How Have We Come This Far? Epilepsy Classification Through the Ages

ILAE Classification of the Epilepsies: Position Paper of the ILAE Commission for Classification and Terminology.

Scheffer IE, Berkovic S, Capovilla G, Connolly MB, French J, Guilhoto L, Hirsch E, Jain S, Mathern GW, Moshé SL, Nordli DR, Perucca E, Tomson T, Wiebe S, Zhang Y-H, Zuberi SM. *Epilepsia* 2017;58:512–521.

The International League Against Epilepsy (ILAE) Classification of the Epilepsies has been updated to reflect our gain in understanding of the epilepsies and their underlying mechanisms following the major scientific advances that have taken place since the last ratified classification in 1989. As a critical tool for the practicing clinician, epilepsy classification must be relevant and dynamic to changes in thinking, yet robust and translatable to all areas of the globe. Its primary purpose is for diagnosis of patients, but it is also critical for epilepsy research, development of antiepileptic therapies, and communication around the world. The new classification originates from a draft document submitted for public comments in 2013, which was revised to incorporate extensive feedback from the international epilepsy community over several rounds of consultation. It presents three levels, starting with seizure type, where it assumes that the patient is having epileptic seizures as defined by the new 2017 ILAE Seizure Classification. After diagnosis of the seizure type, the next step is diagnosis of epilepsy type, including focal epilepsy, generalized epilepsy, combined generalized, and focal epilepsy, and also an unknown epilepsy group. The third level is that of epilepsy syndrome, where a specific syndromic diagnosis can be made. The new classification incorporates etiology along each stage, emphasizing the need to consider etiology at each step of diagnosis, as it often carries significant treatment implications. Etiology is broken into six subgroups, selected because of their potential therapeutic consequences. New terminology is introduced such as developmental and epileptic encephalopathy. The term benign is replaced by the terms self-limited and pharmacoresponsive, to be used where appropriate. It is hoped that this new framework will assist in improving epilepsy care and research in the 21st century.

Operational Classification of Seizure Types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology.

Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshé SL, Peltola J, Roulet Perez E, Scheffer IE, Zuberi SM. *Epilepsia* 2017;58:522–530.

The International League Against Epilepsy (ILAE) presents a revised operational classification of seizure types. The purpose of such a revision is to recognize that some seizure types can have either a focal or generalized onset, to allow classification when the onset is unobserved, to include some missing seizure types, and to adopt more transparent names. Because current knowledge is insufficient to form a scientifically based classification, the 2017 Classification is operational (practical) and based on the 1981 Classification, extended in 2010. Changes include the following: (1) "partial" becomes "focal"; (2) awareness is used as a classifier of focal seizures; (3) the terms dyscognitive, simple partial, complex partial, psychic, and secondarily generalized are eliminated; (4) new focal seizure types include automatisms, behavior arrest, hyperkinetic, autonomic, cognitive, and emotional; (5) atonic, clonic, epileptic spasms, myoclonic, and tonic seizures can be of either focal or generalized onset; (6) focal to bilateral tonic-clonic seizure replaces secondarily generalized seizure; (7) new generalized seizure types are absence with eyelid myoclonia, myoclonic absence, myoclonic–atonic, myoclonic–tonic–clonic; and (8) seizures of unknown onset may have features that can still be classified. The new classification does not represent a fundamental change, but allows greater flexibility and transparency in naming seizure types.

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Instruction Manual for the ILAE 2017 Operational Classification of Seizure Types.

Fisher RS, Cross JH, D'Souza C, French JA, Haut SR, Higurashi N, Hirsch E, Jansen FE, Lagae L, Moshé SL, Peltola J, Roulet Perez E, Scheffer IE, Schulze-Bonhage A, Somerville E, Sperling M, Yacubian EM, Zuberi SM. *Epilepsia* 2017;58:531–542.

This companion paper to the introduction of the International League Against Epilepsy (ILAE) 2017 classification of seizure types provides guidance on how to employ the classification. Illustration of the classification is enacted by tables, a glossary of relevant terms, mapping of old to new terms, suggested abbreviations, and examples. Basic and extended versions of the classification are available, depending on the desired degree of detail. Key signs and symptoms of seizures (semiology) are used as a basis for categories of seizures that are focal or generalized from onset or with unknown onset. Any focal seizure can further be optionally characterized by whether awareness is retained or impaired. Impaired awareness during any segment of the seizure renders it a focal impaired awareness seizure. Focal seizures are further optionally characterized by motor onset signs and symptoms: atonic, automatisms, clonic, epileptic spasms, or hyperkinetic, myoclonic, or tonic activity. Nonmotor-onset seizures can manifest as autonomic, behavior arrest, cognitive, emotional, or sensory dysfunction. The earliest prominent manifestation defines the seizure type, which might then progress to other signs and symptoms. Focal seizures can become bilateral tonic–clonic. Generalized seizures engage bilateral networks from onset. Generalized motor seizure characteristics comprise atonic, clonic, epileptic spasms, myoclonic, myoclonic–atonic, myoclonic–tonic–clonic, tonic, or tonic–clonic. Nonmotor (absence) seizures are typical or atypical, or seizures that present prominent myoclonic activity or eyelid myoclonia. Seizures of unknown onset may have features that can still be classified as motor, nonmotor, tonic-clonic, epileptic spasms, or behavior arrest. This "users' manual" for the ILAE 2017 seizure classification will assist the adoption of the new system.

