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Classification of epileptic seizures and epilepsy syndromes

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Abstract

The efforts of ILAE for providing a standardized classification and terminology of epileptic seizures and epilepsy syndrome; the international classification of epileptic seizures in 1981 and international classification of epilepsy syndromes and epilepsies in 1989, have provided outstanding achievement in promoting epilepsy care, research, and education over the past decades. However, further attempts of ILAE to improve and update the classification systems have not been successful due to significant heterogeneities and still incomplete knowledge on the fundamental pathophysiology of epilepsies. Despite these shortcomings, the Commission on Classification and Terminology of ILAE recently published a new proposal, "Revised Terminology and Concepts for Organization of Epileptic seizures and Epilepsies", which has generated lively discussions and debates throughout the international epilepsy communities. The basic concepts for the change seem to be rational and well taken but the proposal was not a classification, which made the epilepsy communities somewhat confused and disappointed. A new proposal of classification is urgently needed to replace the overdue ILAE-classification.

INTRODUCTION

Classification is the universal vocabulary for communication and exchange of ideas, which is essential for clinical, educational, and research achievements. The classification systems in medicine may have different ranks in hierarchies with a classification system based on pathomechanisms being considered the most reliable and ranked at the highest in hierarchy, while classifications based on etiology, biomarkers, clusters of symptoms and signs, and characteristic symptoms are in descending orders. In epileptology, pathomechanisms of epileptogenesis or ictogenesis are still incompletely understood. Etiologies are unknown in a major proportion of patients while they are quite heterogeneous in patients with known causes of epilepsy. We still do not have any reliable biomarkers for individual cases to be useful for the formulation of classification. Therefore, the current classification systems of epilepsy are based on the electroclinical correlations of individual cases, which are defined as epilepsy syndromes (clusters of signs and symptoms occurring together) and epileptic seizures (the most characteristic symptom), which are at the bottom in hierarchy.

By the leadership of International League Against Epilepsy (ILAE), the international classification of epileptic seizures (ICES) was proposed in 1970 and revised in 1981[1], which has classified seizures into two broad categories, partial and generalized seizures, on the basis of electroclinical correlations. Partial seizures were defined as seizures in which the clinical and EEG changes indicate initial activation of a system of neurons limited to a part of one cerebral hemisphere. They were further divided into simple and complex partial seizures based on the assessment of impairment of consciousness, with or without secondary generalization. Generalized seizures were defined as seizures in which the clinical and EEG changes indicate initial involvement of both hemispheres. They were further divided into generalized tonic-clonic, absence, myoclonic, clonic, tonic, and atonic seizures. The ICES is simple and clinically useful for the selection of antiepileptic drugs (AEDs), thus widely accepted by international medical communities. However, there have been continuing controversies on the scientific basis for the dichotomies of "partial and generalized seizures", and for the use of "impairment of consciousness" as a critical measure of classification.

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Continuing efforts of ILAE to improve the classification to be more clinically useful have resulted in the proposal of the international classification of epilepsy syndromes and epilepsies (ICE) in 1985, which was revised in 1989.[2] Epilepsy syndrome was defined as a distinctive, recognizable clinical disorder by a complex of clinical features, signs and symptoms occurring together. The classification scheme consists of three steps; (i) First, to define seizure types into localization-related (focal or partial) and generalized seizures; (ii) Second, to determine the etiology as one of three categories; idiopathic (there is no underlying cause other than a possible hereditary predisposition), symptomatic (the result of one or more identifiable disorders of the brain), and cryptogenic (presumed to be symptomatic, but the etiology is unknown); and (iii) Third, to categorize into one of known or recognized electroclinical syndromes. Syndromic diagnosis usually provides much more comprehensive information relevant to the etiology, natural courses and prognosis, and therapeutic efficacies. Thus recognizing the patient's epilepsy syndrome has become a firm recommendation in all guidelines of epilepsy management. In clinical practices, many physicians have found that with available clinical information, ICE is a well organized and a very inclusive system, thus most of patients can be assigned into a predetermined diagnostic category. However, there have been growing criticisms against the framework of ICE over past decades. The reasons include: (i) Only a minority of patients can be assigned into specific electroclinical syndromes while many patients are assigned into non-specific diagnostic categories, which may give a false impression of diagnostic precision; (ii) Anatomical localization of lobar epilepsies are not often accurate; (iii) It is essential to incorporate recent advances in epileptology; e.g., neuroimaging data, genetic and molecular information, and newly recognized epilepsy syndromes. In addition, there have been continuing arguments about the dichotomy of "partial and generalized", and controversies to the terminologies of "idiopathic, symptomatic, and cryptogenic".[3]

The Commission of Classification and Terminology of ILAE continues to work towards updating the classification systems. Their efforts were published in 2001 and 2006, which recognized a long list of new electroclinical syndromes, and tried to adopt evidence-based approaches. However, the Commission acknowledged that their proposal is not a new classification system but only complimentary to the ICE of 1989. On the assumption of a general consensus reflecting that the ICE of 1989 is outdated and a new classification system is in urgent need for clinical application of recent advances in epileptology, the ILAE Classification Commission (2005-2009) published their work, titled as "Revised terminology and concepts for organization of seizures and epilepsies", in Epilepsia in 2010[4], which has raised lively discussions and further proposals.

