

COMMENTS ON THE REPORT OF THE COMMISSION ON CLASSIFICATION AND TERMINOLOGY

C P Panayiotopoulos MD PhD FRCP UK Chapter of ILAE

The Report of the Commission on Classification and Terminology is an important document for consideration and reflection as it contains the thoughts of the upmost leading authorities in epilepsies that are also protagonists in the rapid pace of advances made in our field of expertise in medicine.¹

Outstanding achievements in the scientific and social aspects of epilepsies in the last 100 years should be largely attributed to the leaders and committee members of the ILAE; two eminent publications this year marked the 100th anniversary of the ILAE and *Epilepsia*, its official journal.

The ILAE standardized classification and terminology for epileptic seizures and syndromes²⁻⁵ provide a fundamental framework for organizing and differentiating the epilepsies. This categorization is essential in clinical practice, randomized controlled trials, epidemiology and research into these disorders. The efforts of the ILAE to devise classifications of the epilepsies has greatly improved communication among epileptologists and influenced both basic and clinical research.

The Commission's openness in a dedicated forum for debate that any member of the world epileptological community can share an opinion is a greatly appreciated and welcome approach of a productive dialogue. It makes all of us shareholders of these decisions. It is a breath of fresh air particularly in an area that "formal guidelines and practice parameters" are published in major journals practically unchallenged (any correspondence should be submitted within 4-6 weeks from publication!). It is in this sense that I feel privileged to contribute with my thoughts. I also do this with a great sense of responsibility after a thorough study of previous classifications, terminology of the ILAE Commissions and the comments that are already posted in the ILAE website. This is not a knee-jerk reaction of something new but an opinion of a clinician that puts the ILAE classifications in the heart of his work.⁶

Classification of Epileptic Seizures (1981)² and Classification of Epilepsies and Epileptic Syndromes (1989)³ are still the current valid formal ILAE classifications.

These classifications were made through lengthy and thorough assessments by the top epileptologists of the clinical, EEG, imaging, neurosurgical, neuropathological and other available data. The Commissions went at length to explain their procedures and their

reasoning of their decisions. A dictionary of epilepsies has been published earlier (1973).⁷ An important aspect of these classifications is that they provide a brief description of what each epileptic seizure and epileptic syndrome is (as could be best assessed then) which is missing from any subsequent reports on classifications .

Recent advances in the clinical- EEG manifestations of epileptic seizures and syndromes, video-EEG information, functional and structural imaging, investigative procedures and genetics mandated a new thorough and realistic revision of these classifications that the ILAE Commissions have been evaluating since 1997.⁸ The ILAE Task Force on Classification and Terminology under the tireless and dedicated stewardship of Pete Engel (Chair: Jerome Engel, Jr. 1997–2005) produced a report in 2001 as A Proposed Diagnostic Scheme for People with Epileptic Seizures and with Epilepsy,⁴; Engel, 2006 18268 /id} and this was updated and revised in 2006.⁵ A glossary of descriptive terminology for ictal semiology has also been published.⁹ The aim of these reports was to incorporate the tremendous advances and introduce scientific principles and standards into the classification of the epilepsies. This proved to be a challenging and difficult task despite the admirable efforts of the Commissions and their leaders.^{4;5} The subsequent recommendations and reports are not a replacement for the 1981 Classification of Epileptic Seizures² and the 1989 Classification of Epilepsies.³

TERMINOLOGICAL AND TAXONOMIC ISSUES

The newer ILAE proposals concentrate mainly on terminological and taxonomic issues. A significant drawback of these reports is that recognized epileptic seizures and epileptic syndromes are listed by name only in an age-related order. There is no definition or brief description of what each of these seizures/ syndromes/diseases should be despite the significant advance made from then (1981 to 1989) to now.

The different methodologies, approaches, targets and philosophies on classifications and their relevance to epilepsies have been authoritatively discussed in a multi-author editorial in *Epilepsia* (January 2003) entitled '*Cabbages and kings in the classification of seizures and the epilepsies*'.¹⁰ More recently, a series of important essays appeared in *Epilepsy Research* (2006; Supplement 2/3) that provides an excellent insight into what has been achieved and expected in future developments and proposals.

