Issues in epilepsy classification for population studies

Peter Camfield

Department of Pediatrics, Dalhousie University, Halifax, Nova Scotia, Canada; and IWK Health Centre, Halifax, Nova Scotia, Canada

SUMMARY

Population-based studies about epilepsy have been informative about frequency, causes, and outcome of epilepsy. Because epilepsy is a heterogeneous disorder, studying populations of categories of patients is more likely to provide critical insights than is “lumping” all of epilepsy together. The 1981–1989 Classification scheme of the International League Against Epilepsy (ILAE) has been very useful for population-based studies but has some significant shortcomings. Studying a long list of specific epilepsy syndromes is not likely to be useful for population-based studies because the number of patients with each syndrome is so small and comparison with previous research would become very difficult. The author argues that with some significant modifications, the backbone structure of the 1989 Classification scheme could retain its usefulness for further research and clinical care.

KEY WORDS: Classification, Children, Epidemiology.

WHAT FEATURES OF AN EPILEPSY CLASSIFICATION SYSTEM ARE NEEDED FOR POPULATION STUDIES?

Population-based studies about epilepsy describe the full spectrum of the disorder, and indeed it is a wide spectrum. We have learned that most epilepsy is controllable by medication, that there is a spontaneous rate for permanent remission, and that social outcome and comorbidities are important, possibly a greater problem than the seizures (Linehan et al., 2011). Information has become more refined with the identification of risk factors for good and poor outcomes, even though exact prognostication remains elusive for an individual patient (Geelhoed et al., 2005; Berg et al., 2011).

It is obvious that epilepsy is not a single entity—there are a huge array of potential causes and clinical manifestations. Epilepsy syndromes offer a way of grouping patients for more precise prognostication and best choice of treatments. An individual neurologist treating an individual patient may not be terribly hampered by this complexity, but population studies must group together patients for study. Statistical analysis is critical for population studies and tiny groups of patients are an anathema.

A well-constructed classification system for epilepsy and the epilepsies is needed for any population study. Comparison among studies is obviously a cornerstone for science in general and population studies in particular. For comparisons, the classification schema needs to be the same, clear and reliable. Differences among types and rates of epilepsy in various populations should be useful for many public health ventures. For example, in Ecuador or many areas of Africa, new-onset epilepsy has a high probability of being caused by cysticercosis (Garcia et al., 2005; Quet et al., 2010); therefore, elimination of this infection should reduce the rate of epilepsy. In North America, head injury is a much more common cause, and enforcing seatbelt legislation is more likely to reduce the rate of epilepsy (Lowenstein, 2009). For both of these conclusions, population studies needed an effective classification schema. Only certain types of epilepsy would be eliminated by eradication of cysticercosis and only certain types would be decreased by seatbelt use. Simply studying the overall rate of epilepsy in a population would not likely show an effect of a specific intervention for a specific epilepsy disorder.

Rather begrudgingly the world has adopted the 1981–1989 classification scheme of the ILAE (Commission on Classification and Terminology of the International League Against Epilepsy 1981, 1989). This scheme allowed nearly all patients to be classified into three large categories:
Generalized Epilepsy, Focal Epilepsy and Unsure if Generalized or Focal. Generalized and focal epilepsies were then subdivided into Idiopathic, Symptomatic, or Cryptogenic, with some definitions for each category. Specific epilepsy syndromes were then assigned to each subdivision; nearly all patients can be assigned to a first subdivision. Nearly all epilepsy syndromes were then assigned to each subdivision; nearly all patients can be assigned to a first subdivision and hence the structure of this classification scheme has been viewed as useful for population studies (Shinnar et al., 1999). It is also stable over time—most patients do not change from one category to another (Berg et al., 2000). If a child develops childhood absence epilepsy (CAE), years later there may be spontaneous remission, continued CAE, or evolution into juvenile myoclonic epilepsy (JME), but the child’s epilepsy syndrome will still be the overall category of Generalized Idiopathic Epilepsy (Wirrell et al., 1996).

Most of new-onset adult epilepsy will fall into category of Focal Epilepsy, Symptomatic, or Cryptogenic. New onset epilepsy in children has a much more colorful distribution; however, it is important to emphasize that even with current imaging and genetic studies, the largest group by far is Focal, Cryptogenic (Camfield et al., 1993; Berg et al., 2011; Wirrell et al., 2011).

FROM THE PERSPECTIVE OF POPULATION STUDIES, DOES THE CLASSIFICATION OF EPILEPSY NEED TO BE CHANGED?

As argued cogently, there are some very problematic issues in the epilepsy classification system from 1981 to 1989 (Berg et al., 2010). Many new syndromes have been clearly described, particularly based on new genetic findings. Some of these syndromes defy the distinction between Focal and Generalized and Idiopathic versus Symptomatic. Dravet syndrome is particularly poignant—the seizures may be focal or generalized and the cause is genetic, yet this disorder is clearly different than the traditional Idiopathic Epilepsies (Dravet et al., 2005). Some epilepsies categorized as Generalized Symptomatic clearly have a focal cause—West syndrome is a good example. Many patients with West syndrome have clearly identifiable unilateral migrational abnormalities with some focality to both their electroencephalography (EEG) recordings and seizures. A “cure” can be achieved by resection of the lesion. Is there a better case for this being a focal epilepsy? Others with West syndrome have a genetic cause and no evidence of focality—but they are not similar to other patients with Idiopathic Generalized Epilepsies, and the genetic cause is perhaps the only feature that allows them to be considered Symptomatic.

