EPILEPSY CURRENTS

Current Literature
In Clinical Science

ILAE Classification Redux: Ready for Prime Time?

Jacqueline A. French, MD
NYU Comprehensive Epilepsy Center, New York, NY, USA
Correspondence: Jacqueline A. French, MD, Professor, NYU Comprehensive Epilepsy Center, 223 E. 34th St, New York, NY 10016, USA
Jacqueline.french@nyumc.org

In 2010 the International League Against Epilepsy (ILAE) published a proposal for a revised "terminology and concepts for organization" of the epilepsies. (1) This classification was the result of four years of effort by the 2005-2009 ILAE Commission on Classification and Terminology. This classification was immediately adopted by some, shunned by others, and ignored by many. Discussions of this document flooded the pages of journals (2-6) including Epilepsy Currents (7). Most clinicians stood on the sidelines and waited.

It turns out that patience is a virtue. Now, four years later, the 2010-2013 Commission on Classification and Terminology have unveiled a revision of the original document. (8). This revision is an attempt to correct any aspects of the 2010 document that were confusing, misleading, overly controversial or unworkable. This document was available on-line at the ILAE website until January 2014, and is now closed for comments.

Likely most epilepsy specialists are quite confused about the current state of affairs. This review will attempt to briefly summarize some of the changes in the 2010 document, the suggested changes in the 2014 revision, and will then address possible issues that still might need work. Not all issues can be addressed in this brief review. For example, for issues related to re-naming of focal seizures (introducing the word "dyscognitive"), and etiologic subdivisions, the reader is referred to the 2010 document and subsequent reviews.

The last revision of classification of the epilepsies was in 1989, and that document remained a "proposal", never officially accepted. (9) Despite this absence of official confirmation, most epilepsy specialists have been using this classification throughout their careers. They have treated patients based on it, used it as a template to approve new antiepileptic therapies, taught students with it, and used it as the underpinnings of scientific evaluations. In its most simplistic form, the classification identified patients as either having partial epilepsies (idiopathic, e.g. benign rolandic epilepsy, or symptomatic/cryptogenic e.g. temporal lobe epilepsy from mesial temporal sclerosis) or generalized epilepsy (idiopathic, e.g. absence or juvenile myoclonic epilepsy, or symptomatic, e.g. Lennox-Gastaut syndrome).

Epilepsy Currents, Vol. 14, No. 2 (March/April) 2014 pp. 84–85

The 2010 update arose from a frustration that science was marching forward, and this had not been reflected in the way we classify epileptic seizures and syndromes. The biggest scientific advance, and the one that led to the most important changes in classification, were our emerging understanding about epilepsy etiologies, and particularly the role of genetics. Since 1989, we have learned that epilepsies previously thought to be structural in nature actually may often have genetic etiologies, (for example familial focal epilepsies) (10) and epilepsies we presumed to be generalized actually could be terminated by focal resections (e.g. some forms of infantile spasms). This led to a general feeling by the commission that we were being too simplistic with our two categories (focal vs generalized) each divided into two domains (idiopathic vs symptomatic/cryptogenic).

The 2010 document specifically says: "The 1989 classification (9) was an organization built on concepts that no longer correspond to or accurately describe our increasing knowledge of seizures and the epilepsies. **Consequently, the current organization and the concepts on which it is based are abandoned or revised.** Specifically, what was "abandoned" was the concept of a focal epilepsy vs a generalized epilepsy as broad category structure, and what was "revised" were the concepts of "idiopathic", "cryptogenic" and "symptomatic". Instead, we were instructed to think first of electroclinical syndrome (these were largely untouched); second of seizure type (also largely either untouched or re-named), and last of etiology (now subdivided into structural/metabolic, genetic or unknown). One gaping problem with this new world order, was the fact that many patients (in fact the majority of patients over the age of 12) do not have an electroclinical syndrome. This is acknowledged in the following quote from the 2010 manuscript: "Henceforth, the use of the term "syndrome" will be restricted to a group of clinical entities that are reliably identified by a cluster of electroclinical characteristics. Patients whose epilepsy does not fit the criteria for a specific electroclinical syndrome can be described with respect to a variety of clinically relevant factors (e.g., known etiology and seizure types). This does not, however, provide a precise (syndromic) diagnosis of their epilepsy." Unfortunately, patients with what was previously known as "partial epilepsy" fall into those without an electroclinical syndrome.

