Classification is not EZ (Invited Editorial Comment)

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The 1981 International Classification of Epileptic Seizures and the 1989 International Classification of Epilepsies and Epileptic Syndromes have been widely accepted, resulting in an unprecedented standardization of terminology used by the international epilepsy community. These classifications however, are imperfect and have been rightly criticized for a variety of reasons, from the time they were proposed. Since 1997, a Task Force of the International League against Epilepsy (ILAE) has been charged with evaluating the current classifications and recommending changes. Several reports of this Task Force have been published (Engel 1998, Engel 2001, Blume *et al*. 2001), including a proposal for a diagnostic scheme to be used when describing individual patients (Engel 2001), but no *new* classification has yet been proposed. A Core Group of the ILAE Task Force *(table 1)* is currently hard at work finalizing a report that will suggest the use of a rigorous, evidence-based approach to identifying epileptic seizure types and epilepsy syndromes as discrete diagnostic entities, as well as plans for organizing these diagnostic entities into categories or classifications that will be useful for various purposes. In this issue of *Epileptic Disorders*, Loddenkemper *et al.*, from the Cleveland Clinic, have proposed an alternative diagnostic scheme which they refer to as a "classification."

Dr. Hans Lüders, who is senior author of this proposal and a member of the ILAE Task Force Core Group, has been a strong critic of the 1981 and 1989 classifications, and has made important conceptual contributions to the work of the ILAE Task Force. There remains however, a major fundamental difference between the approach to epilepsy classification used at the Cleveland Clinic and that used by the mainstream of the international epilepsy community and supported by the ILAE. A principal component of the standard approach to epilepsy classification is the identification of epilepsy syndromes with specific diagnostic, therapeutic, and prognostic implications. A valid criticism of this approach is the fact that a syndromic diagnosis cannot be made in many patients with epilepsy, although the percentage of patients for whom a syndromic diagnosis is not possible has varied considerably from one study to another, due largely to methodological differences (Manford *et al*. 1992, Berg *et al*. 1999, Freitag *et al*. 2001, Kellinghaus *et al*. 2004). Clearly, syndromic diagnoses are most useful in pediatric epileptology, particularly for children with idiopathic epilepsies, but are of dubious value for many patients with focal symptomatic epilepsies. In addition, it is often difficult to make syndromic diagnoses in patients at the time they appear with new onset epilepsy.

Table 1. ILAE Task force on classification and terminology core group

Jerome Engel, Jr. (Chair) – Los Angeles, CA, USA
Frederick Andermann – Montreal, Quebec, Canada
Giuliano Avanzini – Milan, Italy
Anne Berg – DeKalb, IL, USA
Samuel Berkovic – Melbourne, Australia
Warren Blume – London, Ontario, Canada
Olivier Dulac – Paris, France
Natalio Fejerman – Buenos Aires, Argentina
Hans Lüders – Cleveland, OH, USA
Masakazu Seino – Shizuoka, Japan
Peter Williamson – Lebanon, NH, USA
Peter Wolf – Dianalund and Copenhagen, Denmark

The basic premise of the Cleveland Clinic diagnostic approach has been that emphasis should be placed on a detailed description of the ictal event, and proponents have argued that a syndromic diagnosis is actually unnecessary (Onsurbe *et al*. 1999). Criticisms of this approach include the fact that it is not a classification, but rather, a means to describe clinical characteristics of individual patients, and that detailed descriptions of ictal events usually do not provide sufficient information for determining the diagnostic work-up, treatment, and prognosis, nor are detailed seizure descriptions possible in many patients who are not admitted for video EEG monitoring. The Cleveland Clinic "classification" is particularly useful however, for patients with focal symptomatic epilepsy who are candidates for localized surgical resection.

