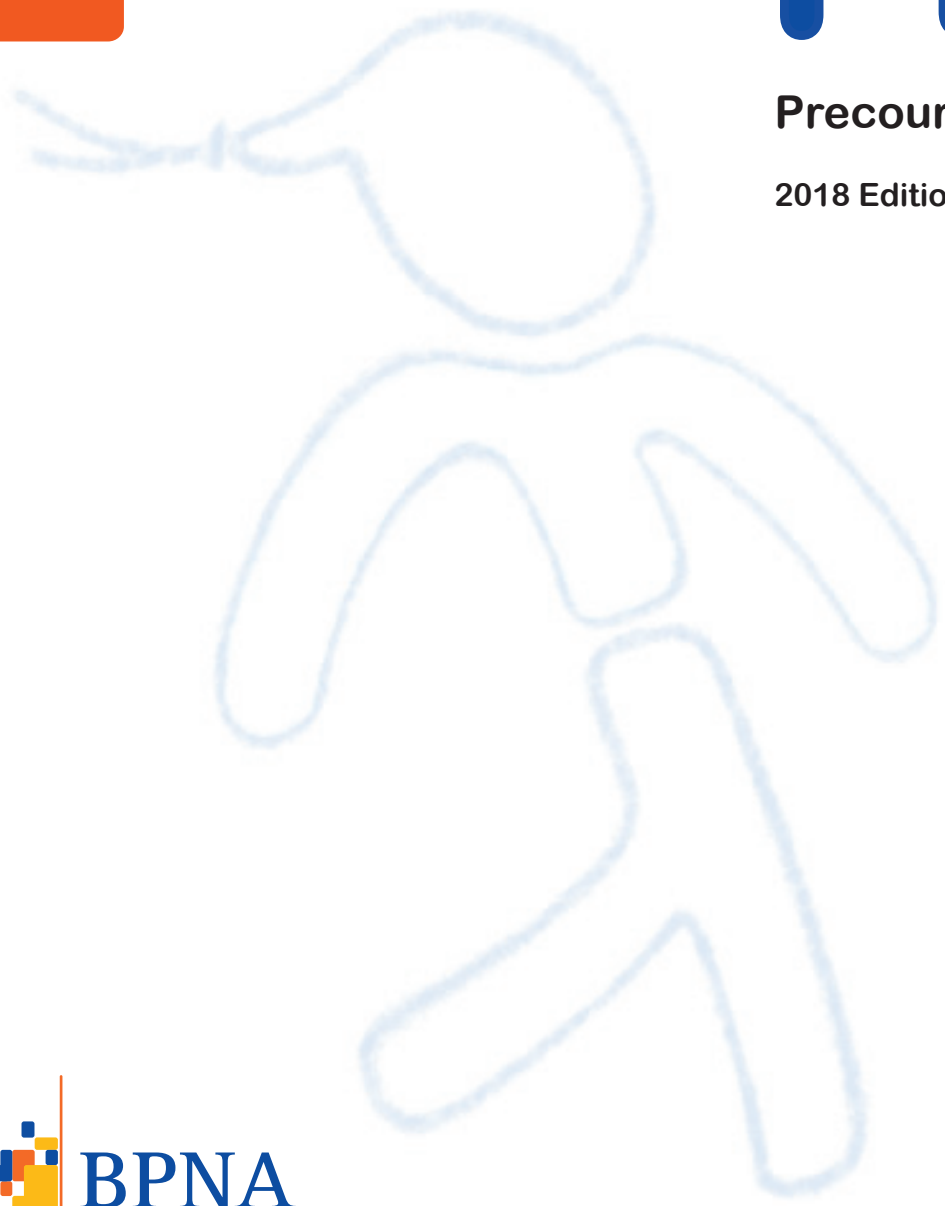
PET 1 2 3
PAEDIATRIC EPILEPSY TRAINING

PET 2

Precourse Workbook

2018 Edition



BPNA
British Paediatric Neurology Association
www.bpna.org.uk
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ILAE International League Against Epilepsy

Welcome to PET2

Paediatric Epilepsy Training (PET) courses were established by the British Paediatric Neurology Association (BPNA) in 2005. They aim to contribute to the ongoing development of health professional expertise and services for children with epilepsies. PET2 and PET3 are designed to complement PET1 and are aimed at paediatricians developing expertise in epilepsies and epilepsy specialist nurses. Participants are encouraged to attend PET1 first and therefore PET1 knowledge is assumed.

PET2 considers diagnosis, classification, investigation and treatment of epilepsies in infancy and early childhood. The format of the course is varied and includes quizzes, workshops, debates, lectures and role play. The course focuses on the application of knowledge in the real clinical world and therefore deliberately examines areas of uncertainty!

Fees towards the course go towards venue hire, refreshments, actor fees, course materials and ongoing course development costs. PET courses are indebted to the ongoing support of the many facilitators who contribute to the course purely on a voluntary basis.

To get the most out of the course, please read the papers provided before attending the course.

a) A helpful **EEG paper** to go alongside the EEG session: AJ Fowle, CD Binne. Uses and Abuses of the EEG in Epilepsy. *Epilepsia*. 2000; 41 (Suppl 3):S1O-S18

b) The 'To treat or not to treat' workshop considers the aims and 'pros and cons' of commencing treatment in a girl who has had two generalised tonic clonic seizures 6 months apart. Please read the papers provided that look at issues relating to this. **Read the papers and consider how treatment would specifically impact in the following areas**:

- Risk of subsequent seizures
- Natural history of the epilepsy
- Safety issues
- Mental health and psychosocial issues
- Risk of death
- Other areas

Also reflect on the following:

- What factors may influence the final decision about commencing treatment?
- Is there a right or wrong decision?
- Whose decision is it?
- What other evidence base may be helpful?

Papers provided to help with the 'To treat or not to treat' workshop:

1. S Shinnar et al. Predictors of multiple seizures in a cohort of children prospectively followed from the time of their first unprovoked seizure. *Annals of Neurology*. 2000; 48: 140-7

2. S Shinnar et al. The risk of seizure recurrence after a first unprovoked afebrile seizure in childhood: an extended follow-up. *Pediatrics*. 1996; 98 (2): 216-25

3. C Camfield et al. Does the number of seizures before treatment influence ease of control or remission of childhood epilepsy? *Neurology*. 1996; 46: 41-44

4. S Davies, I Heyman, R Goodman. A population survey of mental health problems in children with epilepsy. *Developmental Medicine & Child Neurology*. 2003; 45 (5): 292-5

PET2 Timetable

Time	*Session*	*Session Type*
Day 1		
09.00 – 09.30	Registration with tea and coffee	
09.30 – 09.40	1. Welcome and introduction	Whole Group
09.40 – 10.20	2. The epileptic or non-epileptic episode quiz?	Whole Group
10.20 – 11.00	3. Improving accuracy of diagnosis	Workshop
11.00 – 11.30	4. An approach to differential diagnoses	Workshop
11.30 – 11.50	Tea and coffee break	
11.50 – 12.25	5. The diagnosis of epilepsies	Whole Group
12.25 – 12.50	6. Effective EEG in principle	Whole Group
12.50 – 13.30	7. Effective EEG in practice	Workshop
13.30 – 14.15	Lunch	
14.15 – 15.15	8. Epilepsy and disability	Workshop
15.15 – 15.35	Tea and coffee break	
15.35 – 16.35	9. To 'treat' or 'not to treat'	Simulation
16.35	Any questions?	Whole Group
16.45	Close	
19.30	For those who have booked, course dinner in the hotel restaurant	
Day 2		
09.00 – 09.30	Registration with tea and coffee	
09.30 – 09.35	Introduction	Whole Group
09.35 – 10.20	10. Seizures in infants	Whole Group
10.20 – 11.10	11. Epileptic spasms	Workshop
11.10 – 11.30	Tea and coffee break	
11.30 – 12.20	12. Blank episodes in the young child	Whole group
12.20 – 13.00	13. Self-limited and pharmaco-responsive focal childhood epilepsies	Workshop
13.00 – 14.00	Lunch	
14.00 – 15.00	14. Complex epilepsies of early childhood	Whole Group
15.00 – 15.15	Tea and coffee break	
15.15 – 15.55	15. Complex epilepsies in practice	Workshop
15.55 – 16.00	16. Feedback and closing questions	Whole Group
16.00	Close	

Epilepsia, **41**(Suppl. 3):S10–S18, 2000
Lippincott Williams & Wilkins, Philadelphia

Uses and Abuses of the EEG in Epilepsy

Adrian J. Fowle and Colin D. Binnie

Department of Clinical Neurophysiology, King's College Hospital, London, United Kingdom

Summary: Our purpose was to indicate clinical situations in epilepsy in which the EEG provides useful information and those in which it is unhelpful and should be avoided. We performed an overview of the formal evidence available through Medline, Cochrane, and the Internet, as well as a traditional review based on the questions commonly asked of the authors' department in a London teaching hospital. We found that there is insufficient high-quality evidence to informed decisions regarding EEG utility. The EEG has many uses in epilepsy but, without attention to detail in the referral, may be abused. Good liaison between the referrer and the EEG department is essential to make proper use of the EEG. **Key Words:** EEG—Epilepsy—Indications—Utilization—Utility.

EEG TECHNOLOGY

> "Despite the proliferation of EEG departments, extensive research, the development of increasingly complex techniques, and the acquisition of a modicum of medical respectability, it is fair to say that the sanguine hopes of the early electroencephalographers have not been fulfilled."

These are the opening words of the final chapter on "The Future of the EEG in Clinical Practice" by Laidlaw and Stanton (1), written about 30 years after the introduction of EEG as a clinical tool. Approximately 30 years later, can we be any more optimistic about the place of EEG, and what we can predict for the next 30 years?

Much has changed in the past 30 years. The 8- or 16-channel paper EEG machines and transistor amplifiers of that era are replaced by machines capable of digitally recording 32 channels of EEG on a standard computer. It is interesting to note Laidlaw and Stanton's comment, "It is difficult, even for those experienced in EEG work, to appreciate more than 8 channels of EEG tracing at a time" at a time when even ECG is routinely presented as a 12-channel recording. In most modern departments, 20 or 21 channels of EEG and one channel of ECG are now routinely recorded and displayed. The computer-based systems enable one to redefine the montage, derivation, and filter settings not only during recording but also when the EEG is reviewed. These digital electronics systems are also small and robust. Full recordings can be made with a system consisting of a standard laptop computer and a small box of preamplifiers. This equipment can be taken to intensive therapy units (ITUs), to peripheral clinics, and to patients' homes, although working with such a system is less convenient than with a desktop computer based system in a proper EEG laboratory.

Current technology also makes it possible for multichannel EEG and polygraphic data to be recorded for ambulant patients wearing small tape recorders. In specialized laboratories, such data can be recorded with simultaneous digital video for periods of several days, a technique known as video EEG telemetry.

Computer technology helps with the analysis as well as the recording of EEG data, with online frequency analysis becoming readily available in some systems. Potential maps of the brain surface are also produced, using a variety of mathematical models. These techniques are not used routinely.

The complementary investigations offered by neuroimaging departments have also progressed from air encephalograms and angiograms of the 1960s to include computer-assisted tomography (CT) and magnetic resonance imaging (MRI). Functional imaging modalities are also becoming available, with functional MRI (fMRI) and various types of nuclear medicine-based technologies such as positron emission tomography (PET).

In reviewing the use of EEG, it may be helpful first to consider what types of problems these investigations are intrinsically suited to solving. The EEG has a high temporal resolution. It can distinguish spike activity down to 10 ms with ease, or even better for research purposes if

Address correspondence and reprint requests to Dr. Adrian J. Fowle at Department of Clinical Neurophysiology, King's College Hospital, Denmark Hill, London SE5 9RS, U.K.

high sampling rates are used. It has a spatial resolution of perhaps 2 cm but records only activity from the surface of the brain unless invasive electrodes are used. CT and MRI have spatial resolutions down to a few millimeters but temporal resolutions of several seconds. Functional MRI and PET scans fall between these two extremes, but both of these are only available in specialist centers.

It might therefore seem obvious that the EEG is best suited to studying the response of the brain to events in the environment or to internal changes during a seizure. Conversely, the higher spatial resolution of imaging methods is better suited to revealing the anatomy around a lesion. In practice, however, the distinction is not so clear-cut. The function of the brain has not proved easy to deduce from the recorded activity at the surface. Some lesions that are still too small to be detected with current imaging technology may nevertheless produce sufficient functional disturbance to be detected on EEG. EEG has the advantages that it can be taken to the bedside, it is cheaper than most imaging modalities, and does not involve exposure to radiation. It can therefore be repeated more often than imaging studies to chart a patient's progress.

UNDERSTANDING THE EEG

The EEG is a test or series of tests whose exact form can be varied before and during the test to meet the needs of the evolving clinical problem. The ability to vary the test and the final report both depend on the ability to recognize the presence or absence of various EEG phenomena and their significance in the clinical context. These phenomena are waveforms of particular duration, frequency, or shape and their topographic variation over the surface of the scalp. This recognition process is similar to the pattern matching that is used in medical decision-making in many areas. Much work has been performed on computer recognition of EEG features, but thus far it has had little impact on routine EEG practice.

Reading EEGs must be learned through apprenticeship and experience, and it remains an inexact science. The point at which an irregular background activity becomes a small detectable abnormality is open to debate even among experienced practitioners. When the phenomena have been identified, their significance can be determined. For this, the literature provides some guidance for proven associations. Overall, the EEG remains an investigation with a categorical as opposed to continuous outcome, with specificity and outcome that are hard to determine, but which produces data obtainable by no other means.

THE EVIDENCE-BASED APPROACH TO EEG

The entire field of clinical neurophysiology is poorly served by evidence-based medicine. There are many thousands of articles describing trials of antiepileptic drugs (AEDs) and reports of single or series of cases in which EEGs were performed. There are, however, only a few studies in which the correct use of the EEG has been studied in its own right. There are even fewer published consensus statements or systematic reviews.

METHODS

A brief review of the available formal evidence was conducted. Table 1 shows the Internet sites searched on September 12 and 13, 1998. The search terms *EEG, Electroencephalography,* and *Electroencephalogram* were searched separately in those sites offering search engines. In sites offering hierarchical navigation, the *Neurology* tree was followed.

The Cochrane Library (1998, Issue 1) on CD-ROM was searched for the same terms.

Medline on CD-ROM (up to 8/98) was searched using the WinSPIRS program. Searches were made for *Epilepsy* and *Electroencephalography,* using both Mesh terms and free text searches. The Mesh term *Electroencephalography* was exploded and its subheadings analyzed.

TABLE 1. *Evidence-based medicine sites searched on the Internet*

Title	Internet address
Bandolier	http://www.jr2.ox.ac.uk/Bandolier
Centre for Evidence Based Medicine	http://cebm.jr2.ox.ac.uk
Canadian Medical Association, Clinical Practise Guidelines Infobase	http://www.cma.ca/cpgs/neur.htm
Effective Health Care Bulletins	http://www.york.ac.uk/inst/crd/ehcb.htm
Evidence Based Medicine	http://www.ohsu.edu/bicc-informatics/ebm
Internet Database of Evidence Based Abstracts and Articles (IDEA)	http://www.ohsu.edu/bicc-informatics/ebm/ebm_topics.htm
NHS Centre for Reviews and Dissemination: Systematic reviews	http://www.york.ac.uk/inst/crd/listcomp
NHS Economic Evaluation Database	http://nhscrd.york.ac.uk/
NHS Health Technology Assessment (HTA) database	http://nhscrd.york.ac.uk/
NLM Health Services/Technology Assessment Text (includes NIH consensus statements and AHCPR technology assessments and reviews)	http://text.nlm.nih.gov
ScHARR-Lock's Guide to the Evidence	http://www.shef.ac.uk/uni/academic/R-Z/scharr/ir/scebm.html

RESULTS

The Internet and Cochrane searches yielded three abstracts and the full text version of Ehrlichman (2). The Internet search also retrieved two papers (3,4). Eight INAHTA (International Association of Health Technology Assessments) were located in abstract form. One of these was Ehrlichman (2). The other seven covered magnetoencephalography and polysomnography as well as presurgical evaluation of epilepsy. Some of these reviews were still in progress and some were mainly of interest to the author's geographic region.

The Cochrane search also offered a database of over 55,000 drug trials indexed under *Electroencephalography,* with no means of filtering them further.

In Medline, "explode Electroencephalography/all subheadings" yielded 61,910 records. An additional 9,081 records were retrieved by free text searches for *EEG* or *Electroenceph*,* of which 322 records contained one of these words in the title. (Electroenceph* retrieves words beginning with Electroenceph, and therefore such variations as Electroencephalography and Electroencephalogram.)

The free text search for *Epilepsy* produced 41,276 records, whereas "explode Epilepsy/all subheadings" yielded 39,697 records. Combining these with related terms from the thesaurus, such as Landau-Kleffner syndrome, yielded a total of 43,354 records related to epilepsy.

The intersection of the total *EEG* and total *Epilepsy* sets yielded 14,477 records, whereas the intersection of the exploded Mesh searches yielded 12,560 (1,917 fewer).

The Mesh subheading *Utilization* is defined as "Used with equipment, facilities, programs, services, and health personnel for discussions, usually with data, of how much they are used. It includes discussions of overuse and underuse." Thirty papers were retrieved by "explode electroencephalography/utilization," of which only eight were in the intersection with the Mesh epilepsy search. Other subheadings relevant to the present review yielded the following intersections with epilepsy: classification 38; economics 3; methods 603; and standards 13.

DISCUSSION

Despite the current enthusiasm for evidence-based medicine (EBM), there appears to be little formal evaluation of the role of the EEG in the diagnosis and management of epilepsy. There is a Cochrane review group for epilepsy but thus far not for clinical neurophysiology. Medline remains a powerful tool but, in this field at least, does not provide a sufficiently accurate classification of all papers. This review has examined only the quantity of the evidence; the quality of the evidence will be addressed in a future publication.

REFERRAL FOR EEG IN EPILEPSY

In the minds of most doctors, EEG is a tool for investigating epilepsy, although in fact it has other uses. Table 2 shows the questions posed in epilepsy by users of our department. Often more than one of these questions is asked or implied on the same request form, although the wording may not be in the form shown in the table. The list of "Uses of the EEG" is much the same as the list of "Abuses of the EEG" because it is in the detail of the clinical problem that the difference lies. This underlies one of the important points to be made in this review. To get the best out of an EEG requires a dialogue between the referring doctor and the neurophysiologist. A clear statement of the clinical problem and the question that the EEG is to answer should both be provided on the referral form. The neurophysiologist can then decide which, if any, tests are suitable to answer the question. The final report will address the question posed and indicate whether it has been answered, what the answer is, and recommend further studies if appropriate.

The EEG is abused in a general way if insufficient information about the clinical problem is given on the referral form or if the report is not comprehensible to the referring doctor. This lack of communication represents a type of abuse that could be solved by a joint program of education between referring specialities and neuro-

TABLE 2. *Questions posed by referral forms for EEG*

Is it epilepsy?
Epilepsy vs. syncope
Epilepsy vs. nonepileptic attack disorder
Epilepsy vs. aggression
Status epilepticus on ITU
Epilepsy in children
Absence vs. daydreaming
What type of epilepsy is it?
Seizure type
Syndrome
Etiology
Is there a lesion and where?
What is the prognosis?
After a single seizure
After multiple seizures
After surgery
What is the effect of antiepileptic drugs?
In status epilepticus
Is the dose high enough?
Are there side effects?
Could they be stopped?
Can the patient . . .
Drive
Fly

physiology. Much of the remainder of this review concentrates on the specific questions shown in Table 2.

IS IT EPILEPSY?

Given the common perception of EEG, it is perhaps surprising that EEG answers this question only in rather limited circumstances. This question is one of the commonest abuses of EEG, often in the form "to exclude epilepsy," which is almost never possible. The diagnosis of epilepsy is essentially a clinical one. If there is good evidence from a witness of more than one classical generalized tonic–clonic convulsion, or of many absences, the patient has epilepsy.

In the majority of patients with funny turns, faints, and giddy spells, any given interictal EEG will be indistinguishable from normal, but this does not "exclude epilepsy." If nonepileptiform abnormalities are found, this often does not help to distinguish those with and without concomitant epilepsy.

The failure of EEG to answer this question stems from two observations that are themselves much misunderstood: first, that the EEG may be abnormal in normal people and, second, that it may be normal in people with epilepsy. Both of these statements are true and are only expressions of the specificity and sensitivity of the EEG. However, they have been used to denigrate EEG unnecessarily. Not performing an EEG when it would be helpful is another general abuse of the EEG, whose occurrence is hard to assess.

Cross-sectional EEG studies of the "normal population" are difficult to perform. However, studies have been performed in military aircrews and candidates for aircrew training undergoing routine EEGs as part of medical screening (5,6). The incidence of epileptiform activity in asymptomatic men is low (1%). Those with epileptiform activity have roughly a 2.5–5% chance of developing epilepsy in the next few years. These studies have insufficient follow-up data on subjects without epileptiform activity, but this risk is higher than the approximately 2% lifetime risk for epilepsy in the general population, including childhood epilepsy. After exclusion of those with asymptomatic cerebral disorders and of those who subsequently develop epilepsy, the rate of false-positives is about 0.3%.

Zivin and Ajmone-Marsan (7) reviewed the EEGs of patients referred to their department for reasons other than the investigation of a seizure disorder. (This was before the use of modern neuroimaging techniques.) In 2%, epileptiform discharges were found in the EEG. The incidence was much higher, up to 20%, in patients with congenital or perinatal acquired brain abnormalities, brain neoplasms, craniotomies, mental retardation, and biochemical defects. A total of 14% of patients with epileptiform discharges subsequently developed seizures, many in the first 4 weeks after EEG. Although the risk for epilepsy is high in this group, there are still "epileptiform activities" in many patients with cerebral disease who do not have epilepsy. Unfortunately, there is no description in this paper of the incidence of seizures in those without epileptiform discharges.

Later, the same authors (8) reviewed 1,824 EEGs in 308 people with epilepsy. In 92 patients (30%), all the EEGs contained epileptiform discharges. Fifty-four patients (18%) never exhibited epileptiform discharges despite repeated EEGs over several months. Epileptiform discharges were found on some occasions, but not on others, in 162 patients (52%). Overall, epileptiform discharges were found in 55% of patients at the first examination.

Binnie (9) reported the prevalence of epileptic phenomena in patients who clinically had epilepsy. One-third showed abnormalities in every EEG, one-third never, and one-third sometimes. The combination of a wake-and-sleep record yielded epileptiform activity in 80% of these patients.

Taken together, these studies suggest an 80% chance of showing epileptiform activity in a first wake-and-sleep EEG in people with epilepsy. Provided there is no other evidence of cerebral disease, epileptiform activity is rare in those who are and will remain free of epilepsy. Conversely, the finding of epileptiform activity considerably increases the chance for a diagnosis of epilepsy.

It is therefore the practice in our department to offer referring doctors the ability to order a combined routine and sleep EEG as the first investigation in patients with epilepsy, not only to establish that they have epilepsy but also to determine its type, as detailed below. This policy reduces costs and inconvenience to patients in an epilepsy service but is inappropriate for patients with a low chance of having epilepsy, and therefore requires some discrimination by the doctors.

Epilepsy vs. syncope

When can an EEG help answer the "Is it Epilepsy" question? It may help distinguish epilepsy from syncope in some cases, especially if an attack can be recorded with simultaneous EEG and ECG. It should not be forgotten, however, that elderly patients may easily have both cerebrovascular and cardiac causes of drop attacks and may be normal between attacks of either kind. It is also well recognized that small tonic–clonic movements may occur during vasovagal syncope, and are not usually regarded as epileptic seizures. Conversely, absence attacks may occasionally mimic syncope.

Linzer and colleagues (3) systematically reviewed the literature on the diagnosis of syncope to develop a clinical guideline. In total, 534 EEGs were performed in eight studies of syncope. They were diagnostic in only eight cases. Of these eight patients, two had a history of sei-

zures and information was not available for the others. The guidelines recommend EEG "if seizure activity is present on history and physical findings" and also that "patients who have seizure activity, normal results on EEG and no postictal symptoms and patients with seizures who do not respond to anticonvulsant medications should be evaluated for possible cardiac syncope."

Epilepsy vs. nonepileptic attack disorder

Video EEG telemetry can be performed for several days in difficult cases. This slightly increases the chance of detecting significant interictal activity, but the main aim of this approach is to capture the patient's attacks with simultaneous video and EEG. Patients are free to move, as opposed to being on an EEG couch, and some semblance of their normal behavior is observed. Telemetry distinguishes most types of nonepileptic seizures from true epilepsy (2). For example, an attack is not epilepsy if a tonic–clonic convulsion is not accompanied by generalized EEG discharges. It is well recognized that patients may have both epileptic and nonepileptic seizures, and the proportions of each can often be assessed by this technique. It must be remembered that even successful capture of seizures does not guarantee a diagnostic conclusion. For example, simple partial seizures are often not accompanied by any ictal EEG change.

A telemetric investigation that does not show epilepsy is not just a negative result. It may result in the diagnosis of epilepsy being revised, AEDs being withdrawn, and a more appropriate psychiatric management being instigated.

Epilepsy vs. aggression

The question of whether aggressive outbursts represent ictal phenomena is frequently asked, particularly with regard to adolescents. It is largely unrewarding work. Many of these patients are found to have minor epileptiform or other abnormalities on routine EEG. However, on video EEG is becomes apparent that the behavioral disturbances are unrelated to the EEG abnormalities.

Status epilepticus on an ITU

On an ITU the EEG can determine if there is convulsive status epilepticus in a patient whose convulsions are masked by sedation and paralysis. This may be the only means to guide treatment of severe status. Similarly, nonconvulsive status may be revealed only by EEG.

Epilepsy in children

Children who are too young to give a reliable description of their symptoms may exhibit seizure activity on EEG that will support a diagnosis of epilepsy.

Absence vs. daydreaming

Typical absence attacks are associated with a 3-Hz spike-and-wave discharge. The absence of this characteristic discharge during adequate provocation by hyperventilation makes typical absence epilepsy very unlikely. Absence-like symptoms also occur in complex partial seizures; their diagnosis by EEG is similar to the general case described above. This is one of the situations in which an ambulatory EEG recording may be useful.

WHAT TYPE OF EPILEPSY IS IT?

The International League Against Epilepsy (ILAE) has separately classified epileptic seizures (10) and epileptic syndromes (11) (or "the epilepsies," as they are sometimes known). Both classifications are periodically revised to reflect advances in understanding. Both also include clinical and electrographic features. These classifications are important because the prognoses of the various syndromes and their treatments are very different. This is probably the most valuable use of the EEG in epilepsy. It is also one of the hardest arts to master in EEG. As described above, repeated EEG studies and sleep EEG studies may be necessary to obtain sufficient information to answer these questions.

Seizure type

The EEG is used to answer the following questions: Is the seizure generalized or focal? (This is explored in a section below.) What is the morphology of the phenomena seen? What postictal changes are present?

Syndrome

The syndrome classification builds on the knowledge of seizure types. The main distinctions are between generalized and localization-related epilepsy and between idiopathic and symptomatic. The first dichotomy relies heavily on the similar dichotomy in seizure types. The EEG may contribute both to this and to the second dichotomy if abnormalities in the background activity suggest an underlying brain disease from which epilepsy is arising.

Etiology

EEG can rarely determine the etiology of an epilepsy, beyond delineating a seizure type and syndrome. On some occasions however, the pathology causing the epilepsy can be deduced from the EEG.

Video EEG telemetry is also useful for recording seizures to determine their type and possible focus. This is most useful in the context of presurgical evaluation. Video EEG telemetry and amytal (Wada) testing can both be used to determine whether there is spread of seizure activity from one area to another.

IS THERE A LESION AND WHERE?

Neuroimaging techniques have replaced EEG as the primary tool for diagnosing intracranial lesions. However, the EEG can sometimes still provide the first sug-

gestion that the patient might have a lesion. Some lesions whose functional effects can be detected on EEG are nevertheless too small or of the wrong pathology to be detected on current readily available imaging modalities. Some patients have multiple lesions and the EEG may be able to identify the lesion most likely to be causing symptoms. In presurgical evaluation of epilepsy, EEG remains an important part of the battery of investigations. EEG investigations available include routine and sleep EEGs, video telemetry, amytal testing, and depth or intracranial recordings (4).

There are catches for the unwary. First, not all localization-related or partial epilepsy is related to a lesion in the traditional surgical sense, and this causes much confusion in EEG reports. Second, modern epilepsy surgery can sometimes offer treatment to such nonlesional foci. This requires careful communication among the large number of specialists who comprise an epilepsy surgery team.

Generalized epilepsies may produce multifocal discharges on EEG. At a given moment, only one focus may be active, giving a false impression of a localization-related epilepsy. This and other aspects of idiopathic generalized epilepsy have been reviewed and discussed (12). Conversely, focal seizures with rapid secondary generalization may appear to be primarily generalized in nature. There are theoretic but contested arguments that all generalized epilepsies start in a single cortical location. This does not alter the practical distinction between primary and secondary generalization with which we are concerned here.