Classifications in epileptological literature are often compared to the classification of plants for botanists and gardeners as originally proposed by John Hughlings Jackson (1874).¹¹ The botanists, similar to all scientists, need a taxonomy of a scientifically based systematic order, whereas the gardeners, similar to all practising physicians, need arrangements for practical purposes, something to use in daily work.

In this sense, the currently valid classification of epileptic seizures (1981) and epileptic syndromes (1989) should be considered as tools to be used by the “gardeners’ pragmatic arrangement”. “The advantages of it are obvious. It facilitates the identification and the application of knowledge to utilitarian purposes, but it must not be trusted as a natural classification.”

The quest for a “botanists’ scientific classifications” of epilepsies has been the key point of attention in the newer ILAE reports. Such a classification from application of methods used in biology that determines separate species and natural classes is a noble and legitimate target but it appears to be very illusive. It may also have distracted us from truly using and incorporating the advances made in the proposals. In fact most if not all of the newly proposed terminologies are based on the same knowledge existing before 1989.

We should also not lose insight that we still are very much behind in precisely defining universally recognized epileptic seizures and syndromes such as “typical absence seizures” and “childhood absence epilepsy” that are still cited, sometimes with considerable misunderstanding or misuse of their original brief definitions of the 1981 and 1989 classifications.^{12;13}

TERMINOLOGY

Even the definition of epilepsies is eluding us with at least 4 different ILAE proposals that are all referring to “epilepsy” (as if this were a single disease) and we still debate.¹⁴⁻¹⁶ The definition of what epilepsies are may be a good example to prioritise and come into an ILAE consensus.

Definitions and terminology of “epilepsies and epileptic syndromes” have been the subject of a continuing process of discussion and debate through the various ILAE proposals; they have been changing, clarified or replaced with new ones through the various ILAE proposals. There is also considerable concern that certain terminology is “imprecise, misused or misunderstood”.

Terms need to be clarified and redefined when new information arrives, not abandoned or replaced every time that something new comes into light. New terms may not be better to comprehend or to apply and they are equally vulnerable to misunderstanding and misuse as the established ones.

Revised terminology is a significant part of the newest report of the ILAE Commission. Therefore, it is important to present key definitions and terminology “as is” in the ILAE publications. Comments are also made in order to assist the Commission and readers of how these are perceived by a clinical epileptologist.

EPILEPTIC SYNDROME

“An epileptic syndrome is an epileptic disorder characterised by a cluster of signs and symptoms customarily occurring together; these include such items as the type of seizure, aetiology, anatomy, precipitating factors, age of onset, severity, chronicity, diurnal and circadian cycling, and sometimes prognosis. However, in contradistinction to a disease, a syndrome does not necessarily have a common aetiology and prognosis.”³

“Epilepsy syndrome: A complex of signs and symptoms that define a unique epilepsy condition. This must involve more than just the seizure type; thus, for instance, frontal lobe seizures per se do not constitute a syndrome (changed concept)”.⁴

“Epilepsy syndrome, more precisely “electro-clinical syndrome”, is a complex of clinical features, signs and symptoms that together define a distinctive, recognizable clinical disorder. These often become the focus of treatment trials as well as of genetic, neuropsychological, and neuroimaging investigations. Use of the term “syndrome,” and more precisely “electro-clinical syndrome,” will be restricted to a group of clinical entities that are reliably identified by a cluster of electro-clinical and developmental characteristics. These are largely but not exclusively genetic in origin, and tend to have a strong relationship to developmental aspects of the brain. These are distinctive disorders identifiable on the basis of a typical age onset, specific EEG characteristics, seizure types, and often other features which, when taken together, permit a specific diagnosis. The diagnosis in turn often has implications for treatment, management, and prognosis. The term for these entities is “Electro-clinical Syndromes.” While ultimately common usage will likely shorten the term again to “syndrome” alone, this is still specifically defined to mean entities that can be considered electro-clinical syndromes. It would be inappropriate to refer to, for example, epilepsy with a frontal lobe focus and not otherwise specified as a “syndrome.”¹

Comment: It is apparent that the definition of an epileptic syndrome is not much different from one to another in the ILAE proposals. Further, “syndrome” (syn-drome= to run together) is well defined and widely used in medicine probably from the times of Galen. See also definition of syndrome in relevant medical dictionaries: 'a distinct group of symptoms and signs which, associated together, form a characteristic clinical picture or entity', while 'a disease has common aetiology and prognosis despite individual modifications'.¹⁷