The ILAE Task Force has taken a different approach to addressing the shortcomings of syndromic diagnoses. This approach maintains that the diagnosis of a specific syndrome, when possible, is highly desirable because it immediately communicates considerable information about

the patient, with respect to the diagnostic evaluation required, appropriate treatments, and prognosis. The Task Force recognizes however, that many patients have epilepsy conditions that do not fit clearly into well defined syndromes, and recommends that, for these patients, further evaluation, treatment, and prognosis should be based on diagnosis of a specific seizure type (Engel 2001). These ictal diagnostic entities are currently being defined, based on presumed pathophysiological and anatomical substrates, as an adjunct to syndromic diagnosis, as opposed to the purely descriptive ictal phenomenology recommended in the Cleveland Clinic approach. Consequently, when a syndromic diagnosis cannot be made, either because it is too early in the course of the disorder, or the symptom complex is not consistent with an accepted syndrome, diagnostic evaluation, therapy, and prognosis would follow from diagnosis of the seizure type(s). Seizure types as diagnostic entities, rather than descriptive phenomenology therefore, are a new and important feature of the diagnostic scheme proposed by the ILAE (Engel 2001). Seizure-type diagnoses are intended to supplement syndromic diagnoses, or substitute for syndromic diagnoses when these are not possible.

Detailed descriptions of ictal phenomenology, as recommended by Dr. Lüders and his colleagues for classifying epilepsy, do not *per se* carry diagnostic, therapeutic, or prognostic implications. Nor can they be easily organized into categories to constitute a useful classification for clinical or basic research purposes, but rather, constitute a unique description for each individual patient. Perhaps for this reason, the Cleveland Clinic group now appears to have softened their opposition to syndromic diagnoses by including them when they exist, in Dimension 1 of their diagnostic scheme. Although they maintain that localization of the epileptogenic zone (EZ), the principal element of Dimension 1, is the most important part of the diagnostic information in their scheme, clearly this is greatly modified by the syndromic diagnosis, except in patients with focal symptomatic epilepsies. For instance, identifying the entire brain as the EZ would carry no important information for distinguishing a patient with Lennox-Gastaut syndrome from one with childhood absence epilepsy, whereas inclusion of the syndromic diagnosis does this. Conversely, once the syndrome is identified, what is the point of localizing the EZ? Localization of the EZ is of great importance in patients with focal symptomatic epilepsy who are candidates for surgical therapy, but what diagnostic, therapeutic, or prognostic value does it have beyond this? Dimension 2 is not a seizure classification, but merely a detailed description of ictal phenomenology. These descriptions do not have the diagnostic, therapeutic, or prognostic implications of the seizure types proposed in the ILAE diagnostic scheme (Engel 2001). A detailed description of ictal phenomena can be useful for determining the location of the EZ in patients who are surgical candidates, but does not add anything to a syndromic or seizure diagnosis, and can be misleading. For instance, ictal semiology of a focal seizure due to benign childhood epilepsy with centrotemporal spikes can be identical to the ictal semiology due to a focal structural lesion in the rolandic area.

The concept of classification has been openly debated by members of the ILAE Task Force Core Group (Wolf 2003, Engel 2003, Lüders *et al*. 2003, Berg *et al*. 2003, Avanzini *et al*. 2003). Classifications are generally used to recognize and categorize natural classes that can be reproducibly distinguished from all other natural classes (Ax 1996), as in biological taxonomy. In the case of epilepsy classification, the challenge is to identify specific diagnostic entities that can be reproducibly distinguished from all other diagnostic entities. The ILAE Task Force Core Group is making a considerable effort to establish evidence-based criteria for recognizing specific seizure types and syndromes as unique diagnostic entities equivalent to natural classes. Further categorization or classification of these diagnostic entities provides a framework not only for describing individual patients or for teaching, but for organizing patients into relatively homogeneous groupings for epidemiological studies; investigations into basic mechanisms that could eventually lead to novel therapies and prevention; identification of specific etiologies, including genetics; and other research purposes. In this sense, the proposal of Loddenkemper *et al*. is not a classification, but merely a diagnostic scheme similar to the one previously proposed by the ILAE (Engel 2001). For this reason, it becomes necessary to ask whether this new diagnostic scheme includes anything that is not already in the ILAE diagnostic scheme.

Table 2 compares the five dimensions of the Cleveland Clinic, patient-oriented, epilepsy classification proposed by Loddenkemper *et al*., with the five axes of the ILAE diagnostic scheme (Engel 2001).