WHAT IS THE PROGNOSIS?

The EEG has no direct role in the prognostication of seizures or epilepsy. However, the diagnosis of epileptic syndromes, in which EEG plays a major part, may significantly alter the prognosis.

After a single seizure

Previously, it was accepted practice to give AEDs only after two or more seizures. It is becoming more common to treat after one seizure if the history is convincing, particularly if there are abnormalities on the EEG. It is therefore becoming more difficult to observe the natural history of untreated seizures. This topic was reviewed by Rowan and French (13). About 50% of all patients have only one seizure. In children, there is an increased risk for further seizures if the EEG shows organic brain damage, typical 3-Hz spike-and-wave or centrotemporal spikes. There is still a 30–40% risk of recurrence even with a normal EEG. In adults, there is an increased risk for further seizures if the EEG shows generalized spikes and waves. Surprisingly, the presence of focal features does not increase the risk.

After multiple seizures

People with epilepsy have, by definition, recurrent seizures. Treatment may reduce the frequency of rather than abolish seizures. It is to be expected, therefore, that such people will come to the attention of the health services. They are often referred for unnecessary EEG examination by junior medical staff. The EEG is often difficult to interpret after a major seizure and in most cases offers no new information.

An EEG should be requested if seizure type or frequency changes significantly. There is a possibility that a new type of epilepsy for that patient will be apparent, leading to a change in syndrome diagnosis and hence in the prognosis and management.

After surgery

The outcome of epilepsy surgery becomes evident only after extended follow-up. The EEG therefore deserves consideration as an early predictor of the long-term result of surgery. However, postoperative EEG investigations are rarely as detailed as those carried out during preoperative assessment. Only one study reports the use of activating techniques or special electrodes (14). Minor abnormalities can be expected simply as a consequence of surgery. In particular, within 3 months focal slow activity is common. Long-term abnormalities include asymmetries of background activity due to skull defects and a possible breach rhythm, the sharp theta waves that often occur at the site of craniotomy (15). Six months after surgery (16), residual discharges were associated with continuing seizures and with failure to excise the entire irritative zone, as determined by preoperative studies. Twenty percent of patients showed epileptiform activity, of whom 58% had seizures, whereas all but 19% of those without epileptiform activity were seizure-free. There was no association of EEG discharges at 6 months with spikes in the postresection electrocorticogram. At 1 year after surgery (14), residual spikes were found in 22% of patients. Discharges were predictive of continuing seizures, with a sensitivity of 40% and a specificity of 94%. Two years after surgery (17), only 7% of patients with epileptiform EEG discharges were seizure-free, whereas an absence of discharges was accompanied by clinical improvement in 87%. However, other studies have not found postoperative EEG findings to be predictive of outcome (18,19). After amygdalo–hippocampectomy the EEG is often unimproved, irrespective of outcome. This is perhaps not unexpected, as this operation does not purport to remove the irritative zone.

The development of or an increase in focal discharges after callosotomy is often associated with the appearance or exacerbation of partial seizures. After hemispherectomy there is usually a marked improvement in the EEG over the intact hemisphere, which may parallel the often

dramatic improvement in cognitive function that follows this operation.

WHAT IS THE EFFECT OF ANTIEPILEPTIC DRUGS?

In status epilepticus

In patients who are ventilated and paralyzed during status epilepticus, the EEG may be the only indication of whether treatment has succeeded or seizure activity is continuing. It is also helpful as an aid to assessing depth of anesthesia.

In symptomatic epilepsy in which there is continuous epileptiform activity in the EEG and behavioral change, it may not be apparent whether or not the patient is in status epilepticus. It can be useful in this circumstance to give an AED, usually intravenously, under EEG control. If the behavior improves as the epileptiform activity subsides, it is likely that the initial state was indeed status epilepticus.

Is the dose high enough?

Although this is a commonly asked question, it is one that EEG is poorly able to answer in most cases. Treating the EEG, known as "EEG cosmetics," is unhelpful. The dose and type of AED should be determined clinically and in rare cases supported by pharmacologic monitoring. However, apparent exceptions to this general rule are becoming recognized. Studies of transient cognitive impairment (TCI) in children (20) suggest that cognitive processes may be impaired during electrographic seizures that are not clinically apparent. Suppressing these epileptiform discharges may result in improved school performance (21).

Are there side effects?

The EEG changes with quite modest doses of AEDs, in most cases with increased fast activity, although carbamazepine may increase theta activity at therapeutic doses. No qualitatively different effects occur with monotherapy until frankly toxic doses are reached or cerebral depression is induced, which is manifested by slowing of the EEG. Similar changes are seen with polypharmacy when individual drugs may still be within their therapeutic ranges. The EEG can be useful in such situations for identifying toxic interactions.

Could they be stopped?

The risk that seizures will recur in treated patients when treatment is withdrawn has been examined by several authors. The risks are different in adults and children and need to be considered separately. The medical, social, and occupational issues surrounding this issue in both groups make it an extremely important one.

Tennison and colleagues (22) compared the use of short or long periods of drug tapering before discontinuation of AEDs in children. The risk for recurrence was 40% during the follow-up period, averaging 39 months. A number of secondary analyses were performed. These showed the factors with greatest relative risk of seizure recurrence to be mental retardation (3.1), EEG spikes at start of taper period (1.9), and other abnormalities in EEG at start of taper period (1.7). In a similar study (23), the overall relapse rate was 37%. A scoring system was devised using diagnosis (largest weighting factor), age at onset and two different EEG abnormalities (generalized spike–wave after 1 year of treatment; 3-Hz spike–wave after 6 months of treatment). Children with high, medium, and low scores had remission rates of 73%, 40%, and 10% respectively.

Overweg and colleagues (24) studied AED withdrawal in neurologically intact adult patients who were "seizure-free." A multivariate model with weak predictive power was developed, but none of the factors involved EEG. In particular, the development during AED withdrawal of focal spike–wave discharges did not carry a poor prognosis. The EEG was of use in revealing in the prewithdrawal phase that some of the patients were not really seizure-free. In the MRC study (25,26), a small contribution (relative risk 1.3) to the final prognostic model was made by the factor "abnormal EEG in previous year." This study included both adults and children.

Abnormalities present before and unchanged after treatment are predictive of relapse (27). In partial epilepsies (28), the de novo appearance of epileptiform EEG activity during or over 3 years after AED withdrawal was predictive of relapse in patients with secondarily generalized seizures only.

In children, therefore, the EEG provides information that may be of use in the treatment of individual cases. In adults, estimates of the usefulness of EEG in predicting relapse vary. The amount of epileptiform activity as such is of little value, but the EEG is of value for identifying syndromes with different outcomes.

CAN THE PATIENT . . .

Drive

Under United Kingdom legislation, a license to drive an ordinary car is withdrawn after epilepsy or a single seizure. The decision to reinstate the license depends largely on the length of time since the last seizure. However, if the license has been lost because of epilepsy it will not be reinstated if there is generalized spike-and-wave activity in the EEG. Any seizure after the age of 5 years permanently disbars one from driving heavy goods vehicles, passenger service vehicles, and racing and rallying cars, and the EEG has no role in this decision.

Fly

Military aircrews in both the United Kingdom and the United States undergo an EEG as part of general screening programs (5,6). In Europe, EEG testing of applicants

for a commercial pilot's license is now mandatory. The presence of epileptiform activity precludes issue of a license even if no clinical ictal phenomena have been observed.

CONCLUSION

With all the recent enthusiasm for EBM, it is surprising and a little disappointing that there is so little EBM literature on the subject of the EEG. There is a Cochrane review group for epilepsy, but as yet it has not considered the uses of EEG as a topic in its own right. Medline, for many people the first resource for scientific literature, appears to misclassify articles of relevance to EEG even when the title contains the word EEG. Both Cochrane and Medline contain references to many thousands of articles in which the effects of drugs on the EEG or the EEG features of diseases are described. These articles do not constitute evidence to support the use of EEG in the sense in which EBM requires it. In the stringent financial climate faced by medicine in many parts of the world, this lack of evidence of usefulness may be wrongly assumed by some to mean that the EEG is not useful.

The EEG has many uses in epilepsy but may also be abused. The situations in which the EEG can contribute to the diagnosis of epilepsy are rare. Asking for an EEG in this situation is therefore usually an abuse. One exception is a small group of patients with unexplained episodic symptoms, in whom ictal recording by EEG telemetry or ambulatory recording is crucial to the differential diagnosis of epileptic and nonepileptic seizure attacks. Once the diagnosis is established, however, the EEG is probably the most important investigation in helping to define the type of epilepsy, the prognosis, and the initial approach to therapy. In partial seizures, EEG is the investigation of first choice for localization and is an important part of the work-up for the few patients who come to epilepsy surgery.

In general, it is unhelpful to monitor the progress of epilepsy with EEG unless there are unexpected, clinically apparent changes. Nor does the EEG have a role in the monitoring of AED efficacy, although it may help in the investigation of suspected toxicity. In children, the EEG may help to determine when it is safe to discontinue AEDs. In adults, the EEG has a much lesser role in this decision.

Assessing the usefulness of an EEG in a given situation is complicated and is best undertaken by those with some understanding of the technology. Interpretation of the EEG is possible only in the light of the clinical picture. The report that follows an EEG examination may be complicated by the more difficult decisions touched on in this review. For all reasons, it is essential that there is close liaison between the referring clinicians and the EEG department, both for individual tests and for training of junior staff.

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Predictors of Multiple Seizures in a Cohort of Children Prospectively Followed from the Time of Their First Unprovoked Seizure

Shlomo Shinnar, MD, PhD,*†‡§ Anne T. Berg, PhD,‖ Christine O'Dell, RN, MSN,*¶‡ David Newstein, MS,*‡ Solomon L. Moshe, MD,*†#‡ and W. Allen Hauser, MD§

The objective of this study was to assess the risk of multiple recurrences after an initial seizure recurrence in childhood. In a prospective study, 407 children were followed for a mean of 9.6 years from the time of their first unprovoked seizure. Data regarding each seizure recurrence were obtained and analyzed using statistical methods for survival analysis. The cumulative risk of a second seizure was 29%, 37%, 43%, and 46% at 1, 2, 5, and 10 years, respectively. Of the 182 children who experienced a second seizure, 131 (72%) experienced a third seizure, 105 (58%) have had 4 or more seizures, and 52 (29%) have experienced 10 or more seizures. The cumulative risk of a third seizure was 57%, 63%, and 71% at 1, 2, and 5 years, respectively, after the second seizure. After a third seizure, the cumulative risk of another seizure was 69%, 72%, and 81% at 1, 2, and 5 years, respectively. After a second seizure, factors associated with an increased risk of additional recurrences included a remote symptomatic etiology (rate ratio = 1.7) and the occurrence of a second seizure within 6 months of the first seizure (rate ratio = 1.7). After a second seizure, the risk of subsequent seizures was greater than 50% even in the lowest risk group. With the exception of etiology, factors associated with an increased risk of multiple recurrences after the initial seizure were different than those associated with multiple recurrences after a second seizure. Factors associated with multiple recurrent seizures may be different than those associated with an initial recurrence. As most patients who experience a second seizure experience further seizures, these data suggest that two seizures are a sufficient epidemiological criterion for the definition of epilepsy.

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Most children with a single unprovoked seizure do not experience a recurrence.[1–16] Only one study in a primarily adult population has examined the risk of further seizures after a second seizure.[17] The data from the adult study suggest that a single seizure may be an isolated event, but once two seizures have occurred, the likelihood of further seizures is 70% or greater, and one is thus dealing with a chronic process.[17,18] We have followed 407 children from the time of their first unprovoked seizure. Details of the cohort and the risk of seizure recurrence after the initial seizure have been published previously.[1,2] This analysis focuses on the risk of subsequent recurrences after an initial seizure recurrence and risk factors for further recurrences in this cohort.

Materials and Methods

Subjects

In a prospective cohort study, 407 children with a first unprovoked seizure who were seen at Montefiore Medical Center, Jacobi Medical Center, North Central Bronx Hospital, or the private practices of the authors between October 1983 and August 1992 were enrolled and followed until September 1, 1998. Eligible candidates for the study were patients aged 1 month to 19 years who presented with their first unprovoked afebrile seizure. Details of the inclusion and exclusion criteria for this cohort as well of the initial evaluation have been reported previously.[1,2]

At the time of the initial visit, informed consent was obtained from the parent and child. Details, including seizure characteristics, duration, number of seizures in 24 hours, and any treatment given, were collected. Additional information

From the Departments of *Neurology, †Pediatrics, #Neuroscience, and ¶Nursing, and ‡Epilepsy Management Center, Montefiore Medical Center, The Albert Einstein College of Medicine, Bronx, and §The Gertrude Sergievsky Center, Columbia College of Physicians and Surgeons, New York, NY; and ‖Department of Biological Sciences, Northern Illinois University, DeKalb, IL.

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Address correspondence to Dr Shinnar, Epilepsy Management Center, Montefiore Medical Center, 111 East 210th Street, Bronx, NY 10467.

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regarding prior provoked seizures, prior neurological insults, birth history, and family history was also coded. A physical and neurological examination was performed on all children. Electroencephalograms (EEGs) were scheduled for all patients. Neuroimaging studies were performed when clinically indicated. Etiology and seizure type were classified in accordance with International League Against Epilepsy criteria.[18–20]

Follow-Up

After enrollment, subjects were followed by telephone interviews at least every 3 months for ascertainment of any seizure recurrence. In those children with a recurrence, records of any emergency medical care were reviewed and the children were re-evaluated. A recurrence was defined as any unprovoked seizure occurring more than 24 hours after the first seizure. The mean follow-up period was 9.6 years. Of the 407 subjects, 391 (96%) have been followed for more than 2 years and 372 (91%) for more than 5 years. The 16 subjects followed less than 2 years include 1 patient who died and 15 lost to follow-up.

Analysis

As the length of the follow-up interval influences the probability of observing a recurrence, the statistical methods took account of the variable length of follow-up for each child.[21–27] Risks of a first, second, and ninth recurrence at 6 months and at 1, 2, 5, and 10 years after the initial seizure as well as risks of a second, third, and ninth recurrence at 6 months and at 1, 2, 5, and 10 years after a first recurrence (second seizure) were determined by the product-limit method, and the results were displayed as Kaplan-Meier curves. Ninety-five percent confidence intervals (CIs) for the Kaplan-Meier estimates of recurrence risks were calculated at 1, 2, 5, and 10 years using an approximate Greenwood formula for the SE.[24,27]

The Cox proportional hazards model was used to obtain crude and adjusted rate ratios for each independent variable and for the multivariate analysis.[21,24–27] To determine the appropriateness of the proportional hazards assumption (ie, constant rate ratio over time), a term was included for the independent variable multiplied by the log of time (in years) in each unadjusted analysis. Where there was evidence for lack of proportionality over time based on either visual inspection of the log-(−log) survival plots or a test of time dependence using the log of time, we examined cutoff points at 3-month intervals during the first year and at 1 and 2 years as well as at later points if necessary to determine whether there was an abrupt change in the rate ratio at one point in time or whether the rate ratio changed continuously over time. A single cutoff point was used unless the continuous log representation provided a significantly better ($p < 0.05$) fit for the statistical model.[27]

Results

Overall Recurrence Risk

Of the 407 subjects in the study, 182 (45%) have experienced a recurrence. The overall product-limit estimate of recurrence was 22% at 6 months (95% CI: 18%, 26%), 29% at 1 year (95% CI: 25%, 33%), 37% at 2 years (95% CI: 33%, 42%), 43% at 5 years (95% CI: 38%, 48%), and 46% at 10 years (95% CI: 41%, 51%) (Fig 1). The median time to recurrence was 6.2 months (range, 0.03 months to 10.1 years).

Of those who experienced a second seizure, 131 (72%) experienced a third seizure, 105 (58%) experienced 4 or more seizures, and 52 (29%) experienced 10 or more seizures (Table 1, Fig 2). The primary analysis is the risk of another seizure after a second seizure has occurred. We also analyzed the risk of three or more seizures using only the data available at the time of first seizure.

Risk of a Third Seizure after a Second Seizure

The 182 children who had a second seizure have been followed for a mean of 8.4 years after their second seizure (see Table 1). The risk of a third seizure was 57%, 63%, and 72% at 1, 2, and 5 years, respectively, after the second seizure (see Fig 2). After a third seizure, the cumulative risk of another seizure was 66%, 70%, and 81% at 1, 2, and 5 years, respectively.

UNIVARIATE ANALYSIS. Univariate analysis of factors associated with a differential risk of subsequent recurrences after a second seizure (first recurrence) is shown in Table 2. Remote symptomatic etiology (Fig 3) and an interval of less than 6 months between the first and second seizures were associated with an increased risk of having a third seizure. The increased recurrence risk associated with a remote symptomatic etiology is not time-dependent and persists throughout the analysis period. In contrast, an interval less than 6 months between the first and second seizures was associated with an increased recurrence risk only during the first 3 months after the second seizure (relative risk [RR] = 2.99; 95% CI: 1.75, 5.12; $p = 0.0001$), after which it

Fig 1. Probability of seizure recurrences after a first unprovoked seizure (N = 407). Kaplan-Meier curves for cumulative risk of a second (R1), third (R2), fourth (R3), and tenth (R9) seizure in children who have had a first unprovoked seizure calculated from the time of the first seizure.

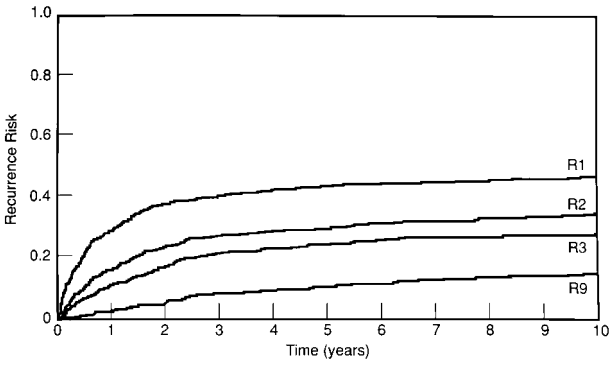

Table 1. Characteristics of Cohort of 407 Children Followed from Time of First Unprovoked Seizure

	Overall	Cryptogenic/Idiopathic Etiology	Remote Symptomatic Etiology
No. of children	407	342	65
Mean age at first seizure (yr)	6.8	6.8	7.0
Mean follow-up after first seizure (yr)	9.6	9.6	9.7
Recurrent seizures	182 (45%)	135 (39%)	47 (72%)
Mean follow-up after second seizure (yr)	8.4	8.4	8.6
Total number of seizures to date			
1 (no recurrences)	225 (55%)	207 (60%)	18 (28%)
2 (one recurrence)	51 (13%)	46 (13%)	5 (8%)
3	26 (6%)	18 (5%)	8 (12%)
4	13 (3%)	10 (3%)	3 (5%)
5	12 (3%)	10 (3%)	2 (3%)
6–9	28 (7%)	20 (6%)	8 (12%)
≥10	52 (13%)	31 (10%)	21 (32%)

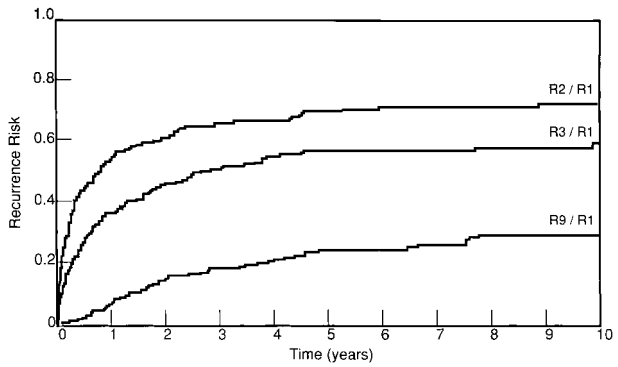

Fig 2. Probability of subsequent seizure recurrences after a second seizure (first recurrence) (N = 182). Kaplan-Meier curves for cumulative risk of a third (R2), fourth (R3), and tenth (R9) seizure in children who have had two unprovoked seizures calculated from the time of the second seizure.

no longer influenced recurrence risk (RR = 0.92; 95% CI: 0.53, 1.57; $p = 0.002$ for difference in the RRs).

Eighty (44%) of the 182 children were treated with anti-epileptic drugs (AEDs) after the first recurrence. On univariate analysis, treatment after the second seizure (first recurrence) did not affect the risk of subsequent seizures. However, children with remote symptomatic seizures were more likely to be treated after a first recurrence (60%) than children with cryptogenic first seizures (38%) ($p = 0.01$), as were children whose first recurrence occurred within 6 months (56%) compared with children whose first recurrence occurred after 6 months (33%) ($p < 0.01$).

An abnormal EEG (RR = 1.08; 95% CI: 0.81, 1.67; $p = 0.41$) and a seizure occurring while asleep (RR = 0.86; 95% CI: 0.61, 1.23; $p = 0.41$), which were associated with an increased recurrence risk after a first seizure, were not associated with an increased risk of further seizures after a second seizure. The occurrence of status epilepticus (RR = 0.84; 95% CI: 0.51, 1.41; $p = 0.51$) or of multiple seizures as the presenting first seizure episode was also not associated with an increased risk of subsequent recurrences.

MULTIVARIATE ANALYSIS. On multivariate analysis (Table 3), remote symptomatic etiology and an interval less than 6 months between the first and second seizures remain significant. After adjusting for etiology and time to second seizure, treatment after the second seizure is also highly significant and is associated with a greater than 50% reduction in the risk of subsequent seizures for the first 3 months. No other variables entered the model.

Predictors of Multiple Recurrences after a Second Seizure

The univariate and multivariate analyses for the occurrence of a fourth and tenth seizure after a second seizure has occurred are shown in Tables 2 and 3. Etiology and an interval less than 6 months between the first and second seizures have a similar association with the risk of a fourth seizure as they did with the risk of a third seizure. Treatment after the second seizure is also important after adjusting for etiology, and the effect does not vary significantly over time (see Table 3). In addition, a history of prior febrile seizures and having multiple seizures in 1 day as the initial seizure have a modest but statistically significant association with an increased risk of a fourth seizure after a second seizure (see Tables 2 and 3).

In predicting the occurrence of 10 or more seizures after a second seizure, a remote symptomatic etiology and an interval less than 6 months between the first and second seizures are significantly associated with an increased risk of having 10 or more seizures in both univariate and multivariate analyses (see Tables 2 and 3). The effect of the interval of less than 6 months is largely limited to the first year after the second seizure.

Table 2. Risk of Multiple Recurrences following a Second Seizure: Proportional Hazards Model (N = 182)[a]

	Risk of Third Seizure (n = 131)			Risk of Fourth Seizure (n = 105)			Risk of Ten Seizures (n = 52)		
Risk Factor	Rate Ratio	95% CI	*p*	Rate Ratio	95% CI	*p*	Rate Ratio	95% CI	*p*
Remote symptomatic etiology	1.69	(1.17, 2.45)	0.005	1.65	(1.10, 2.49)	0.02	2.20	(1.26, 3.83)	0.005
Time to second seizure < 6 mo[a]	1.60[a]	(1.14, 2.26)	0.007	2.10[a]	(1.42, 3.10)	0.0002	2.10[a]	(1.19, 3.72)	0.01
Treatment after second seizure[a]	0.92[a]	(0.65, 1.29)	0.62	0.86	(0.59, 1.27)	0.45	1.19	(0.69, 2.05)	0.53
Abnormal electroencephalogram	1.08	(0.81, 1.67)	0.41	1.13	(0.77, 1.68)	0.53	0.90	(0.52, 1.55)	0.70
Prior febrile seizures	1.32	(0.88, 1.98)	0.17	1.60	(1.04, 2.47)	0.04	1.42	(0.77, 2.62)	0.26
Todd's paresis	0.94	(0.51, 1.74)	0.84	1.30	(0.69, 2.42)	0.42	2.05	(0.97, 4.36)	0.06
>1 seizure within 24 hr of the first seizure	1.23	(0.82, 1.83)	0.31	1.57	(1.02, 2.40)	0.04	1.06	(0.56, 2.03)	0.85

[a]Analysis is shown without effect of time-dependent covariates. Variables for which time-dependent covariates are significant are indicated, and the effects of the time-dependent covariates on these variables are shown in the multivariable analysis in Table 3.

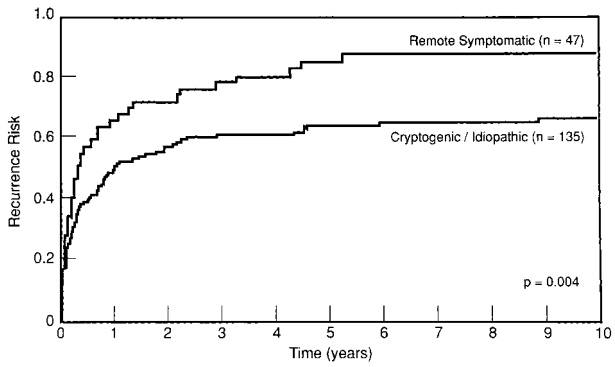

Fig 3. Probability of subsequent seizure recurrences after a second seizure in children with cryptogenic/idiopathic and remote symptomatic seizures (N = 182). Kaplan-Meier curves.

Predictors of Multiple Recurrences at the Time of Initial Seizure

A separate analysis of predictors of multiple recurrences based on information available at the time of the first seizure was performed (Tables 4 and 5). The Kaplan-Meier curves illustrating the risk for multiple seizures after the initial seizure are shown in Figure 1. As previously reported,[1,2] remote symptomatic etiology, abnormal EEG, being asleep at the time of the first seizure, a history of prior febrile seizures, and the presence of a Todd's paresis were all associated with an increased risk of a second seizure in both univariate and multivariate analyses. An analysis of the time dependence of the effect showed that the influence of etiology on recurrence risk, although present throughout, was significantly stronger after the first 2 years (see Table 5). There was no evidence that the strength of the association with recurrence risk was time-dependent for any of the other variables.

Not surprisingly, factors associated with a differential risk of a second seizure are also associated with an increased risk of a third seizure. Etiology and the EEG as well as a history of prior febrile seizures were significant and independent predictors of the risk of a third seizure at the time of the first seizure (see Tables 4 and 5). In predicting the risk of having 10 or more seizures at the time of the first seizure, a remote symptomatic etiology and the presence of a Todd's paresis were the only two significant predictors (see Tables 4 and 5). There was no evidence of departure from proportionality over time for any of the variables, including etiology, in the analysis of predictors of 10 or more seizures at the time of the first seizure.

Discussion

How Many Seizures Is Epilepsy?

After two seizures, the risk of subsequent seizures goes up to 70% or more. Although factors such as etiology and the interval between the first and second seizures are associated with a differential risk of recurrence, the recurrence risk is greater than 60% in all subgroups. Furthermore, the risk of an additional seizure does not substantially change after a third seizure. This supports the epidemiological definition of epilepsy as two or more unprovoked seizures.[18] The overall recurrence risk after a second seizure in this study is similar to that recently reported in a largely adult population.[17]

Although from an epidemiological standpoint, the data justify requiring at least two seizures for the definition of epilepsy, this may not always be the case in other settings. The risk of a seizure recurrence in a child with a first seizure of remote symptomatic etiology or cryptogenic/idiopathic etiology and an epileptiform EEG is quite comparable to the recurrence risk after a second seizure.[1–3] Therefore, if one is designing a drug trial for new-onset seizures, it may be quite rational to include children with one seizure and additional risk factors for recurrence.[28] In particular, the recurrence risk in this cohort in children with benign Rolandic epilepsy, who all have a characteristic epilep-

Table 3. Risk Factors for Subsequent Seizures after a Second Seizure: Multivariable Analysis Using Cox Proportional Hazards Model[a]

Risk Factor	Risk of Third Seizure (n = 131)			Risk of Fourth Seizure (n = 105)			Risk of Ten Seizures (n = 52)		
	Rate Ratio	95% CI	*p*	Rate Ratio	95% CI	*p*	Rate Ratio	95% CI	*p*
Remote symptomatic etiology	1.69	(1.16, 2.47)	0.007	1.74	(1.14, 2.66)	0.01	2.13	(1.22, 3.71)	0.008
Second seizure within 6+ mo									
In first 3 months (12 mo for 10 seizures)	4.00	(2.28, 7.00)	<0.0001	5.07	(2.19, 11.7)	0.0002	6.94	(1.56, 30.7)	0.01
After 3 months (12 mo for 10 seizures)	0.86	(0.49, 1.50)	<0.0001[b]	1.92	(0.83, 4.46)	0.05[b]	1.43	(0.32, 6.33)	0.06[b]
Treatment after second seizure[a]	—	—	—	0.56	(0.37, 0.85)	0.006	—	—	—
First 3 mo	0.37	(0.22, 0.63)	0.0003	—	—	—	—	—	—
After 3 mo	1.28	(0.75, 2.18)	0.001[b]	—	—	—	—	—	—
>1 seizure within 24 hr of the first seizure	—	—	—	1.73	(1.12, 2.68)	0.01	—	—	—
Prior febrile seizures	—	—	—	1.56	(1.00, 2.44)	0.05	—	—	—

[a]Effect of variable is best modeled with a time-dependent covariate.
[b]Probability value on interaction represented by time-dependent covariate. This indicates that the RR after 3 (or 12) months have passed after the initial recurrence is significantly different from the RR before that time.

