

Usefulness of the new seizure and epilepsy classifications in clinical practice

Andreas Schulze-Bonhage*



Practice Points

- The new seizure classification is more precise and indicative of seizure severity.
- The terms 'complex-partial' and 'simple-partial' have been abandoned due to difficulties in assessing consciousness reliably in many cases. Alterations in cognition are instead described as 'dyscognitive' and are specified in the particular domain, for example, attention or memory.
- The new epilepsy classification has given up the dichotomy between 'generalized' and 'localization-related' epilepsies due to evidence that 'generalized' seizures also have a circumscribed focal origin.
- In the new classification system, 'idiopathic' is replaced by 'genetic' and 'symptomatic' by 'structural-metabolic'.
- There is more emphasis on the underlying pathology reflecting progress in imaging and genetics during the last two decades.
- Despite terminological improvements, there is little change in the organization of epilepsies. Adapting the diagnosis to the new recommendations is therefore easy, but, on the other hand, progress in understanding and taxonomy is limited.

SUMMARY The classification of seizures and epilepsies was revised by the International League Against Epilepsy in 2001 and 2010, respectively. Using the new seizure glossary gives more precise information on seizures, which is helpful to better understand the severity of the disease, assess ictal and peri-ictal impairments and to target treatment. The new epilepsy classification resolves some terminological problems of the pre-existing scheme (e.g., giving up the classifier 'generalized' vs 'localization-related'), but has provided little progress in terms of a new organization of the epilepsies. Changes in seizure classification may thus be of more practical benefit compared with the use of the suggested epilepsy classification scheme.

*Epilepsy Center, University Hospital Freiburg, Breisacher Str. 64, D-79106 Freiburg, Germany; Tel.: +49 761 27053660; andreas.schulze-bonhage@uniklinik-freiburg.de

Classification systems of diseases have always been a matter for debate. This is mainly due to two reasons: one is the limited knowledge of the disease spectrum to be organized that renders each classification preliminary, the other is related to the aims that a classification supports, whether primarily scientific or for everyday practice.

Classification systems for seizures and epilepsies started in the 19th century [1], and recent versions date back to 1981 [2] and 1989 [3]. The International League Against Epilepsy thus established commissions to revise them. With increasing availability of video-EEG-monitoring, semiological seizure description has become more precise, showing that some of the key terms used in the old seizure classification system were problematic and that a considerable percentage of seizures could not be adequately classified. Similarly, there was a feeling that the old epilepsy classification was outdated [4], as our methodology to characterize epilepsies has expanded particularly in the fields of imaging and genetics, and because the main classification system of ‘generalized’ versus ‘localization-related’ cannot be upheld in view of scientific findings. Also, increasing experience has shown that classification was problematic in a relevant patient subpopulation.

Different principal views on the requirements for and the use of a classification system render it a difficult endeavor to find a consensus on a new classification, which is reflected particularly in the process of syndrome classification and in the ongoing discussion following the publication of the new proposal of the commission led by Anne Berg in 2010 [4–13]; based on this debate, this new proposal was not accepted by all national chapters of the ILAE. Here, some of the key issues changed in seizure classification are reported and discussed with regard to the practical considerations of their usage. It should be mentioned that other proposals for classifications have been made by individual groups, which are not discussed in detail within the scope of this article.

Seizure classification

The old seizure classification [2] had two main categories: partial/focal seizures and (primary) generalized seizures. Whereas focal seizures were considered to arise from a circumscribed brain region, seizures with initial bilateral EEG discharges were called ‘generalized’ and were

conceptualized to arise from a ‘centrencephalic’ midthalamic area by Jasper and Penfield, or to emerge from the interaction of the reticular and thalamocortical relay cells in the thalamus (‘thalamic clock’) as suggested by Buzsáki (for review, see [14]). Focal seizures were classified based on the key criterion as to whether consciousness was preserved (‘simple partial’ seizures) or not (‘complex partial’ seizures), whereas other features like motor or vegetative phenomena were largely ignored. Furthermore, focal seizures were thought to sometimes ‘generalize’ over the brain.

The new glossary for seizure description by Blume *et al.* no longer uses the categorization of partial seizures as being simple partial or complex partial [15]. Instead, it contains a more elaborate description scheme that addresses many semiological elements, such as detailed aspects of motor features, types of automatisms and lateralizing aspects of seizure semiology, and the evolution of semiological elements over time.

