



Classifying Seizures and Epilepsies: Limits of Science and Semantics

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"If I wished to show a student the difficulties of getting at truth from medical experience, I would give him the history of epilepsy to read." Oliver Wendell Holmes (1)

If the medical experience of epilepsy is obscured by uncertainties, then its classification is mired in the mud of expert opinion. The newly revised terms and concepts for "organizing" (also known as "classifying") seizures and epilepsy provide a humble and modern perspective, with many superb suggestions (2). The central points are well articulated and valid: 1) divorcing classification from "expert opinion" and marrying it to science; 2) acknowledging what is unknown; and 3) simplifying and clarifying terminology. Yet, the revision lacks the crisp clarity needed to educate students, patients, and colleagues. And some recommendations lack a clear scientific or semantic basis.

The authors wisely suggest that we replace the term "idiopathic" with "genetic," "symptomatic" with "structural/metabolic," and "cryptogenic" with "unknown." Everyone understands "genetic" and "unknown," but confusion fills the eyes of medical students when they try to comprehend the distinction between "idiopathic" and "cryptogenic." The suggested classification offers clearer and more practical etiologic organization of the epilepsies. For example, in patients with frontal lobe epilepsy without imaging or metabolic abnormalities, the cause is "unknown," unless either familial clustering or genetic mutation for autosomal dominant nocturnal frontal lobe epilepsy is identified ("genetic" cause), or postsurgical pathologic examination reveals abnormality such as cortical dysplasia ("structural" cause). Doctors vote with words—general neurologists never use the pedantic term "cryptogenic epilepsy"—"unknown" works much better. Yet, genetics are never simple. How do we categorize the etiology in someone who has a gene that is strongly associated with clinical epilepsy but whose first seizure followed a head trauma with loss of consciousness for 30 minutes? Genetic or structural? Presumably both. What if the gene has a less strong association with epilepsy? Just traumatic? More information does not guarantee simpler decisions.

The classification scheme also addresses specific seizure types, providing a simplification of generalized epileptic seizures and arguing that there is no "natural" classification of focal (partial) seizures. Eleven subtypes of generalized seizures are offered, but no subtypes of focal epilepsy. Genes, clinical

features, and EEG findings distinguish partial (focal) seizures arising in the frontal lobes with motor automatisms and partial (focal) seizures arising in the temporal lobe with auditory symptoms. What is unnatural in this distinction: the genes, the anatomy, or the behavior? The new classification argues that the distinction between tonic and myoclonic-tonic seizures rests on fundamental biology, while the distinction between simple and complex partial seizures is an arbitrary line drawn on a natural continuity. And, why did myoclonic-tonic-clonic get left out if myoclonic-tonic is in? Darwin recognized that the fight between "lumpers" and "splitters" can be critical to deciphering natural history, but it is often an artifact of perspective. Ultimately, consensus may limit truth—committees excel at compromise and avoiding conflict, but what is the price?

A classification of the epilepsies is essential to understand and communicate. Science and medicine need a straightforward and accurate vocabulary to describe seizures and epilepsies. The revision acknowledges the many gaps in our knowledge, the shortcomings of prior classifications, and the goal to avoid accepting "assumptions and assertions as the basis for classification and to acknowledge areas for which we do not have good information for making decisions." The human mind and language are organized into hierarchies and categories. The revision half-preserved the deeply entrenched and intuitively attractive—albeit artificial dichotomy—that splits the epilepsies into generalized and focal. We are no longer obliged to designate an epilepsy as partial or generalized, but those terms are preserved as descriptors of manifestations or correlations.

The classification of partial seizures has significantly changed. The term "partial" has been replaced by "focal." Why? There is no clear explanation. Both terms have linguis-



tic limitations. Although partial seizures come from a “part” of the brain, the same technically can be true of generalized seizures. Further, partial seizures could falsely suggest that the seizure is not a “complete” seizure, but rather “part” of a seizure. Focal derives from focus, which etymologically derives from “a point,” as in a focal point. Focal epilepsy conjures the image of a cortical dot, fueling misconceptions that the source is small and localized, when it is sometimes a widely distributed network. The definition of focal seizures—networks limited to one hemisphere—leaves in limbo those seizures that seem to arise nearly simultaneously from both hemispheres, where invasive electrodes show a “dance” of evolving spikes and rhythms in both mesial temporal regions that suddenly morph into a bilateral complex partial or generalized seizure without a clear hemisphere of onset. These seizures are neither “focal” nor “unilateral.” The marginal—and uncertain—value of “focal” over “partial” may not outweigh the potential confusion stirred by the change. After 3 decades in the literature and common use, there should be an excellent reason for change. Is it biology, semantics, or the momentum of expert consensus?