EPILEPSY DISEASE

“Epilepsy disease: A pathological condition with a single, specific, well-defined aetiology. Thus, progressive myoclonus epilepsy is a syndrome, but Unverricht–Lundborg is a disease (new concept)”.⁴

Comment: “Disease” is clearly differentiated from “syndrome” in any medical dictionary and in the ILAE classifications (see above definitions). It is therefore of surprise to read in the

newer ILAE report : “Disease versus syndrome: Although there is reason to distinguish the concepts of disease and syndrome, these terms are not consistently used in medicine. Ultimately, it was decided not to insist on the disease-syndrome distinction in referring to the epilepsies at this time, although either or both terms may be used depending on the context and custom.” ¹

The term “Constellations” introduced in the recent report (in addition to electro-clinical syndromes) is unlikely to attract any approval or popularity. Most of these so-called “constellations based on specific lesions or other specific causes” are diseases.

Of note also is that “Progressive myoclonus epilepsy” are not a syndrome but a group of heterogeneous genetic diseases such as Lafora and Unverricht-Lundborg disease. Also, relevant to the following discussion on classification by age, they may start from infancy to adulthood.

IDIOPATHIC EPILEPSY SYNDROME

“**Idiopathic epilepsies** are defined by age-related onset, clinical and electroencephalographic characteristics, and a presumed genetic etiology. There is no underlying cause other than a possible hereditary predisposition. Idiopathic epilepsies and syndromes are described as disorders “not preceded or occasioned by another,” according to the Oxford English Dictionary.” ³

“**Idiopathic epilepsy syndrome:** A syndrome that is only epilepsy, with no underlying structural brain lesion or other neurological signs or symptoms. These are presumed to be genetic and are usually age dependent (unchanged term)”. ⁴

Comment: The word ‘idiopathic’ comes from the Greek words *idios* (meaning self, own and personal) and *pathic* (meaning suffer).¹⁸ Idiopathic is not synonymous with benign. There are some idiopathic epilepsies that have a bad prognosis or lifelong duration and, conversely, there are symptomatic epilepsies with a few seizures that may not even require treatment. Also, idiopathic is not synonymous with “pharmaco-responsive”; even within the same syndrome (idiopathic or else) some patients are pharmaco-responsive while others are pharmaco-resistant. Idiopathic is not and should not be equated with prognostic outcome and response to treatment though this is usually better than in symptomatic and cryptogenic epilepsies.

Despite all these clarifications and the unequivocal meaning of what an idiopathic epileptic syndrome is, the new ILAE Commission proposes to abandon this term with the following justification:

“The term (idiopathic), however, is also used to convey the idea of a highly pharmaco-responsive form of epilepsy. Many, although not all, of the traditional “idiopathic” epilepsies

also spontaneously remit during a predictable age range (a separate quality or dimension) and were generally thought to be unaccompanied by other consequences or disabilities, although this is clearly not the case as a variety of subtle cognitive and behavioral disorders are seen in association with these forms of epilepsies.⁸ Cause is no longer equated with prognosis, and the implication that “idiopathic” implies “benign” is intentionally discarded.”¹

Reiterating these clarifications on idiopathic should be sufficient without the need to abandon the term and replace it with “unknown” which is much broader.

“Idiopathic” and “cryptogenic” refer to epilepsies that their cause is not definitely known. The only difference from the newly proposed group of “epilepsies of unknown aetiology”¹ is that idiopathic are more likely to be of genetic and cryptogenic of symptomatic cause. When certain aetiology is found, these syndromes are not any more idiopathic, cryptogenic or unknown; they are re-classified appropriately as symptomatic, genetic or other syndromic categorisations.

SYMPTOMATIC EPILEPSY SYNDROME

“Symptomatic epilepsies and syndromes are considered the consequence of a known or suspected

disorder of the central nervous system “.³

“Symptomatic epilepsy syndrome: A syndrome in which the epileptic seizures are the result of one or more identifiable structural lesions of the brain (unchanged term)”.⁴

Comment: It is true that “symptomatic” may not be the best term to characterise these epilepsies; other synonyms such as “lesional” and “structural” have been proposed. “Epilepsy is symptomatic of something”. See also use of the word in “symptomatic treatment”, “symptomatic relief” and so on. However, this term has now been well established and with further clarification of its meaning it may continue to serve its purpose. It should not be “substituted for the concept of a poor prognosis for seizure control”;¹ this is clarified and easily understood.