Table 4. Risk of Seizure Recurrences after a First Unprovoked Seizure: Proportional Hazards Model (N = 407)

Risk Factor	Risk of Second Seizure (n = 182)			Risk of Third Seizure (n = 131)			Risk of Ten Seizures (n = 52)		
	Rate Ratio	95% CI	*p*	Rate Ratio	95% CI	*p*	Rate Ratio	95% CI	*p*
Remote symptomatic etiology[a]	2.32[a]	(1.67, 3.24)	<0.0001	3.20	(2.22, 4.63)	<0.001	4.04	(2.32, 7.03)	<0.0001
Abnormal electroencephalogram	2.16	(1.60, 2.91)	<0.0001	2.15	(1.51, 3.05)	<0.0001	1.72	(1.00, 2.98)	0.05
Seizure while asleep	1.61	(1.20, 2.17)	0.0002	1.37	(0.97, 1.95)	0.07	1.28	(0.73, 2.24)	0.38
Prior febrile seizures	1.54	(1.08, 2.20)	0.02	1.79	(1.19, 2.67)	0.005	1.92	(1.04, 3.55)	0.04
Todd's paresis	1.81	(1.08, 3.03)	0.02	1.49	(0.81, 2.77)	0.20	2.95	(1.39, 6.27)	0.005
>1 seizure within 24 hr of the first seizure	1.04	(0.73, 1.47)	0.83	1.15	(0.76, 1.72)	0.48	1.05	(0.55, 2.01)	0.87

[a]Analysis is shown without effect of time-dependent covariates. The effect of remote symptomatic etiology is time-dependent. The effects of the time-dependent covariate on this variable are shown in the multivariable analysis in Table 5.

Table 5. Risk Factors for Seizure Recurrences after a First Unprovoked Seizure: Multivariable Analysis Using Cox Proportional Hazards Model

Risk Factor	Risk of Second Seizure (n = 182)			Risk of Third Seizure (n = 131)			Risk of Ten Seizures (n = 52)		
	Rate Ratio	95% CI	*p*	Rate Ratio	95% CI	*p*	Rate Ratio	95% CI	*p*
Remote symptomatic etiology[a]				2.64	(1.82, 3.84)	<0.0001	4.10	(2.35, 7.15)	<0.0001
First 24 mo	1.61[a]	(1.11, 2.34)	0.01						
After 24 mo	4.00[a]	(2.75, 5.83)	0.03[b]						
Abnormal electroencephalogram	1.95	(1.44, 2.64)	<0.0001	1.93	(1.35, 3.84)	0.0003			
Prior febrile seizures	1.63	(1.13, 2.33)	0.008	1.75	(1.17, 2.63)	0.007			
Seizure while asleep	1.41	(1.04, 1.90)	0.03						
Todd's paresis	1.68	(1.00, 2.82)	0.05				3.07	(1.44, 6.53)	0.004

[a]Effect of variable is best modeled with a time-dependent covariate.
[b]Probability value on interaction represented by time-dependent covariate. This indicates that the RR after 3 (or 12) months have passed after the initial recurrence is significantly different from the RR before that time.

tiform EEG,[29] is quite similar after one seizure to the recurrence risk after two seizures. Including such patients may make it easier to conduct placebo-controlled trials.[30]

Predicting 10 or More Seizures

Another area of interest is early identification of patients who will go on to have many seizures. These children would be candidates not only for early treatment with AEDs but possibly for more aggressive early intervention.[31–33] Few children who present with a first unprovoked seizure develop intractable epilepsy. This is partly because the syndromes most likely to progress to intractable epilepsy rarely present with a single unprovoked seizure.[34] If one examines the subgroup with 10 or more seizures in this cohort, which constitutes only 13% of the cohort, only remote symptomatic etiology and early initial recurrence are associated with an increased risk of 10 or more seizures after a second seizure. Remote symptomatic etiology is consistently associated with a higher recurrence risk after a first seizure,[1–5,6,10–13] with a higher risk of recurrence after AED withdrawal in patients who are seizure-free,[35,36] with a lower probability of attaining remission,[37–39] and with a higher risk of developing intractable epilepsy.[31] It is also a risk factor in this population for having many seizures, as 32% of the 65 children with a remote symptomatic first seizure in this cohort experienced 10 or more seizures compared with 9% of children with a cryptogenic/idiopathic first seizure ($p < 0.001$).

After adjustment for etiology, treatment reduces recurrence risk by half but only for the first 3 months. The reduction of recurrence risk in this observational study is comparable to the reduction reported in randomized placebo-controlled treatment trials after a first unprovoked seizure in children and adults.[14,15] Those studies did not analyze whether the effect is time-dependent. A time-dependent effect for the efficacy of AED treatment was also observed in the Medical Research Council study of discontinuing AEDs in patients with epilepsy who were seizure-free for 2 or more years.[40] In that study, which randomized subjects to either discontinue medications or remain on AEDs, the recurrence risk was twice as high in those who discontinued AEDs, but the increased risk only persisted for a finite period of time, after which the 2 groups had similar recurrence risks.[41] In our observational study, treatment did not influence the risk of having 10 or more seizures. As the probability of a clinical decision to initiate AED therapy substantially increased with each recurrence, this finding is somewhat difficult to interpret. These findings are similar to those of the randomized Italian study of treatment after a first seizure,[41] which found no effect of delaying treatment on long-term outcome in the sense that delaying treatment until at least the third seizure did not affect long-term outcome as measured by the risk of having 10 or more seizures.

The association between the time interval between the first and second seizures is not surprising, as it may reflect how aggressive the underlying process is. The effect is time-dependent and transient. Initial seizure frequency, which is inversely related to the interval between seizures, has been associated with the probability of attaining remission in patients with childhood-onset epilepsy.[33,39]

Factors such as a Todd's paresis, prior febrile seizures, and the occurrence of multiple seizures within 24 hours are of marginal significance in the overall analysis, although they may contribute to some of the multiple analyses performed. In contrast to a recent abstract suggesting that the occurrence of multiple seizures in 1 day is associated with a worse prognosis,[42] these data support the International League Against Epilepsy position[18] and other reports[1,2,5,43,44] that multiple seizures in a 24-hour interval have the same prognostic significance as a single isolated seizure.

When Is Treatment with AEDs Indicated?

In general, the decision to initiate AED therapy is based on weighing the relative risks of further seizures versus the risks of AED therapy.[45] Given the high risk of recurrent seizures, most adult neurologists initiate treatment after a second seizure.[17] In children, in addition to the recurrence risks, treatment decisions should take account of whether the seizures are part of a benign self-limited syndrome such as benign Rolandic epilepsy as well as seizure frequency and duration.[45–47] The authors often do not treat otherwise normal children with infrequent brief seizures even after two or three seizures have occurred.[45,46] Data from randomized clinical trials of children and adults who present with a first unprovoked seizure have shown that AED therapy reduces the risk of seizure recurrence by approximately half.[14,15] Early treatment does not affect the probability of attaining long-term remission, however.[41] Our data further suggest that the effect on recurrence may be of relatively limited duration. Studies in developing countries, where treatment delays were due to the unavailability of AEDs, have shown no difference in response rate in those with many prior seizures compared with new-onset patients.[48,49] In general, the prognosis seems to be a function of the specific epilepsy syndrome. AED therapy suppresses seizures but does not alter the underlying course of the illness.[47,50–52] The decision to treat should therefore be made on the grounds that the patient has had a sufficient number of events to justify therapy and not with the hope of somehow preventing the development of "chronic" epilepsy.[53] Although the probability of a seizure recurrence seems to be the same in children and adults, the relative risks and benefits of AED therapy,

which take account of not only the statistical probability of further seizures but also the possible consequences of another seizure and the potential adverse effects of AED therapy, are quite different in children than in adults.[45,46,54]

Conclusions

Most children who experience two seizures experience further seizures. Thus, the definition of epilepsy as two or more unprovoked seizures occurring more than 24 hours apart is appropriate for epidemiological studies. Etiology is the most important factor influencing long-term prognosis in this group of children. Treatment decisions in these children need to be individualized based on the statistical recurrence risk and the relative risks of both seizures and AED therapy.

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The Risk of Seizure Recurrence After a First Unprovoked Afebrile Seizure in Childhood: An Extended Follow-up

Shlomo Shinnar, MD, PhD*‡¶**; Anne T. Berg, PhD#; Solomon L. Moshe, MD*‡§¶; Christine O'Dell, RN, MSN*‖¶; Marta Alemany*¶; David Newstein, MS*¶; Harriet Kang, MD*‡¶; Eli S. Goldensohn, MD*¶; and W. Allen Hauser, MD**

ABSTRACT. *Objective.* **To assess the long-term recurrence risks after a first unprovoked seizure in childhood.**

Methods. **In a prospective study, 407 children who presented with a first unprovoked seizure were then followed for a mean of 6.3 years from the time of first seizure.**

Results. **One hundred seventy-one children (42%) experienced subsequent seizures. The cumulative risk of seizure recurrence was 29%, 37%, 42%, and 44% at 1, 2, 5, and 8 years, respectively. The median time to recurrence was 5.7 months, with 53% of recurrences occurring within 6 months, 69% within 1 year, and 88% within 2 years. Only 5 recurrences (3%) occurred after 5 years. On multivariable analysis, risk factors for seizure recurrence included a remote symptomatic etiology, an abnormal electroencephalogram (EEG), a seizure occurring while asleep, a history of prior febrile seizures, and Todd's paresis. In cryptogenic cases, the risk factors were an abnormal EEG and an initial seizure during sleep. In remote symptomatic cases, risk factors were a history of prior febrile seizures and age of onset younger than 3 years. Risk factors for late recurrences (after 2 years) were etiology, an abnormal EEG, and prior febrile seizures in the overall group and an abnormal EEG in the cryptogenic group. These are similar to the risk factors for early recurrence.**

Conclusions. **The majority of children with a first unprovoked seizure will not have recurrences. Children with cryptogenic first seizures and a normal EEG whose initial seizure occurs while awake have a particularly favorable prognosis, with a 5-year recurrence risk of only 21%. Late recurrences do occur but are uncommon.** ***Pediatrics*** **1996;98:216–225;** ***seizure, epilepsy, prognosis, status epilepticus, electroencephalography.***

ABBREVIATIONS. AED, antiepileptic drug; EEG, electroencephalogram; CI, confidence interval.

Knowledge of the natural history after a single unprovoked seizure and the risk factors for recurrence is a necessary prerequisite for making rational decisions regarding long-term treatment with antiepileptic drugs (AEDs). The reported risks of recurrence after a first unprovoked seizure in studies that included adults and/or children vary from 27% to 71%.[1–17] A recent meta-analysis has shown that many of the differences can be attributed to differences in methods and the distribution of important risk factors in the different populations studied.[2] All but one of these studies[7] have reported only short-term follow-ups of 2 to 4 years or less. Therefore, little data is available on the long-term recurrence risks and prognosis of these children. In a previous article,[1] we reported on the short-term outcomes of a cohort of 283 children prospectively followed from the time of their first seizures for a mean of 2.5 years. We now report the long-term outcomes of this cohort, which has been expanded to 407 children and followed for a mean of 6.3 years.

From the Departments of *Neurology, ‡Pediatrics, §Neuroscience, and ‖Nursing, and the ¶Epilepsy Management Center, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York; #Social Science Research Institute, Northern Illinois University, DeKalb, Illinois; and **Gertrude Sergievsky Center, Columbia College of Physicians and Surgeons, New York, New York.

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Reprint requests to (S.S.) Epilepsy Management Center, Montefiore Medical Center, 111 E 210th St, Bronx, NY 10467.

METHODS

Children

In a prospective cohort study, 407 children with a first unprovoked afebrile seizure seen at Montefiore Medical Center, Bronx Municipal Hospital Center, North Central Bronx Hospital, or the private practices of the authors between October 1983 and August 1992 were enrolled and followed.

Eligible candidates for the study were children 1 month to 19 years of age who presented with their first unprovoked afebrile seizures. Consistent with current guidelines and previous epidemiologic work, children with a cluster of seizures all of which occurred within 24 hours were considered to have had one seizure and were included. Also included were children with status epilepticus (defined as a seizure lasting more than 30 minutes or as a series of seizures without regaining consciousness lasting more than 30 minutes[1,18–21]). Children with prior neonatal seizures, febrile convulsions, immediate posttraumatic seizures, or other provoked seizures who now presented with first unprovoked seizures were also included.[1,6,19,21] Details of the inclusion and exclusion criteria for this cohort have been previously reported.[1]

Children identified in the emergency departments at the time of their first seizure who had seizure recurrences in the interval before being seen by the investigators for the specific purposes of the study were included and considered as having recurrences. Excluded were children who presented with typical absence seizures, myoclonic seizures, and infantile spasms, as well as those who presented with their first generalized tonic-clonic seizure but were found to have had prior absence, myoclonic, or partial seizures.

A seizure was considered unprovoked when there was no identifiable proximate insult (eg, fever or head trauma) that could account for it.[6] A seizure was classified as remote symptomatic if the child had static encephalopathy from birth and/or had sustained a prior neurological insult, such as a stroke or significant head trauma (associated with a depressed skull fracture, loss of

consciousness for more than 30 minutes, or intracranial bleeding).[19,21] In the initial report,[1] all other unprovoked seizures were considered idiopathic. In the newly proposed classification scheme of the International League Against Epilepsy, the term cryptogenic is used for seizures we and others[1,2,6,7,15,17,19] previously called idiopathic, and idiopathic is reserved for the genetic epilepsies.[21] The terminology in this report conforms with the new classification. To be consistent with our prior work and the fact that these cases were classified prospectively, all cases that were not remote symptomatic were considered cryptogenic. This still conforms with the new classification, because idiopathic is now considered a subgroup of cryptogenic. We did not further subdivide the cryptogenic group.

The seizures were classified as cryptogenic or remote symptomatic at entry to the study using only the results of the initial diagnostic work-up. No information from the follow-up was used to reclassify etiology, because additional diagnostic information would be more available in those with recurrences who, therefore, would have had more testing done. Also, to have predictive value at the time of the initial seizure, the classification must be based on information available at that time. A history of birth trauma, a difficult perinatal course, neonatal or other provoked seizures, or mild head trauma in a neurologically healthy child did not preclude the diagnosis of a cryptogenic seizure.[1,19,21] A family history of seizures was defined as a history of one or more unprovoked seizures in a first-degree relative. Seizures were classified as generalized tonic or tonic-clonic, atypical absence, atonic, simple partial, complex partial, or partial with secondary generalization, in accordance with the revised international classification of seizures.[18]

At the time of the initial visit, informed consent was obtained from the parent, and assent from the child was obtained when appropriate. Details were collected about the exact nature of the seizure, including seizure characteristics, duration, number of seizures in 24 hours, and any treatment given. Additional history regarding prior provoked seizures, prior neurologic insults, birth history, and family history of seizures was also coded. A physical and neurologic examination was performed on all children. Electroencephalograms (EEGs) were scheduled for all patients. Further laboratory examinations such as computed tomography or magnetic resonance imaging were performed when clinically indicated.

Electroencephalography

EEGs were obtained for 383 (94%) of the 407 children. More than 90% of the EEGs were interictal, obtained more than 48 hours after the seizures. The remainder were obtained within 48 hours after the seizures. When feasible, EEGs were obtained when the children were both awake and asleep. In many younger children and in some older, neurologically impaired children, only sedated sleep records could be obtained. All EEGs were interpreted by at least one of the authors (E.S.G., H.K., and S.L.M.), who were blinded to the outcome. EEGs were classified as normal or abnormal. Specific epileptiform abnormalities (focal spikes, multifocal spikes, centrotemporal spikes, a generalized spike and wave, and a photoconvulsive response) as well as focal and generalized slowing were coded separately. EEG findings on the first 347 children have been previously reported.[22]

Follow-up

After enrollment, the children were followed by telephone interviews at least every 3 months for ascertainment of any seizure recurrence. Formal neurologic assessments were done when clinically indicated. Because seizures in this population rarely occur in the physician's office, ascertainment of seizure recurrence is done by history. Therefore, telephone ascertainment should be as reliable as information obtained by direct contact in clinical follow-up. The majority of children had several clinic follow-ups as well. In those children with recurrences, records of any emergency medical care were reviewed, and the children were seen for re-evaluation. A recurrence was defined as any unprovoked seizure occurring more than 24 hours after the first seizure. Febrile seizures occurring after the initial unprovoked seizure were noted but classified as provoked seizures rather than recurrences.

Analysis

Because the length of follow-up influences the probability of observing a recurrence, the statistical methods of analysis took into account the variable length of follow-up for each child.[23-29] Univariate analyses for dichotomous variables were performed using Kaplan-Meier survival analysis,[23,26,28,29] and statistical significance was calculated from the Cox model.[26-29] Results are displayed as Kaplan-Meier survival curves, with the cumulative probability of seizure recurrence plotted as a function of time from the first seizure. Ninety-five percent confidence intervals (CIs) for the Kaplan-Meier estimates of recurrence risks were calculated at 2, 5, and 8 years using an approximate Greenwood formula for the SE.[26,29] Continuous variables were examined using t tests. The Cox proportional hazards model was used to obtain crude and adjusted rate ratios for each independent variable.[26-29] All P values are two tailed.

RESULTS

The study group included 234 (57%) boys and 173 (43%) girls. The predominantly inner-city minority population was representative of the mixture of patients seen at our institutions. It consisted of 155 (38%) Hispanic children, 114 (28%) white children, 120 (29%) black children, and 18 (4%) children of other ethnic origins. The mean age at the time of first seizure was 6.8 years.

The mean follow-up period was 6.3 (range, 0.1 to 10.8) years. Of the 407 children, 388 (95%) have been followed for more than 2 years, 324 (80%) for more than 4 years, 232 (57%) for more than 6 years, and 129 (32%) for more than 8 years. To date, 41 children (10%) have been lost to follow-up after observation periods of 9.1 to 7.1 (mean, 3.4) years.

Overall Recurrence Risk

Of the 407 children in the study, 171 (42%) had recurrences by January 1, 1995. The mean time to recurrence was 11.3 (median, 5.7) months. The risk of recurrence was greatest in the first few months after the first seizure: 36 (21%) of the 171 recurrences occurred in the first month, 92 (53%) within 6 months, and 150 (88%) within 2 years of the initial seizure. Only 5 (3%) had their first recurrences more than 5 years after the initial seizure. The overall Kaplan-Meier estimate of recurrence was 22% at 6 months (95% CI, 18% to 26%), 29% at 1 year (95% CI, 25% to 33%), 37% at 2 years (95% CI, 32% to 42%), 42% at 5 years (95% CI, 37% to 47%), and 44% at 8 years (95% CI, 39% to 49%) (Fig 1).

Predictors of Recurrence

In the overall study group, significant predictors of recurrence in the overall group included etiology, EEG, whether the seizure occurred while awake or asleep, seizure type (partial versus generalized), a history of prior febrile convulsions, presence of Todd's paresis, and a family history of seizures together with an abnormal EEG (Table 1). In the cryptogenic group (n = 342), an abnormal EEG, a seizure occurring while asleep, Todd's paresis, and age were significant predictors of seizure recurrence. A family history of seizures was also important but only in cryptogenic children who also had an abnormal EEG. In the remote symptomatic group (n = 65), a history of prior febrile seizures and age of onset younger than than 3 years were associated with an

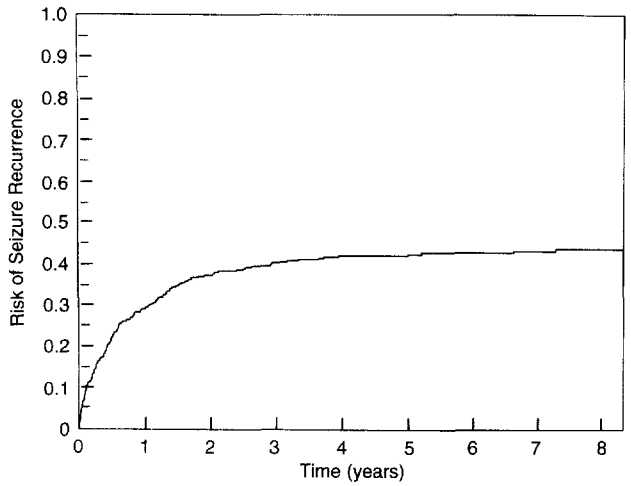

Fig 1. Probability of seizure recurrence after a first unprovoked seizure (n = 407): Kaplan-Meier curve.

additional increased risk of recurrence (Table 1). The duration of the initial seizure, including status epilepticus, and the number of seizures in the 24 hours following the initial episode did not affect the risk of recurrence. Individual risk factors are presented in detail below.

Etiology of Seizures

Individuals with remote symptomatic first seizures had a higher recurrence risk than those with a cryptogenic first seizure. Forty-four (68%) of the 65 children with remote symptomatic first seizures had recurrences, compared with 127 (37%) of the 342 children with cryptogenic first seizures. For the remote symptomatic group, the Kaplan-Meier risks of recurrence were 57% (95% CI, 45% to 70%) and 66% (95% CI, 54% to 78%) at 2 and 5 years, respectively, compared with recurrence risks of 33% (95% CI, 28% to 38%) and 37% (95% CI, 32% to 43%), respectively, in the cryptogenic group ($P < .0001$; Fig 2).

EEG

In children with a cryptogenic first seizure, the EEG was the most important predictor of outcome (Table 1). An epileptiform EEG was associated with a higher recurrence risk than a nonepileptiform EEG, although focal slowing was also associated with a high risk of recurrence. The Kaplan-Meier estimates of the risk of recurrence were 52% (95% CI, 45% to 60%) and 59% (95% CI, 51% to 67%) at 2 and 5 years, respectively, in children with an abnormal EEG, compared with recurrence risks of 28% (95% CI, 22% to 35%) and 32% (95% CI, 25% to 38%), respectively, in those with normal EEGs ($P < .0001$). The recurrence risks for children with normal EEGs and with nonepileptiform and epileptiform EEG abnormalities are shown in Fig 3. The recurrence risk in the 100 children with cryptogenic first seizures and epileptiform abnormalities on EEG was independent of the type of epileptiform abnormality. Recurrent seizures occurred in 60% of these children, including 57% of the 37 children with centrotemporal spikes on their EEGs, 60% of the 33 children with other focal epileptiform abnormalities on their EEGs, and 67% of the 30 children whose EEGs showed generalized spike and wave abnormalities.

Abnormal EEGs were more common in children with remote symptomatic first seizures (60%) than in those with cryptogenic first seizures (40%; $P = .003$). However an abnormal EEG was not associated with a differential risk of seizure recurrence in the remote symptomatic group (Table 1).

Abnormal EEGs were strongly associated with age. In children younger than 3 years, 18 (17%) of 104 children had an abnormal EEG, compared with 148 (53%) of 279 children older than 3 years. This was true for both the cryptogenic and remote symptomatic groups.

Sleep State at Time of First Seizure

Information on sleep state was available in 404 patients (99%). The onset of the first seizure occurred during the awake state in 271 (67%) and during sleep in 133 (33%). Those that occurred in sleep were associated with recurrence risks of 50% (95% CI, 41% to 58%) and 53% (95% CI, 45% to 62%) at 2 and 5 years, respectively, compared with 31% (95% CI, 25% to 36%) and 36% (95% CI, 30% to 42%) in those that occurred while the children were awake ($P < .001$; Table 1). A seizure occurring during sleep was associated with an increased recurrence risk whether it occurred during a daytime nap or at night. In contrast, whether the initial seizure occurred during the day (8 AM to midnight) or night (midnight to 8 AM) was not associated with a differential risk of recurrence (Table 1).

An association between sleep state and recurrence risk was present in the cryptogenic but not in the remote symptomatic group (Table 1). In the cryptogenic group, the occurrence of the first seizure in sleep was associated with a higher recurrence risk both in children with normal EEGs and those with abnormal EEGs (Fig 4). There was a strong association between the occurrence of a first seizure during sleep and an abnormal EEG. In the 50 children who had their first seizure while asleep and who had an abnormal EEG, the recurrence risks at 2 and 5 years were 63% (95% CI, 47% to 76%) and 65% (95% CI, 52% to 79%), respectively (Fig 4). The onset of a first seizure during sleep in children with cryptogenic first seizures and abnormal EEGs was associated with similar recurrence risks in the 21 such children with centrotemporal spikes on their EEGs, 15 (71%) of whom had recurrences, and the 29 such children with other EEG abnormalities, 17 (59%) of whom had recurrences. The 136 children with cryptogenic first seizures, normal EEGs, and first seizures that occurred while awake had particularly low recurrence risks of 19% (95% CI, 12% to 25%) and 21% (95% CI, 14% to 28%) at 2 and 5 years, respectively. In those children who did have seizure recurrences, the recurrences occurred in the same sleep state in 72% of the cases ($P < .001$).

Family History of Unprovoked Seizures

There were family histories of unprovoked seizures in first-degree relatives in 48 (14%) of the 342 children with cryptogenic first seizures for whom

TABLE 1. Risk Factors for Recurrence

Risk Factor	Proportionate Hazards Model								
	Overall (n = 407)			Cryptogenic (n = 342)			Remote Symptomatic (n = 65)		
	Rate Ratio	95% CI*	*P*	Rate Ratio	95% CI	*P*	Rate Ratio	95% CI	*P*
Remote symptomatic etiology	2.2	1.6–3.1	<.0001	...	...	...	...	...	...
Abnormal EEG†	2.3	1.7–3.2	<.0001	2.6	1.8–3.7	<.0001	1.1	0.6–2.0	.78
Seizure while asleep	1.7	1.2–2.3	<.0001	1.9	1.3–2.7	<.0005	1.1	0.6–2.0	.80
Family history of seizures and abnormal EEG	2.7	1.5–4.9	.001	3.5	1.9–6.6	<.0001	0.6	0.1–4.7	.66
Partial seizure	1.4	1.0–1.9	<.04	1.3	0.9–1.9	.14	1.2	0.6–2.1	.64
Prior febrile seizures	1.6	1.1–2.3	<.02	1.3	0.8–2.0	.31	2.7	1.4–5.3	.003
Todd's paresis	1.9	1.1–3.2	<.02	2.1	1.2–3.8	<.02	1.3	0.5–3.6	.63
Age ≤3 y	0.8	0.5–1.1	.14	0.6	0.4–0.9	.02	2.8	1.4–5.4	<.003
Status epilepticus	1.3	0.9–2.1	.19	1.2	0.7–2.0	.48	1.6	0.7–3.5	.24
>1 seizure in 24 h	1.1	0.7–1.5	.72	1.2	0.8–1.8	.43	0.8	0.4–1.8	.63
Family history of seizures	0.9	0.6–1.5	.76	1.2	0.7–1.9	.55	0.2	0.03–1.7	.16
Treatment >14 d	1.0	0.7–1.5	.97	0.7	0.4–1.3	.30	1.3	0.7–2.6	.39
Time of day (midnight–8 AM)	1.1	0.8–1.7	.53	1.1	0.7–1.7	.74	1.2	0.6–2.5	.66

* CI indicates confidence interval.
† EEG indicates electroencephalogram.

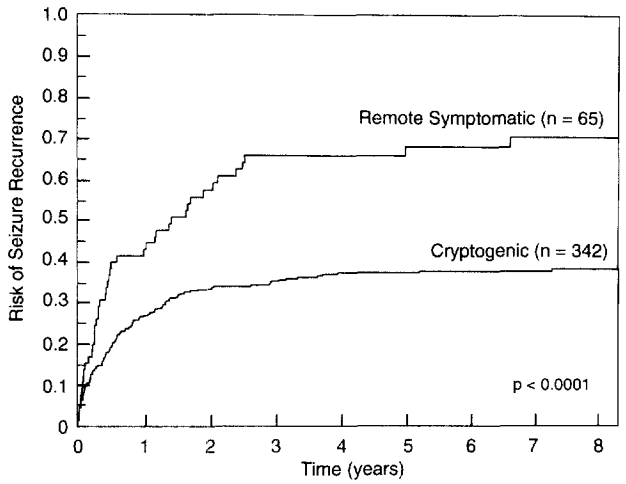

Fig 2. Probability of seizure recurrence after cryptogenic and remote symptomatic first seizures (n = 407): Kaplan-Meier curve.