Perhaps the revision’s greatest change is in banishing the terms “simple” and “complex partial” seizures. Two explanations are offered. First, “simple” and “complex” were often misused and misunderstood. True. Twenty years ago, an occasional neurology resident confused a simple partial seizure with complex hallucinations (e.g., voices or a child’s image) with a complex partial seizure that impaired consciousness. However, that error is now very, very rare. The second argument is scientific—the border between impaired and preserved consciousness is a continuum. Yet, in the vast majority of cases, the distinction is clear. Even among young children, most parents can tell if consciousness is preserved and their child remains connected. Continua are not restricted to partial seizures. Tonic and myoclonic seizures can overlap in duration, and EEG features in some patients. Do we therefore exclude the categories because of a continuum? Does a 5% overlap justify elimination of terms? Or is it 1%. Where are the data? Few distinctions have as much clinical relevance as the distinction between simple partial and complex partial seizures: whether or not a person can drive, operate dangerous equipment, play some contact sports, etc. Yet the value of these terms is even greater: complex partial seizures have been the primary measure of antiepileptic drug and device trials for the past 30 years. The yardstick that almost everyone in academic epilepsy, regulatory agencies, and pharmacology agreed on was abandoned. A suggestion has been made that we call complex partial seizures “focal dyscognitive seizures.” However, ictal cognitive dysfunction does not always suggest associated impairment of consciousness or awareness, but may merely reflect very localized electrophysiologic disruption of specific anatomic areas, such as language centers with ictal expressive or receptive dysphasia, or limbic structures with cognitive auras (forced intrusive thinking, derealization, depersonalization). Seizures that slightly impair arithmetic or memory skills are dyscognitive but should not lead to loss of driving privileges.

In focusing on classification, organization, and semantics, we can also lose the bigger picture of what we call epilepsy. This is not an issue concerned with the revised terms and concepts as much as it is with recognizing the limits of our current

clinical science. For example, the potentially confusing borderland between simple and complex partial seizures is highlighted by the current revision. Yet, we believe that there is a crystal clear distinction between simple partial seizures and nonepileptic phenomena in the psychiatric, medical, migraine, and normal populations. The majority of simple partial seizures are not associated with EEG changes (3). And, in controlled studies of psychiatric populations and generalized epilepsy populations, the frequency of aura symptoms is remarkably similar to those in the patients with partial epilepsy! (4, 5) Therefore, whether we call them partial seizures with purely affective or autonomic features or simple partial seizures with affective or autonomic features, the real question is—are they seizures? Presence of EEG changes during symptoms as well as stereotypic features that begin suddenly, are brief in duration, and with identical symptoms that progress to impaired consciousness or tonic-clonic seizure are clear. But what about the vast majority of symptoms in this category? If they occur in isolation in a patient with an affective disorder, do we call them psychiatric? If they occur in isolation in a patient with mesial temporal sclerosis and convulsions, do we call them a partial seizure? Is this science or circular reasoning infused with confirmation bias? Now consider that half of patients with refractory partial epilepsy have psychiatric disorders and the implications that has for drug and device trials if the new classification confuses apples (complex partial seizures) for oranges (nonepileptic events that mimic focal seizures).

Change is challenging. Consensus is complex. Classifying seizures and epilepsies only seems to magnify the limits of our science and semantics. The International League Against Epilepsy (ILAE) Commission on Classification and Terminology should be congratulated on their provocative and valuable contribution. Let a new conversation in an endless discussion begin.

“Diseases should be recognized, as far as possible, not by any of the common names imposed upon them, as fever or epilepsy, but as individual collections of symptoms, each of which differs from every other collection.” Oliver Wendell Holmes (1)

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