Commentary

Nearly 50 years ago, Professor H. Gastaut, through the International League Against Epilepsy (ILAE), initiated the concept of an international classification of epileptic seizures and epilepsies (1). This classification was to serve as a common vocabulary, a framework for diagnosis, for those treating patients with epilepsy. Classification improves clinical care by helping to guide investigations for underlying cause, identify preferred therapies, and predict outcome. Nearly from its inception, epilepsy classification has been subject to review and revision to better reflect advances in diagnostic abilities and understanding of this disease.

By 1981, seizures were classified as either being of partial onset (focal or localization-related) or generalized onset (bilateral or widespread). Partial seizures were further described as being simple partial (no impairment of consciousness) or complex partial (impaired consciousness), and whether or not they secondarily generalized (2). The 1989 Proposal for Revised Classification of Epilepsies and Epileptic Syndromes (ICES) became the standard way of conceptualizing seizures, epilepsies, and epileptic syndromes (3). Epileptic syndromes were defined by clinical signs and symptoms, including seizure types, age at onset, precipitating factors, as well as outcome in some. It was made clear that syndromes did not always have common etiologies or outcomes (3).

The 1981 and 1989 proposed classifications are the schema most epilepsy providers still think of today. Seizures are either "partial" or "generalized." If seizures begin within one hemisphere and are associated with impaired awareness, they are "complex partial." If awareness is unaffected, they are "simple partial." Epilepsy is either "idiopathic" (presumed genetic), "symptomatic," or "cryptogenic" (presumed symptomatic; 3). However, this classification system is far from perfect. As diagnostic techniques improve, how does this affect our concept of "cryptogenic"? What is truly meant by retained awareness? Is the person who is able to answer all questions correctly while having a nondominant temporal lobe seizure but who is later amnestic for the event truly aware? Is the child on continuous midazolam infusion in the ICU for epilepsia partials continua really having a "simple" partial seizure? The child's parents would certainly argue there is nothing simple about the situation!

These concepts were appropriately challenged in 2010 when the ILAE presented the Revised Terminology and Concepts for Organization of Seizures and Epilepsies (4). The idea of generalized and partial/localization related seizures was altered due to improved understanding that seizures occur due to hyperexcitability and synchrony of neurons within networks, rather than specific areas of neocortex (5). Generalized seizures have onset within and rapidly engaging bilateral networks but not necessarily the entire cortex. Seizures arising within a network limited to one hemisphere were termed "focal seizures" and were described by their features (including awareness) rather than using the terms "simple" or "partial" (4). Furthermore, epilepsy was determined to be of genetic, structural/metabolic, or unknown cause (4).

The 2010 proposal was not meant to be a permanent change but rather initiate a complete paradigm shift. It served as a platform for further feedback, discussion, and development until the ILAE Classification Task Force published these new proposals for classification of seizure types and classification of the epilepsies.

In the newly proposed classification scheme described by Fisher, Scheffer, and others, the 2010 proposed paradigm shift has taken on new dimensions. Classification now occurs at three levels: seizure type, epilepsy type, and epilepsy syndrome. It is recognized that we may not always have sufficient

understanding of a patient's epilepsy—or we may not have the diagnostic resources available—to be able to classify at all three levels. Seizure and epilepsy type can still be unknown. Not all epilepsies fall into a specific electroclinical syndrome.

There have been additional, substantial changes made. Focal seizures should now just be described by what is witnessed or felt during the seizure. Specific descriptive terms have been proposed, which include automatisms, autonomic, emotional, cognitive, motor, and sensory features. This universal vocabulary will hopefully lead to better understanding of seizure types. Furthermore, rather than classifying seizures as "complex," "simple," "dyscognitive," or any other name previously used to describe awareness, we are now encouraged to simply note whether awareness is retained or impaired. Like the 2010 proposal replacing the ambiguous term "partial" with "focal," this recent change makes it readily understood by patients, families, and physicians whether the seizures impact the patient's ability to interact with his or her environment, which has significant implications for independence and driving. Finally, at each level, we are encouraged to identify potential etiology—described as being genetic, structural, metabolic, infectious, immune, unknown, or a combination thereof—and possible comorbidities. Identifying comorbidities at each level serves to remind us that comorbidities in epilepsy are the rule, not the exception. All patients, including those with epilepsy syndromes previously felt to have good outcome (such as Benign Childhood Epilepsy with Centrotemporal Spikes and Childhood Absence Epilepsy), are at high risk to have cognitive, psychiatric, and social complications of their disease.

Why do we need a new classification scheme? Most providers are quite comfortable with the 1989 proposal. Do we gain anything from this complete paradigm shift? Yes!

If seizure and epilepsy classification are to serve as the framework for diagnosis and treatment of epilepsy, to provide a common language for those who treat epilepsy around the world, then our language must reflect our understanding. How could we effectively communicate now using only a 1989 vocabulary? The notion seems comical. Our understanding of epilepsy as a disease—seizure propagation, causes, treatments, outcomes—has changed dramatically over the last 30 years. Now it is time for our terminology to change. While no classification scheme is ever likely to be perfect, this new proposal brings us forward by leaps and bounds.

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