Classification criteria of epileptic seizures and syndromes

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Abstract

Care must be exercised not to intermingle with classification of seizures and classification of epilepsies in an inconsistent fashion. Criteria for each class must be defined as clearly as possible, and these criteria must be those which are necessary for classifying any given case. The international classification first proposed by the ILAE in 1970 was an attempt to distinguish seizures from epilepsies; the seizure types defined in the 2001 diagnostic scheme are conceptually akin to the syndromes in the 1989 classification in the sense that they imply etiological, therapeutic, and prognostic significance. However, there exists no room in the new diagnostic scheme to accommodate electro-clinical seizure types, which have been used for more than three decades. The concept of epileptic syndrome in the 1989 classifications seems to have been changed to epileptic seizure type in the 2001 diagnostic scheme, and seizure type of the latter virtually becomes synonymous with epileptic syndrome of the former. In the 2001 diagnostic scheme, seizure type can be used to supplement syndrome, and can stand alone when syndrome diagnosis cannot be made. In other words, seizure types may replace syndromes, or vice versa. We should not return to an era prior to 1970 where no distinction exists between epilepsies and seizures. In a cohort of patients with active epilepsy, to what extent is syndrome classification applicable? In 300 consecutive patients hospitalized in a tertiary center, syndromic diagnosis was applicable to only 61%. Similarly, another 100 consecutive patients, classification of epilepsy was possible but not defined as a syndrome in 32% patients, according to the 1989 classification. The 1989 syndrome classification assigned in each category “other epilepsies not defined as a syndrome.” These epilepsies are diagnosed only dichotomously; idiopathic focal or generalized, symptomatic focal or generalized, or undetermined whether focal or generalized. In other words, even if we could complete a list to include all the new syndromes that may exist, it is very unlikely that it would cover all epilepsies.

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Keywords: Concept of classification criteria; Distinction between epileptic seizures and epilepsies; Syndromes epilepsies; Two dichotomies, 4-part classification

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1. Introduction

The development of a rational treatment approach and prognostication of patients with epilepsy are often based on a specific profile of seizure events, or the suggested diagnosis of specific disorder based on presenting symptoms and available clinical information. Although classifications based on neurobiological knowledge would be highly desirable, the present state of information on the anatomical, pathophysiological, genetic, and biochemical mechanisms and substrata of epileptic seizures and epilepsies still make such a task rather difficult.

A very important concept inherent in classification of epileptic seizures and of epilepsies published in 1970 was the distinction between the two. The distinction was made more explicit in the 1981 revised seizure classification (Commission Report, 1981) and the syndrome/epilepsy classification published in 1985 and 1989. Seizures are classified according to clinical seizure type, ictal and interictal EEG expression, and are defined as electro-clinical seizure types, while syndromes are defined as an epileptic disorder characterized by a cluster of signs and symptoms customarily occurring together (Commission Report, 1985 and 1989).

In 1997 an attempt was made to reevaluate the current classifications for epileptic seizures and epilepsy (Engel, 1998), and proposed a diagnostic scheme for describing individual patients, which includes a list of generally agreed-upon epileptic seizure types and epilepsy syndromes (Engel, 2001). A glossary of terms was also published to be used when describing ictal phenomena (Blume et al., 2001), and a series of essays on concepts of classification to be considered in the process of creating a new classification system (Fisher, 2003). This chapter addresses some of these issues which cause confusion in the classification of epileptic seizures and epilepsies.

2. Classification criteria for seizures and syndromes from 1970 to 2001

2.1. Definition of seizures and epilepsies

The ILAE and IBE recently proposed the definitions of epileptic seizures and epilepsy, stating that “an epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiologic, cognitive, psychological, and social consequences of the condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure” (Fisher et al., 2005). In the time-honored Dictionary of Epilepsy published by WHO, Gastaut (1973)
mentioned “a given condition may often be described as either epilepsy or an epileptic seizure. Although the distinction is sometimes arbitrary, the two terms are used in the following ways: epilepsy when referring to the etiology or the site of the lesion, epileptic seizure when referring to the nature of the phenomenon of the frequency or circumstances of occurrence, e.g., oropharyngeal epileptic seizure, autonomic epileptic seizure, hallucinatory epileptic seizure, and evoked epileptic seizure”.

