epilepsy with variable foci: a new partial epilepsy syndrome with suggestion of linkage to chromosome 2. *Ann Neurol* 44:890–899.
- Scheffer IE, Turner SJ, Dibbens LM, Bayly MA, Friend K, Hodgson B, Burrows L, Shaw M, Wei C, Ullmann R, Ropers H-H, Szepletowski P, Haan E, Mazarib A, Afawi Z, Neufeld MY, Andrews PI, Wallace G, Kivity S, Lev D, Lerman-Sagie T, Derry CP, Korczyn AD, Geicz J, Mulley JC, Berkovic SF. (2008) Epilepsy and mental retardation limited to females: an under-recognized disorder. *Brain* 131:918–927.
- Stromme P, Mangelsdorf ME, Shaw MA, Lower KM, Lewis SM, Bruyere H, Lucherath V, Gedeon AK, Wallace RH, Scheffer IE, Turner G, Partington M, Frints SG, Fryns JP, Sutherland GR, Mulley JC, Geicz J. (2002) Mutations in the human ortholog of *Aristaless* cause X-linked mental retardation and epilepsy. *Nat Genet* 30:441–445.
- Taylor I, Berkovic SF, Kivity S, Scheffer IE. (2008) Benign occipital epilepsies of childhood: clinical features and genetics. *Brain* 131:2287–2294.
- Vadlamudi I, Kjeldsen MJ, Corey LA, Solaas MH, Friis ML, Pellock JM, Nakken KO, Milne RL, Scheffer IE, Harvey SA, Hopper JL, Berkovic SF. (2006) Analyzing the etiology of benign rolandic epilepsy: a multicenter twin collaboration. *Epilepsia* 47:550–555.
- York GK, Steinberg DA. (2009) Hughlings Jackson's suggestion for the treatment of epilepsy. *Neurology* 73:1155–1158.