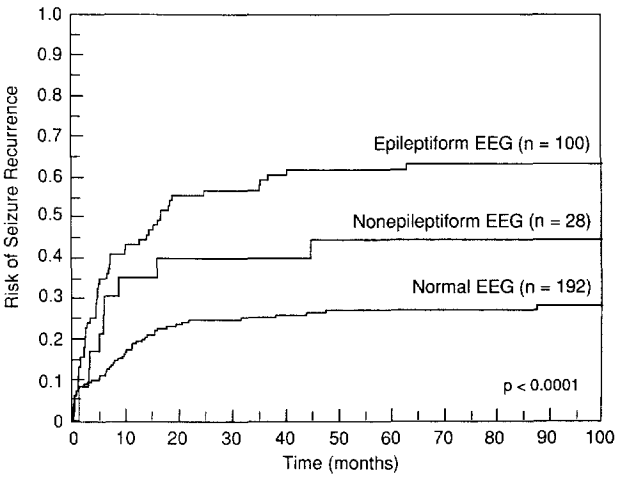

Fig 3. Probability of seizure recurrence after a cryptogenic first seizure as a function of the electroencephalogram (n = 320): Kaplan-Meier curve.

family histories were available and in 4 (6%) of the 65 children with remote symptomatic first seizures. Overall there was no increased recurrence risk among those with family histories of seizures (Table 1). For the group with cryptogenic first seizures and abnormal EEGs, a family history of unprovoked seizures in a first-degree relative was associated with an increased risk of recurrence ($P < .001$; Table 1).

Seizure Classification

There was sufficient information to classify the initial seizure in accordance with the international classification[18] in all cases. Because of study entry criteria, children who had typical absence and myoclonic seizures are not represented in the study group, because they virtually never come to medical attention at the time of their first episodes. In the overall group, partial seizures were associated with a higher risk of recurrence (Table 1). However, partial seizures were more common in the remote symptomatic group than in the cryptogenic group ($P = .012$). In the cryptogenic group, partial seizures were more common in children with abnormal EEGs than in children with normal EEGs ($P < .001$). Once the effect of etiology and EEG are controlled for, partial seizures were not associated with a differential recurrence risk (Table 1).

Todd's Paresis

Twenty six (6%) children had Todd's paresis following their initial seizure. Seizures recurred in 16 (61%) of the children with Todd's paresis, including 12 (57%) of 21 children with cryptogenic first seizures and 4 (80%) of 5 children with remote symptomatic first seizures. The presence of Todd's paresis was associated with a statistically significant increased risk of recurrence in the overall group ($P < .02$) and the cryptogenic group ($P < .02$; Table 1).

Prior Febrile Convulsions

Overall there was an association between a history of prior febrile seizures and recurrence (Table 1). Thirty-five (54%) of the 65 children with prior histories of febrile seizures had recurrences, compared with 134 (39%) of the 340 children with no prior

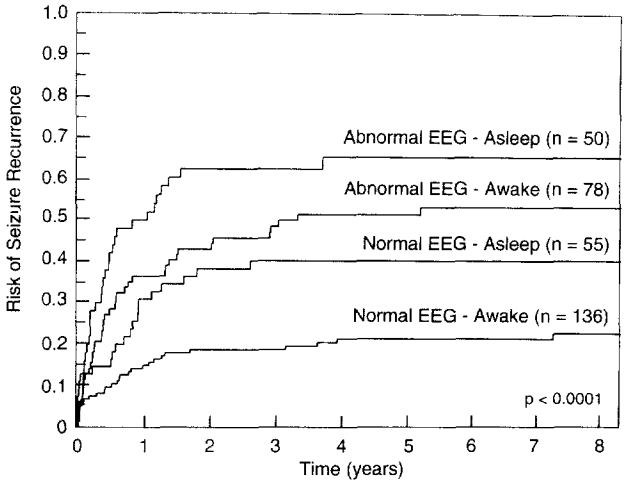

Fig 4. Probability of seizure recurrence after a cryptogenic first seizure as a function of sleep state and the electroencephalogram (n = 319): Kaplan-Meier curve.

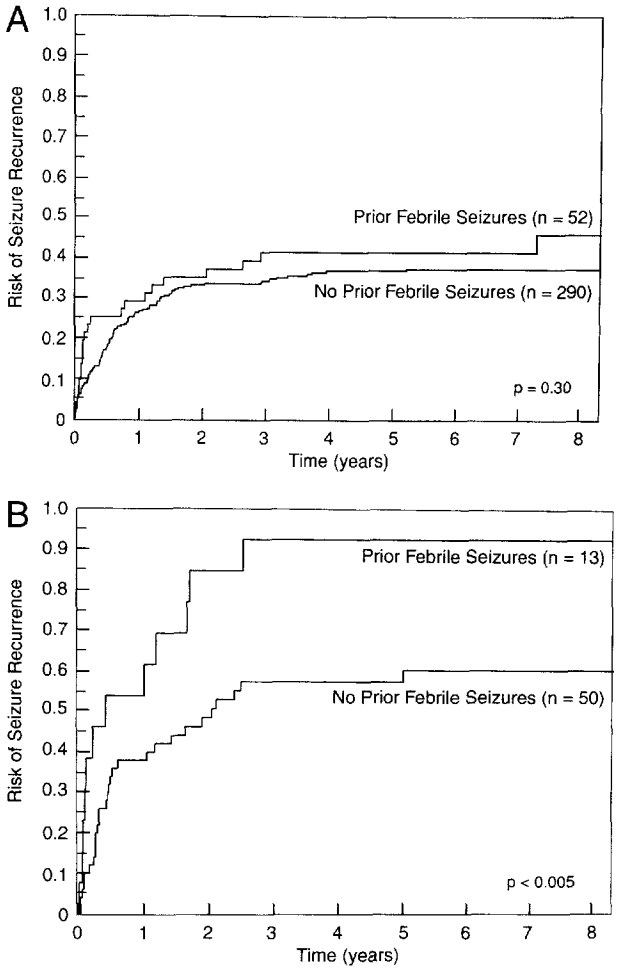

Fig 5. Probability of seizure recurrence after a first unprovoked seizure as a function of prior febrile seizure, Kaplan-Meier curve: A, cryptogenic cases (n = 342); B, remote symptomatic cases (n = 63).

febrile seizures (P = .017). The recurrence risk for those with prior febrile seizures was 45% (95% CI 33%,57), and 52% (95% CI, 39% to 64%) at 2 and 5 years compared with 35% (95% CI, 30% to 40) and 40% (95% CI, 34% to 45%) in those with no prior febrile seizures (P < .02).

The association of prior febrile seizures and seizure recurrence was limited to the remote symptomatic group. In the cryptogenic group, the recurrence risks for those with prior febrile seizures were 35% (95% CI, 22% to 48%) and 41% (95% CI, 28% to 55%) at 2 and 5 years, respectively, compared with 33% (95% CI, 28% to 38%) and 37% (95% CI, 31% to 42%) in those with no prior febrile seizures (P = .31; Fig 5, A). In children with remote symptomatic first seizures, however, a history of prior febrile seizures was a significant risk factor for recurrence (Table 1 and Fig 5, B). The recurrence risks in the 13 remote symptomatic cases with prior febrile seizures were 85% (95% CI, 65% to 100%), and 92% (95% CI, 78% to 100%) at 2 and 5 years, respectively, compared with 48% (95% CI, 34% to 62%) and 57% (95% CI, 43% to 71%) in the 50 cases with no prior febrile seizures (P < .005).

Age at First Seizure

The mean age at the time of first seizure was 6.8 years. There were 109 (27%) children younger than 3 years, 298 (46%) between 3 and 10 years, and 109 (27%) 10 years or older at the time of their first seizures. In the overall group, there was no relationship between age at first seizure, whether analyzed as a continuous or discrete variable, and the risk of recurrence (Table 1). However, there was a differential effect of age in the cryptogenic and remote symptomatic subgroups (Fig 6, A and B). In the cryptogenic group, those younger than 3 years had the lowest recurrence risk compared with older children (P < .03; Table 1 and Fig 6, A), whereas in the remote symptomatic group, those younger than 3 years had the highest recurrence risk (P < .01). It should be noted that in the cryptogenic group, those younger than 3 years have the lowest rate of abnormal EEGs.

Status Epilepticus

The occurrence of status epilepticus as the first seizure did not influence the recurrence risk. Forty eight children (12%; 38 cryptogenic and 10 remote symptomatic) presented with status epilepticus (duration, >30 minutes) as their first unprovoked seizure. None had new neurologic deficits after the episodes of status epilepticus. To date, 24 (50%) have had seizure recurrences, including 16 (42%) cryptogenic and 8 (80%) remote symptomatic cases. Initial presentation with status epilepticus was not a risk factor for seizure recurrence (Table 1). For the cryptogenic group, the Kaplan-Meier risks of recurrence were 38% (95% CI, 22% to 53%) and 45% (95% CI, 28% to 61%) at 2 and 5 years, respectively, in children who presented with status epilepticus, compared with recurrence risks of 33% (95% CI, 27% to 38%) and 36% (95% CI, 31% to 42%), respectively, in those who presented with brief initial seizures (P = .47).

Of the 24 children with initial episodes of status epilepticus who had a seizure recurrence, 5 (21%) had recurrences with status epilepticus. Of the 147 children who presented with initial brief seizures and had seizure recurrences, only 2 (1%) had recurrences with status epilepticus (P < .001). Overall, of

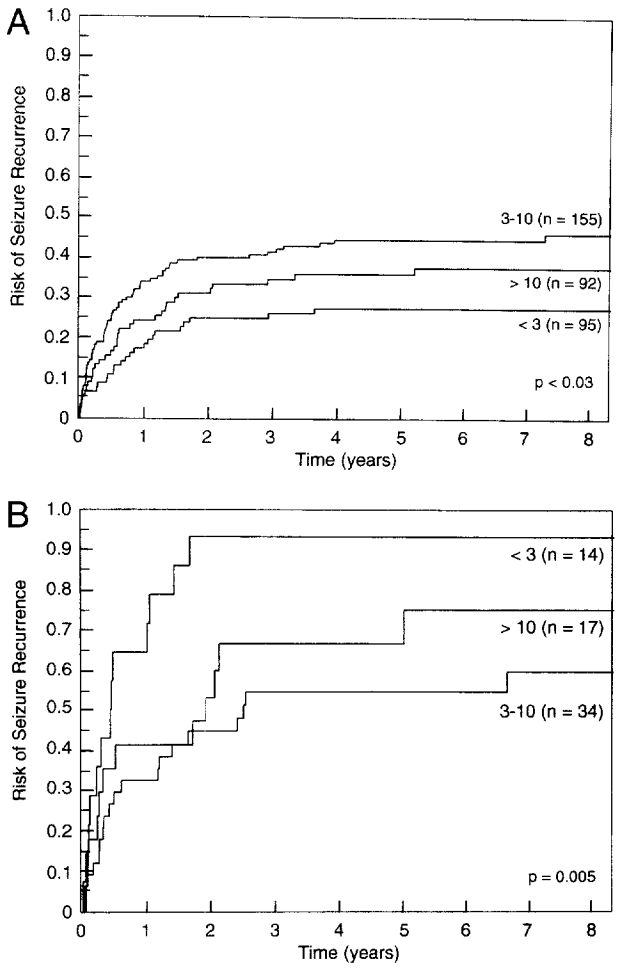

Fig 6. Probability of seizure recurrence after a first unprovoked seizure as a function of age at first seizure: Kaplan-Meier curve. A, cryptogenic cases (n = 342); B, remote symptomatic cases (n = 65).

the 171 children with recurrent seizures, only 7 (4%) had recurrences with status epilepticus.

Number of Seizures in 24 Hours

Among the 407 children in the study, 94 (23%) had more than one seizure within 24 hours as their initial episode. The 41% recurrence risk in this group is not significantly different than the 42% recurrence risk in the group who presented with one seizure. The recurrence risks in those who presented with multiple seizures were 40% (95% CI, 30% to 50%) and 42% (95% CI, 31% to 52%) at 2 and 5 years, respectively, compared with 36% (95% CI, 31% to 42%) and 42% (95% CI 36% to 47%), respectively, in those who presented with an isolated initial seizure.

Treatment

Eighty-six percent of the children were either not treated at all with AEDs after the initial seizures or were treated for less than 2 weeks. Of those with cryptogenic first seizures, 87% were not treated or were treated for less than 2 weeks. Thirty-two children (8%) were treated for more than 3 months, often after early seizure recurrences. Even children with perceived risk factors for recurrence, such as an abnormal EEG, remote symptomatic etiology, or status epilepticus, were usually not treated with long-term antiepileptic drug therapy. In this observational study, there were no differences in recurrence rates between treated and untreated children (Table 1).

Multivariable Analysis

A multivariable analysis was performed using a proportionate hazards model (Table 2). Variables with statistically significant associations with recurrence risk in the univariate analyses (Table 1) were included in the model. Separate models were created for the overall group as well as for the cryptogenic and remote symptomatic groups.

In the overall cohort, an abnormal EEG, remote symptomatic etiology, prior febrile seizures, Todd's paresis, and onset of the initial seizure in sleep remained in the model. Partial seizures and family history even in association with an abnormal EEG, did not. In the cryptogenic group, only the EEG and sleep state at onset were associated with recurrence risk. In the remote symptomatic group, a history of prior febrile seizures and a first seizure at younger than 3 years were significant independent predictors of recurrence.

Late Recurrences

Of the 171 recurrences, 149 (88%) occurred within 2 years of the initial seizures, and 167 (98%) occurred within 5 years. Twenty-two (9%) of the 242 children who were seizure free for 2 years after the initial seizure had seizure recurrences, including 15 (7%) of 216 cryptogenic cases and 7 (27%) of 26 remote symptomatic cases (P = .004). In the 242 children

TABLE 2. Risk Factors for Recurrence: Multivariable Analysis Using Cox Proportional Hazards Model

Risk Factor	Proportionate Hazards Model		
	Rate Ratio	95% Confidence Interval	P
Overall group (n = 407)			
Abnormal electroencephalogram	2.1	1.6–3.0	<.001
Remote symptomatic etiology	1.7	1.2–2.4	.006
Prior febrile seizures	1.6	1.1–2.3	.019
Todd's paresis	1.7	1.0–2.9	.038
Seizure while asleep	1.5	1.1–2.1	.008
Cryptogenic cases (n = 342)			
Abnormal electroencephalogram	2.5	1.7–3.6	<.0001
Seizure while asleep	1.7	1.2–2.5	<.003
Remote symptomatic cases (n = 65)			
Prior febrile seizures	2.3	1.2–4.5	<.02
Age ≤3 y	2.4	1.2–4.9	<.02

who were seizure free for 2 years after the initial seizure, the risks of late recurrence were 5% (95% CI, 2% to 7%), 8% (95% CI, 4% to 11%), and 10% (95% CI, 6% to 14%) at 3, 5, and 8 years, respectively, after the initial seizures. The risks of late recurrence were 6% (95% CI, 3% to 9%) and 8% (95% CI, 4% to 12%) at 5 and 8 years, respectively, in the 216 children with cryptogenic first seizures, compared with 20% (95% CI, 4% to 36%) and 31% (95% CI, 11% to 50%) at 5 and 8 years, respectively, in the 26 children with remote symptomatic first seizures ($P = .0004$).

Factors associated with late recurrence are shown in Tables 3 and 4. The variables predicting late recurrence are the same as those predicting early recurrence and have very similar rate ratios, except that sleep state is no longer predictive. Because of the small number of children and late recurrences (n = 7) in the remote symptomatic group, an analysis of risk factors was not feasible in this group. Multivariable analysis of late recurrences (Table 4) also shows a pattern similar to that seen in the overall multivariable analysis.

For the 164 children who met the more stringent criterion of being seizure free 5 years after the initial seizure, the risks of a late recurrence were 1.2% (95% CI, 0.0% to 3.0%), 2.0% (95% CI, 0.0% to 4.3%), and 2.9% (95% CI, 0.1% to 5.7%) at 6, 7, and 8 years, respectively, after the initial seizure. Because only 5 children had recurrences more than 5 years after the initial seizure, one cannot do a meaningful analysis of risk factors for very late recurrences.

DISCUSSION

In this prospective study of children identified at the time of their first unprovoked seizure, the risk of recurrence after 8 years of follow-up is less than 50%. This risk is very similar to those reported in the three other prospective studies, primarily in adults.[6,7,9,15] It is also similar to the recurrence risk in the untreated group in a recent randomized, multicenter Italian study if one excludes those with suspected prior seizures, a group that was excluded from our study.[17] The above four studies,[6,7,9,15,17] like ours, recruited patients directly from the emergency department and carefully excluded those with histories of prior seizures. Studies using different methods for identifying and recruiting patients have reported much higher recurrence risks.[2,8,10,11] The methodological reasons for these higher recurrence risks have been reviewed previously.[2]

The large size and the long duration of follow-up of this prospectively recruited group have allowed a detailed study of risk factors for seizure recurrence. Five factors were associated with the risk of recurrence. These include etiology, EEG, sleep state, Todd's paresis, and a history of prior febrile seizures. Etiology and EEG have been consistently associated with an increased recurrence risk in other studies[2,6,7,11–15,17]. The association of onset of seizures in sleep with recurrence risk was previously reported and persists in this analysis.[30] With the substantially increased sample size and longer duration of follow-up, we were able to confirm the importance of risk factors such as Todd's paresis and febrile convulsions, which were only marginally significant in our earlier analysis of 283 children with a mean follow-up of 30 months.[1] Todd's paresis and histories of prior provoked seizures in remote symptomatic cases have also been reported as risk factors in the one other prospective study with an extended follow-up period.[7] However, risk factors of marginal significance in the prior analysis,[1] such as partial seizures in the remote symptomatic group, turned out not to be associated with the risk of recurrence.

In the cryptogenic group, the key risk factors for recurrence are the EEG and the sleep state. Using these two variables, one can identify a large group with very low risk of recurrence (ie, cryptogenic with a normal EEG and the seizure occurring while awake) and smaller groups with a very high risk of recurrence (cryptogenic with an abnormal EEG and a seizure while asleep; Fig 4).

In the remote symptomatic group, a history of prior febrile seizures, including both simple and complex febrile seizures, was associated with a very high recurrence risk. This suggests that, in this group, febrile seizures may be an age-specific marker for a predisposition for epilepsy.[31] Conversely, in the much larger cryptogenic group, a history of prior febrile seizures did not alter the recurrence risk in this study and several others.[2,11,12]

A younger age of onset was associated with a higher recurrence risk in the remote symptomatic group. This variable remained in the multivariable analysis, and thus the relationship is not simply attributable to the association of early age of onset with

TABLE 3. Risk Factors for Late Recurrence (After 2 Years)

Risk Factor	Proportionate Hazards Model					
	Overall (n = 242)			Cryptogenic (n = 216)		
	Rate Ratio	95% CI*	*P*	Rate Ratio	95% CI	*P*
Remote symptomatic etiology	4.4	1.8–10.8	.0012	...	...	...
Abnormal electroencephalogram	3.5	1.5–8.5	.0052	3.4	1.2–9.8	.024
Seizure while asleep	1.0	0.4–2.6	.99	0.7	0.2–2.4	.55
Partial seizure	0.7	0.3–1.9	.53	0.7	0.2–2.3	.61
Prior febrile seizures	2.6	1.0–6.7	.05	2.4	0.8–7.8	.13
Todd's paresis	1.1	0.2–8.5	.89	0.0	...	...
Age ≤3 y	0.4	0.1–1.3	.13	0.6	0.2–2.0	.36
Status epilepticus	1.5	0.5–5.2	.49	1.4	0.3–6.3	.65
Family history of seizures	0.7	0.2–2.9	.61	1.1	0.2–4.7	.93

* CI indicates confidence interval.

TABLE 4. Risk Factors for Late Recurrence (After 2 Years): Multivariable Analysis Using Cox Proportional Hazards Model

Risk Factor	Proportionate Hazards Model		
	Rate Ratio	95% Confidence Interval	*P*
Overall group (n = 242)			
Remote symptomatic etiology	3.4	1.3–8.9	.012
Abnormal electroencephalogram	2.8	1.1–6.9	.031
Prior febrile seizures	2.5	0.9–6.9	.081
Cryptogenic cases (n = 216)			
Abnormal electroencephalogram	3.4	1.2–9.8	.024

febrile seizures. In the cryptogenic cases, a younger age of onset was associated with a more favorable prognosis on univariate analysis but did not remain in the multivariable analysis. This finding may be attributable to the low frequency of abnormal EEGs in that age group.[22] A similar finding, that a younger age of onset is associated with an increased recurrence risk in remote symptomatic cases but not in cryptogenic cases, was recently reported in a study of discontinuing AEDs in children with epilepsy who were seizure free while taking AEDs.[32] This may be attributable to the known association of a younger age of onset with a more severe neurologic handicap.[32,33]

Status epilepticus as the initial seizure was not uncommon in the cryptogenic group but was not a risk factor for seizure recurrence. The only other study to examine the predictive value of status epilepticus separately in cryptogenic and remote symptomatic cases[6,7] reported similar results. The risk of subsequent status epilepticus in the cryptogenic group is very low, particularly if the initial seizure was brief, and need not unduly influence treatment decisions. What is still unresolved and requires further follow-up is whether after a longer latency period of 10 or more years there will be an increased rate of further seizures in the children who had episodes of status epilepticus. Some retrospective data from tertiary care centers evaluating patients with intractable temporal lobe epilepsy suggest a very long latency period between prolonged early childhood convulsions and subsequent intractable epilepsy.[34–37] Longer-term follow-up of this cohort is being planned to determine whether status epilepticus is associated with the late subsequent development of intractable temporal lobe epilepsy. In remote symptomatic cases, the numbers were small, but meta-analysis suggests that these children are at an increased risk for seizure recurrence.[2,7] Children with status epilepticus of a remote symptomatic cause are also at an increased risk of recurrent episodes of status epilepticus.[20,38,39]

A number of observational studies have reported that treatment with AEDs does not influence the risk of recurrence.[6,11–13] However, two controlled, randomized trials clearly demonstrate that AED therapy after a first seizure reduces the risk of seizure recurrence by approximately 50%.[16,17] The emphasis of the current study, which was initiated in 1983, was on the natural history of an untreated cohort, and the majority of subjects in this study were not treated with AEDs after the initial seizure. Even children who presented with remote symptomatic seizures, status epilepticus, abnormal EEGs, or prior febrile seizures were not treated. Thus, the recurrence risks reported here likely reflect the natural history of this disorder.

Recent randomized, controlled studies of treatment with AEDs have shown that treatment after the first seizure reduces the recurrence risk by approximately 50% but does not affect the probability of attaining remission.[16,17,40] The authors of one study limited to children thought that the benefits of therapy were outweighed by the significant incidence of adverse effects from therapy. They concluded that treatment should not be routinely initiated after the initial seizure.[16] The more recent multicenter Italian study,[17] which included children and adults, initially found a reduction of recurrence risk. After further follow-up, they found that therapy after the initial seizure did not influence long-term remission rates and also do not recommend treatment after a single seizure.[40] Other epidemiologic data also suggest that early treatment with AEDs does not alter the long-term prognosis of these seizure disorders.[41,42]

Most recurrences occur early. A first recurrence after 2 years is uncommon and after 5 years is rare. With the exception of sleep state, the risk factors for late recurrence seem to be the same as those for early recurrence. As discussed above, it remains to be seen whether with very long follow-up further recurrences will occur, particularly in those children with status epilepticus as their first seizure. Some recent retrospective studies suggest that the latency period for development of epilepsy after an initial episode of status epilepticus may be 10 years or more.[34,43] Although this possibility is of concern, it should not alter current treatment decisions.[42,44,45]

The decision to treat or not to treat a child after a first unprovoked seizure is an individualized one. The physician must take into account not only the risk of seizure recurrence and its consequences but also the risks of AEDs. The impact of seizure recurrence in children and adolescents is predominantly social unless recurrence is associated with prolonged status epilepticus.[44,45] Even then, current studies suggest that the sequelae are minimal if the seizure is not caused by an acute neurologic insult and is unprovoked.[20,34,35,38,39,46–48] Only 7 (4%) of the 171 recurrences met the criteria for status epilepticus, and none had sequelae.

In deciding which children should be treated after a first unprovoked seizure, one needs to balance the recurrence risk and the long-term prognosis against the potential morbidity of antiepileptic drug therapy.[44,45,49] Children with cryptogenic first seizures oc-

curring while awake and with normal EEGs have a very low risk of recurrence and will usually not be treated. Children with cryptogenic first seizures occurring while asleep and with abnormal EEGs have a high risk of recurrence. However, many of these children in our cohort met the criteria for benign Rolandic epilepsy, a self-limited, benign focal epilepsy of childhood, the usual course of which consists of brief infrequent seizures occurring in drowsiness and sleep.[50] Several authors have suggested that treatment in this benign, self-limited disorder may not be needed despite the high recurrence risk of a second or third seizure.[44,45,51] Treatment decisions need to be individualized and based on an informed assessment of risk and benefit. These data provide information with regard to recurrence risks and long-term outcomes, which is necessary for making informed treatment decisions. We remain of the opinion that even children with risk factors for recurrence should not be routinely treated after a first unprovoked seizure.

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VITAL SIGNS

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New York Times. March 5, 1996.

Articles

Does the number of seizures before treatment influence ease of control or remission of childhood epilepsy? Not if the number is 10 or less

Carol Camfield, MD, FRCP(C); Peter Camfield, MD, FRCP(C); Kevin Gordon, MD, FRCP(C); and Joseph Dooley, MB, FRCP(C)

Article abstract—Using a population-based regional cohort of 479 children with epilepsy, we studied the effect of the number of pretreatment afebrile seizures on seizure control and remission. The number of pretreatment seizures varied from 1 to 20. For the first 10 pretreatment seizures, there was no significant difference or trend in (1) the proportion of children who were seizure free long enough to attempt stopping medication (mean, 70%), (2) the number of breakthrough seizures before control was achieved, or (3) the proportion of children who were seizure free after stopping medication for the first time (mean, 70%). More patients with more than 10 pretreatment seizures had complex partial seizures (59%) than those with 10 or fewer seizures (16%) ($p < 0.00001$). We conclude that there does not appear to be any penalty for seizure control or early remission of epilepsy if medication is delayed for up to 10 pretreatment seizures.

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The diagnosis of epilepsy is conventionally made after two unprovoked seizures. Daily antiepileptic medication is often prescribed at this point, with the expectation that further seizures will be avoided. It is not clear whether prevention of further seizures alters the tendency of many children to outgrow their epilepsy. Experimental kindling of epilepsy in animals raises the point that each seizure "greases the track" for the next seizure, i.e., seizures beget seizures.[1] The relevance of kindling of experimental seizures in animals to epilepsy in children is uncertain. In kindling models, subclinical electrical stimulation eventually leads to spontaneous seizures. More than 10 stimulation events are required before seizures occur, and the stimulation must occur very regularly and at short intervals. There does not appear to be a clear human equivalent to subclinical stimulation.[1] Nonetheless, the existence of experimental kindling may make clinicians anxious to give children who have recurrent seizures antiepileptic medication as soon as possible.

If the course of epilepsy in children follows a similar pattern to that of experimental kindling, there should be a relationship between the number of seizures before treatment and both the ease of seizure control and the rate of eventual remission of epilepsy. If seizures do not beget seizures, it may be reasonable to withhold medication, for selected children, until several seizures have occurred. Some children with epilepsy might avoid drug treatment completely.

We address the question, Does the number of seizures before antiepileptic drug (AED) treatment influence the ease of seizure control or the chance that medication can be successfully withdrawn?

Methods. The IWK Children's Hospital in Halifax is the only tertiary pediatric center in the province of Nova Scotia (population of approximately 850,000). All pediatric neurologists in the province are located at this hospital, and we have an extensive pediatric neurology traveling clinic system throughout the province. All EEGs for the province are interpreted by the pediatric neurologists at IWK Children's Hospital.

Our previous studies suggest that virtually all children presenting to a physician with a first seizure need to have an EEG.[2] Therefore, we are confident that all those presenting with a second seizure have had at least one EEG; hence, EEG records were a comprehensive source for identifying pediatric seizure patients in the province. The detailed methods of case ascertainment have been previously published.[3] In brief, all EEG reports for children in Nova Scotia in the study period 1977–1985 were reviewed. For each possible patient, information was gathered from the hospital's or the neurologist's charts or by direct contact with the family doctor. When information was incomplete, parent(s) or the patient was contacted directly both for

From the Department of Pediatrics, Dalhousie University and the IWK Children's Hospital, Halifax, Nova Scotia, Canada.
Received February 7, 1995. Accepted in final form April 19, 1995.
Address correspondence and reprint requests to Drs. Camfield, IWK Children's Hospital, Box 3070, Halifax, Nova Scotia, B3J 3G9 Canada.

Table 1 *Inclusion and exclusion criteria*

Inclusion criteria
Two or more unprovoked afebrile seizures
First two afebrile seizures between July 1977 and July 1985
Resident of Nova Scotia at time of first two afebrile seizures
Followup information during 1987–90 (2–12 years)
Age at first two seizures: 1 month to 16 years
Exclusion criteria
Myoclonus; absence (typical or atypical), akinetic, or atonic seizures; and infantile spasms
Acute provoking factors for seizures (e.g., fever, acute head trauma)
Evidence of progressive neurologic disease (brain tumor or degenerative disease)
Unknown number of pretreatment seizures, unless clearly more than 10

Table 2 *Number of patients becoming seizure free and successfully discontinuing medication*

AED started after seizure no.	n	No. tried off AED (%)	No. successfully stopping AED (%)
1	74	48 (65)	27 (57)
2	151	114 (76)	79 (69)
3	74	57 (77)	40 (71)
4	27	20 (74)	17 (85)
5	18	12 (70)	9 (75)
6	12	9 (75)	7 (78)
7	9	4 (44)	3 (75)
10	17	12 (71)	11 (92)
>10	99	55 (56)	39 (71)

initial and followup information from 1987 to 1990. Nearly all patients (97%) had been seen by our pediatric neurology service at some point in the evolution of their disorder.