Nevertheless, even among epilepsy specialists, the distinction between epilepsies and epileptic seizures was not necessarily clear. In the preamble of the first proposal for the International Classification of the Epilepsies, Merlis (1970) stated that “care must be exercised not to intermix classification of seizures and classification of epilepsies in an inconsistent fashion, that is criteria for each class must be defined as clearly as possible, and that these criteria must be those which are necessary and sufficient for classifying any given case”.

2.2. Criteria of the 1970 epilepsy and seizure classification

In the 1970 epilepsy classification, the format in defining criteria for generalized and focal epilepsies was: (A) clinical criteria: (1) seizure form, (2) presence of neurological or psychological evidence of brain pathology, (3) age of onset, (4) etiology, and (B) EEG criteria: (1) interictal, (2) ictal (Table 1). A clinical and EEG classification of epileptic seizures was proposed by Gastaut (1970) on behalf of the ILAE. The criteria for classifying seizures were: (1) clinical seizure type, (2) electrographic seizure type, (3) electrographic interictal expression, (4) anatomical substrate, (5) etiology, and (6) age. It is obvious that, as far as the classification criteria of epilepsies and seizures are concerned, the former overlap the latter (Table 2).

Since the introduction of the 1970 seizure classification, sophisticated methods for studying epileptic seizures have become commonplace. These methods include video documentation of epileptic seizures with simultaneous EEG recording, and instant replay capability. The advances enabling repeated review of transient ictal events facilitated further elaboration of classification. The 1985 and 1989 advent of digital EEG instruments and the capability of storing information on CDs has resulted in further progress in video-EEG recording.

2.3. Criteria of the 1981 seizure classification and 1989 syndrome classification

The outcome of this effort was a revised classification which was approved in 1981. The basic structure of the 1970 classifications was retained, but the following significant changes were introduced. For seizure classification criteria, only (a) clinical seizure type, (b) ictal, and (c) interictal EEG expressions have been retained (Table 3). The anatomical substrate, etiology, and the age factor have been deleted as they were largely based on historical information. In a description of seizures (rather than epilepsy), the result of direct observation by means of video-EEG should be the only consideration (Commission Report, 1981).

The commission met frequently in the early 1980s and proposed classification of epilepsies and epileptic syndromes in 1985 and the revised classification in 1989. In both of them, “an epileptic syndrome is defined

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Table 1
The classification criteria of epilepsies (Merlis, 1970)

<table>
<thead>
<tr>
<th>Clinical criteria</th>
<th>Seizures</th>
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<tbody>
<tr>
<td></td>
<td>Neurologic status</td>
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<td></td>
<td>Age of onset</td>
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<tr>
<td></td>
<td>Etiology</td>
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<tr>
<td>Electroencephalographic criteria</td>
<td>Interictal EEG</td>
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<td></td>
<td>Ictal EEG</td>
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Table 2
The classification criteria of epileptic seizures (Gastaut, 1970)

<table>
<thead>
<tr>
<th>Clinical seizure type</th>
<th>Electroencephalographic seizure type</th>
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<tbody>
<tr>
<td>EEG seizure type</td>
<td>Electroencephalographic interictal expression</td>
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<tr>
<td>Etiology</td>
<td>Age</td>
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Table 3
The 1981 classification criteria of epileptic seizures

<table>
<thead>
<tr>
<th>Clinical seizure type</th>
<th>EEG seizure type</th>
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<tbody>
<tr>
<td>EEG interictal expression</td>
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</table>
as an epileptic disorder 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 prognosis. We have adopted this distinction between seizures and syndromes for decades, and found it workable in principle in clinical practice (Commission Report, 1985 and 1989). In 1985, a monograph titled “Epileptic Syndromes” was published that followed the second edition in 1992, the third edition in 2002, and fourth edition in 2005 (Roger et al., 1985, 1992, 2002, 2005). In Japan, a 400-page monograph was published to illustrate individual syndromes with vignettes in 1998 (Seino and Ohtahara, 1998).