How useful is this changed classification?

Giving up alterations of consciousness as a key classification criterion is based on good reasons. “Consciousness exists, but it resists definition” states the *Oxford Companion on Philosophy* [16]. As consciousness is essentially a subjective phenomenon, all attempts to define it from an outer view remain speculative. Patients with ictal loss of control of motor functions or ictal aphasia may not be able to respond, patients with impaired memory consolidation may not remember what has happened during a seizure. In practice, operationalizing consciousness by awareness, memory and reactivity often fails, even when video recordings of seizures are analyzed and when structured ictal testing is performed. Furthermore, there is a huge group of young children in whom abilities to report the subjective state of consciousness are severely limited, rendering any statement as to the preservation or absence of consciousness purely speculative.

The term ‘dyscognitive’ is now used to define ictal deficits in cognitive domains that can be assessed objectively when interacting with a patient during a seizure, such as attention, memory, perception or preserved executive functions. This approach describes conscious mental states instead of consciousness as a unified faculty and thus better corresponds to present day theories of consciousness [16]. Furthermore, these alterations in cognitive functioning are no

longer used as a higher-ranking category but are considered to be at the same level as tonic, clonic or dystonic motor phenomena or various types of automatisms.

Unlike the new classification of epilepsies, the term ‘generalized’ seizures is no longer used in this glossary. This causes inconsistencies between the suggested new classification of epilepsies from 2010 and the earlier seizure classification from 2001. ‘Generalized epilepsies’ were classified as they were thought to be characterized by ‘generalized’ seizures. As there is good reasoning to abandon the term ‘generalized’ in syndrome classification, a similar approach should be used in seizure description (e.g. changing ‘generalized tonic-clonic’ to a descriptive term like ‘bilateral convulsive’ seizures) (Figure 1).

In presurgical diagnostics, a detailed semiological description like the one suggested by Blume *et al.* [15] has been used for a long time as it contains valuable lateralizing and localizing information to identify the symptomatogenic brain areas. There was some criticism stating that a detailed seizure description apart from this particular situation might cause unnecessary work in primary care for epilepsy patients as opposed to its usefulness in specialized centers. However, a precise seizure description is relevant

for assessing ictal patient impairment and for decisions based thereon, be it in the field of counseling or treatment. For example, patients with epigastric aura, automotor seizures with oral automatisms, right-sided tonic arm contraction and ictal aphasia, patients with gelastic seizures during which their reactivity is impaired, and patients with nocturnal bilateral hypermotor seizures with pelvic thrusting would probably have all classified as having ‘complex partial’ seizures, even if there had never been an attempt to test for consciousness. It is obvious that the new glossary give a lot more information. In young children, in whom consciousness is in no way assessable, the old classification system completely failed. Moreover, misconceptions have now been eliminated: for example, patients with oral automatisms and preserved consciousness were unclassifiable in the old scheme as seizures with automatisms were considered to be only one form of complex partial seizures, although their presence, despite intact verbal communication, is frequently encountered in temporal lobe epilepsy arising from the nondominant hemisphere.

The presence of partial-onset seizures was essential for regulatory drug trials. How do we apply drugs when this is no longer a criterion? We can certainly go on using drugs for