The category of Cryptogenic is troublesome for population studies because it blurs so much with Symptomatic and is highly dependent on the sophistication of the imaging studies.

The current proposal for “organization” of the epilepsies has taken a very neutral approach and organized epilepsy syndromes by the usual age of onset (Berg et al., 2010). There are many specific syndromes. If a person has epilepsy that does not fit the definition for a given specific syndrome, then the epilepsy cannot be classified. This would not be a problem for population studies if most patients had a specific syndrome and most syndromes were relatively common. However, it is clear that more than half of children with epilepsy cannot be assigned a specific syndrome (Wirrell et al., 2011)—in particular the broad categories of Focal Cryptogenic and Symptomatic Generalized remain very large. Are population studies doomed to ignore most of childhood epilepsy as completely unclassified? As noted previously, there is a great deal of commonality among children with cryptogenic focal epilepsy—they are often otherwise normal and have an excellent long-term prognosis, at least as good as many of the more clearly defined syndromes. Most of the clearly defined syndromes are rare. Their importance to an individual patient is unquestionable, but their influence on population studies is currently low.

Population studies need to use a classification system that is also useful in clinical practice. Sticking strictly with the 1981–1989 system is no longer tenable because this system has misleading categories. It would, however, be highly desirable to retain some of the important organizing features of the 1981–1989 system so that groups of patients could be studied.

SUGGESTIONS FOR THE EVOLUTION OF AN EPILEPSY CLASSIFICATION SYSTEM FOR POPULATION STUDIES

There needs to be recognition that a classification system that cannot deal with the majority of children with epilepsy is inadequate. Restoration of some large categories is needed (Table 1). In this section I have made some suggestions for how the large categories of the 1981–1989 classification system might be retained. These are suggestions only and aimed at furthering discussion.

The term cryptogenic is easily replaced with “cause unknown” (Berg, 2010). Because children with cryptogenic focal epilepsy are so common, perhaps a descriptive and neutral term could be developed. A suggestion would be Focal Epilepsy in Normal Children without Known Etiology (FENCNE).

More difficult is the term “idiopathic.” As noted in the table, among the Idiopathic Generalized Epilepsies there is a great deal of commonality among patients. They are neurologically and intellectually normal. Their EEGs show generalized spike-wave with a normal background,
and their seizure types are typically restricted to generalized tonic–clonic, absence, and myoclonus. Some patients evolve from one specific syndrome in this category to another, particularly CAE to JME. Although many have relatives affected by epilepsy, this feature is not universal. A neutral term for the category such as Generalized Spike Wave Epilepsy (GSWE) would require a few caveats but would allow for population studies and comparison with previous studies.

Idiopathic Focal Epilepsy has become a troublesome term because it is not so clear that the two most common syndromes have a definite genetic etiology—Benign Epilepsy with Occipital Paroxysms and BenignRolandic Epilepsy. Both syndromes are linked because the children are otherwise normal, and have focal seizures and virtually guaranteed long-term remission. These syndromes account for at least 15% of childhood epilepsy and are important for population studies, especially because they are not acquired brain disorders. A new more neutral name could retain this commonality. I suggest Focal Epilepsies with Excellent Prognosis (FEWEP).

The category Symptomatic Generalized Epilepsy encompasses many of the most chronic epilepsies in childhood. There are many syndromes, many causes, and typically a depressing long-term outcome. At least one third of these patients do not fit into a known specific syndrome and would be unclassifiable in the current schema (Camfield & Camfield, 2008). They do not all have an epileptic encephalopathy. West syndrome is the best defined of these syndromes but as noted above, it is often not a Generalized Epilepsy. Patients in this category have in common a variety of generalized seizure types (accepting that it is unclear if spasms are generalized or focal), an EEG with irregular and/or generalized slow spike and wave or multi-focal spikes, disturbed EEG background, and almost always mental retardation. A term such as Generalized Epilepsy with Diffuse Brain Disorder (GEDBD) might encapsulate this group and allow further population studies.

Symptomatic Focal Epilepsy implies an identified focal lesion. The prognosis is variable but the concept is important because it points to the possibility of surgical treatment. I would suggest the term Focal Epilepsy With a Lesion (FEWFL) that would combine patients for population studies.

There remain a number of epilepsies that are not covered by renaming the larger categories of the 1981–1989 classification. Most of these could be gathered into two additional larger categories—Epileptic Encephalopathy (EE) and Monogenetic Disorders with Epilepsy as the Main Manifestation (MDEMM). EE would include disorders such as continuous spike-wave in slow sleep, Landau-Kleffner syndrome, and migrating partial seizures. Monogenetic disorders would include disorders such as focal epilepsy with variable foci or familial temporal lobe epilepsy. Both EE and MDEMM are relatively uncommon and will not likely be the major concentration of population studies.

**Conclusions**

Retaining large groupings of epilepsy syndromes is in the best interests of population research, research that has had and will have a major impact on the way that we understand epilepsy.

**Disclosures**

The author has no conflicts of interest to report. I confirm that I have read the Journal’s position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

**References**