CRYPTOGENIC AND PROBABLY SYMPTOMATIC EPILEPSY SYNDROME

“Cryptogenic epilepsies are presumed to be symptomatic, but the aetiology is not known. The term cryptogenic refers to a disorder whose cause is hidden or occult. The cryptogenic epilepsies are also age related but often do not have well-defined electro- clinical characteristics”.³

“Probably symptomatic epilepsy syndrome: This is synonymous with, but preferred to, the term ‘cryptogenic’, used for defining syndromes that are believed to be symptomatic but no aetiology has been identified (new term)”.⁴

Comment: The number of cryptogenic epilepsies is decreasing in favour of the symptomatic ones with the use of high-resolution MRI, which identifies previously undetected structural brain abnormalities. However, as Peter Wolf has pointed out, ‘some cryptogenic conditions may also turn out to be idiopathic, and this could be true even for the one well-known case where, at the syndrome level, the aetiology remains unclarified but a specific, “idiopathic” pathogenesis may still be revealed, i.e. mesiotemporal lobe epilepsy with hippocampal sclerosis’.¹⁹

Despite all these clarifications and the unequivocal meaning of what cryptogenic epilepsies are (at least in the original classification of 1989)³, the new ILAE Commission proposes to abandon this term with the following justification: “cryptogenic” was defined in 1989 as meaning “presumed symptomatic” apparently in the sense of “lesional”. It is, however, from among these “cryptogenic” epilepsies that syndromes such as autosomal dominant nocturnal frontal lobe epilepsy and autosomal dominant partial epilepsy with auditory features have been discovered.”¹ However, the latter is absolutely consistent with the view that cryptogenic is a general term that includes “syndromes of causes that are hidden or occult”.

Please, see also relevant comment in idiopathic which I repeat:

“Idiopathic” and “cryptogenic” refer to epilepsies that their cause is not definitely known. The only difference from the newly proposed group of “epilepsies of unknown aetiology”¹ is that idiopathic are more likely to be of genetic and cryptogenic of symptomatic cause. When certain aetiology is found, these syndromes are not any more idiopathic, cryptogenic or unknown; they are re-classified appropriately as symptomatic, genetic or other syndromic categorisations.

BENIGN EPILEPSY SYNDROME

Benign epilepsy syndrome: A syndrome characterised by epileptic seizures that are easily treated or require no treatment and remit without sequelae (clarified concept).⁴

Benign: The names of many syndromes contain the word “benign.” Two key features of “benign” epilepsy syndromes are that they: a. Involve seizures which are self-limited in that spontaneous remission, regardless of treatment, occurs at an expected age and is the anticipated outcome in the vast majority of cases, b. The consequences, if any, of the seizures are generally not disabling over the course of the active seizure disorder. This does

not preclude an increased risk of subtle to moderate cognitive and behavioral disorders prior to, during, or extending beyond the active phase of the seizures".¹

Comment: The prefix "benign" in a number of epileptic syndromes is to contrast them from the stigmatising word "epilepsy" and to differentiate them from the most severe forms of epilepsies such as "epileptic encephalopathies". Benign in medicine indicates conditions that are not recurrent or progressive; not malignant; have little or no detrimental consequences, favourable for recovery and generally not life-threatening. See also benign tumours.

With all these in mind, it may be difficult to understand the reasoning that the term benign epileptic syndrome should be abandoned and I quote "With our increasing awareness, however, of the cognitive and behavioural comorbidities, psychiatric disorders, migraine, and even sudden death that may accompany any form of epilepsy, the term "benign" itself seems inappropriate as it may lead to false hopes and unrealistic expectations."¹ This is the most worrying statement, a stone of death to all of us, who have campaigned for year that on evidence, a significant number of patients and mainly children have some forms of epilepsies (or just one or a few epileptic seizures) that are entirely benign with little or no detrimental consequences as documented with long term prospective studies over the last 50 years (see relevant syndromes with the prefix "benign" in the 1989 classification most of which were accepted in the subsequent ILAE reports). The main consequences for the vast majority of these patients and their families are psychosocial resulting from equating them with "epilepsy".