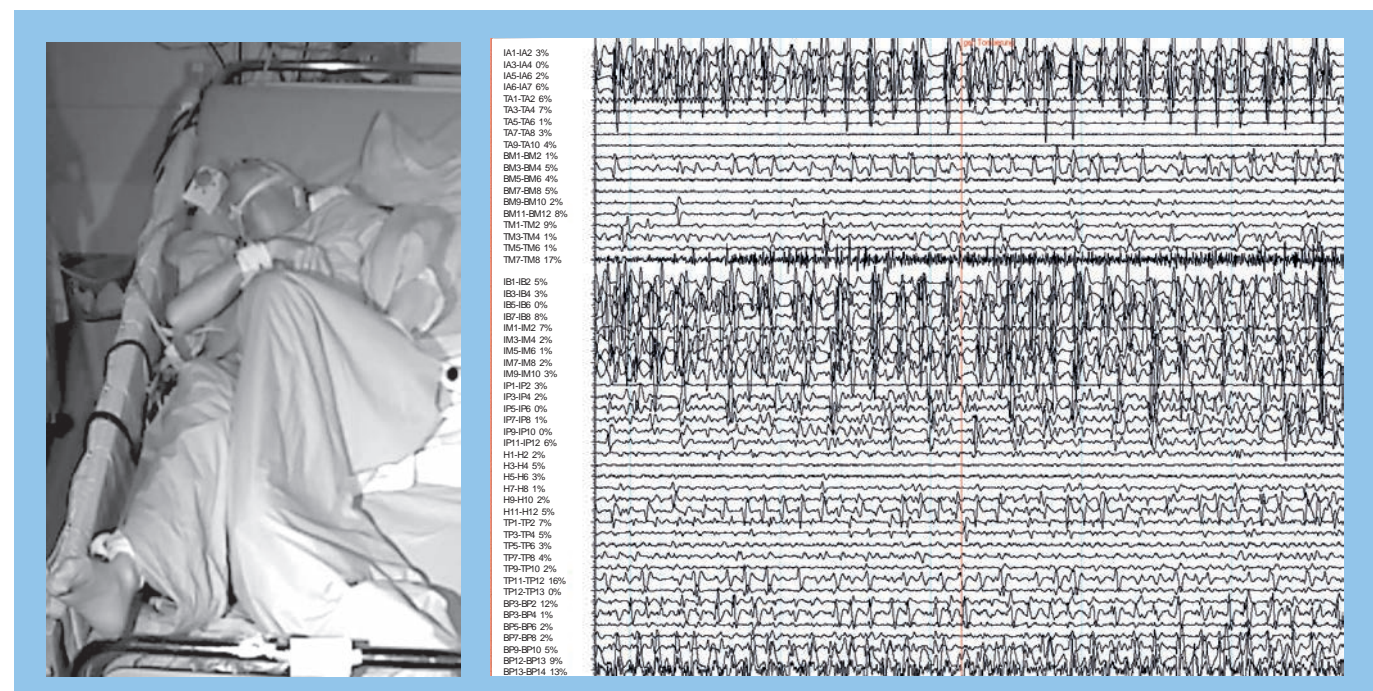


Figure 1. Intracranial recordings with stereo-EEG during the phase of ‘secondary generalization’ of a seizure. Note the involvement of only parts of the brain in the ictal epileptic activity despite bilateral motor phenomena (asymmetric extension of arms and legs).

'localization-related epilepsy' when reclassifying this to 'structural-metabolic'. Furthermore, one has to consider that already using drugs for 'generalized' versus 'localization-related' seizures is inferior to a syndromatic approach; for example, when applying ethosuximide in childhood absence epilepsy but not in idiopathic generalized epilepsy in general, when applying carbamazepine in autosomal dominant nocturnal frontal lobe epilepsy although this was considered an 'idiopathic' epilepsy [17], and when using carbamazepine or phenytoin to control bilateral tonic-clonic seizures, independent from the assumption of a 'primarily generalized' or 'focal' seizure onset.

Having 'complex partial' versus 'simple partial' seizures was also used as a criterion for assessing the driving capacity of patients. However, independent of the aforementioned problems occurring when attempting to assess the presence of absence of consciousness, it is not the only relevant semiological element, and a proper evaluation of the capacity to drive a car or work at a particular job depends on the preservation of a normal reactivity. Reactivity is impaired when a patient is unconscious, but it may well be impaired during a visual aura with a scotoma or positive visual phenomena, during an acoustic aura distracting the attention of a patient, during a dyscognitive seizure with slowed mentation, during a vegetative seizure with bradycardia and during motor seizures of various kinds. Reporting seizure semiology as suggested in the new glossary thus renders it easier rather than more difficult to draw valid conclusions in the medicolegal domain.

Furthermore, a detailed semiological description helps in everyday life to determine the severity and impairments of a patient. Using the new seizure glossary does not make this assessment more difficult but instead pinpoints relevant aspects based on a proper description of the seizure semiology. It also allows targeting of particular treatment aims in reducing the seizure burden; for example, by abolishing positive or negative motor phenomena or even postictal impairments, which affect the quality of life of patients.