The inclusion and exclusion criteria are listed in table 1. Epilepsy was defined as two or more unprovoked seizures. Children treated with daily AED therapy after their first seizure were only included if they eventually had a second seizure. We emphasize that children were excluded if they had myoclonus; absence (typical or atypical), akinetic or atonic seizures; or infantile spasms.

In this study we only considered the patient's initial medication period. In all patients, daily AED treatment was started after diagnosis. Some patients continued on medication until their final followup. Others attempted to discontinue medication after a seizure-free period. The decision to discontinue medication was made by the family and attending physician based on clinical factors. Many children withdrew from AED treatment successfully, but others relapsed and restarted daily medication. Some attempted to discontinue medication a second or third time; however, only their first attempt is considered in this report.

The number of pretreatment seizures was coded as 1 to 20, with greater numbers coded as >20. Because few patients had 11 to 21 pretreatment seizures, we grouped together all those with more than 10 pretreatment seizures. Children with an unknown number of pretreatment seizures were excluded unless that number was clearly more than 10. If a child had a first seizure that was unprovoked, fully recovered consciousness, and then had a recurrence on the same day, the second seizure was defined as the first recurrence.[4]

If a child became seizure free for a period that the child's physician and family agreed was sufficient, medication was tapered and then discontinued. The child was then defined as seizure free if he or she experienced no more seizures off medication until the end of followup.

Breakthrough seizures were defined as seizures occurring after medication was prescribed but before medication was withdrawn for those patients who were seizure free for a sufficient period. Information about compliance at the time of breakthrough seizures was not available. Our previous studies have indicated that compliance in this population is usually excellent.[5,6]

Results. *Clinical characteristics.* There were 479 children who met the entry criteria. The mean age of first seizure was 81.5 months (median, 77; range, 1–195). The mean time from first to second seizure was 4.9 months (median, 2; range, 1–72) with 70% of patients having the second seizure within 1 month of the first. The mean length of followup after the first seizure was 85.1 months (median, 85; range, 3–188).

The neurologic examination was normal in 373 patients (78%) and revealed a major abnormality in 53 (11%). Intelligence was judged to be normal in 326 patients (68%), whereas 57 (12%) had a mental handicap and another 77 (16%) had a learning disorder.

The first seizure type was generalized tonic-clonic in 120 patients (25%), simple partial in 19 (4%), complex partial in 124 (26%), partial with secondary generalization in 177 (26%), rolandic in 29 (6%), and "other" in 10 (2%). The initial medication prescribed was phenobarbital in 211 patients (44%), carbamazepine in 177 (37%), phenytoin in 53 (11%), valproic acid in 10 (2%), and "other" in 28 (6%).

Seizure-free period during AED treatment. Overall, 331 patients (70%) became seizure free long enough to attempt discontinuation of medication. The mean seizure-free period while being treated with AED was 31 ± 17 (SD) months. If the number of pretreatment seizures was 10 or fewer, the specific number did not influence the proportion of patients who became seizure free long enough to attempt discontinuation of medication (table 2). Only 55 of the 99 patients (56%) with more than 10 pretreatment seizures were seizure free for a sufficient time to attempt discontinuation of medication, compared with 276 of 380 patients (73%) with 10 or fewer seizures ($p = 0.001$, chi-square test).

Discontinuation of AED treatment. When patients discontinued AED treatment, overall, 232 of the 331 patients (70%) remained seizure free off AED therapy. For the 232 seizure-free patients, the mean followup after AED discontinuation was 39 ± 19 (SD) months. For each pretreatment seizure number, the number of patients successfully stopping AED treatment was the same (see table 2). The only exception was the group treated after a single seizure. Of this group, 27 of 48 patients (57%) were seizure free after

Table 3 Breakthrough seizures after starting AED

AED started after seizure no.	n	Number of breakthrough seizures (%)			
		0	1–3	4–10	>10
1	47	15*	40	28	17
2	115	52	22	10	22
3	56	51	28	11	9
4	20	55	15	15	15
5	13	54	30	8	8
6–10	25	48	12	32	4

Data about breakthrough seizures were not available for those patients with more than 10 seizures before treatment.

* These children were eventually taken off medication and then had at least one recurrence.

AED discontinuation, compared with 205 of 284 patients (72%) with more than one pretreatment seizure ($p = 0.04$, chi-square test).

Breakthrough seizures while receiving AED treatment. Once AED treatment was started, the number of breakthrough seizures before complete control did not differ from the number of pretreatment seizures, again with the exception of those patients with only one pretreatment seizure (table 3). This analysis applies only to the 276 patients with 10 or fewer pretreatment seizures plus sufficient seizure control to attempt discontinuation of medication. Unfortunately, because of our coding system, data for this issue were not available for those patients with more than 10 pretreatment seizures. Of those patients with only one pretreatment seizure, 7 of 47 (15%) had no more seizures when medication was started, compared with 119 of 229 patients (52%) with more than one pretreatment seizure ($p < 0.0001$, chi-square test).

Children with one pretreatment seizure. The mean time from first to second seizure for patients treated after only one pretreatment seizure was significantly longer than for those treated after more seizures (mean, 14.9 versus 4.4 months; $p < 0.00001$, Mann-Whitney test).

Children with more than 10 pretreatment seizures. Those patients with more than 10 pretreatment seizures were more likely to have complex partial seizures than those with fewer pretreatment seizures (60 of 99 versus 62 of 380; $p < 0.00001$, chi-square test). They also had a younger average age of onset of epilepsy (mean, 71.6 versus 84.1 months; $p = 0.05$, Mann-Whitney test). They were not more likely to have neurologic, intellectual, or behavioral disabilities (see reference 3 for definitions).

Discussion. Based on our experience, the number of seizures before a child is started on AED treatment has little influence on the ease of seizure control, the likelihood of becoming seizure free long enough to consider discontinuing medication, or the chance of seizure recurrence after stopping treatment for the first time. Children with more than 10 pretreatment seizures appear to have a reduced chance of completely controlling their seizures with daily AED treatment, but if controlled, the chance of successfully stopping medication is unchanged. We did not include children with initial absence, akinetic, or atonic seizure; myoclonus; or infantile spasms in this study. These disorders virtually always present with seizures too numerous to count.

Our study was population based and the decision of when to start medication was made by the family and physician. We doubt that treatment was deliberately withheld in many of these children until there were multiple seizures. Between 1977 and 1985, our usual practice was to start daily medication after one or two seizures. Children with more than two pretreatment seizures most likely did not present to a physician until multiple seizures had occurred. AEDs were nearly always discontinued if a child was seizure free for 2 to 4 years. Overall, only 18 of the 479 children were seizure free, having made no attempt to stop medication, for more than 4 years. Because we found no trend in the difficulty of seizure control or remission of epilepsy with increasing pretreatment seizure (<10), a randomized trial would probably not yield different results. In a randomized Italian study of 397 adults and children, the investigators found no difference in long-term remission when medication was started after the first or second seizure.[7,8]

Children treated after having more than 10 seizures had a different clinical profile than those treated earlier. They were younger at onset and more likely to have complex partial seizures, suggesting that these seizures are not easily recognized by parents. However, once these children became seizure free with medication, there was no reluctance to attempt medication withdrawal. Only 5% of children with more than 10 pretreatment seizures were seizure free, having made no attempt to stop medication, for more than 4 years compared with 3.4% of those with fewer pretreatment seizures. The rate of successful medication discontinuation was the same with all pretreatment seizure numbers.

We cannot conclude that earlier treatment would have made a difference in seizure control for those with more than 10 pretreatment seizures. Perhaps younger children with many seizures before treatment have a form of epilepsy that is unlikely to remit. In a previous study using multivariate analysis, we noted that more than 20 seizures before treatment was predictive of a low rate of long-term remission, independent of seizure type.[3] Therefore, the effect of a very large number of pretreatment seizures is only partially explained by the overrepresentation of complex partial seizures in this group.

Only one-half of children with a first seizure have a recurrence.[2] Based on our data, it appears that children treated after a single seizure have a more difficult clinical course than those treated after multiple seizures; however, this impression is undoubtedly the result of our inclusion criteria. To be included, children had to have had two or more seizures. Those treated after a first seizure were included if they had an additional seizure on medica-

tion or further seizures when medication was discontinued. Those who had no recurrences after their first seizure were excluded from the study.

In adults, the impact of multiple seizures before treatment is controversial. Elwes et al suggested that "a high frequency of tonic-clonic seizures before treatment" was associated with unsatisfactory seizure control.[9] On the other hand, Sander concluded that there was little evidence in untreated populations to implicate an adverse effect on remission from multiple seizures.[10] Studies, specifically in children, have not directly focused on the issues raised in this paper.[11] In two population-based studies of childhood epilepsy, the investigators noted that frequent "early" seizures are predictive of a poor prognosis.[12,13] In both studies, the early seizures occurred after medication was started.

In 1881, Gowers wrote of epilepsy: "The tendency is for self perpetuation: each attack facilitates the occurrence of another."[14] We disagree, at least for children who have had 10 or fewer seizures before treatment. We suspect that the current "standard of practice" is to prescribe daily medication for children who have had two seizures. Our paper offers reassurance to families who choose to delay medication until a child with epilepsy has had a substantial number of seizures.[15] There does not appear to be any penalty for seizure control or remission if medication treatment is delayed for up to 10 seizures. If early medication does not have an effect on the long-term prognosis of childhood epilepsy, then, initially, the only rationale for treatment would be avoidance of injury or avoidance of adverse social consequences. We are unaware of studies addressing the frequency or severity of injury based on pretreatment seizure number. The social outcome of our patients was not related to the number of pretreatment seizures.[16] The rationale for medication treatment for children who have had 10 or fewer seizures requires further study.

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A population survey of mental health problems in children with epilepsy

Sharon Davies MBBS MRCPsych, Specialist Registrar, Great Ormond Street Hospital;
Isobel Heyman* MBBS PhD MRCPsych, Consultant Child and Adolescent Psychiatrist;
Robert Goodman MBBS PhD FRCPsych, Professor of Brain and Behavioural Medicine, Department of Child and Adolescent Psychiatry, Institute of Psychiatry, King's College London and Maudsley Hospital, London, UK.

**Correspondence to second author at* Department of Child and Adolescent Psychiatry, Institute of Psychiatry, King's College London and Maudsley Hospital, London SE5 8AZ, UK.
E-mail: i.heyman@iop.kcl.ac.uk

The 1999 British Child and Adolescent Mental Health Survey, a nationwide epidemiological study of rates of psychiatric disorder in children aged 5 to 15 years, provided the opportunity to investigate the mental health of children with epilepsy. These children and their families experience disability specifically because of additional emotional, behavioural, and relationship problems, and this is the first epidemiological study that directly measures these impairments. Information was obtained by interviewing a main carer and teacher for 10 316 children; 67 children with epilepsy were identified (35 males, 32 females; mean age 10 years 2 months, SD 2 years 11 months, range 5 to 15 years), and compared with the 47 children with diabetes (27 females, 20 males; mean age 10 years 4 months, SD 3 years 4 months, range 5 to 15 years) and 10 202 controls (50% male; mean age 9 years 11 months, SD 3 years 1 month, range 5 to 15 years). DSM-IV psychiatric diagnoses were derived from the Development and Well-Being Assessment in combination with the interview and a specialist clinician rating. Parental reports of emotional and behavioural problems, their impact, and associated peer problems were also obtained. Rates of psychiatric disorder were 37% (95% confidence interval [CI] 22 to 49) in epilepsy, 11% (95% CI 2 to 19%) in diabetes, and 9% (95% CI 9 to 10%) in control children. Parents of children with epilepsy consistently reported more problems, with greater impact and associated peer problems. Epilepsy, but not diabetes, was independently (adjusted for age, sex, and severe learning difficulties) associated with all behavioural variables in regression analyses. Emotional, behavioural, and relationship difficulties are common in children with epilepsy, and constitute a significant burden to the children and their families, indicating the need for effective mental health services for these children.

Children with epilepsy are at increased risk for mental health problems in comparison with the general population and with children with chronic illnesses not involving the CNS. Children with both epilepsy and structural CNS abnormalities are more likely to have emotional and behavioural symptoms, which in many cases are severe enough to warrant a psychiatric diagnosis (Dunn and Austin 1999). In 1970, a landmark study in child psychiatric epidemiology showed rates of psychiatric disorder of 7% in the general population, 12% in children with physical disorders not involving the CNS, 29% in those with idiopathic seizures, 38% in children with structural brain abnormalities, and 58% in those with both seizures and structural brain abnormalities (the Isle of Wight Study; Rutter et al. 1970). The impact and burden of this psychiatric morbidity have not been well studied but seem to contribute significantly to the overall disability experienced by children with epilepsy. The psychosocial impairments in these children are significantly greater than those found in children with other chronic disorders such as diabetes or asthma (Hoare 1984a, Austin et al. 1994).

The epidemiological study reported here was designed to measure the mental health of a large sample of children in the UK and is unique in employing structured interviews with parents and children. The results of the interviews were combined with teacher rating scales and independent clinician's ratings to generate diagnoses that incorporate clinical judgements (Goodman et al. 2001). Parents were also asked directly about the impact of psychosocial symptoms on their child's overall functioning, in order to provide a more direct measure of disability than was available from the Isle of Wight Study (Rutter et al. 1970). Apart from this extra information, the two studies have similar designs and employ conceptually equivalent diagnostic schemes for child psychiatric disorder, which, therefore, permits a direct comparison of rates of disorder over the 30-year interval.

Method

We used data from a cross-sectional survey of the mental health of a representative sample of 10 438 British children (83% of those approached) aged 5 to 15 years (Meltzer et al. 2000). Centralized computerized records from the Child Benefit Register (CBR) were used as a sampling frame to select children aged 5 to 15 years throughout England, Wales, and Scotland. Families with no detailed postal code in the database or those undergoing a current revision of their record (due to death of the child or change of address) were excluded. The total number of children finally included in the sampling frame was 6 422 202, an estimated 90% coverage of the whole population. The sampling frame was further stratified by Regional Health Authority, and within that, by sociodemographic groupings. Postal sectors were then selected at random within that frame with a probability proportional to the size of the sector. To facilitate the logistics of the survey, a few areas were oversampled but proper weights were introduced into the analysis to adjust for unequal sampling probabilities. From the final list of 475 postal sectors selected from the 8265 sectors covering the whole country, the CBR was instructed to sample 30 children within each postal sector and a letter was subsequently sent to the families by the CBR on behalf of the Office for National Statistics survey team. Of the 14 250 families contacted, 931 parents (6.5%) chose to opt out by calling the CBR and a further 790 addresses (5.5%) were found to be

incorrect. This left a sample of 12 529 children eligible for interview, of whom 10 438 were interviewed.

Psychiatric disorder was assessed using the Development and Well-Being Assessment (DAWBA; Goodman et al. 2000) to collect detailed information from parents, teachers, and young people aged 11 years or more. A structured interview about the relevant DSM-IV criteria (American Psychiatric Association 1994) was administered by lay interviewers, who also recorded verbatim accounts of any reported problems (Goodman et al. 2000; www.dawba.com). Experienced clinicians reviewed both the verbatim accounts and the answers to structured questions about symptoms and their impact before assigning diagnoses according to DSM-IV criteria. The diagnostic assessment used strict symptom and impairment criteria and generated prevalences towards the lower end of the previously reported range for European and North American epidemiological studies. Peer relations and the impact of emotional and behavioural difficulties were assessed by a standard questionnaire (Goodman 1999, 2001; www.sdqinfo.com). Although the survey was primarily one of child mental health, the information gathered included a section on associated illnesses. Parents of 10 316 (99%) of the children provided information on the presence or absence of 34 health problems or conditions.

Epilepsy was reported in 67 children, of whom 42 had 'uncomplicated epilepsy' and 25 had 'complicated epilepsy' as indexed by one or more of the following: severe learning difficulties; cerebral palsy; any stiffness or deformity of the foot, leg, fingers, arms or back; any muscle disease or weakness; a condition present since birth such as talipes equinovarus or cleft palate; any difficulty with coordination; or speech or language problems. Severe learning difficulties were diagnosed when a child's vocabulary quotient was under 60 (Dunn et al. 1997), or when a teacher's estimate of cognitive age was less than half of the child's chronological age. Of the eight children with epilepsy and severe learning difficulties, seven also had one or more of the other complicating factors. In the parental report of epilepsy, we did not have information on seizure type, length of illness, or whether or not treatment was being given.

Diabetes was reported to be present in 48 children, one of whom also had uncomplicated epilepsy and was included in the epilepsy group. This rate is in accordance with that quoted by Diabetes UK (British Diabetic Association, www.diabetes.org.uk) for the rate of juvenile diabetes in the UK population. There have been some reports that eating disorders are more common in young people with diabetes (Verrotti et al. 1999). Our study did not find increased rates of any specific psychiatric disorder in the diabetic group, but the power of the study would be unlikely to be sufficient to detect this. Informed parental consent was obtained for all participants.

Results

The rate of any psychiatric disorder was 37% (25 of 67, 95% confidence interval [CI] 22 to 49%) in the children with epilepsy; 11% (5 of 47, 95% CI 2 to 19%) in the children with diabetes; and 9% (946 of 10 202, 95% CI 9 to 10%) in the remaining children ($\chi^2=61.2$, 2df, $p<0.001$). The rate in the epilepsy group was significantly higher than in either of the other two groups after partitioning with protected significance levels. In forward conditional logistic regression using SPSS (version 10.0), independent predictors of psychiatric disorder were severe learning difficulties, gender, epilepsy, and age (in that order, $p<0.001$ for all), but not diabetes.

Table I provides additional information for a wider range of diagnoses, after splitting the epilepsy group into uncomplicated and complicated epilepsy; all comparisons across the four groups are statistically significant (minimum $\chi^2=11.8$, 3df, $p<0.01$).

Figure 1 shows the parental identification of any emotional or behavioural problem in their child, its impact, and the level of peer relationship problems; all group differences are statistically significant ($p<0.001$ for χ^2 or one-way analysis of variance). Regression analyses were performed with age, gender, severe learning difficulties, uncomplicated epilepsy, complicated epilepsy, and diabetes as independent variables, and with psychiatric diagnoses and the parent-reported variables shown in Figure 1 as independent variables (using stepwise linear regression and forward conditional logistic regressions from SPSS). At least one epilepsy variable was a significant predictor in all instances, whereas diabetes was not a significant predictor in any instance. Uncomplicated epilepsy was a significant independent predictor of the three parent-reported variables shown in Figure 1, and also of emotional disorders, oppositional-conduct disorders, and the presence of at least one psychiatric diagnosis. Complicated epilepsy was a significant independent predictor of the three parent-reported variables shown in Figure 1, and also of emotional disorders, hyperactivity disorders, pervasive developmental (autistic) disorders, and the presence of at least one psychiatric diagnosis.

Discussion

In this epidemiological study, children with epilepsy had high rates of psychiatric disorder and associated impairment;

Table I: Diagnosis by group

Group (n)	*Percentage with psychiatric disorder (n)*				
	Any	*Emotional*	*Conduct*	*ADHD*	*PDD*
Complicated epilepsy (25)	56.0 (14)	16.0 (4)	24.0 (6)	12.0 (3)	16.0 (4)
Uncomplicated epilepsy (42)	26.2 (11)	16.7 (7)	16.7 (7)	0	0
Diabetes (47)	10.6 (5)	6.4 (3)	8.5 (4)	2.1 (1)	0
All other (10 202)	9.3 (946)	4.2 (427)	4.7 (483)	2.2 (228)	0.2 (25)

Any, any psychiatric disorder; Emotional, any emotional disorder; Conduct, any conduct disorder, including oppositional defiant disorder; ADHD, any attention-deficit–hyperactivity disorder; PDD, any pervasive developmental disorder (autistic disorder).

this was not due simply to the association between epilepsy and severe learning difficulties. Both the uncomplicated and complicated epilepsy groups showed a substantial increase in emotional and behavioural disorders. However, only the complicated epilepsy group (identified as having additional neurological problems or severe learning difficulties) was associated with a markedly increased rate of hyperactive and pervasive developmental (autistic) disorders. The fact that mental health problems were much more commonly associated with epilepsy than with diabetes, indicates that the psychiatric consequences of epilepsy are not an inevitable correlate of a chronic and potentially life-threatening disorder that requires daily treatment; neurological abnormalities and social stigma are likely to be key risk factors (Taylor 1996).

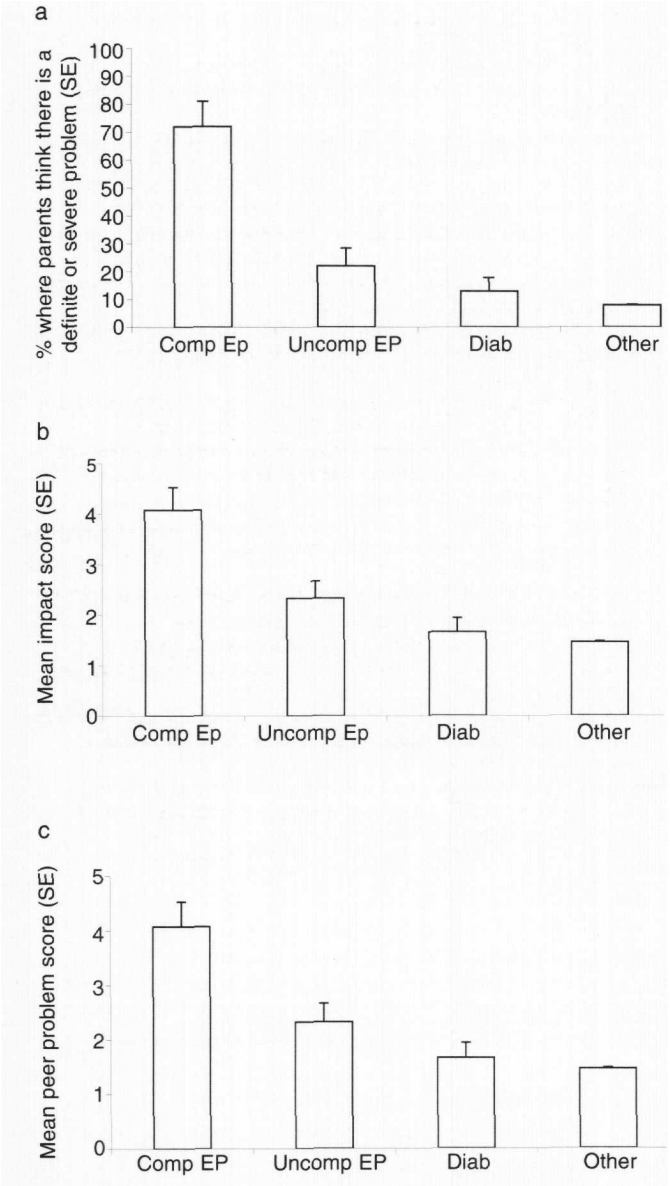

Figure 1: *Parent reports on: (a) Is there an emotional or behavioural problem? (b) What impact does it have? (c) Are there peer problems? Comp EP, complicated epilepsy; Uncomp EP, uncomplicated epilepsy; Diab, diabetes.*

Other studies have shown that a psychiatric disorder can emerge in children early in the course of their illness (Hoare 1984b) or even before the onset of seizures (Austin et al. 2001).

The rates of psychiatric disorder reported in this study are remarkably similar to those reported 30 years ago by the pioneering Isle of Wight study, both for uncomplicated epilepsy (26% now vs 29% then) and for complicated epilepsy (56% now vs 58% then). One implication is that these strong brain–behaviour links are not an artefact of a particular diagnostic scheme or type of assessment – a conclusion reinforced by the high frequency with which parents themselves think that their children with epilepsy have additional emotional and behavioural problems. Obtaining parental impressions may be particularly important in this group of children, as they may not fit neatly into diagnostic categories (Taylor and Lochery 1991). For example, children with severe epilepsy may have social communication problems not meeting full diagnostic criteria for an autistic spectrum disorder, but this disability can be identified by asking parents about peer relationships and general adjustment, as did. Similarly, some children with epilepsy have disinhibited, labile, and unpredictable behaviour, which parents clearly rate as a problem but which cannot be classified as a hyperactivity disorder.

Although we diagnosed epilepsy in this study by parent report without corroboration from medical records, it is reassuring that our prevalence rate (6.4 out of every 1000) is in line with other reported prevalence rates which cluster around 4 to 6 out of 1000 children (Cowan et al. 1989). We did not have the statistical power or clinical information in this study to establish whether the risk of psychiatric disorder varied with characteristics of the epilepsy, such as seizure frequency, type, or length of illness. Previous studies suggest that greater seizure frequency does seem to have an increased psychosocial impact (Camfield et al. 2001). Some seizure types, perhaps particularly those involving the temporal lobe, may be more linked to psychopathology; this has been surprisingly little study of this in children (Ott et al. 2001) although specific clinic series have revealed associations such as a link between right-sided temporal lobe lesions, epilepsy, and autistic spectrum disorder (Taylor et al. 1999). Antiepileptic medications are often suggested as a cause of behavioural problems, and there are many case reports and clinical series suggesting that the side effects of drugs should not be ignored. However, good seizure control is one of the strongest predictors of improved behaviour, and attempts at a systematic study of the effects of anticonvulsants have failed to find evidence of a strong clinical effect on behaviour (Bourgeois 1998).

Although our study focused on epilepsy as the most common neurodevelopmental disorder, our findings are potentially relevant to a substantially greater number of children with other neurodevelopmental conditions such as head injury, cerebral palsy, and hydrocephalus. Rates of the common childhood psychiatric disorders are high in all of these children; response to treatment is equivalent to that in other groups; and, if successful, treatment results in an improved quality of life for the children and their carers (Goodman and Graham 1996).

Conclusion

It is sobering that all the changes in paediatric and child mental health practice over the past 30 years have not apparently reduced the psychiatric associates of epilepsy, despite the

availability of effective, evidence-based treatments for many childhood psychiatric disorders. There are few or no published data on treatment outcomes of psychiatric disorder in children with epilepsy, but clinical experience suggests that these children's mental health problems respond to treatment. In treatment studies, children with medical problems such as epilepsy are often excluded from the analysis, so we do not have trial evidence about whether disorders are equally responsive to treatment, or whether children with epilepsy might need modified treatments. The few published treatment studies suggest equivalent responsiveness to treatment, for example in attention-deficit–hyperactivity disorder (Feldman et al. 1989). The shortage of relevant research studies seems to reflect clinical practice, where psychiatric diagnoses are often missed in children with epilepsy, for example the common disorders of depression and anxiety (Ettinger et al. 1998), or if identified are considered to be an integral part of the epilepsy and are not treated specifically. This study confirms very high rates of psychiatric disorder in children with epilepsy and suggests underdetection and undertreatment of mental health problems in this group. Routine monitoring of psychological adjustment by mental health professionals should be a standard part of the multidisciplinary package of care for children with epilepsy, with early, assertive intervention when necessary to prevent the additional disability that emotional and behavioural disorders confer. Specialist epilepsy centres need ready access to neuropsychological and neuropsychiatric expertize, particularly for children with severe and treatment-resistant epilepsy, and for those with underlying structural brain abnormalities.

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ILAE OFFICIAL REPORT

A practical clinical definition of epilepsy

*Robert S. Fisher, †Carlos Acevedo, ‡Alexis Arzimanoglou, §Alicia Bogacz, ¶J. Helen Cross, #Christian E. Elger, **Jerome Engel Jr, ††Lars Forsgren, ‡‡Jacqueline A. French, §§Mike Glynn, ¶¶Dale C. Hesdorffer, ##B.I. Lee, ***Gary W. Mathern, †††Solomon L. Moshé, ‡‡‡Emilio Perucca, §§§Ingrid E. Scheffer, ¶¶¶Torbjörn Tomson, ###Masako Watanabe, and ****Samuel Wiebe

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Robert S. Fisher
Department of Neurology & Neurological Sciences, Stanford University School of Medicine

Summary

Epilepsy was defined conceptually in 2005 as a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures. This definition is usually practically applied as having two unprovoked seizures >24 h apart. The International League Against Epilepsy (ILAE) accepted recommendations of a task force altering the practical definition for special circumstances that do not meet the two unprovoked seizures criteria. The task force proposed that epilepsy be considered to be a disease of the brain defined by any of the following conditions: (1) At least two unprovoked (or reflex) seizures occurring >24 h apart; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; (3) diagnosis of an epilepsy syndrome. Epilepsy is considered to be resolved for individuals who either had an age-dependent epilepsy syndrome but are now past the applicable age or who have remained seizure-free for the last 10 years and off antiseizure medicines for at least the last 5 years. "Resolved" is not necessarily identical to the conventional view of "remission or "cure." Different practical definitions may be formed and used for various specific purposes. This revised definition of epilepsy brings the term in concordance with common use.