THE NEW ILAE PROPOSAL ON CLASSIFICATION AND COMMENTARIES

Classification of epileptic seizures

The new proposal for the classification of seizures is largely unchanged from the framework of ICES of 1981. However, a network concept for the definition of partial and generalized seizures is adopted, in which partial seizures are conceptualized as seizures originating within networks limited to one hemisphere while generalized seizure as originating at some point within, and rapidly engaging, bilaterally distributed networks. Other specific changes include: (i) Neonatal seizures are no longer regarded as a separate entity; (ii) Subclassification of absence seizures is altered to include myoclonic absence and absence with eyelid myoclonia; (iii) Subclassification of myoclonic seizures includes myoclonic tonic and myoclonic atonic seizures; (iv) Epileptic spasm is included as a separate entitiy; and (v) For focal seizures, the distinction between the different types is eliminated. However, if necessary, it is recommended to use "descriptors of focal seizures according to degree of impairment during seizures", which are essentially identical to the previous concept of simple and complex partial seizures.

Commentaries about the new proposal by the epilepsy care professional community were mainly focused at (1) the network concept about the partial and generalized epilepsies and (2) elimination of subtypes of focal seizures. The traditional concept of partial and generalized seizures was based on the distribution of abnormally hyperexcitable brain regions (or epileptogenic zone), *focal vs. diffuse*, which may still be correct and easier to explain the clinical features of seizures. Although recent advances in fMRI and electrophysiology have raised interests for the network concept in ictogenesis and ictal spreading, the precise identification of network characteristics of partial

and generalized seizures have yet to be clarified. In fact, there are many clinical examples of partial seizures originating within, and rapidly engaging bilaterally distributed networks. It has also been reported that in generalized absence seizures, a localized somatosensory cortex is responsible for seizure onset involving the thalamocortical network.[5] Commentaries were also generally against the idea of eliminating subtypes of focal seizures. The new proposal recommends to describe seizures according to their semiologic features without trying to fit them into an artificial category, as the Commission feels that the semiologic features of focal seizures are too diverse and variable to be categorized into accurate entities. However, most commentators have stressed that the recommendation of describing seizures, in fact, requires extensive free text and expertise of caring physicians in description. Also, they were much concerned about the seizure description in free text to make communications and comparisons of data more difficult. Another argument against the proposal was the elimination of simple and complex partial seizures while providing the descriptors of focal seizures, an essentially identical in meaning. The modification of generalized epilepsies were generally considered appropriate.

Classification of epilepsies

The new proposal for the classification of epilepsies has made very radical changes in the basic framework of classification and terminologies, which are: (i) Replacement of three terms related to the etiological categories (idiopathic, symptomatic, and cryptogenic) by new terms; genetic, structural-metabolic, and unknown etiologies; (ii) Elimination of terminologies of localization-related and generalized epilepsies, and (iii) Change of orderly 3 steps of classification scheme into a form of database consisting of (a) electroclinical syndromes, (b) distinct constellations, (c) epilepsies associated with structural or metabolic conditions, and (d) epilepsies of unknown causes. These changes are apparently aiming at picking one entity most appropriate to the patient from a database instead of trying to fit the patient's condition into one of categories specified in the classification scheme of ICE. However, the new proposal has essentially mixed syndromes and causes together in a parallel structure, thus cannot be considered as a classification system of usual sense, which has generated a very fierce arguments against its adoption in place of ICE-1989. Although the commission has admitted that the new proposal is not a new classification, they insisted its high value as an attempt to break away from what had become an inadequate, misleading terms and concepts and to offer some alternatives to reflect changing concept afforded by the last two decades of scientific breakthroughs in genomics, neuroimaging, and neurophysiology.[7]

Commentaries about the new proposal have generally agreed that the inclusion of "genetic epilepsy" is necessary, but are against the idea of replacing the term of "idiopathic" by "genetic". They were also concerned about the idea of giving up the orderly classification system of IEC to adopt the list of database aiming at more flexibilities in clinical practice. In his commentary, Wong proposed a two-tier classification system combining the new proposal and etiological classification[8], which were favored by other opinion leaders. In addition, the new proposal triggered the proposal of a new etiological classification of epilepsies employing four categories of idiopathic, symptomatic, provoked, and cryptogenic, which has revived another debates about the different concepts related to terminologies.[9]

CONCLUSION

The efforts of ILAE to improve the classification of epileptic seizures and epilepsies have continued over the past two decades but without any major success. This was largely due to rapidly developing but still incomplete understanding of the basic mechanisms of epilepsy. The recent proposal by the ILAE's Classification Commission to revise the concept and terminologies of ICE-1989 was considered more rational and scientific, but faced fierce arguments against the idea of abandoning old terminologies and classification system. This was mainly because the new proposal was not a new classification scheme. However, the new proposal generated very lively discussions and renewed interests of international epilepsy community for a better future classification system.

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