Old & new classification of epilepsy syndromes

The old classification of epilepsies and epilepsy syndromes has caused troubles to all teachers of

epileptology when trying to explain the structure behind it. The concepts involved in the classification system were as variable as considering the irritative zone, extent of EEG discharges, suspected epileptogenic lobe, genetics, clinical course, age at onset, semiology, trigger mechanisms and presence or absence of imaging findings, without an obvious logical scheme behind it.

One major distinction of epilepsies was the term 'localization-related' versus 'generalized'. As mentioned above, concepts of seizure generation have changed a lot during the last decades, and to date, seizures classically named 'generalized' like absence seizures or 'primarily generalized' tonic-clonic seizures are now also believed to originate in a local area of the cortex, but propagated faster and wider than in other seizures, which tend to remain more 'focal' [14].

The new epilepsy classification continues to use historically established electroclinical syndromes but no longer uses this distinction [13]. Giving up a terminology that can no longer be upheld in view of scientific progress is certainly a correct step. False implications of 'generalized' syndromes that can be caused by a circumscribed lesion (such as West syndrome) can be avoided, and erroneous classifications such as syndromes that can be precipitated by specific stimuli as necessarily generalized are no longer included.

So how to classify epilepsies then? One maintained principle is a division related to the age at initial manifestation of the epilepsy. This is an aspect that holds for some childhood epilepsy syndromes but due to a great variability of initial manifestation has its limitations.

In the formerly 'symptomatic' epilepsies, the new classification puts more stress on etiology, in effect, on epilepsies due to a structural lesion or metabolic alteration in brain physiology as opposed to a primarily genetic background. Replacing 'symptomatic epilepsies' with 'structural-metabolic' epilepsies has caused some debate as one may argue that not all symptomatic epilepsies are really associated with structural or metabolic changes [12]. On the other hand, the term 'idiopathic' has been considered preferable to 'genetic' as geneticists have so far failed to elucidate the background of the vast majority of epilepsies now called 'genetic'. Furthermore, it has been argued that a certain genetic background also plays a role in the formerly symptomatic epilepsies [18] so that a dichotomy is introduced at a level where in fact a continuum of genetic and

acquired factors plays a role. These aspects have to be taken seriously and may argue against the use of the term ‘genetic’ as a term to separate entities.

In practical terms, the formerly ‘idiopathic’ syndromes are mostly just transferred to a ‘genetic’ syndrome. This may pose problems in communication, as suffering from a ‘genetic’ epilepsy may sound even more stigmatizing than having a more mysterious sounding ‘idiopathic’ epilepsy. With the increasing knowledge of genetics in society, however, naming a disease according to its true cause should not be prohibited in the field of epileptology, as it is in other fields of neurology.

The new proposal introduces the term ‘constellation’ for mesial temporal lobe epilepsy with hippocampal sclerosis, Rasmussen syndrome, hypothalamic hamartomas with gelastic seizures and hemiconvulsion–hemiplegia epilepsy, instead of calling them syndromes. In the view of this author, there is little reason to withhold the term ‘syndrome’ for them as they all fulfill the requirements to form a complex of clinical features, signs and symptoms that together define a distinctive, recognizable clinical disorder to no less a degree than other syndromes that are accepted.

In practical terms, a better consideration of the cause of epilepsy reflects the rapid progress imaging techniques have made and their easy accessibility in patient care in many countries. Lumping together all ‘symptomatic’ epilepsies in one group does not take into account the practical relevance of the etiology. Etiology is a key determinant both for the efficacy of pharmacotherapy [19] and of epilepsy surgery [20]. For example, post-stroke epilepsies have a much higher chance of being successfully treated with antiepileptic drugs than hippocampal sclerosis or cortical dysplasia. This is relevant for informing patients on their prognosis when treatment is started, and it is relevant for setting early the course in treatment (i.e., timing of presurgical evaluation and surgical treatment).

Etiology is also relevant for outcome of surgery; for example, seizure freedom may be expected in 80–90% in patients undergoing lesionectomy of a glioneuronal developmental tumor or in patients undergoing hemispherectomy following perinatal infarction of the territory of the medial cerebral artery. Seizure freedom is achieved only approximately 60–70% in patients with hippocampal sclerosis, and less

frequently in patients with tuberous sclerosis or hypothalamic hamartoma. This is important information for patients and doctors, and thus ought to be given a corresponding significance in the diagnosis.