That children with rolandic seizures and related benign childhood syndromes may develop usually mild and reversible linguistic, cognitive and behavioural abnormalities during the active phase of the disease has been well reported. However, the effect of anti-epileptic drugs, the impact of stigmatizing because of epilepsy, bias in selection of the most serious cases and other factors have not been excluded in most of these studies. The development, social adaptation and occupations of adults with a previous history of such seizures was found normal in prospective studies of many years of follow up and this is also my experience.²⁰ These are subjects to further research prior to accepting them as a reason for detaching from them the word "benign". Even more unjustifiable is the threat of SUDEP for these patients that may exist but to what extend and for which of them?

Many patients with "benign" epilepsies do as good and sometimes better than of febrile seizures, which is an example of "benignity" despite that some of them may not do well (see complex febrile seizures). Another alternative is to classify them as "*Conditions with epileptic seizures that are traditionally not diagnosed as a form of epilepsy per se*" with benign neonatal seizures and febrile seizures which is a categorisation accepted in all classifications from 1989. [See below under relevant title]

Proposed terms such as “pharmaco-responsive” may be more problematic than “benign” because (a) at least one third of these children do not need pharmacological treatment and (b) patients with the same syndrome may be “pharmaco-responsive” or “pharmaco-resistant”. “Self-limited” may be better but this also applies to a significant number of other unrelated epilepsies and this term has also been used to define epileptic seizures (see “self-limited epileptic seizures” in a previous ILAE report – see below).⁴

That benign and idiopathic are not synonymous have been unequivocally clarified above (see idiopathic epilepsy syndrome).

GENETIC EPILEPSY

“The concept of genetic epilepsy is that the epilepsy is, as best as understood, the direct result of a known or presumed genetic defect(s) in which seizures are the core symptom of the disorder. The knowledge regarding the genetic contributions may derive from specific molecular genetic studies that have been well replicated and even become the basis of diagnostic tests (e.g. SCN1A and Dravet syndrome) or the central role of a genetic component may rely on evidence from appropriately designed family studies. Designation of the fundamental nature of the disorder as being genetic does not exclude the possibility that environmental factors (outside the individual) may contribute to the expression of disease. At the present time, there is virtually no knowledge to support specific environmental influences as causes of or contributors to these forms of epilepsy.... It is possible that the genetic defect may have other effects in addition to the seizures but, as best we can tell, these other effects are not interposed between the genetic effect and the seizures”.¹

Comment: Genetic epilepsies are the best example to include and expand in the classification of epilepsies in order to take advantage of the tremendous advances made in recent years. No one else could do this better than the current ILAE Commission which includes the protagonists of this progress.^{21;22} The familial autosomal dominant focal epilepsies have already recognised by the ILAE Task Force.⁴ The same may apply to other genetic epilepsies (monogenic or polygenic) as they are definitely discovered. For others such as childhood absence epilepsy, juvenile myoclonic epilepsy and rolandic epilepsy we may have to wait for more concrete evidence to emerge. Until then, they can be nested in their corresponding grouping of IGEs and benign childhood focal epilepsies. The Commission discusses childhood absence epilepsy and benign childhood focal epilepsies that I wish to expand because these exemplify some of the problems that I wish to focus upon: (a) The Commission considers childhood absence epilepsy (CAE) as “genetic epilepsy” and this may be right.¹ However, the Commission also considers CAE as “very specific and highly recognizable entity” with which I would entirely agree but this is not consensual as recently debated in *Epilepsia* where even what is a “typical absence seizure” was disputed.^{12;13} (b)