KEY WORDS: **Epilepsy, Seizure, Definition, Unprovoked, Recurrence.**

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*Department of Neurology & Neurological Sciences, Stanford University School of Medicine, Stanford, California, U.S.A.; †SCH, Past President Chilean League Against Epilepsy, Santiago, Chile; ‡Epilepsy, Sleep and Pediatric Neurophysiology Department, University Hospitals of Lyon (HCL) and Lyon Neuroscience Research Center (CRNL), Lyon, France; §Neurological Institute of Clinical Hospital, Universidad Mayor de la República. Montevideo, Uruguay; ¶UCL-Institute of Child Health, Great Ormond Street Hospital for Children, London & Young Epilepsy, Lingfield, United Kingdom; #Department of Epileptology, University of Bonn Medical Centre, Bonn, Germany; **Neurology, Neurobiology, and Psychiatry and Biobehavioral Sciences, UCLA Seizure Disorder Center, David Geffen School of Medicine at UCLA, Los Angeles, California, U.S.A.; ††Department of Pharmacology and Clinical Neuroscience/Neurology, Umeå University, Umeå, Sweden; ‡‡Department of Neurology, NYU School of Medicine, New York, New York, U.S.A.; §§CEO, Epilepsy Ireland, Dublin, Ireland; ¶¶GH Sergievsky Center and Department of Epidemiology, Columbia University, New York, New York, U.S.A.; ##Yonsei Epilepsy Research Institute, Yonsei University College of Medicine, Seoul, Korea; ***Departments of Neurosurgery and Psychiatry & BioBehavioral Medicine, Mattel Children's Hospital, David Geffen School of Medicine, University of California, Los Angeles, California, U.S.A.; †††Saul R. Korey Department of Neurology, Dominick P. Purpura Department of Neuroscience and Department of Pediatrics, Laboratory of Developmental Epilepsy, Montefiore/Einstein Epilepsy Management Center, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, New York, U.S.A.; ‡‡‡Department of Internal Medicine and Therapeutics University of Pavia and C. Mondino National Neurological Institute, Pavia, Italy; §§§Departments of Medicine and Paediatrics, Florey Institute, Austin Health and Royal Children's Hospital, The University of Melbourne, Melbourne, Victoria, Australia; ¶¶¶Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden; ###Department of Psychiatry, National Center of Neurology and Psychiatry, Tokyo, Japan; and ****University of Calgary, Calgary, Alberta, Canada

Address correspondence to Robert S. Fisher, Neurology, Stanford University School of Medicine, Room A343, 300 Pasteur Drive, Stanford, CA 94305-5235, U.S.A. E-mail: robert.fisher@stanford.edu

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In 2005, a Task Force of the International League Against Epilepsy (ILAE) formulated conceptual definitions of "seizure" and "epilepsy" (Table 1).[1] Conceptual definitions can be translated for specific purposes into operational (practical) definitions.

The ILAE commissioned a Task Force to formulate an operational definition of epilepsy for purposes of clinical diagnosis. This article summarizes the recommendations of the Task Force, including appended notes and case examples explaining the reasons for these recommendations and occasional dissenting views. In December of 2013, the ILAE Executive Committee adopted the recommendations as a position of the ILAE.

Why alter the definition of epilepsy? Doing so might cause confusion among patients who could be left uncertain as to whether they have or do not have epilepsy. Epidemiologists and other researchers would need to decide whether to use the new or old definition and how this might affect trends and comparisons. Rules and regulations might have to be changed. Arrayed against these potential negatives are positive aspects to reevaluation of the definition. The current definition requires two unprovoked seizures occurring at least 24 h apart.[2] Some epileptologists recognize and feel a need to address circumstances with high risk for future seizures after a first unprovoked seizure. For example, one Delphic study group in Spain[3] voted with high consensus in favor of treatment in five of seven hypothetical scenarios after a first seizure. A decision for treatment does not necessarily equate to a diagnosis of epilepsy, but it can be taken as a marker for belief in a strong enduring predisposition for further seizures. Conversely, a diagnosis of epilepsy does not necessarily require treatment. The current definition does not allow a patient to outgrow epilepsy, yet many older individuals have all but forgotten their two childhood seizures. A definition should conform to how clinicians and patients think, and usefully merge with other individual considerations in helping to make treatment decisions.

Practical Clinical Definition of Epilepsy

Conceptually, epilepsy exists after at least one unprovoked seizure, when there is high risk for another, although the actual required risk is subject to debate. After a single unprovoked seizure, risk for another is 40–52%.[4] With two unprovoked nonfebrile seizures, the chance by 4 years of having another is 73%, with a 95% confidence interval (CI) of 59–87%, subsequently herein portrayed as approximately 60–90%.[5]

The "two unprovoked seizure" definition of epilepsy has served us well, but it is inadequate in some clinical circumstances. A patient might present with a single unprovoked seizure after a remote brain insult, such as a stroke, central nervous system (CNS) infection, or trauma. A patient with such brain insults has a risk of a second unprovoked seizure that is comparable to the risk for further seizures after two unprovoked seizures.[6] When two individuals with a history of at least one unprovoked seizure have the same high risk for having another, an argument can be made that both have epilepsy. Under limits of the current definition, another patient might have photosensitive epilepsy, yet not be considered to have epilepsy because the seizures are provoked by lights. Another might be free of seizures and seizure medications for 50 years, yet still have epilepsy. In order to bring the practical (operational) clinical definition of epilepsy into concordance with how epileptologists think about epilepsy, the ILAE Task Force recommends broadening the definition of epilepsy to include the circumstances enumerated in Table 2. The Task Force also added a time limit to the definition.

Several elements of this definition require clarification.

Table 1. Conceptual definition of seizure and epilepsy – 2005 report

An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.
Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures, and by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure.

Disease

Epilepsy has traditionally been referred to as a disorder or a family of disorders, rather than a disease, to emphasize that it is comprised of many different diseases and conditions. The term disorder implies a functional disturbance, not necessarily lasting; whereas, the term disease may (but not always) convey a more lasting derangement of normal function. Many heterogeneous health problems, for example, cancer or diabetes, comprise numerous subdisorders and are still considered to be diseases. The term "disorder" is poorly understood by the public and minimizes the serious nature of epilepsy. The ILAE and the International Bureau for Epilepsy (IBE) have recently agreed that epilepsy is best considered to be a disease.

Two unprovoked seizures

Epilepsy exists in a patient who has had a seizure and whose brain, for whatever reason, demonstrates a pathologic and enduring tendency to have recurrent seizures. This tendency can be imagined as a pathologic lowering of the seizure threshold, when compared to persons without the condition. Table 2, item 1, represents the current commonly employed definition of epilepsy as at least two unprovoked seizures occurring >24 h apart. A seizure that is provoked by a transient factor acting on an otherwise normal brain to temporarily lower the seizure threshold does not count toward a diagnosis of epilepsy. The term "provoked sei-

Table 2. Operational (practical) clinical definition of epilepsy

Epilepsy is a disease of the brain defined by any of the following conditions

1. At least two unprovoked (or reflex) seizures occurring >24 h apart
2. One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years
3. Diagnosis of an epilepsy syndrome

Epilepsy is considered to be *resolved* for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years.

zure" can be considered as being synonymous with a "reactive seizure" or an "acute symptomatic seizure."[7] Etiology should not be confused with provocative factors, as some etiologies will produce an enduring tendency to have seizures. A brain tumor, for example, might cause a person to have an epileptic seizure, but not as a transient insult.

The condition of recurrent reflex seizures, for instance in response to photic stimuli, represents provoked seizures that are defined as epilepsy. Even though the seizures are provoked,[8] the tendency to respond repeatedly to such stimuli with seizures meets the conceptual definition of epilepsy, in that reflex epilepsies are associated with an enduring abnormal predisposition to have such seizures.

A seizure after a concussion, with fever, or in association with alcohol-withdrawal, each would exemplify a provoked seizure that would not lead to a diagnosis of epilepsy. The term "unprovoked" implies absence of a temporary or reversible factor lowering the threshold and producing a seizure at that point in time. Unprovoked is, however, an imprecise term because we can never be sure that there was no provocative factor. Conversely, identification of a provocative factor does not necessarily contradict the presence of an enduring epileptogenic abnormality. In an individual with an enduring predisposition to have seizures, a borderline provocation might trigger a seizure, whereas in a nonpredisposed individual, it might not. The Definitions Task Force recognizes the imprecise borders of provoked and unprovoked seizures, but defers discussion to another venue.

High recurrence risk

Table 2, item 2 defines another path for diagnosing epilepsy. Its intent is to encompass circumstances for which some practitioners[9] and expert epileptologists[3] manage patients as if epilepsy is present after a single unprovoked seizure, because of a very high risk of recurrence. Such examples may include patients with a single seizure occurring at least a month after a stroke (Hesdorffer et al. 2009)[6] or a child with a single seizure conjoined with a structural or remote symptomatic etiology and an epileptiform electroencephalography (EEG) study.[10] Another example is a patient in whom diagnosis of a specific epilepsy syndrome associated with persistent threshold alteration can be made after the occurrence of a single seizure. A first seizure might present as status epilepticus,[11,12] but this does not in itself imply epilepsy. Recurrence risks are not known for the majority of individual cases. However, if a treating physician is aware that the lesion has generated an enduring predisposition for unprovoked seizures with a risk comparable to those who have had two unprovoked seizures (which we all agree is epilepsy), then that person too should be considered to have epilepsy. Choosing a specific threshold risk number might be excessively precise, but for general comparison, this risk is about 60–90% after two unprovoked seizures.[I] A threshold level of 60% appropriately exceeds the 50% level of recurrence risk found at 5 years after a single seizure in the United Kingdom multicentre study of early epilepsy and single seizures (MESS) study.[13]

It is important to note that a single seizure plus a lesion or a single seizure plus epileptiform EEG spikes does not automatically satisfy criteria for this operational definition of epilepsy, because data may vary among different studies and specific clinical circumstances. In the Dutch Epilepsy Study,[10] children with epileptiform EEG patterns after their first seizure had a 2-year risk for recurrence of 71%, but in the study by Shinnar et al.,[12] children with a first idiopathic seizure and abnormal EEG patterns had recurrence risk of 56% at 3 years. No formula can be applied for additive risks, since data are lacking on how such risks combine; such cases will have to be decided by individualized considerations. Recurrence risk is a function of time, such that the longer the time since the last seizure, the lower the risk.[14]

The revised definition places *no burden* on the treating physician to specify recurrence risk in a particular circumstance. In the absence of clear information about recurrence risk, or even knowledge of such information, the default definition of epilepsy originates at the second unprovoked seizure. On the other hand, if information is available to indicate that risk for a second seizure exceeds that which is usually considered to be epilepsy (about 60%), then epilepsy can be considered to be present.

Epilepsy syndrome

It makes little sense to say that someone has an epilepsy syndrome[15] but not epilepsy. If evidence exists for an epilepsy syndrome, then epilepsy may be presumed to be present, even if the risk of subsequent seizures is low. This is the case with benign epilepsy with centro-temporal spikes (BECTS).

Exceptional syndromic cases may exist in which obvious behavioral seizures may not occur at all, as can be the case with continuous spike and waves during sleep and the Landau-Kleffner Syndrome.[16]

Implications for treatment

Diagnosing epilepsy after a single unprovoked seizure when there is high risk for recurrence may or may not lead to a decision to initiate treatment. The proposed practical definition may provide support to a physician who wishes to treat a patient with high recurrence risk after a single unprovoked seizure. However, a treatment decision is distinct from a diagnosis, and should be individualized depending upon the desires of the patient, the individual risk-benefit ratio and the available options. The physician should weigh the possible avoidance of a second seizure with associated risks against the risk for drug-related side effects and costs for the patients.

To be clear, the diagnosis of epilepsy and a decision to treat are two related but different issues. Many epileptologists treat for a time after an acute symptomatic seizure (for example, with Herpes encephalitis), with no implication of epilepsy. In contrast, patients with mild seizures, with seizures at very long intervals, or those declining therapy might go untreated even when a diagnosis of epilepsy is beyond dispute.

Unprovoked seizures separated in time

The time span between two unprovoked seizures that together qualify as epilepsy is subject to ambiguity. Seizures clustering within 24 h confer approximately the same risk for later seizures as does a single seizure.[17] The Task Force retained the current thinking that unprovoked seizures clustering in a 24 h period be considered to be a single unprovoked seizure for purposes of predicting recurrence risk.

Some authorities[17] consider epilepsy to be present, but in remission, after 5 years of seizure freedom. However, the definition of epilepsy does not specify an outer time limit for occurrence of the second unprovoked seizure to mark the onset of epilepsy. Therefore, epilepsy could be considered present if an unprovoked seizure occurred at age 1 and at age 80, a condition sometimes referred to as oligoepilepsy.[18] The Task Force acknowledges that, in such circumstances, the causes of the seizures occurring at the two time points might be different, and if so then epilepsy would not be present.[II] Otherwise, the Task Force did not agree on a specific interval of time between seizures that would "reset the clock" for counting an event as a second seizure. A rationale for setting such an interval might emerge from future research.

Epilepsy resolved

Is epilepsy, once diagnosed, always present? The traditional definition does not allow for its disappearance. Should a person who has been seizure-free and off medication for decades after absence seizures as a child still be considered to have epilepsy? Likewise, are patients with mesial temporal lobe epilepsy who have been seizure-free off medications for 10 years after resection of their hippocampal sclerosis considered to still have epilepsy? Seizure freedom for long intervals of time can result from one of several different underlying circumstances and treatments. An abnormal tendency to have unprovoked seizures may remain, but the seizures are successfully controlled by therapy. Children can outgrow their epilepsy, as with BECTS. Some persons might have had a definitive treatment, such as brain surgery, rendering them permanently seizure-free.

The Task Force sought a definition that would allow a possible end to the burden of having epilepsy. Medical literature uses the term "remission" to imply an abeyance of a disease, but this term is not well-understood by the public, and remission does not convey absence of the disease. "Cure" implies a risk for future seizures no greater than that of the baseline unaffected population, but after a history of epilepsy such a low risk is never achieved. The Task Force therefore adopted the phrase "resolved."[III] When epilepsy is resolved, it implies that the person no longer has epilepsy, although it does not guarantee that it will not return.

What time intervals and circumstances should characterize resolved epilepsy?[IV] Recurrence risk depends on the type of epilepsy, age, syndrome, etiology, treatment, and many other factors. Juvenile myoclonic epilepsy is known to be subject to an elevated risk of seizures for several decades,[19] but remissions do still occur. Structural brain lesions, such as malformations of cortical development,[20] may elevate risk of seizures long term. Seizures may recur at variable intervals after remission due to removal of an epileptogenic lesion, such as a cavernous malformation.[21] A study[22] of 347 children achieving at least 5-year "complete remission" including at least 5-years free of antiseizure drugs identified late seizure relapses in 6%. One occurred as long as 8 years after the prior seizure. Data were not given for those remaining free of seizures after a 10-year complete remission, but the number would be <6%. After temporal lobe epilepsy surgery,[23] 54.2% of patients relapse within 6 months; whereas, only 1.9% relapse 4 years after surgery. Similar results were seen in another study,[24] with only 0.6% having seizures in the last year of follow-up, provided that they had been seizure-free for 3 years after surgery.

The risk of seizure recurrence after unprovoked seizures diminishes with time, although the risk may never reach levels for normal individuals who have not had a prior seizure. Most relapses are early. After a single unprovoked seizure, 80%[14,17] to 90%[25] of those who had a second did so within 2 years. In one study,[5] after a second unprovoked seizure, subsequent seizures occurred within 4 years, but none in the ensuing 3 years, suggesting that the risk may not be zero but is low. The National General Practice Study of Epilepsy in the United Kingdom[14] identified a 3-year recurrence risk of 44% after a seizure-free period of 6 months, 32% after 12 months,

and 17% after 18 months. No adequate data are available on seizure recurrence risk after being seizure-free and off medication for extended periods of time. Delayed relapses are rare after 5 years.[26] By 10 years off antiseizure medicines, the annual risk for seizures probably is very low.[27,V]

Clinicians will have to individualize a determination of whether epilepsy is resolved. The Task Force chose to define epilepsy as being resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure-free for the last 10 years, with no seizure medicines for the last 5 years. Delineation of circumstances in which epilepsy is definitively cured is beyond the scope of this paper.

Imperfect information

From the clinician's perspective, the new practical definition linking epilepsy to a predefined probability of seizure recurrence brings greater clarity and clinical relevance to the diagnostic process. However, optimal application of this definition often requires specialized diagnostic and interpretative skills—specifically, in assessing recurrence risks, or in diagnosing syndromes—which may not be broadly available in all settings, particularly at the primary care level. Even more important is the inevitable uncertainty in many situations about the potential epileptogenicity of an magnetic resonance imaging (MRI)–demonstrated lesion. For instance, one or more brain cysts in an individual with neurocysticercosis[28] may be incidental findings with no epileptogenic activity in a particular individual. Risk does not equate with causation. When in doubt, practitioners should consider referring a patient to a specialized epilepsy center with experience in diagnosis.

In the absence of a seizure documented by video-EEG recording and typical for a person's recurrent unprovoked seizures, there will be situations where a diagnosis of epilepsy remains uncertain. One approach to these ambiguities would be to define a condition called "probable (or possible) epilepsy."[VI] Such an approach has been adopted with other diseases, such as multiple sclerosis with the McDonald criteria,[29] amyotrophic lateral sclerosis with the El Escorial criteria,[30] migraine,[31] and vascular dementia.[32] The ILAE Task Force recognized the subtle, but important, difference between telling a patient that "you have probable epilepsy" versus "you probably have epilepsy." In the absence of secure information, the latter statement, or another statement simply expressing uncertainty, seemed a more straightforward assertion. Therefore, the Task Force has not defined probable epilepsy as a specific entity, but has left that possibility open for the future.

Consequences of the Practical Definition

Definitions have consequences. From the viewpoint of the patient, epilepsy is associated with stigma and psychological, social, cognitive, and economic repercussions so important as to be built into the conceptual definition of epilepsy.[1] The new practical definition could improve outcomes by sensitizing clinicians about the need to give greater consideration to the risk of recurrence after a single unprovoked seizure, and making the clinicians more comfortable in initiating treatment after some initial unprovoked seizures. This must be individualized, since a diagnosis of epilepsy does not necessarily require prescription of an antiseizure drug, and treatment might be justified in some patients for whom a definitive diagnosis of epilepsy has not been made. A practical definition allowing earlier diagnosis will be especially useful for prevention of unnecessary risks of physical injuries or social consequences resulting from recurrent seizures in patients deemed to be susceptible to a high risk for recurrence. The revised definition also provides an expanded opportunity for disease-modifying interventions that prevent the progression of epilepsy and onset of comorbidities.

How revision of the definition of epilepsy will affect the measured prevalence of epilepsy is unpredictable. Future epidemiologic studies may choose to use the older operational definition for consistency. If the revised definition is used, some patients previously considered to have epilepsy will no longer carry an epilepsy diagnosis because of the provisions for epilepsy being resolved. Other individuals who meet the "single seizure with high risk for another" criteria might be added to the epilepsy group.

The definition of epilepsy will affect diagnosis and treatment in both resource-rich and resource-poor societies. The Task Force has been careful to define epilepsy in a way that can be applied in general with or without expensive technology that may not be universally available.

The correct diagnosis of epilepsy in people who might not have been diagnosed previously may have both negative and positive consequences. For example, economic consequences might include reimbursement by a national health service for medications whose cost otherwise would have to be covered by the affected person. On the other hand, many people with epilepsy have difficulty in obtaining life or medical insurance. Some cannot purchase a first home without a life insurance policy secured at the time of home purchase. Stigma could profoundly affect some people not previously considered to have epilepsy, with serious and misguided consequences such as loss of access to education or marriage bans. Allowing epilepsy to be declared "resolved" may lift the stigma from some who should no longer be considered to have epilepsy. Positive economic and health consequences will accrue when more accurate diagnosis results in appropriate preventative treatment before a second seizure occurs.

People with reflex epilepsies previously have been disenfranchised by the requirement that seizures be unprovoked. The inclusion of reflex epilepsy syndromes in a practical clinical definition of epilepsy now brings these individuals into the epilepsy community.

The revised practical definition described in this report is intended for clinical diagnosis, and might not be suitable for all research studies. Different operational definitions will be used depending on specific purposes, and comparisons could still be made using the traditional "two-unprovoked-seizure" definition of epilepsy whenever appropriate. Investigators must clearly identify the definition used in any study or publication.

A revised definition has implications for legislation and health economics. Regulations affecting individual life activities, such as driving restrictions, relate more to seizure frequency or to risk of seizure recurrence than to a diagnosis of epilepsy, but this is not always the case. In some countries a diagnosis of epilepsy per se limits the period of validity of a driving permit, or the type of permit that can be acquired. Guidelines about participation in certain sports may stipulate restrictions for people with a diagnosis of epilepsy, irrespective of seizure history. Insurance coverage and social benefits might also be affected by the diagnostic label. To the extent that a revised practical definition might affect the number of people diagnosed with epilepsy, there could be cost repercussions for the individual and for the society. Costs to society may not necessarily be higher, however, particularly if the new operational diagnosis codifies the current approach of epileptologists and leads to improved management of individuals who are likely or unlikely to have future seizures.

Conclusion

Epilepsy previously has been defined as at least two unprovoked seizures >24 h apart. The revised practical definition implies that epilepsy also can be considered to be present after one unprovoked seizure in individuals who have other factors that are associated with a high likelihood of a persistently lowered seizure threshold and therefore a high recurrence risk. Such risk should be equivalent to the recurrence risk of a third seizure in those with two unprovoked seizures, approximately at least 60%. The latter risk level occurs with remote structural lesions, such as stroke, CNS infection, certain types of traumatic brain injury, diagnosis of a specific epilepsy syndrome, or in some circumstances with the presence of other risk factors. Those with recurrent reflex seizures, for example, photosensitive seizures, are also considered to have epilepsy. This definition of epilepsy brings the term in concordance with common use by most epileptologists.[VII] Epilepsy is not necessarily life-long, and is considered to be resolved if a person has been seizure-free for the last 10 years, with at least the last 5 year off antiseizure medicines, or when that person has passed the age of an age-dependent epilepsy syndrome. The new definition is more complicated than is the old definition. Studies providing detailed knowledge of seizure recurrence risk are few, so most diagnoses of epilepsy will of necessity still be made by documentation of two unprovoked seizures. As more knowledge of recurrence risks is accrued for specific etiologies, application of the epilepsy definitions will become more precise and more useful.

Case Examples[VIII]

1. *Two seizures*. A 25-year-old woman has two unprovoked seizures, 1 year apart. *Comment*: This person has epilepsy, according to both the old and new definitions.
2. *Stroke and seizure*. A 65-year-old man had a left middle cerebral artery stroke 6 weeks ago and now presented with an unprovoked seizure. *Comment*: With a seizure in this time relation to a stroke (or brain infection or brain trauma) the literature[6] suggests a high (>70%) risk of another unprovoked seizure. Therefore, in the new (but not the old) definition, this man would have epilepsy.
3. *Photic seizures.* A 6-year-old boy has had two seizures 3 days apart while playing a videogame involving flashing lights. There have been no other seizures. EEG shows an abnormal photoparoxysmal response. *Comment*: This boy has epilepsy according to the new definition (but not the old), even though the seizures are provoked by lights, since there is an abnormal enduring predisposition to have seizures with light flashes.
4. *Benign Epilepsy with Centrotemporal Spikes (BECTS).* A 22-year-old man had seizures with face twitching when falling asleep at ages 9, 10, and 14 years; he has had none since. EEG at age 9 years demonstrated centrotemporal spikes. Medications were discontinued at age 16. *Comment*: For this young man, epilepsy is resolved, because of passing the relevant age range of an age-dependent syndrome. The old definition has no provision for considering epilepsy to be resolved.
5. *Single seizure and dysplasia*. A 40-year-old man had a focal seizure characterized by left hand twitching that progressed to a tonic–clonic seizure. This was his only seizure. Magnetic resonance imaging (MRI) shows a probable transmantle dysplasia in the right frontal lobe and EEG shows right frontotemporal interictal spikes. *Comment*: Although many clinicians would reasonably treat this man with antiseizure medications, the recurrence risk for seizures is not precisely known, and therefore epilepsy cannot yet be said to be present according to either definition. Future epidemiologic studies might clarify this situation.
6. *Two seizures long ago*. An 85-year-old man had a focal seizure at age 6 and another at age 8 years. EEG, MRI, blood tests, and family history were all unrevealing. He received antiseizure drugs from age 8 to age 10 years, when they were discontinued. There have been no further seizures. *Comment*: According to the new definition, epilepsy is resolved, since he has been seizure-free for >10 years and off seizure medication for at least the last 5 years. This is not a guarantee against future

seizures, but he has a right to be viewed as someone who does not currently have epilepsy.

7. *Long-interval seizures.* A 70-year-old woman had unprovoked seizures at ages 15 and 70. EEG, MRI, and family history are unremarkable. *Comment*: Both old and new definitions consider this woman to have epilepsy. Despite the diagnosis, many clinicians would not treat because of the low frequency of seizures. Should investigations somehow show that the causes of the two seizures were different, then epilepsy would not be considered to be present.
8. *Questionable information*. A 20-year-old man has had three unobserved episodes over 6 months consisting of sudden fear, difficulty talking, and a need to walk around. He is not aware of any memory loss during the episodes. There are no other symptoms. He has no risk factors for epilepsy and no prior known seizures. Routine EEG and MRI are normal. *Comment*: Declaring this man to have epilepsy is impossible by either the old or new definition. Focal seizures are on the differential diagnosis of his episodes, but both definitions of epilepsy require confidence that the person has had at least one seizure, rather than one of the imitators of seizures. Future discussions may define the boundaries of "possible and probable epilepsy."

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Notes

I. Specifying a level of risk for recurrence to quantify the concept of "enduring predisposition" was difficult for the Task Force. All agreed that an individual with two unprovoked seizures had epilepsy. The risk for a third seizure in such an individual is about 3 in 4, but the 95% confidence intervals are about 60–90%. Therefore, the Task Force agreed that an individual having a similar risk after one unprovoked seizure should logically be considered also to have epilepsy. The number >60% is intended to be an approximate guideline, rather than a sharp cutoff.

II. Some suggested a time limit within which the two spontaneous seizures must occur to diagnose epilepsy. In the absence of consensus and evidence on which to base a specific time, lifetime occurrence was retained as the default.

III. The motivation for this aspect of the definition was twofold. First, many clinicians, patients, and families consider epilepsy to be in the past when seizures no longer occur and no antiseizure medications are employed. Second, the Task Force desired to remove lasting stigma associated with a lifetime diagnosis of epilepsy. Other terms considered included remission, terminal remission, complete remission, inactive epilepsy, epilepsy absent, epilepsy not present, epilepsy no longer present, and cure. Many of these did not convey the concept that epilepsy was gone. Cure implied complete success of some treatment or passage of time, such that risk was that of the baseline population.

IV. Evidence to guide a specific required seizure-free number of years is limited, and existing risk functions show a continuous decline over time, rather than a natural breakpoint. Some argued for 5 years, but as many as 5% annually may have a seizure after a 5-year seizure-free interval. Being seizure-free for the most recent 10 years and off medications for the most recent 5 years predicts future freedom from seizures in a high percentage of cases.

V. Although evidence exists for a (low) relapse rate after 5 years of seizure freedom, no evidence was available at time of writing for relapse rates after being seizure-free for 10 years, which therefore was selected to be a time longer than 5 years, for which relapse rate would be consider likely very low.

VI. Whether to define a condition called "probable epilepsy," "possible epilepsy," or both, generated the most debate in the deliberations, and ultimately the issue was settled by majority view rather than full consensus. Probable epilepsy was considered for two different circumstances: the first in which one seizure had occurred and risks were high but not very high for having another. The second circumstance encompassed limited information in cases that seemed to be epilepsy, but reliable seizure descriptions or other key data were lacking. Allowing a diagnosis of probable epilepsy in the second circumstance could harmfully short-cut necessary diagnostics to clarify the diagnosis. The Task Force did see value in defining probable epilepsy, but believed that extensive future consideration would be needed in order to make its definition operationally consistent and useful.

VII. An earlier draft of the manuscript was posted for comments on the ILAE website. A total of 315 comments, some very extensive, were received. The majority of opinions were positive, but there also were some very thoughtful and strongly felt disagreements. It was considered

unreasonable to place a burden on a treating physician for knowing the precise risk for a subsequent seizure. The authors agreed with this criticism. Many commenters were for and many others against calling epilepsy a disease, rather than a disorder. This decision was commandeered by the respective IBE and ILAE Executive Committees in favor of the term "disease." The phrase "no longer present" was not embraced by those responding to comments, and it was changed to "resolved." Many commenters wished for epilepsy to be resolved at 5 years of seizure freedom, on or off antiseizure drugs. The Task Force wanted resolved to mean a risk sufficiently low that epilepsy could be put aside, and achieving that requires a more stringent time interval, so we settled on 10 years of seizure freedom, 5 years off medicines. Several commenters wanted to eliminate the slippery concept of provoked versus unprovoked seizures. Such a change would have been quite fundamental, altering our view of acute symptomatic seizures, now comprising 40% of all seizures. We left that discussion for another venue. In general, the authors believed that the "wisdom of the crowd" strengthened and clarified the arguments and, more importantly, moved the definition closer to how working clinicians think of epilepsy.