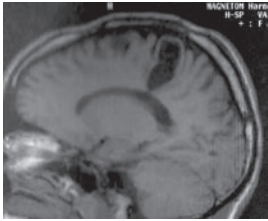
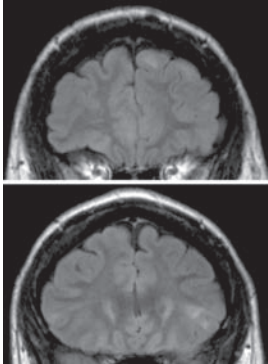
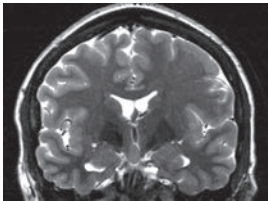
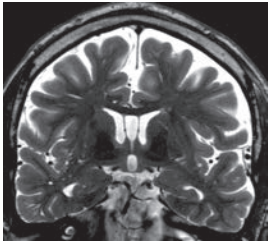
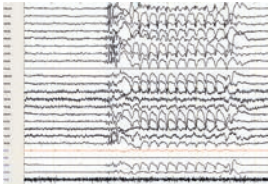
Lumping together all epilepsies with complex partial seizures has also turned out to not be fruitful for progress in medical treatment. When designing antiepileptic drugs that work on all symptomatic epilepsies, obviously, only the final common pathway is addressed, and we end up with more and more exchangeable blockers of voltage-gated ion channels and modulators of GABAergic transmission without achieving a breakthrough in terms of complete seizure control beyond what has been the possible since the 1960s.

Integrating etiology in the classification of epilepsies may thus pave the way to more targeted therapies, particularly in integration of knowledge on the particular pathophysiology of brain alterations in the process of drug development. For example, it has to be assumed that optimal interference with seizures due to mossy fiber sprouting in the dentate gyrus are different from those involved in the overexcitability in dysplasias related to abnormal connectivity and neurophysiological alterations in immature or altered pyramidal cells.

Conclusion & future perspective: there are two sides of the coin

In practical terms, a transfer of diagnoses from the old to the new classification system for epilepsies is easy. Instead of speaking of ‘symptomatic localization-related epilepsy with complex-partial seizures’, we may now say ‘structural’ epilepsy due to a glioneuronal tumor in the right frontal lobe with nocturnal left-sided tonic motor seizures. Using the term ‘unknown’ for unclear etiologies may not be superior to ‘cryptogenic’ for the expert but may avoid confounding cryptogenic and idiopathic, as has often occurred, or using cryptogenic with different meanings (Table 1) [21].

The new classification can thus be easily used in place of the old one. This is due to the fact that previously existing syndromes of epilepsy have been touched on only very little. This also means, however, that the progress in using the new classification is limited to a partially improved terminology and to giving up some erroneous aspects of the organization. The

Table 1. Classification of epilepsy syndromes according to the old and new scheme.		
Old classification (1989)	Imaging/EEG	New classification (2010)
Symptomatic focal epilepsy with simple partial seizures with motor symptoms		Post-traumatic structural epilepsy with left-sided clonic motor seizures
Symptomatic focal epilepsy with complex partial seizures		Structural epilepsy due to tuberous sclerosis with asymmetric tonic seizures suggesting left hemispheric generation
Symptomatic focal epilepsy with complex partial (?) seizures		Constellation hypothalamic hamartoma with gelastic seizures
Cryptogenic focal epilepsy with complex partial seizures		Epilepsy of unknown cause with asymmetric tonic seizures suggesting right hemispheric generation
Idiopathic generalized epilepsy with myoclonic seizures (Janz syndrome)		Genetic epilepsy with bilateral myoclonic seizures (Janz syndrome)
Note that in many cases a transfer is easy. The new classification contains more information on the underlying pathology and offers advantages in the precision of seizure description and in avoiding ambiguities when consciousness is difficult to assess, here in the case of brief gelastic seizures. Classification of epilepsy in tuberous sclerosis as structural is based on the assumption that seizures arise from cortical tubera and not directly from the genetic defect underlying the formation of tumors.		

next step, a multiaxial system of classification, including etiology, semiology, electrophysiology and possibly related social aspects [10] has not yet been taken although its possible value has also been emphasized by members of the commission. Finding a consensus on changes in terminology seems to have absorbed so much

energy that such a major second step of reorganization was beyond the scope. The commission accordingly termed the new proposal an ‘interim organization’ of epilepsies. Further progress that reclassifies epilepsies in a more fundamental, taxonomic manner is still some way off in the future.