3. A diagnostic scheme for epileptic seizures and epilepsy, 2001

3.1. Criteria of seizure and syndrome classification

The ILAE Commission on Classification and Terminology proposed in 2001 a diagnostic scheme that makes use of standardized terminology and concepts to describe individual patients (Engel, 2001). The diagnostic scheme is divided into five axes, organized to facilitate a clinical approach to the development of hypotheses necessary to determine the diagnostic studies and therapeutic strategies to be undertaken in individual patients. Axis 1: ictal phenomenology, Axis 2: seizure type, Axis 3: syndrome, Axis 4: etiology, and Axis 5: impairment. In these five axes epileptic seizure type is defined as: an ictal event believed to represent a unique pathophysiological mechanism, and anatomic substrate. This is a diagnostic entity with etiology, therapeutic, and prognostic implications (new concept) (Table 4). Epilepsy syndrome was defined as: a complex of signs and symptoms that define a unique epilepsy condition. This must involve more than just seizure type, thus frontal lobe seizures per se, for instance, do not constitute a syndrome (changed concept) (Table 5).

Contrary to the 1981 revised seizure classification, in which classifying criteria were clinical and EEG type in addition to the interictal EEG expression, i.e. electro-clinical seizure type, in the 2001 seizure classification, clinical manifestations were moved to ictal phenomenology or Axis 1, while seizure types represent a unique pathophysiological mechanism and anatomical substrate. Most importantly, a seizure type is a diagnostic entity with etiology, therapeutic, and prognostic implications. The term “diagnosis” is defined as: (1) the art of distinguishing one disease from another, (2) the determination of the nature of a case of disease (Dorland’s Medical Dictionary). Insofar as epilepsy is referring to the etiology or disease, epilepsy is “diagnosed,” whereas epileptic seizure is referring to the nature of the phenomenon or symptom, and seizure type is “recognized.” A seizure type that refers to a symptom cannot be a diagnostic entity.

3.2. A discrepancy

On the other hand, in a commentary authored in 1998 by the commission chairman, it is explicitly noted that the classification of syndromes provides information on prognosis and has etiological implications, but the classification of epileptic seizures does not (Engel, 1998). If this notion is correct, it apparently contradicts the definition of seizures that appears in the 2001 classification. Insofar as epileptic seizure types imply diagnostic entity with etiology, therapeutic, and prognostic implications, seizure type or Axis 2 becomes akin to syndrome or Axis 3. Thus, the electro-clinical

Table 4

<table>
<thead>
<tr>
<th>Criteria used to select specific seizure types as unique diagnostic entities (2001) (new concept)</th>
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<tbody>
<tr>
<td>Pathophysiological mechanisms</td>
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<tr>
<td>Neuronal substrates</td>
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<tr>
<td>Response to AEDs</td>
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<tr>
<td>Ictal EEG patterns</td>
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<tr>
<td>Propagation patterns and postictal features</td>
</tr>
<tr>
<td>Syndromes that are associated with this seizure type</td>
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Table 5