VIII. These examples were presented on June 24, 2013, to the audience of the ILAE Congress Presidential symposium, with >1,000 epileptologists in attendance. Audience votes on whether epilepsy was present in these cases correlated very strongly with the terms of the revised definition. Although not a scientifically valid survey, the responses indicated that epileptologists thought of epilepsy in ways consistent with the revised definition.

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ILAE COMMISSION REPORT

Instruction manual for the ILAE 2017 operational classification of seizure types

[1]Robert S. Fisher, [2]J. Helen Cross, [3]Carol D'Souza, [4]Jacqueline A. French, [5]Sheryl R. Haut, [6]Norimichi Higurashi, [7]Edouard Hirsch, [8]Floor E. Jansen, [9]Lieven Lagae, [10]Solomon L. Moshé, [11]Jukka Peltola, [12]Eliane Roulet Perez, [13]Ingrid E. Scheffer, [14]Andreas Schulze-Bonhage, [15]Ernest Somerville, [16]Michael Sperling, [17]Elza Márcia Yacubian, and [18,19]Sameer M. Zuberi on behalf of the ILAE Commission for Classification and Terminology

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Dr. Robert S. Fisher, past president of AES and editor of *Epilepsia* and epilepsy.com, led the Seizure Classification Task Force.

Summary

This companion paper to the introduction of the International League Against Epilepsy (ILAE) 2017 classification of seizure types provides guidance on how to employ the classification. Illustration of the classification is enacted by tables, a glossary of relevant terms, mapping of old to new terms, suggested abbreviations, and examples. Basic and extended versions of the classification are available, depending on the desired degree of detail. Key signs and symptoms of seizures (semiology) are used as a basis for categories of seizures that are focal or generalized from onset or with unknown onset. Any focal seizure can further be optionally characterized by whether awareness is retained or impaired. Impaired awareness during any segment of the seizure renders it a focal impaired awareness seizure. Focal seizures are further optionally characterized by motor onset signs and symptoms: atonic, automatisms, clonic, epileptic spasms, or hyperkinetic, myoclonic, or tonic activity. Nonmotor-onset seizures can manifest as autonomic, behavior arrest, cognitive, emotional, or sensory dysfunction. The earliest prominent manifestation defines the seizure type, which might then progress to other signs and symptoms. Focal seizures can become bilateral tonic–clonic. Generalized seizures engage bilateral networks from onset. Generalized motor seizure characteristics comprise atonic, clonic, epileptic spasms, myoclonic, myoclonic–atonic, myoclonic–tonic–clonic, tonic, or tonic–clonic. Nonmotor (absence) seizures are typical or atypical, or seizures that present prominent myoclonic activity or eyelid myoclonia. Seizures of unknown onset may have features that can still be classified as motor, nonmotor, tonic–clonic, epileptic spasms, or behavior arrest. This "users' manual" for the ILAE 2017 seizure classification will assist the adoption of the new system.

KEY WORDS: Classification, Seizures, Focal, Generalized, Epilepsy (taxonomy).

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[1]Stanford Department of Neurology & Neurological Sciences, Stanford, California, U.S.A.; [2]UCL-Institute of Child Health, Great Ormond Street Hospital for Children, London, United Kingdom; [3]Bombay Epilepsy Society, Mumbai, India; [4]Department of Neurology, NYU Langone School of Medicine, New York, New York, U.S.A.; [5]Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, New York, U.S.A.; [6]Department of Pediatrics, Jikei University School of Medicine, Tokyo, Japan; [7]Unite Francis Rohmer, Strasbourg, France; [8]Department of Pediatric Neurology, Brain Center Rudolf Magnus, University Medical Center, Utrecht, The Netherlands; [9]Pediatric Neurology, University Hospitals KU Leuven, Leuven, Belgium; [10]Saul R. Korey Department of Neurology, Department of Pediatrics and Dominick P. Purpura Department Neuroscience, Montefiore Medical Center, Bronx, New York, U.S.A.; [11]Department of Neurology, Tampere University Hospital, Tampere, Finland; [12]Pediatric Neurorehabilitation Unit, CHUV, Lausanne, Switzerland; [13]Florey Institute and University of Melbourne, Austin Health and Royal Children's Hospital, Melbourne, Victoria, Australia; [14]Epilepsy Center, University Medical Center Freiburg, Freiburg, Germany; [15]Faculty of Medicine, Prince of Wales Clinical School, University of New South Wales, Sydney, New South Wales, Australia; [16]Department of Neurology, Jefferson Comprehensive Epilepsy Center, Thomas Jefferson University, Philadelphia, Pennsylvania, U.S.A.; [17]Department of Neurology and Neurosurgery, Epilepsy Research and Treatment Unit, São Paulo, Brazil; [18]The Paediatric Neurosciences Research Group, Royal Hospital for Children, Glasgow, United Kingdom; and [19]College of Medicine, Veterinary & Life Sciences, University of Glasgow, Glasgow, United Kingdom

Address correspondence to Robert S. Fisher, Neurology, SNHC, Room 4865, 213 Quarry Road, Palo Alto, CA 94304, U.S.A. E-mail: robert.fisher@stanford.edu

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Key Points

- The ILAE provided a revised basic and expanded seizure type classification, with initial division into focal versus generalized onset or unknown onset seizures
- Focal seizures are optionally subdivided into focal aware and focal impaired awareness seizures. Specific motor and nonmotor classifiers may be added
- Generalized-onset seizures can be motor: tonic–clonic, clonic, tonic, myoclonic, myoclonic–tonic–clonic, myoclonic–atonic, atonic, and epileptic spasms
- Generalized-onset seizures can also be nonmotor (absence): typical absence, atypical absence, myoclonic absence, or absence with eyelid myoclonia
- Additional descriptors and free text are encouraged to characterize the seizures. Mapping of old to new terms can facilitate adoption of the new terminology

The International League Against Epilepsy (ILAE) has released a 2017 version of seizure-type classification (accompanying manuscript). Revision of the classification that has been used in modified form since 1981[1] was motivated by several factors. Some seizure types, for example tonic seizures or epileptic spasms, can have either a focal or generalized onset. Lack of knowledge about the onset makes a seizure unclassifiable. Some terms used to classify seizures lack community acceptance or public understanding, including "dyscognitive," "psychic," "partial," "simple partial," and "complex partial." Determining whether a person has impaired consciousness during a seizure can be confusing for nonclinicians. Some important seizure types are not included in the 1981 classification. The new classification addresses these relevant issues. Material that follows explains how to apply the 2017 seizure-type classification.

Methods

Classification of a seizure begins with historical elicitation or observation of certain symptoms and signs (sometimes referred to as the semiology of seizures) that are known to be associated with common seizures. The key symptoms and signs cannot be matched in one-to-one relationships with seizure types because some symptoms appear in more than one seizure type. Behavior arrest, for example, occurs in both focal impaired awareness seizures and absence seizures. Tonic–clonic activity can be present from onset in a generalized seizure or emerge in the course of a focal-onset seizure. Conversely, a seizure type often associates with multiple symptoms. Naming a seizure type an "automatism seizure" would not allow the distinction between a focal seizure with impaired awareness and an absence seizure. Because these two seizure types are treated differently and have different prognoses, maintenance of distinct seizure types is useful, even though some interpretation beyond direct observation may be needed to classify the seizures. Distinction of seizure types usually can be made by recognizing a characteristic sequence of symptoms and other clinical observations. Typical absence seizures, for instance, show more rapid recovery of function than do focal impaired awareness seizures. In some instances, ancillary information from electroencephalography (EEG), imaging, or laboratory studies is needed to properly classify a seizure. For these cases, classification of seizure type begins to merge imperceptibly with diagnosis of epilepsy syndromes.[2,3] Because we lack a fundamental pathophysiologic understanding of differing seizure presentations, grouping of symptoms and signs into seizure types reflects an operational opinion about which groupings are sufficiently distinct and common as to merit a specific name.[4] This classification is derived for practical clinical use, but it also can be used by researchers and other groups with specific purposes.

Results

The ILAE 2017 seizure classification presents basic and expanded versions, depending on the desired degree of detail. The basic version is the same as the expanded version, but with collapse of the subcategories.

Basic classification

Figure 1 shows the basic classification. Seizures are first categorized by type of onset. Focal-onset seizures are defined as "originating within networks limited to one hemisphere. They may be discretely localized or more widely distributed. Focal seizures may originate in subcortical structures." Generalized from onset seizures are defined as "originating at some point within, and rapidly engaging, bilaterally distributed networks."[5] A seizure of unknown onset may still evidence certain defining motor (e.g., tonic–clonic) or nonmotor (e.g., behavior arrest) characteristics. With further information or future observed seizures, a reclassification of unknown-onset seizures into focal or generalized-onset categories may become possible. Therefore, "unknown-onset" is not a characteristic of the seizure, but a convenient placeholder for our ignorance. When a seizure type begins with the words "focal," "generalized," or "absence," then the word "onset" may be presumed.

Further classification is optional. The next level of focal seizure classification is by level of awareness. Awareness is operationally defined as knowledge of self and environment. Assay of awareness is a pragmatic surrogate marker used to determine whether level of consciousness is impaired. During a focal aware seizure, consciousness will be intact. Awareness specifically refers to awareness during a seizure, and not to awareness of whether a seizure has

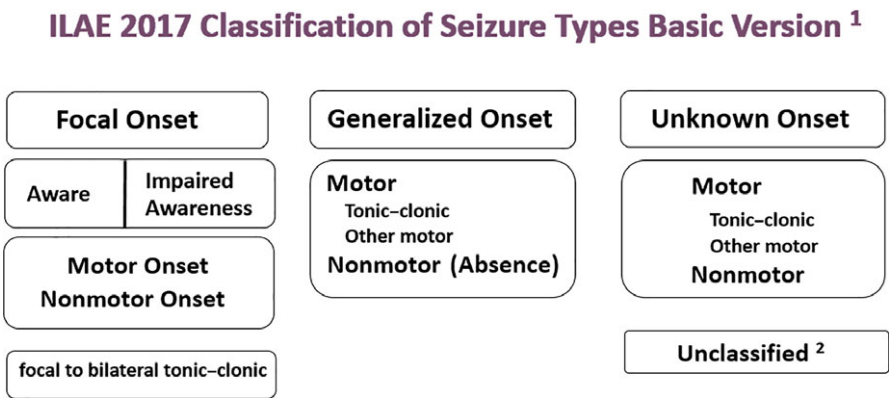

Figure 1.
The basic ILAE 2017 operational classification of seizure types. [1]Definitions, other seizure types, and descriptors are listed in the accompanying paper and glossary of terms. [2]Due to inadequate information or inability to place in other categories.
Epilepsia © ILAE

occurred. If awareness of the event is impaired for *any portion* of the seizure, then the seizure is classified as a focal seizure with impaired awareness. As a practical matter, a focal aware seizure implies the ability of the person having the seizure to later verify retained awareness. Occasional seizures may produce transient epileptic amnesia[6] with retained awareness, but classification of such seizures would require exceptionally clear documentation by observers. Some might use the shorthand "focal unaware." In doing so, it is crucial to note that awareness may be impaired without being fully absent. Word order is not important, so "focal aware seizure" means the same thing as a "focal seizure with retained awareness."

Responsiveness is a separate clinical attribute that can be either intact or impaired for seizures with or without retained awareness. Although responsiveness is an important descriptive aspect of seizures, it is not used in the ILAE 2017 classification to designate specific seizure types. The basic classification further allows classification into motor onset or nonmotor-onset (for example, sensory) symptoms. Further specification invokes the expanded classification, discussed below.

The seizure type "focal to bilateral tonic–clonic" is in a special category because of its common occurrence and importance, even though it is reflective of a propagation pattern of seizure activity rather than a unique seizure type. The phrase "focal to bilateral tonic–clonic" replaces the older term "secondarily generalized tonic–clonic." In the new classification, "bilateral" is used for propagation patterns of seizures and "generalized" for seizures of generalized onset.

Generalized-onset seizures are divided into motor and nonmotor (absence) seizures. Level of awareness is not used as a classifier for generalized seizures, since the large majority (although not all) of generalized seizures are associated with impaired awareness. By definition of the generalized branch of the classification, motor activity should be bilateral from the onset, but in the basic classification, the type of motor activity need not be specified. In cases where bilateral onset of motor activity is asymmetrical, it may be difficult in practice to determine whether a seizure has focal or generalized onset.

Absence seizures (the prefix "generalized onset" may be assumed) present with a sudden cessation of activity and awareness. Absence seizures tend to occur in younger age groups, have more sudden start and termination, and they usually display less complex automatisms than do focal seizures with impaired awareness, but the distinctions are not absolute. EEG information may be required for accurate classification. Focal epileptiform activity may be seen with focal seizures and bilaterally synchronous spike-waves with absence seizures.

Seizures of unknown onset can be categorized as motor, including tonic–clonic, nonmotor, or unclassified. The term unclassified comprises both seizures with patterns that do not fit into the other categories or seizures presenting insufficient information to allow categorization.

Expanded classification

The expanded classification (Fig. 2) provides another level of seizure names, built on the framework of the basic classification. The vertical organization of the focal-onset category is not hierarchical, since naming the level of awareness is optional. A focal seizure can be classified as focal aware (corresponding to the 1981 term "simple partial seizure") or focal impaired awareness (corresponding to the 1981 term "complex partial seizure"). Focal aware or impaired awareness seizures can optionally be classified by adding one of the motor onset or nonmotor-onset terms below, reflecting the earliest prominent sign or symptom other than awareness. Alternatively, a focal seizure name can omit mention of awareness as being inapplicable or unknown and classify the focal seizure directly by the earliest motor or nonmotor characteristic.

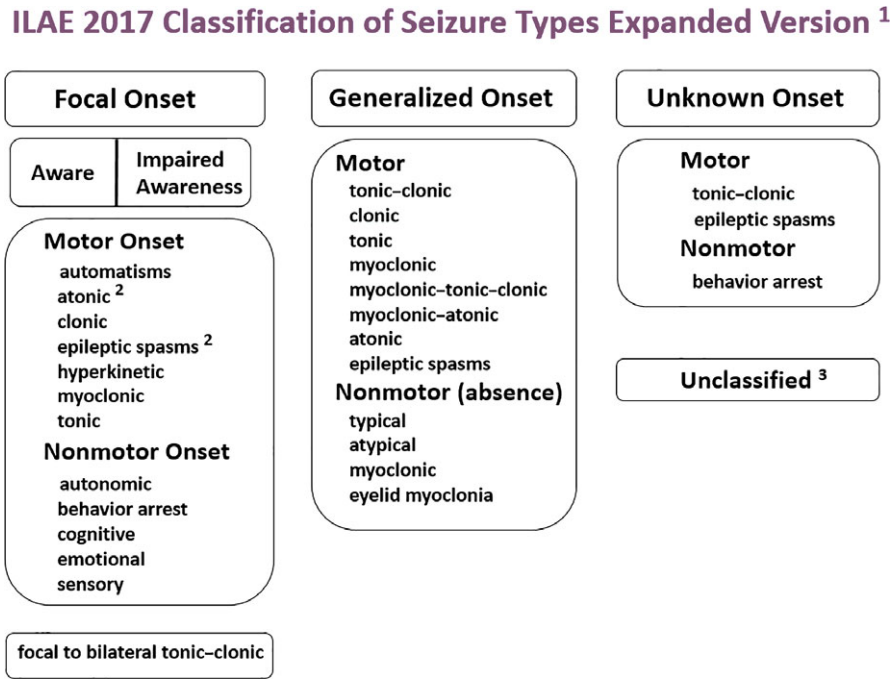

Figure 2.
The expanded ILAE 2017 operational classification of seizure types. The following clarifications should guide the choice of seizure type. For focal seizures, specification of level of awareness is optional. Retained awareness means the person is aware of self and environment during the seizure, even if immobile. A focal aware seizure corresponds to the prior term simple partial seizure. A focal impaired awareness seizure corresponds to the prior term complex partial seizure, and impaired awareness during any part of the seizure renders it a focal impaired awareness seizure. Focal aware or impaired awareness seizures optionally may further be characterized by one of the motor-onset or nonmotor-onset symptoms below, reflecting the first prominent sign or symptom in the seizure. Seizures should be classified by the earliest prominent feature, except that a focal behavior arrest seizure is one for which cessation of activity is the dominant feature throughout the seizure. In addition, a focal seizure name can omit mention of awareness when awareness is not applicable or unknown, and thereby classify the seizure directly by motor-onset or nonmotor-onset characteristics. Atonic seizures and epileptic spasms would usually not have specified awareness. Cognitive seizures imply impaired language or other cognitive domains or positive features such as déjà vu, hallucinations, illusions, or perceptual distortions. Emotional seizures involve anxiety, fear, joy, other emotions, or appearance of affect without subjective emotions. An absence is atypical because of slow onset or termination or significant changes in tone supported by atypical, slow, generalized spike and wave on the EEG. A seizure may be unclassified due to inadequate information or inability to place the type in other categories. [1]Definitions, other seizure types, and descriptors are listed in the accompanying paper and glossary of terms. [2]Degree of awareness usually is not specified. [3]Due to inadequate information or inability to place in other categories.

For focal-onset seizures, the clinician should assay level of awareness as described for the basic classification. Ask the patient whether awareness for events occurring during the seizures was retained or impaired, even when the person seizing was unresponsive or unable to understand language. If someone walked into the room during a seizure, would that person's presence later be recalled? Questioning witnesses may clarify the nature of behavior during the seizure. It is important to attempt to distinguish the ictal versus the postictal state, since awareness returns during the latter. If the state of awareness is uncertain, as, for example, is usually the case for atonic or epileptic spasm seizures, the seizure is classified as focal but awareness would not be specified. Description of level of awareness is optional and applied only when known. A "focal aware seizure," with or without further characterization, corresponds to the old term "simple partial seizure" and a "focal impaired awareness seizure" corresponds to the old term "complex partial seizure." Subsequent terms in the focal column of the expanded classification can further specify the type of focal aware and focal impaired awareness seizures. Alternatively, the degree of awareness can be left unspecified and a seizure classified as a focal seizure with one of the motor onset or nonmotor-onset characteristics listed in Figure 2.

Focal motor onset behaviors include these activities: atonic (focal loss of tone), tonic (sustained focal stiffening), clonic (focal rhythmic jerking), myoclonic (irregular, brief focal jerking), or epileptic spasms (focal flexion or extension of arms and flexion of trunk). The distinction between clonic and myoclonic is somewhat arbitrary, but clonic implies sustained, regularly spaced stereotypical jerks, whereas, myoclonus is less regular and in briefer runs. Other less obviously focal motor behaviors include hyperkinetic (pedaling, thrashing) activity and automatisms. An

automatism is a more or less coordinated, purposeless, repetitive motor activity. Observers should be asked whether the subject demonstrated repetitive purposeless fragments of behaviors that might appear normal in other circumstances. Some automatisms overlap other motor behaviors, for instance, pedaling or hyperkinetic activity, thereby rendering classification ambiguous. The 2017 ILAE classification arbitrarily groups pedaling activity with hyperkinetic seizures, rather than with automatism seizures. Automatisms may be seen in focal seizures and in absence seizures.

A focal motor seizure with behavior arrest involves cessation of movement and unresponsiveness. Because brief behavioral arrest at the start of many seizures is common and difficult to identify, a focal behavioral arrest seizure should comprise behavioral arrest as the predominant aspect of the *entire* seizure. Focal autonomic seizures present with gastrointestinal sensations, a sense of heat or cold, flushing, piloerection (goosebumps), palpitations, sexual arousal, respiratory changes, or other autonomic effects. Focal cognitive seizures can be identified when the patient reports or exhibits deficits in language, thinking or associated higher cortical functions during seizures and when these symptoms outweigh other manifestations of the seizure. Déjà vu, jamais vu, hallucinations, illusions, and forced thinking are examples of induced abnormal cognitive phenomena. A more correct, although less euphonious, term would be "focal impaired cognition seizure," but impaired cognition may be assumed, since seizures never improve cognitive function. Focal emotional seizures present with emotional changes, including fear, anxiety, agitation, anger, paranoia, pleasure, joy, ecstasy, laughing (gelastic), or crying (dacrystic). Some of these phenomena are subjective and must be recalled and reported by the patient or caregiver. Emotional symptoms comprise a subjective component, whereas, affective signs may or may not be accompanied by subjective emotionality. Impairment of awareness for events during the seizure does not classify the seizure as a focal cognitive seizure, because impairment of awareness can apply to any focal seizure. A focal sensory seizure can produce somatosensory, olfactory, visual, auditory, gustatory, hot–cold sense, or vestibular sensations.

The clinician must decide whether an event is a unified single seizure, with evolving manifestations as the seizure propagates, or alternatively, two separate seizures. Such a distinction can sometimes be difficult. A smooth, continuous evolutions of signs, symptoms, and EEG patterns (where available) favors the event being a single seizure. Repetition of a stereotyped sequence of signs, symptoms, and EEG changes at different times supports a unitary seizure type. Unitary focal seizures are named for the initial manifestation and presence or absence of altered consciousness at any point during the seizure. In contrast, discontinuous, interrupted or nonstereotyped events point to classification of more than one seizure type. Consider an event starting with déjà vu, repetitive purposeless lip-smacking, loss of awareness, forced version to the right, and right-arm stiffening. This steady evolution implies a unitary seizure, which would be classified as a focal impaired awareness cognitive seizure. It would be useful to append (as optional description, not a seizure type) information about the progression to automatisms and tonic version. In another scenario, the clinician might encounter a seizure with fear and loss of awareness. The patient recovers and 30 min later has an event with tingling in the right arm during clear awareness. Such a sequence reflects two separate seizures, the first being a focal impaired awareness emotional seizure and the second a focal aware sensory seizure.

Other focal seizure types are sometimes encountered, for example, focal tonic–clonic seizures, but not sufficiently often to be named as a specific seizure type. Rather than include the term "other" in each category, a decision was made to revert to nonspecific use of the larger category, such as motor onset or nonmotor-onset when the next level of detail is unclear or the seizure is not listed as a specific seizure type.

The classification of generalized-onset seizures is similar to that of the 1981 classification, with addition of a few new types. Awareness usually is impaired with generalized onset seizures, so level of awareness is not used as a classifier for these seizures. The main subdivision is into motor and nonmotor (absence) seizure types. The terms "motor" and "nonmotor (absence)" are present in order to allow characterization of generalized-onset motor or nonmotor seizures about which nothing else can be said, but "motor" and "nonmotor (absence)" may be omitted if the seizure name is unambiguous, for example, "generalized tonic seizure." The word "generalized" can be omitted for seizures such as absence that present only with generalized onset.

Tonic–clonic remains the term replacing the "grand mal" seizure type, although popular usage of the old French phrase will undoubtedly persist. Because there is a new seizure type characterized by myoclonic movements preceding tonic (stiffening) and clonic (sustained rhythmic jerking) movements, it is important to document the early movements of a tonic–clonic seizure as being tonic. The clonic phase of a tonic–clonic seizure typically shows regularly decreasing frequency of jerks over the course of the event. During a tonic–clonic seizure, awareness is lost before or contemporaneously with the stiffening and jerking movements. Some tonic–clonic seizures may invoke a nonspecific feeling of an impending seizure or a brief period of head or limb version, neither of which invalidates a generalized onset, since biologic processes never exhibit perfect synchrony. The clinician has to judge whether a truly focal onset is present.

Generalized clonic seizures begin, progress, and end with sustained rhythmic jerking of limbs on both sides of the body and often head, neck, face, and trunk. Generalized clonic seizures are much less common than are tonic–clonic seizures, usually occur in infants, and should be distinguished from jitteriness or shuddering attacks.[7]

Generalized tonic seizures manifest as bilateral limb stiffening or elevation, often with neck stiffening. The classification presumes that the tonic activity is not followed by clonic movements. The tonic activity can be a sustained abnormal posture, either in extension or flexion, sometimes accompanied by tremor of the extremities. Tonic activity can be difficult to distinguish from dystonic activity, defined as sustained contractions of both agonist and antagonist muscles producing athetoid or twisting movements, which when prolonged, may produce abnormal postures.

Generalized myoclonic seizures can occur in isolation or in conjunction with tonic or atonic activity. Myoclonus differs from clonus by being briefer and not regularly repetitive. Myoclonus as a symptom has possible epileptic and nonepileptic etiologies.

Generalized myoclonic–tonic–clonic seizures begin with a few myoclonic jerks followed by tonic–clonic activity. These seizures are commonly seen in patients with juvenile myoclonic epilepsy[8] and occasionally with other generalized epilepsies. It is arguable whether the initial jerks are myoclonic or clonic, but they are rarely sufficiently sustained to be considered clonic.

A myoclonic–atonic seizure involves brief jerking of limbs or trunk, followed by a limp drop. These seizures, previously called myoclonic–astatic seizures, are most commonly seen in Doose syndrome,[9] but can also be encountered in Lennox-Gastaut and other syndromes.

Atonic means without tone. When leg tone is lost during a generalized atonic seizure, the patient falls on the buttocks or sometimes forward onto the knees and face. Recovery is usually within seconds. In contrast, tonic or tonic–clonic seizures more typically propel the patient into a backward fall.

Epileptic spasms previously were referred to as infantile spasms, and the term "infantile spasms" remains suitable for epileptic spasms occurring at infantile age. An epileptic spasm presents as a sudden flexion, extension, or mixed extension–flexion of predominantly proximal and truncal muscles. They commonly occur in clusters and most often during infancy.

Generalized nonmotor seizure types comprise several varieties of absence seizures. The Task Force retained the distinction between typical and atypical absence, because the two types of seizures usually are associated with different EEG findings, epilepsy syndromes, therapies, and prognoses. According to the 1981 classification, which was based on analysis of numerous video-EEG recordings,[1] absence seizures are considered atypical when they are associated with changes in tone that are more pronounced than in typical absence or the onset or cessation is not abrupt. An EEG may be required to secure the distinction between typical and atypical absence seizures.

A myoclonic absence seizure[10] refers to an absence seizure with rhythmic three-per-second myoclonic movements, causing ratcheting abduction of the upper limbs leading to progressive arm elevation, and associated with three-per-second generalized spike-wave discharges. Duration is typically 10–60 s. Impairment of consciousness may not be obvious. Myoclonic absence seizures occur in a variety of genetic conditions and also without known associations.

Eyelid myoclonia are myoclonic jerks of the eyelids and upward deviation of the eyes, often precipitated by closing the eyes or by light. Eyelid myoclonia can be associated with absences, but also can be motor seizures without a corresponding absence, making them difficult to categorize. The 2017 classification groups them with nonmotor (absence) seizures, which may seem counterintuitive, but the myoclonia in this instance is meant to link with absence, rather than with nonmotor. Absence seizures with eyelid myoclonia, seizures, or EEG paroxysms induced by eye closure and photosensitivity constitutes the triad of Jeavons syndrome.[11]

Seizures of unknown onset can be motor or nonmotor. The most important use of this classification is for tonic–clonic seizures for which the beginning was obscured. Further information might allow reclassification as a focal or generalized-onset seizure. Epileptic spasms and behavior arrest are other possible seizure types of unknown onset. Epileptic spasms may require detailed video-EEG monitoring to clarify the nature of onset, but doing so is important because a focal onset may correspond to a treatable focal pathology. An unknown-onset behavior arrest seizure could represent a *focal impaired awareness behavior arrest seizure* or an *absence seizure*. A seizure might be unclassified due to inadequate information or inability to place the seizure in other categories. If an event is not clearly a seizure, then it should not be called an unclassified seizure; rather, this classification is reserved for unusual events likely to be seizures, but not otherwise characterized.

Every seizure classification involves some degree of uncertainty. The Task Force adopted the general guideline of an 80% level of certainty that onset was focal or generalized; otherwise, the seizure should be listed as of unknown onset. The 80% level was chosen arbitrarily to match the commonly applied 80% false-negative cutoff for statistical analysis.