The Commission suggests that in some “traditional “idiopathic” electro-clinical syndromes such as benign rolandic epilepsy (Vadlamudi L. et al., 2006)²³ and the benign occipital epilepsies of childhood, both Panayiotopoulos and Gastaut types (Taylor I, et al., 2008)²⁴ it is likely that genetic factors are involved but present evidence (e.g. low or absent concordance in siblings) does not suggest that genetic factors are paramount “ and therefore they should be categorised amongst the category of unknown aetiologies.¹ Benign childhood focal seizures and related epileptic syndromes is one of the most fascinating topic in paediatric epileptology that by itself needs a thorough re-assessment as we had pleaded on many occasions; the Commission had plenty of new prospective evidence to consider and incorporate other than the two cited references. What about “early onset benign childhood occipital epilepsy” that the Commissions have honoured me with an eponymic nomenclature “Panayiotopoulos type” from their first report?^{1,4,5} Converging evidence from multiple and independent sources (EEG, MEG, clinical and so on) document that this syndrome by large is a multifocal (not an occipital) epilepsy, linked with rolandic and much less often with ICOE-Gastaut and that some more severe forms are probably due to SCN1A mutations (as we recently reviewed in the Brain).²⁰ Also, contrary to the only one cited reference (of a retrospective study with only one typical case of PS)²⁴ this is different to the idiopathic childhood occipital epilepsy of Gastaut (a purely occipital epilepsy) as was also statistically validated (which is the type of evidence that the Commission rightly emphasises its significance). Genetic studies of rolandic spikes and rolandic epilepsy have also been recently published.²⁵ Therefore, like CAE the verdict is still open.

GENERALISED VERSUS FOCAL EPILEPTIC SEIZURES AND RELATED EPILEPTIC SYNDROMES

Similarities and overlapping of pathophysiological or genetic aspects between generalised and focal seizures/syndromes are significant but this should not distract us by the fact that their differences are of much greater magnitude than their similarities or overlapping. It is by emphasising their differences, that therapeutic disasters such as prescribing carbamazepine in absence seizures have been minimised.

That the differences between generalised and focal (partial) seizures are not as sharp as was initially thought is not new and was certainly known by our mentors of the 1981 and 1989 seizure and syndrome classifications. The Commission rightly clarifies what “generalised” and “focal” epileptic seizures are.¹ It also rightly maintains them as two distinctive groups of epileptic seizures probably in recognition that though both focal and generalized seizures may all start from a specific region or specific network some areas/networks may be easier to generalize and spread than others. This, both pathophysiological and clinically renders it important to still use focal or generalized as descriptive terms rather than to cover all the complexities of seizure generation.

However, discarding the distinction of “generalised” and “focal” for epileptic syndromes is highly contentious and problematic. Abandoning the term “generalised” epileptic syndromes is an unwanted example of how existing evidence may be interpreted in diametrically different ways; it is reversing the previous proposal that juvenile myoclonic epilepsy, juvenile absence epilepsy and “idiopathic generalized epilepsy with GTCS only” are a syndrome of “IGE of adolescence”²⁶ that I have argued against. Further, abandoning the term “generalised” epileptic syndromes creates the paradox that syndromes such as “epilepsy with generalized tonic-clonic seizures only” are not classified as generalised epilepsy though by name it manifests exclusively with “generalized tonic-clonic seizures alone”. The same applies for CAE and other IGEs that may be evidenced ONLY with generalised seizures.

SIMPLE AND COMPLEX PARTIAL SEIZURES

Simple and complex partial seizures are well established terms of practical significance and should not be abolished. The Commission considers that we should discard them because they ‘inappropriately created the impression that impairment of consciousness had certain mechanistic implications related to limbic system involvement’ and that ‘complex partial seizures’ has been erroneously used as a synonym of ‘temporal lobe epilepsy’⁴ and/or “the terms “simple’ and “complex” were often misused or misunderstood. Moreover, the distinction based on impairment of consciousness, although of great pragmatic social importance (eg for driving competence), was impossible to define in a precise scientific manner.”¹ Though these are correct, there are significant practical reasons (medico-legal cases, driving and job-related performance) for distinguishing seizures with or without impairment of consciousness. The problems with them may be as much as in the original considerations of the 1981 Classification which I quote: “A more persuasive argument existed for abolishing the words “simple” and “complex” in favour of “partial seizures with retention of consciousness” and “partial seizures with disturbance of consciousness”.²

Again if the problem is misunderstanding and misuse then ‘simple’ and ‘complex’ focal seizures should be maintained while emphasising that (1) ictal impairment of consciousness is a symptom of either neocortical or limbic seizures and (2) complex focal seizures may originate from any cerebral lobe and therefore they are not synonymous with temporal lobe epilepsy. In regard to “impairment of consciousness” this again needs to be appropriately defined even if the term complex partial seizures had to be eliminated. “Impairment of consciousness” is also a defining symptom of absence seizures.