These patients were left in a no-man's land in which their epilepsy could be "organized" based on underlying etiology or seizure types, but not in way that would easily communi-

cate from clinician to clinician the fundamental nature of the condition. As an example, consider two patients who have had traumatic brain injury at age 2. One has severe developmental delay, slow spike-wave on EEG, and stereotypic focal onset seizures as well as atonic seizures. A second patient with the same history has a normal IQ, focal motor seizures and focal frontal encephalomalacia. These two patients have fundamentally different epilepsy, and are treated in fundamentally different ways, that cannot be acknowledged without reverting to a conceptual framework that includes "focal epilepsy".

The 2014 revision now takes a step back and acknowledges the concept of focal and generalized epilepsy, but only in a halfhearted way. They suggest "While the terms "generalized epilepsy" and "focal epilepsy" remain useful *descriptors* for many cases, there are, however, clinical settings in which a dichotomous approach is not supported by the electroclinical data. Therefore such an approach cannot form the basis of a biological classification."

Of course, there is wisdom in these words. The concept of "focal epilepsy" and "generalized epilepsy" are probably not correct for determining a biological classification, nor are the terms "symptomatic, cryptogenic and idiopathic". The problem is that for many other purposes they work exceedingly well. In fact, when teaching house staff, one of the fundamentals of training is: "before you treat the patient, figure out if their epilepsy is focal or generalized". Now, this concept is de-emphasized. The 2010 document had also abandoned any grouping of the "syndromes formerly known as idiopathic generalized epilepsy" or "IGE". These could be identified by individual syndrome (juvenile myoclonic epilepsy, absence epilepsy) but there was no category that acknowledged the fundamental similarities in this group. Now, the 2014 document suggests that we call these the "genetic generalized epilepsies". This is problematic for several reasons. The first is that in a number of these patients there is no confirmation of a genetic syndrome to date, although there is a presumption that genes play a role. The second problem is that this will produce a great deal of confusion between these genetic generalized epilepsies, and other genetic generalized syndromes such as Dooses syndrome and Dravet syndrome. Just imagine the discussion with a trainee-"remember, JME is one of the genetic generalized syndromes". Yes, Dravet syndrome is genetic, yes, it is generalized, but it is not "genetic generalized epilepsy".

Clearly the new revision will need some "real world testing" to determine whether it is road ready, functional and usable. Probably, it is not yet time to include it in recertification and fellowship exams (as some are already suggesting), or require its use in papers and grants.

Will we ever have a "finalized" new classification? Perhaps classifications should always be a work in progress. Yet, to use two conflicting classifications simultaneously, could lead to they type of chaos that is the opposite of "organization".

References

1. Berg, A. T., S. F. Berkovic, M. J. Brodie, J. Buchhalter, J. H. Cross, W. van Emde Boas, J. Engel, J. French, T. A. Glauser, G. W. Mathern, S. L. Moshé, D. Nordli, P. Plouin and I. E. Scheffer (2010). "Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005-2009." *Epilepsia* 51(4): 676-685.
2. Christensen, J. and P. Sidenius (2012). "Epidemiology of epilepsy in adults: implementing the ILAE classification and terminology into population-based epidemiologic studies." *Epilepsia* 53 Suppl 2: 14-17.
3. Engel, J. (2006). "ILAE classification of epilepsy syndromes." *Epilepsy Res* 70 Suppl 1: S5-10.
4. Gómez-Alonso, J. and P. Bellas-Lamas (2011). "[The new International League Against Epilepsy (ILAE) classification of epilepsies: a step in the wrong direction?]." *Rev Neurol* 52(9): 541-547.
5. Shinnar, S. (2010). "The new ILAE classification." *Epilepsia* 51(4): 715-717.
6. Uttam, A. K., R. Joshi, R. Dwivedi, K. Prasad, M. V. Padma, R. Bhatia, M. B. Singh and M. Tripathi (2013). "Applicability of the new ILAE classification for epilepsies (2010) in persons with epilepsy at a tertiary care center in India." *Epilepsia* 54(4): 751-756.
7. Berg, A. T. (2011). "Classification and epilepsy: the future awaits." *Epilepsy Curr* 11(5): 138-140.
8. URL: http://www.ilae.org/Visitors/Centre/Organization.cfm
9. Proposal for revised classification of epilepsies and epileptic syndromes. Commission on Classification and Terminology of the International League Against Epilepsy. *Epilepsia* 1989;30:389-399.
10. Andermann, F., E. Kobayashi and E. Andermann (2005). "Genetic focal epilepsies: state of the art and paths to the future." *Epilepsia* 46 Suppl 10: 61-67.