<table>
<thead>
<tr>
<th>Classification criteria of epileptic syndromes (2001) (changed concept)</th>
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</thead>
<tbody>
<tr>
<td>Epileptic seizure types</td>
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<tr>
<td>Age of onset</td>
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<tr>
<td>Progressive nature (i.e. epileptic encephalopathies)</td>
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<tr>
<td>Interictal EEG</td>
</tr>
<tr>
<td>Associated interictal signs and symptoms</td>
</tr>
<tr>
<td>Pathophysiological mechanisms, anatomical substrates, and etiologies</td>
</tr>
<tr>
<td>Genetic basis</td>
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</tbody>
</table>
seizure types in the 1981 seizure classification have lost their place in the classification framework and have been extinguished (Fig. 1). Further, syndrome or Axis 3 is defined as “a complex of signs and symptoms that define a unique epileptic condition.” It needs no saying that the distinction between seizure type and syndrome is equivocal. Accordingly, both of them appear to be conceptually similar to epileptic syndrome in the previous classifications.

3.3. The 2001 seizure type equates with the 1989 syndrome

The concept of epileptic syndrome in the 1989 classification seems to have been changed to epileptic seizure type in the 2001 diagnostic scheme, and seizure type of the latter virtually becomes synonymous with epileptic syndrome of the former. It is noteworthy how similar the concept of these two definitions is. In fact, it is explicitly stated in the diagnostic scheme that “seizure type can be used to supplement syndrome, and can stand alone when syndrome diagnosis cannot be made” (Engel, 2001). In other words, seizure types may replace syndromes, or vice versa. Thus, a single patient may have either syndrome or seizure type in the diagnostic scheme, whereas both seizure type and epilepsy/syndrome have to be given to a single patient in order to represent seizure manifestations and etiology of epilepsy in previous classifications. Without recognizing seizure type(s), we are unable to proceed to diagnosing syndrome in a given patient. In communication between physicians, education, clinical trials, registration of new drugs, and epidemiology and also when legal problems have arisen, we have followed this tradition for over three decades. Speaking metaphorically of the relationship between seizures and syndromes, we cannot “set the cart before the horse.”

This has necessarily resulted in the problem that there exists no category in the 2001 diagnostic scheme that equates with seizure type in the conventional classifications. It appears to be downgraded to “a description of the ictal semiology; descriptive ictal terminology that is not always necessary” (Engel, 2001). Notwithstanding, we have built up a tradition in everyday practice in which information about clinical seizure manifestations is so indispensable that a clinician always begins careful consultation from the clinical features of a patient’s attack.

4. Epilepsy syndromes and other epilepsies

“Syndrome classification is not applicable to all patients with epilepsy, but only a limited number of patients” (Engel, 2001). In a cohort of patients with active epilepsy, to what extent is syndrome classification applicable? In 300 consecutive patients hospitalized in a tertiary center where investigations including interictal EEG, ictal video-EEG, MRI in all, and inter- and ictal SPECT and MEG in selected cases
were thoroughly carried out, syndrome classification was applicable to only 61% (Seino, 2004). In another 100 consecutive hospitalized patients, syndromes were identified in 39%, syndromes were probable in 19%, classification of epilepsy was possible but not defined as a syndrome in 32%, and situation-related seizures were found in 10% according to the 1989 classification (Seino, 2004). The 1989 syndrome classification assigned in each category “other epilepsies not defined as syndromes.” These epilepsies are classified only by dichotomy; idiopathic generalized, symptomatic generalized, or undetermined whether focal or generalized. In other words, even if we could complete a list to include all the new syndromes that may exist, it is very unlikely that it would cover all epilepsies.

How can we classify these epilepsies that account for at least one third of patients? The dichotomous classification criteria of seizures and epilepsies has been intentionally excluded in the 2001 diagnostic scheme, however, it offers only room for these patients with other epilepsies, which are not defined as a syndrome. Syndrome is the selected “elite” other non-specific epilepsies.