Dimension 1, epilepsy localization, is included as part of the etiological diagnosis in Axis 4 of the ILAE diagnostic scheme. The syndrome diagnosis, which is also included where possible in Dimension 1 of the Cleveland Clinic scheme, is the same as Axis 3 of the ILAE diagnostic scheme. It is worth noting that Axis 3 recognizes that a syndromic diagnosis is not always possible.

Dimension 2 of the Cleveland Clinic scheme is essentially the same as Axis 1 of the ILAE classification, with minor differences in terminology (Blume *et al*. 2001). Unlike Dimension 2 of the Cleveland Clinic scheme, Axis 1 of the ILAE scheme allows the clinical situation to determine the degree of descriptive detail. Axis 1 also includes seizure frequency, which is Dimension 4 of the Cleveland Clinic scheme. Axis 2 of the ILAE scheme, seizure type as a diagnostic entity however, does not appear in the Cleveland Clinic scheme, which is an important omission. Consequently, there is nothing contained in the first four dimensions of the Cleveland Clinic scheme that is not also contained in the ILAE scheme, while the important

Table 2. Comparison of the Cleveland Clinic and ILAE diagnostic schemes

Cleveland Clinic		**ILAE**	
Dimension 1	Epilepsy localization[1]	*Axis 1*	Ictal phenomenology
Dimension 2	Seizure semiology[2]	*Axis 2*	Seizure type[5]
Dimension 3	Etiology[3]	*Axis 3*	Syndrome
Dimension 4	Seizure frequency[4]	*Axis 4*	Etiology
Dimension 5	Related medical condition If applicable[6]	*Axis 5*	Impairment[6]

[1]Localization is included in Axis 4; this Dimension also includes syndrome (Axis 3)
[2]This is the same as Axis 1 although a detailed description is not mandatory in Axis 1
[3]This is the same as Axis 4
[4]Seizure frequency is included in Axis 1
[5]This is a unique concept not included in the Cleveland Clinic scheme
[6]These two categories are different, but optional

seizure-type diagnostic entity of the ILAE scheme is missing from the Cleveland Clinic scheme.

The fifth categories of the two schemes are entirely different; Dimension 5 of the Cleveland Clinic scheme lists related medical conditions if applicable, while Axis 5 of the ILAE diagnostic scheme is an optional assessment of impairment, using a WHO scale. Although debate is justified as to whether either of these two categories needs to be included in a formal diagnostic scheme, this does not reflect a major concern for choosing one approach over the other, or justify the need for a new diagnostic scheme.

The issue, therefore, is primarily whether a diagnostic scheme which emphasizes localization of the EZ would accurately define more patients, provide more clinically useful information, and be more easily communicated than a scheme which emphasizes seizure types and syndromes as diagnostic entities. Localization of the EZ is extremely difficult even in the best of circumstances and can be achieved only in a small minority of patients in the general population (Manford *et al*. 1992), while a seizure-type diagnosis is usually possible when a syndrome diagnosis is not. Localization of the EZ in itself provides little or no information about the diagnostic evaluation required, therapy needed, or, most importantly, prognosis, whereas diagnosis of a specific seizure type and syndrome do. Finally, it is not clear how localization of the EZ, or the Cleveland Clinic diagnostic approach itself, would be used to easily communicate information among physicians in a manner comparable to stating that a patient has mesial temporal lobe epilepsy or typical absence seizures. What we now need of course, is independent field-testing to compare the clinical utility of various diagnostic schemes (Kälviäinen *et al*. 2005).

Personally, and I must speak here for myself and not the ILAE Task Force, I appreciate the work that the Cleveland Clinic group continues to do to pursue the possible applications of their "classification" system, and recognize that it has contributed importantly to the work of the ILAE Task Force [Axis 1 of the diagnostic scheme (Blume *et al*. 2001)]. However, I see no compelling need for this new diagnostic approach when the scheme proposed by the ILAE Task Force contains essentially the same information, as well as the additional important diagnostic entity of seizure type. Furthermore, the primary emphasis of this new proposal on the location of the EZ has clinical importance only for a small minority of patients with focal symptomatic epilepsy who are candidates for surgery. A variation of the Cleveland Clinic diagnostic scheme however, might be adapted by the ILAE Task Force, specifically for patients with focal symptomatic epilepsy. □

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