The two recent ILAE reports introduce age at onset as the primary organizational factor for the electro-clinical syndromes.^{1;5} This is a remarkable, unsafe and unwanted deviation from all previous classifications and efforts for a relatively homogeneous categorization of epilepsies which is often achievable.^{3;4} Syndromes that are likely to be linked together on vast electro-clinical (and often genetic) evidence are separated apart and intermixed with a number of heterogeneous epilepsies.

That medical disorders including epilepsies and their evolution have significant differences from neonates to the elderly is well known otherwise we would not have neonatologists, paediatricians, adult physicians and gerontologists. This I have also emphasised in my book⁶ organised by chapters describing syndromes by approximate age at onset (neonates, infants, children) but without neglecting their so many significant differences (clinical, aetiological, management) which is why epilepsies in infancy and childhood are presented in separate chapters of idiopathic epilepsies, epileptic encephalopathies, severe neocortical syndromes and benign childhood focal epilepsies. I can not foresee how one could follow the new organisational order with chapters in infancy for example going from West syndrome to Myoclonic epilepsy in infancy, benign infantile seizures to Dravet syndrome and so one.

However and more importantly than practical issues is that age at onset is a broad criterion to accept as the primary organisational factor in any classification; some electroclinical syndromes have a small range of age onset (and indeed months or few years before complete remission) while in others their range of age onset expands for many decades.

Progressive myoclonic epilepsies may start at any age from infancy to adulthood (see for example neuronal ceroid lipofusconoses) and even a specific genetic epilepsy can start from very early or late age in life amongst family members.

The uncertainties and unsafe use of such listing (classification?) by age at onset becomes apparent by comparing the current table 3¹ with that of the ILAE Task Force of 2006.⁵ There are significant differences in between them, despite the same principle of classification by age at onset and the same existing evidence that the listing has been made. Syndromes previous listed in childhood and/or of less specific age relationships are now moved to adolescence (now also expanded to include adulthood) and so forth.

ADDITIONAL MATTERS TO CONSIDER

There are many other additional matters to consider and I am sure that I have missed many of them but here is what it comes on the surface of my list.

Terminology and classification that has been introduced by the ILAE Task Force but abandoned in the newer report.

There are many examples of terms and proposals that have been newly introduced in the ILAE Task Force reports^{4,5} that were short lived; these are now abandoned (mostly rightly) in the new report though their introduction was based on the same evidence.¹ I used two of them to exemplify of what may have been apparently avoidable to consider in future planning of the ILAE classifications.

Continuous seizure types was introduced for status epilepticus as distinct from self-limited seizure types.⁴ This naturally was soon abandoned; continuous seizure type was not better understood than status epilepticus which may also be self-limited.

Epileptic seizure type was introduced as a diagnostic entity with aetiological, therapeutic and prognostic implications^{4,5} with “eyelid myoclonia with and without absences” as an example of it but this has now been discarded with no further justification.¹

“Partial” versus “focal” seizures: Please consider the upset that occurred in our communications by establishing “partial” instead of “focal” seizures in 1981 which is now rightly reversed though these are synonymous. I quote “The present proposal does not represent a unanimity of views. There are those who would prefer the substitution of “focal” for “partial” in the description of seizures. The compromise to retain “partial” stems from the compromise arrived at on this very point in the formulation of the 1969 classification”.²

Conditions with epileptic seizures that are traditionally not diagnosed as a form of epilepsy per se.

This includes benign neonatal seizures and febrile seizures. It is the same as “Conditions with epileptic seizures that do not require a diagnosis of epilepsy” that initially included Benign neonatal seizures, Febrile seizures, Reflex seizures, Alcohol-withdrawal seizures, Drug or other chemically induced seizures, Immediate and early posttraumatic seizures, Single seizures or isolated clusters of seizures, Rarely repeated seizures (oligoepilepsy)⁴ following the example of “Situation-related seizures” of the 1989 classification³ that included Febrile convulsions, Isolated seizures or isolated status epilepticus, Seizures occurring only when there is an acute metabolic or toxic event due to factors such as alcohol, drugs, eclampsia, nonketotic hyperglycemia. Subsequently the list was rightly amended as most of these could be acute symptomatic seizures⁵ but why changing the terminology again? And why other syndromes that may manifest with a single or just a few age-related seizures can not find a place in this group? (see comments in benign).