5. Two dichotomies, a 4-part classification

5.1. Idiopathic versus symptomatic epilepsies

For a century, from the time of Delasauve (1854) to that of Penfield and Jasper (1954), the epilepsies were divided into two major categories: (1) epilepsies with no identifiable brain lesion as functional, idiopathic, essential, genuine, genetic, true, or centroencephalic; (2) epilepsies associated with an identifiable lesion as lesional, structural, organic, symptomatic, secondary, or partial or focal (Gastaut, 1983). It was empirical knowledge that the former implied epilepsies with generalized seizures while the latter implied epilepsies with focal seizures. It was not until 1960 that recognition was given to the existence of symptomatic epilepsies with a variety of generalized seizures from onset, which are electro-clinically obviously different from seizures in idiopathic generalized epilepsies. In the following 15 years, the existence of idiopathic localization-related epilepsies was recognized. Thus, the two separate dichotomies of classifying epilepsies resulted in a 4-part classification separating idiopathic and symptomatic generalized epilepsies from their counterparts of idiopathic and symptomatic localization-related epilepsies. In each category, several syndromes were identified according to their age of onset. Further, in each category, other epilepsies which are not defined as a syndrome were added (Wada and Seino, 1990).

5.2. Cryptogenic and undetermined epilepsies

The 1989 syndrome classification recognized that the dichotomy is not applicable in all cases because occasionally both generalized and focal features may be present in one patient. Therefore, the third category of epilepsies, undetermined as to focal or generalized in nature, was added in the 1989 syndrome classification. In recognition of epilepsies having an undetermined seizure type, the proposed classification designates the following four syndromes as having both partial and generalized seizures at least once during the course of evolution: neonatal seizures, severe myoclonic epilepsy in infancy, epilepsy with continuous spike-wave during slow wave sleep, and acquired aphasia. For the diagnosis of severe myoclonic epilepsy in infancy, for example, the presence of both generalized myoclonic jerks and focal seizures frequently associated with signs of autonomic disturbance is mandatory. Other than the four syndromes classified as undetermined epileptic syndromes, there are other undetermined epilepsies not classified as syndromes. This category is important where both focal and generalized seizures coexist in a single patients and syndrome diagnosis is not applicable.

Although the roles of epileptic predisposition and cerebral lesions are discussed traditionally as independent causes of idiopathic and symptomatic epilepsy, respectively, these factors often coexist. However, a particular case may be arbitrarily classified as either idiopathic or symptomatic depending on which one predominates. Only when given epilepsy fulfills the criteria of idiopathic epilepsy insofar as etiology is concerned but belies electro-clinical correlation with respect to seizure symptomatology, is one entitled to use the term of “cryptogenic” (Classification Report, 1989), although the term has been changed to “probably symptomatic” and finally excluded because of the ambiguity of the concept.
5.3. How other epilepsies not defined as syndrome are classified?

There are two possible reasons for the inability to determine whether the epilepsy is focal or generalized: (1) the patient has both focal and generalized seizures; there are focal and generalized EEG seizure discharges, and (2) unequivocal evidence of either focal or generalized seizure onset is absent, usually due to unwitnessed seizure (Commission Report, 1985 and 1989). In the undetermined epilepsies, other epilepsies not defined as a syndrome were also accommodated.

In other words, there exists a seamless transition between the pole of idiopathic epilepsy and the other pole of symptomatic epilepsy. To the contrary, there exists a clear distinction between epilepsies with focal seizures and epilepsies with generalized seizures. It is evident that classifying focal seizures apart from generalized seizures based on electro-clinical correlation is essential in order to select appropriate anti-epileptic drugs and avoid inappropriate drugs that may result in worsening seizures, and to select appropriate candidates for surgically remediable epilepsy patients. It is also evident that the outcome of the medical and surgical treatments can be foreseen based on the syndrome/epilepsy classification.

Wolf (2003) stated “What is wrong with the 1981 ICES? I believe that nothing fundamental is wrong concerning its taxonomic principles and system. Nevertheless, it is outdated.” Nobody would oppose the richness of a list of new epilepsy syndromes. However, it is unlikely that the number of patients who conform to syndrome classifications would increase as the description of syndromes increases.

References