Financial & competing interests disclosure

The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment,

consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

No writing assistance was utilized in the production of this manuscript.

References

Papers of special note have been highlighted as:

■ of interest

- 1 Esquirol JM. *Des Maladies Mentales*. Bailliere JP (Ed.). Paris, France, Tome 2 (1838).
- 2 Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised clinical and electrographic classification of epileptic seizures. *Epilepsia* 22, 489–501 (1981).
- 3 Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 30, 389–399 (1989).
- 4 Wolf P. Of cabbages and kings: some considerations on classifications, diagnostic schemes, semiology, and concepts. *Epilepsia* 44, 1–4 (2003).
- 5 Beghi E. New classification proposals for epilepsy: a real advancement in the nosography of the disease? *Epilepsia* 52, 1197–1198 (2011).
- 6 Berg AT, Scheffer IE. New concepts in classification of the epilepsies: entering the 21st century. *Epilepsia* 52, 1058–1062 (2011).
- 7 Berg AT, Scheffer IE. What is at stake in a classification. *Epilepsia* 52, 1205–1208 (2011).
- 8 Duncan JS. The evolving classification of seizures and epilepsies. *Epilepsia* 52, 1204–1205 (2011).
- 9 Engel J Jr. The etiologic classification of epilepsy. *Epilepsia* 52, 1195–1197 (2011).
- 10 Lüders HO, Amina S, Baumgartner C *et al*. Modern technology calls for a modern approach to classification of epileptic seizures and the epilepsies. *Epilepsia* 53, 405–411 (2012).
- 11 Shorvon S. Using etiology as one axis of classification. *Epilepsia* 52, 1208–1209 (2011).
- 12 Shorvon S. The etiologic classification of epilepsy. *Epilepsia* 52, 1052–1057 (2011).
- 13 Berg A, Berkovic S, Brodie M *et al*. Revised terminology and concepts for organization of seizures and epilepsies: report of the ILAE Commission on Classification and Terminology, 2005–2009. *Epilepsia* 51, 676–685 (2010).
- New commission report suggesting the new epilepsy classification.
- 14 Meeren H, van Luijckelaar G, Lopes da Silva, Coenen A. Evolving concepts on the pathophysiology of absence seizures. The cortical focus theory. *Arch. Neurol.* 62, 371–376 (2005).
- 15 Blume WT, Lüders HO, Mizrahi E, Tassinari C, van Emde Boas W, Engel J Jr. Glossary of descriptive terminology for ictal semiology: report of the ILAE task force on classification and terminology. *Epilepsia* 42, 1212–1218 (2001).
- Currently accepted International League Against Epilepsy classification of semiology.
- 16 Flanagan O. Consciousness. In: *Oxford Companion on Philosophy*. Oxford University Press, Oxford, UK (1995).
- 17 Picard F, Chauvel P. [Autosomal dominant nocturnal frontal lobe epilepsy: the syndrome]. *Rev. Neurol. (Paris)* 155, 445–449 (1999).
- 18 Berkovic SF, Mulley JC, Scheffer IE, Petrou S. Human epilepsies: interaction of genetic and acquired factors. *Trends Neurosci.* 29, 391–397 (2006).
- 19 Semah F, Picot MC, Adam C *et al*. Is the underlying cause of epilepsy a major prognostic factor for recurrence? *Neurology* 51, 1256–1262 (1998).
- 20 Tonini C, Beghi E, Berg AT *et al*. Predictors of epilepsy surgery outcome: a meta-analysis. *Epilepsy Res.* 62, 75–87 (2004).
- 21 Engel J Jr, Fejerman N, Berg AT, Wolf P. Classification of the epilepsies. In: *Epilepsy. A Comprehensive Textbook, 2nd Edition*. Engel J, Pedley TA (Eds). Lippincott Williams & Wilkins, PA, USA (2008).