CONSISTENCY OF TERMINOLOGY AND PRINCIPLES

It is surprising how often terminology is not consistent between ILAE proposals and even in the same report.

The term “primary reading epilepsy” is still used though “primary” is an obsolete term that has been long abandoned in the classification of epileptic syndromes.

“Epilepsy with myoclonic-astatic seizures” is still used though the term astatic seizures has been abandoned in favour of atonic seizures.

“Febrile seizures plus” is used to denote an epileptic syndrome “Epilepsy with febrile seizures plus” though these are types of seizure.

It is also surprising how often principles and arguments of classification that are used for one may not be used for another syndrome.

For example the word “likely” (without referring to its statistical dimensions) is often used in favour of one or against another view or seizure/syndrome. Statistical validation is rightly a defining value but even when this exists is not taken into account.

The problem of course is not only with the ILAE reports; it is much more wide and the ILAE may take the lead for this in at least on what may be detrimental for epilepsies.

Evidence based medicine is our ultimate and desirable goal, but this is also often misunderstood or misused.²⁷

New terms some of which are derogatory such as “cognitive teratogenicity” are allowed to be introduced.

Terms such a “secondary generalization” are ill applied even by the regulatory authorities in the licensing of antiepileptic drugs erroneously equating this with “secondarily generalized tonic clonic seizures”. Formal guidelines make recommendations for the use of antiepileptic drugs in “generalized epileptic seizures” though the drug is effective only in one of these and may be deleterious for another type of generalized seizure.

There may be also other matters that do not come now in mind but may be found in my book⁶ or other of my publications.

PRACTICAL PROPOSALS

The authors of the Commission’s report are the leaders that take ILAE into the second centenary which is expected to be greater than the first one. There is also a wealth of research, experience and interest in epilepsies which expands all over the world than limited to a few countries which was the situation in the first centenary. This is evidenced by the increasing numbers of eminent publications and contributions from all over the world and a new generation of brilliant clinicians and scientists, the future stars of epileptology.

The Commission had offered us their report for comments and as one can assess from those that have been already submitted and this one of mine, it is easy to praise, doubt, criticise or project your own ideas and approaches. The difficulty is of how can these be put into practice and this is what I would attempt in this last part of my comments.

It is apparent to me that despite significant efforts, time and thought, the classification of epilepsies so far has been unsuccessful with methods used in biology that determine separate species and natural classes. In attending this target, we have been distracted from defining the basic elements of epilepsies (seizures, syndromes and diseases). We still rely on their brief definitions made 20 years ago despite that this is where the advances made can be easily incorporated and shine. Therefore, my practical proposal to the ILAE leaders is to delegate the task of defining each one of these seizures, syndromes, diseases each in a small group (around 5?) of experts with documented contribution in that particular subject and preferentially of different views and of different approaches. They should be asked to offer a brief description precisely stating areas of consensus and areas of uncertainties; disagreements should also be clearly stated and justified. These then can be collated and assessed by the ILAE Commission, accepted or published for further consultation. This can yield satisfactory results in a very short time because of wealth of experience, the willingness of physicians to collaborate and available fast means of communication. It is disheartening to realise that childhood absence epilepsy is still the subject of speculations in regard to what its definition means in the ILAE 1989 classification. Am I confident that the views we expressed in the report on CAE with the late Pierre Loiseau (see ILAE website (http://www.ilae-epilepsy.org/ctf/childhood_absence.html)) correct? Of course not, and this is where matters can be improved with my proposal of a small and flexible team work.

Another proposal which would be much easier to fulfill is that terminology used in epileptology (whether officially accepted or not) should be clearly defining in its meaning and also pointing where this is misunderstood or misused as the report does on a number of occasions.

C P Panayiotopoulos MD, PhD, FRCP
UK Chapter of ILAE
Consultant Emeritus
Department of Clinical Neurophysiology and Epilepsies
St. Thomas' Hospital, London SE1 7EH
e-mail: tom.panayiotopoulos@gstt.sthames.nhs.uk

PS. I may have gone too long and I am sorry of possible typographical, grammatical or other errors. English is not my mother language, the time I have to submit this commentary is limited and I feel that I should share my views in this invitation. I usually test my documents by asking the opinion of many other colleagues (known and unknown to me) and I am

honoured and privileged with their generous responses. Then, the final text is professionally text-edited before it is submitted for publication.

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