Common descriptors

Focal seizures provoke a variety of potential sensations and behaviors too diverse to be incorporated into a classification. To facilitate a common terminology about seizures, the Task Force listed some common descriptors of behaviors during focal seizures (Table 1), but these are not intrinsic to the classification. In other words, the common descriptors can be added to the seizure classification to clarify the manifestations of individual seizures, but the descriptors do not define unique seizure types in this classification. Descriptors are therefore at a "lower level" than are signs, such as tonic, that define a seizure type. Laterality is a

Table 1. Common descriptors of behaviors during and after seizures (alphabetically)

Cognitive	Automatisms
Acalculia	Aggression
Aphasia	Eye-blinking
Attention impairment	Head-nodding
Déjà vu or jamais vu	Manual
Dissociation	Oral-facial
Dysphasia	Pedaling
Hallucinations	Pelvic thrusting
Illusions	Perseveration
Memory impairment	Running (cursive)
Neglect	Sexual
Forced thinking	Undressing
Responsiveness impairment	Vocalization/speech
	Walking
Emotional or affective	Motor
Agitation	Dysarthria
Anger	Dystonic
Anxiety	Fencer's posture (figure-of-4)
Crying (dacrystic)	Incoordination
Fear	Jacksonian
Laughing (gelastic)	Paralysis
Paranoia	Paresis
Pleasure	Versive
Autonomic	Sensory
Asystole	Auditory
Bradycardia	Gustatory
Erection	Hot-cold sensations
Flushing	Olfactory
Gastrointestinal	Somatosensory
Hyper/hypoventilation	Vestibular
Nausea or vomiting	Visual
Pallor	
Palpitations	Laterality
Piloerection	Left
Respiratory changes	Right
Tachycardia	Bilateral

special type of descriptor, but an important one in clinical practice. The Task Force acknowledged the importance of a detailed individual free-text description of a seizure, in addition to the classification.

Glossary

Table 2 provides a glossary of terms used in this and the accompanying paper. The definitions are not universal, but are focused on the aspects of language pertinent to seizures. For instance, sensory is defined in terms of sensory seizures, not all sensation. Wherever possible, prior accepted definitions from the ILAE glossary of 2001[12] were maintained, in order to support continuity of usage, but this glossary updates some terminology. Reference can be made to earlier literature for definitions of old terms. Terms no longer recommended for use are omitted.

Mapping old to new terms

Table 3 provides mapping of old official and popular terms to the 2017 seizure type classification.

Abbreviations

Table 4 provides suggested abbreviations for the main seizure types.

Summary of rules for classifying seizures

1. Onset: Decide whether seizure onset is focal or generalized, using an 80% confidence level. Otherwise, onset is unknown.
2. Awareness: For focal seizures, decide whether to classify by degree of awareness or to omit awareness as a classifier. *Focal aware seizures* correspond to the old *simple partial seizures and focal impaired awareness seizures* to the old *complex partial seizures*.
3. Impaired awareness at any point: A focal seizure is *a focal impaired awareness seizure* if awareness is impaired at any point during the seizure.
4. Onset predominates: Classify a focal seizure by its first prominent sign or symptom. Do not count transient behavior arrest.
5. Behavior arrest: A *focal behavior arrest seizure* shows arrest of behavior as the prominent feature of the entire seizure.
6. Motor/nonmotor: A *focal aware or impaired awareness seizure* may be further subclassified by motor or nonmotor characteristics. Alternatively, a focal seizure can be characterized by motor or nonmotor characteristics, without specifying level of awareness. Example, a *focal tonic seizure*.
7. Optional terms: Terms such as motor or nonmotor may be omitted when the seizure type is otherwise unambiguous.
8. Additional descriptors: After classifying seizure type based on initial manifestations, it is encouraged to add descriptions of other signs and symptoms, suggested descriptors or free text. These do not alter the seizure type. Example: *focal emotional seizure* with tonic right arm activity and hyperventilation.
9. Bilateral versus generalized: Use the term "bilateral" for tonic–clonic seizures that propagate to both hemispheres and "generalized" for seizures that apparently originate simultaneously in both hemispheres.
10. Atypical absence: Absence is atypical if it has slow onset or offset, marked changes in tone, or EEG spike-waves at <3 per second.
11. Clonic versus myoclonic: Clonic refers to sustained rhythmic jerking and myoclonic to regular unsustained jerking.
12. Eyelid myoclonia: *Absence with eyelid myoclonia* refers to forced upward jerking of the eyelids during an absence seizure.

Table 2. Glossary of terms

Word	Definition	Source
Absence, typical	A sudden onset, interruption of ongoing activities, a blank stare, possibly a brief upward deviation of the eyes. Usually the patient will be unresponsive when spoken to. Duration is a few seconds to half a minute with very rapid recovery. Although not always available, an EEG would show generalized epileptiform discharges during the event. An absence seizure is by definition a seizure of generalized onset. The word is not synonymous with a blank stare, which also can be encountered with focal onset seizures	Adapted from Ref. 12
Absence, atypical	An absence seizure with changes in tone that are more pronounced than in typical absence or the onset and/or cessation is not abrupt, often associated with slow, irregular, generalized spike-wave activity	Adapted from Ref. 11
Arrest	See behavior arrest	New
Atonic	Sudden loss or diminution of muscle tone without apparent preceding myoclonic or tonic event lasting ~1–2 s, involving head, trunk, jaw, or limb musculature	12
Automatism	A more or less coordinated motor activity usually occurring when cognition is impaired and for which the subject is usually (but not always) amnesic afterward. This often resembles a voluntary movement and may consist of an inappropriate continuation of preictal motor activity	12
Autonomic seizure	A distinct alteration of autonomic nervous system function involving cardiovascular, pupillary, gastrointestinal, sudomotor, vasomotor, and thermoregulatory functions	Adapted from Ref. 12
Aura	A subjective ictal phenomenon that, in a given patient, may precede an observable seizure (popular usage)	12
Awareness	Knowledge of self or environment	New
Bilateral	Both left and right sides, although manifestations of bilateral seizures may be symmetric or asymmetric	New
Clonic	Jerking, either symmetric or asymmetric, that is regularly repetitive and involves the same muscle groups	Adapted from Ref. 12
Cognitive	Pertaining to thinking and higher cortical functions, such as language, spatial perception, memory, and praxis. The previous term for similar usage as a seizure type was psychic	New
Consciousness	A state of mind with both subjective and objective aspects, comprising a sense of self as a unique entity, awareness, responsiveness, and memory	New
Dacrystic	Bursts of crying, which may or may not be associated with sadness	12
Dystonic	Sustained contractions of both agonist and antagonist muscles producing athetoid or twisting movements, which may produce abnormal postures	Adapted from Ref. 12
Emotional seizures	Seizures presenting with an emotion or the appearance of having an emotion as an early prominent feature, such as fear, spontaneous joy or euphoria, laughing (gelastic), or crying (dacrystic)	New
Epileptic spasms	A sudden flexion, extension, or mixed extension–flexion of predominantly proximal and truncal muscles that is usually more sustained than a myoclonic movement but not as sustained as a tonic seizure. Limited forms may occur: Grimacing, head nodding, or subtle eye movements. Epileptic spasms frequently occur in clusters. Infantile spasms are the best known form, but spasms can occur at all ages	Adapted from Ref. 12
Epilepsy	A disease of the brain defined by any of the following conditions: (1) At least two unprovoked (or reflex) seizures occurring >24 h apart; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; (3) diagnosis of an epilepsy syndrome. Epilepsy is considered to be resolved for individuals who had an age-dependent epilepsy syndrome but are now past the applicable age or those who have remained seizure free for the last 10 years, with no antiseizure medicines for the last 5 years	3
Eyelid myoclonia	Jerking of the eyelids at frequencies of at least 3 per second, commonly with upward eye deviation, usually lasting <10 s, often precipitated by eye closure. There may or may not be associated brief loss of awareness	New
Fencer's posture seizure	A focal motor seizure type with extension of one arm and flexion at the contralateral elbow and wrist, giving an imitation of swordplay with a foil. This has also been called a supplementary motor area seizure	New
Figure-of-4 seizure	Upper limbs with extension of the arm (usually contralateral to the epileptogenic zone) with elbow flexion of the other arm, forming a figure-of-4	New
Focal	Originating within networks limited to one hemisphere. They may be discretely localized or more widely distributed. Focal seizures may originate in subcortical structures	5
Focal onset bilateral tonic–clonic seizure	A seizure type with focal onset, with awareness or impaired awareness, either motor or non-motor, progressing to bilateral tonic–clonic activity. The prior term was seizure with partial onset with secondary generalization	New

Continued

Table 2. Continued.

Word	Definition	Source
Gelastic	Bursts of laughter or giggling, usually without an appropriate affective tone	12
Generalized	Originating at some point within, and rapidly engaging, bilaterally distributed networks	5
Generalized tonic–clonic	Bilateral symmetric or sometimes asymmetric tonic contraction and then bilateral clonic contraction of somatic muscles, usually associated with autonomic phenomena and loss of awareness. These seizures engage networks in both hemispheres at the start of the seizure	Adapted from Refs 5, 12
Hallucination	A creation of composite perceptions without corresponding external stimuli involving visual, auditory, somatosensory, olfactory, and/or gustatory phenomena. Example: "Hearing" and "seeing" people talking	12
Behavior arrest	Arrest (pause) of activities, freezing, immobilization, as in behavior arrest seizure	New
Immobility	See activity arrest	New
Impaired awareness	See awareness. Impaired or lost awareness is a feature of focal impaired awareness seizures, previously called complex partial seizures	New
Impairment of consciousness	See impaired awareness	New
Jacksonian seizure	Traditional term indicating spread of clonic movements through contiguous body parts unilaterally	12
Motor	Involves musculature in any form. The motor event could consist of an increase (positive) or decrease (negative) in muscle contraction to produce a movement	12
Myoclonic	Sudden, brief (<100 msec) involuntary single or multiple contraction(s) of muscles(s) or muscle groups of variable topography (axial, proximal limb, distal). Myoclonus is less regularly repetitive and less sustained than is clonus	Adapted from Ref. 12
Myoclonic–atonic	A generalized seizure type with a myoclonic jerk leading to an atonic motor component. This type was previously called myoclonic–astatic	New
Myoclonic–tonic–clonic	One or a few jerks of limbs bilaterally, followed by a tonic–clonic seizure. The initial jerks can be considered to be either a brief period of clonus or myoclonus. Seizures with this characteristic are common in juvenile myoclonic epilepsy	Derived from Ref. 1
Nonmotor	Focal or generalized seizure types in which motor activity is not prominent	New
Propagation	Spread of seizure activity from one place in the brain to another, or engaging of additional brain networks	New
Responsiveness	Ability to appropriately react by movement or speech when presented with a stimulus	New
Seizure	A transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain	4
Sensory seizure	A perceptual experience not caused by appropriate stimuli in the external world	12
Spasm	See epileptic spasm	
Tonic	A sustained increase in muscle contraction lasting a few seconds to minutes	12
Tonic–clonic	A sequence consisting of a tonic followed by a clonic phase	12
Unaware	The term unaware can be used as shorthand for impaired awareness	New
Unclassified	Referring to a seizure type that cannot be described by the ILAE 2017 classification either because of inadequate information or unusual clinical features. If the seizure is unclassified because the type of onset is unknown, a limited classification may still derive from observed features	New
Unresponsive	Not able to react appropriately by movement or speech when presented with stimulation	New
Versive	A sustained, forced conjugate ocular, cephalic, and/or truncal rotation or lateral deviation from the midline	12

New, a new definition, created in this article.

Examples

1 Tonic–clonic: A woman awakens to find her husband having a seizure in bed. The onset is not witnessed, but she is able to describe bilateral stiffening followed by bilateral shaking. EEG and magnetic resonance imaging (MRI) findings are normal. This seizure is classified as *unknown onset tonic–clonic*. There is no supplementary information to determine if the onset was focal or generalized. In the old classification, this seizure would have been unclassifiable with no further qualifiers.

2 Focal onset bilateral tonic–clonic: In an alternate scenario of case 1, the EEG shows a clear right parietal slow-wave focus. The MRI shows a right parietal region of cortical dysplasia. In this circumstance, the seizure can be classified as *focal to bilateral tonic–clonic*, despite the absence of an observed onset, because a focal etiology has been identified, and the overwhelming likelihood is that the seizure had a focal onset. The old classification would have classified this seizure as partial onset, secondarily generalized.

3 Absence: A child is diagnosed with Lennox-Gastaut syndrome of unknown etiology. EEG shows runs of slow spike-waves. Seizure types include absence, tonic, and focal motor seizures. The absence seizures are prolonged, have indistinct onset and cessation, and sometimes result in falls. In this case, the absence seizures are

Table 3. Mapping of old to new seizure classifying terms

Old term for seizure	New term for seizure [choice] (optional)
Absence	**(Generalized) absence**
Absence, atypical	(Generalized) absence, atypical
Absence, typical	(Generalized) absence, typical
Akinetic	Focal behavior arrest, generalized absence
Astatic	[Focal/generalized] atonic
Atonic	**[Focal/generalized] atonic**
Aura	Focal aware
Clonic	[Focal/generalized] clonic
Complex partial	**Focal impaired awareness**
Convulsion	[Focal/generalized] motor [tonic–clonic, tonic, clonic], focal to bilateral tonic–clonic
Dacrystic	Focal [aware or impaired awareness] emotional (dacrystic)
Dialeptic	Focal impaired awareness
Drop attack	[Focal/generalized] atonic, [focal/generalized] tonic
Fencer's posture (asymmetric tonic)	Focal [aware or impaired awareness] motor tonic
Figure-of-4	Focal [aware or impaired awareness] motor tonic
Freeze	Focal [aware or impaired awareness] behavior arrest
Frontal lobe[a]	Focal
Gelastic	Focal [aware or impaired awareness] emotional (gelastic)
Grand mal	**Generalized tonic–clonic, focal to bilateral tonic–clonic, unknown-onset tonic–clonic**
Gustatory	Focal [aware or impaired awareness] sensory (gustatory)
Infantile spasms	**[Focal/generalized/unknown] onset epileptic spasms**
Jacksonian	Focal aware motor (Jacksonian)
Limbic	Focal impaired awareness
Major motor	Generalized tonic–clonic, focal-onset bilateral tonic–clonic
Minor motor	Focal motor, generalized myoclonic
Myoclonic	**[Focal/generalized] myoclonic**
Neocortical[a]	Focal aware or focal impaired awareness
Occipital lobe[a]	Focal
Parietal lobe[a]	Focal
Partial	Focal
Petit mal	**Absence**
Psychomotor	**Focal impaired awareness**
Rolandic	Focal aware motor, focal to bilateral tonic–clonic
Salaam	[Focal/generalized/unknown onset] epileptic spasms
Secondarily generalized Tonic–clonic	Focal to bilateral tonic–clonic
Simple partial	**Focal aware**
Supplementary motor	Focal motor tonic
Sylvian	Focal motor
Temporal lobe[a]	**Focal aware/impaired awareness**
Tonic	**[Focal/generalized] tonic**
Tonic–clonic	**[Generalized/unknown] onset tonic–clonic, focal to bilateral tonic–clonic**
Uncinate	Focal [aware impaired awareness] sensory (olfactory)

Note that there is not a one-to-one correspondence, reflecting reorganization as well as renaming.

The most important terms are set in bold.

[a]Anatomic classification may still be useful for some purposes, for example, in evaluation for epilepsy surgery.

Table 4. Abbreviations for the most important seizure types

Seizure type	Abbreviations
Focal aware seizure	FAS
Focal impaired awareness seizure	FIAS
Focal motor seizure	FMS
Focal nonmotor seizure	FNMS
Focal epileptic spasm	FES
Focal to bilateral tonic–clonic seizure	FBTCS
Generalized tonic–clonic seizure	GTCS
Generalized absence seizure	GAS
Generalized motor seizure	GMS
Generalized epileptic spasm	GES
Unknown onset tonic–clonic seizure	UTCS

classified as *atypical absence* due to their characteristics, the EEG pattern, and underlying syndrome. The absence seizures would have had the same classification in the old system.

4 Tonic: A child has brief seizures with stiffening of the right arm and leg, during which responsiveness and awareness are retained. This seizure is a *focal aware tonic seizure* (the words "motor onset" can be assumed). In the old system, the seizure would have been called *tonic*, with a perhaps incorrect assumption of generalized onset.

5 Focal impaired awareness: A 25-year-old woman describes seizures beginning with 30 s of an intense feeling that "familiar music is playing." She can hear other people talking, but afterwards realizes that she could not determine what they were saying. After an episode, she is mildly confused, and has to "reorient herself." The seizure would be classified as *focal impaired awareness*. Even though the patient is able to interact with her environment, she cannot interpret her environment, and is mildly confused. Prior classification would have been complex partial seizure.

6 Autonomic: A 22-year-old man has seizures during which he remains fully aware, with the "hair on my arms standing on edge" and a feeling of being flushed. These are classified as *focal aware nonmotor autonomic seizures*, or more succinctly, *focal aware autonomic seizures*. The old classification would have called them simple partial autonomic seizures.

7 Focal clonic: A 1-month-old boy has rhythmical jerking of the left arm that does not remit when repositioning the arm. Corresponding EEG shows right frontal ictal rhythms. These seizures are *focal motor onset clonic seizures*, or more parsimoniously, *focal clonic seizures*. Because the level of awareness cannot be ascertained, awareness is not involved in classifying this seizure. The old classification would not have had a name for this seizure.

8 Sequential seizure manifestations: A seizure begins with tingling in the right arm of a 75-year-old man. The

patient says that it then progresses to rhythmic jerking of the right arm lasting about 30 s. He retains awareness and memory for the event. This seizure is a *focal (non-motor-onset) sensory seizure*. Additional description would be useful, namely *focal sensory seizure* with somatosensory features progressing to right arm clonic activity. If the sensory and motor events were to be discontinuous or the clinician had reason to consider the event to be two separate (bifocal or multifocal) seizures, then each component would be classified as a separate seizure. The old classification would have called this a *simple partial sensorimotor seizure*. An advantage of the 2017 classification is specification of the sensory onset, which may have clinical importance.

9 Myoclonic–atonic: A 4-year-old boy with Doose syndrome has seizures with a few arm jerks and then a rapid drop with loss of tone. These are now classified as *myoclonic–atonic seizures*. Prior unofficial usage would have called these *myoclonic–astatic seizures*.

10 Myoclonic–tonic–clonic seizures: A 13-year-old with juvenile myoclonic epilepsy has seizures beginning with a few jerks, followed by stiffening of all limbs and then rhythmic jerking of all limbs. These would be classified as *myoclonic–tonic–clonic seizures*. No corresponding single seizure type existed in the old classification, but they might have been called myoclonic or clonic seizures followed by tonic–clonic seizures.

11 Focal epileptic spasms: A 14-month-old girl has sudden extension of both arms and flexion of the trunk for about 2 s. These seizures repeat in clusters. EEG shows hypsarrhythmia with bilateral spikes, most prominent over the left parietal region. MRI shows a left parietal dysplasia. Resection of the dysplasia terminated the seizures. Because of the ancillary information, the seizure type would be considered to be *focal epileptic spasms* (the term "motor onset" can be assumed). The previous classification would have called them infantile spasms, with information on focality not included. The term "infantile" can still be used when spasms occur in infancy.

12 Unclassified: A 75-year-old man known to have epilepsy reports an internal sense of body trembling and a sense of confusion. No other information is available. EEG and MRI are normal. This event is *unclassified*.

Discussion

This companion to the paper presenting the rationale and structure of the ILAE 2017 seizure classification provides an instructional manual for use of the classification. No amount of explanation can, however, eliminate the inherent ambiguities of a classification in real clinical use. For instance, generalized onset tonic–clonic seizures may be slightly asymmetrical with initial head version. How focal must an asymmetry be to imply a focal onset? The answer lies in individual judgment for each seizure. How uncertain must a clinician be about the nature of the onset to classify a seizure as being of unknown onset? The Task Force set a guideline of "80%" confidence to call a seizure focal or generalized, but this bright line will undoubtedly blur in practice.

Ambiguities arise when a seizure presents multiple signs and symptoms early in the event, for example, tonic arm stiffening and automatisms. The classifier should choose the earliest prominent symptom, but different observers might produce different seizure names depending on the interpretation of reported or observed symptoms and signs. These ambiguities can be partially ameliorated by knowing the typical patterns of common seizures. A behavior arrest, followed by eye-blinking and head-nodding for 5 s, and then immediate recovery, is likely to be a typical absence seizure, even though each individual symptom can occur in multiple seizure types. Appending optional descriptors after the seizure type may better communicate the nature of a seizure, for example, adding "with laughing" to a "focal impaired awareness emotional seizure."

Several motor signs now appear in conjunction with either focal or generalized-onset seizure types, but it cannot be assumed that the pathophysiology is the same for both categories. A focal tonic seizure may have a different mechanism than that of a generalized tonic seizure, and each seizure type may evidence different prognoses, responses to treatments, demographics, and associations with epilepsy syndromes. Even within the focal category, focal tonic activity as part of a focal impaired awareness seizure (recall the common occurrence of twisting movements during complex partial seizures) may be a different entity from focal tonic seizures in a child with Lennox-Gastaut syndrome. Identifying these new seizure types should facilitate learning more about them and the syndromes with which they are associated.

A learning and adoption curve will develop for those in the epilepsy community who use the 2017 classification. Over time, consensus will emerge regarding which seizure types are best representative of various important groups of symptoms and signs. Past experience forecasts gradual adoption of the new classification, with transient use of terms from multiple prior generations of classifications. Real-world use of the 2017 classification will likely motivate revisions. The desired outcome for the ILAE 2017 classification is greater ease of communication about seizure types among clinicians, the nonmedical community, and researchers. Future empirical classifications will be developed until knowledge is sufficient to construct a classification based on the fundamental reasons that there are different seizure types.

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ILAE POSITION PAPER

Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology

Robert S. Fisher, †J. Helen Cross, ‡Jacqueline A. French, §Norimichi Higurashi, ¶Edouard Hirsch, #Floor E. Jansen, **Lieven Lagae, ††Solomon L. Moshé, ‡‡Jukka Peltola, §§Eliane Roulet Perez, ¶¶Ingrid E. Scheffer, and ##Sameer M. Zuberi**

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Dr. Robert S. Fisher, past president of American Epilepsy Society and editor of *Epilepsia* and epilepsy.com, led the Seizure Classification Task Force.

Summary

The International League Against Epilepsy (ILAE) presents a revised operational classification of seizure types. The purpose of such a revision is to recognize that some seizure types can have either a focal or generalized onset, to allow classification when the onset is unobserved, to include some missing seizure types, and to adopt more transparent names. Because current knowledge is insufficient to form a scientifically based classification, the 2017 Classification is operational (practical) and based on the 1981 Classification, extended in 2010. Changes include the following: (1) "partial" becomes "focal"; (2) awareness is used as a classifier of focal seizures; (3) the terms dyscognitive, simple partial, complex partial, psychic, and secondarily generalized are eliminated; (4) new focal seizure types include automatisms, behavior arrest, hyperkinetic, autonomic, cognitive, and emotional; (5) atonic, clonic, epileptic spasms, myoclonic, and tonic seizures can be of either focal or generalized onset; (6) focal to bilateral tonic–clonic seizure replaces secondarily generalized seizure; (7) new generalized seizure types are absence with eyelid myoclonia, myoclonic absence, myoclonic–atonic, myoclonic–tonic–clonic; and (8) seizures of unknown onset may have features that can still be classified. The new classification does not represent a fundamental change, but allows greater flexibility and transparency in naming seizure types.

KEY WORDS: Classification, Seizures, Focal, Generalized, Epilepsy, Taxonomy.

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*Stanford Department of Neurology & Neurological Sciences, Stanford, California, U.S.A.; †UCL-Institute of Child Health, Great Ormond Street Hospital for Children, London, United Kingdom; ‡Department of Neurology, NYU Langone School of Medicine, New York, New York, U.S.A.; §Department of Pediatrics, Jikei University School of Medicine, Tokyo, Japan; ¶Unite Francis Rohmer, Strasbourg, France; #Department of Pediatric Neurology, Brain Center Rudolf Magnus, University Medical Center, Utrecht, The Netherlands; **Pediatric Neurology, University Hospitals KU Leuven, Leuven, Belgium; ††Saul R. Korey Department of Neurology, Department of Pediatrics and Dominick P. Purpura Department Neuroscience, Einstein College of Medicine and Montefiore Medical Center, Bronx, New York, U.S.A.; ‡‡Department of Neurology, Tampere University Hospital, Tampere, Finland; §§Pediatric Neurology and Rehabilitation Unit, CHUV, Lausanne, Switzerland; ¶¶Florey Institute and University of Melbourne, Austin Health and Royal Children's Hospital, Melbourne, Victoria, Australia; ##The Paediatric Neurosciences Research Group, Royal Hospital for Children, Glasgow, United Kingdom; and ***College of Medicine, Veterinary & Life Sciences, University of Glasgow, Glasgow, United Kingdom

Address correspondence to Robert S. Fisher, Neurology, SNHC, Room 4865, 213 Quarry Road, Palo Alto, CA 94304, U.S.A. E-mail: robert.fisher@stanford.edu

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The International League Against Epilepsy (ILAE), through the Commission for Classification and Terminology, has developed a working classification of seizures and epilepsy. Following the proposed reorganization in 2010,[1,2] further clarification has been discussed and feedback sought from the community. One area that required further elucidation was the organization of seizure types. A Seizure Type Classification Task Force was established in 2015 to prepare recommendations for classification of seizure types, which are summarized in this document. A companion document guides the intended use of the classification.

Descriptions of seizure types date back at least to the time of Hippocrates. Gastaut[3,4] proposed a modern classification in 1964. Various basic frameworks for seizure classification can be considered. Manifestations of certain seizures are age-specific and depend on the maturation of

Key Points

- The ILAE has constructed a revised classification of seizure types; the classification is operational and not based on fundamental mechanisms
- Reasons for revision include clarity of nomenclature, ability to classify some seizure types as either focal or generalized, and classification when onset is unknown
- Seizures are divided into those of focal, generalized, unknown onset, with subcategories of motor, nonmotor, with retained or impaired awareness for focal seizures

the brain. Previous classifications have been based on anatomy, with temporal, frontal, parietal, occipital, diencephalic, or brainstem seizures. Modern research changed our view of the pathophysiologic mechanisms involved and has shown epilepsy to be a network disease and not only a symptom of local brain abnormalities.[5] From a network perspective, seizures could arise in neocortical, thalamocortical, limbic, and brainstem networks. Although our understanding of seizure networks is evolving rapidly,[6] it is not yet sufficient to serve as a basis for seizure classification. In 1981, an ILAE Commission led by Dreifuss and Penry[7] evaluated hundreds of video–electroencephalography (EEG) recordings of seizures to develop recommendations that divided seizures into those of partial and generalized onset, simple and complex partial seizures, and various specific generalized seizure types. This classification remains in widespread use today, with revisions in terminology and classification of seizures and epilepsy by the ILAE,[2,8–14] and with suggested insights, modifications, and criticisms by others.[15–24] We chose not to develop a classification based solely on observed behavior—instead, reflecting clinical practice, the 2017 classification is interpretive, allowing the use of additional data to classify seizure types.

The intention of the 2001[12] and 2006[13] reports on reclassification was to identify unique diagnostic entities with etiologic, therapeutic, and prognostic implications, so that when a syndromic diagnosis could not be made, the therapy and prognosis would be based on seizure type. Such a classification would permit grouping of reasonably pure cohorts of patients for discovery of etiologies, including genetic factors, research into fundamental mechanisms, involved networks, and clinical trials. The ILAE Seizure Type Classification Task Force (hereafter called "the Task Force") chose to use the phrase "operational classification," because it is impossible at this time to base a classification fully on the science of epilepsy. In the absence of a full scientific classification, the Task Force chose to use the basic organization initiated in 1981 and subsequently modified[1,2] as a starting point for the revised operational classification.

Methods

What is a seizure type?

A seizure is defined as "a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain."[25] It is the clinician's first task to determine that an event has the characteristics of a seizure and not one of the many imitators of seizures.[26] The next step is classification into a seizure type.

The Task Force operationally defines a seizure type as a useful grouping of seizure characteristics for purposes of communication in clinical care, teaching, and research. Mention of a seizure type should bring to mind a specific entity, albeit sometimes with subcategories and variations on a theme. Choices must be made by interested stakeholders to highlight groupings of seizure characteristics that are useful for specific purposes. Such stakeholders include patients, families, medical professionals, researchers, epidemiologists, medical educators, clinical trialists, insurance payers, regulatory agencies, advocacy groups, and medical reporters. Operational (practical) groupings can be derived by those with specific interests. A pharmacologist, for example, might choose to group seizures by efficacy of medications. A researcher doing a clinical trial might consider seizures as disabling or nondisabling. A surgeon might group by anatomy in order to predict the eligibility for and likely success of surgical therapy. A physician based in an intensive care unit with predominantly unconscious patients might group seizures in part by EEG pattern.[27] The principal aim of this classification is to provide a communication framework for clinical use. Seizure types are relevant to clinical practice in humans; whereas, it is acknowledged that seizure types in other species, experimental and natural, may not be reflected in the proposed classification. One goal was to make the classification understandable by patients and families and broadly applicable to all ages, including neonates. The ILAE Commission on Classification & Terminology recognizes that seizures in the neonate can have motor manifestations, or alternatively little or no behavioral manifestations. A separate Neonatal Seizure Task Force is working to develop a classification of neonatal seizures. The 2017 seizure classification is not a classification of electroencephalographic ictal or subclinical patterns. The guiding principle of the Seizure Type Task Force was advice from Albert Einstein to "make things as simple as possible, but no simpler."

Motivation for change

Adapting to a change in terminology can be effortful and needs to be motivated by a rationale for change. Seizure type classification is important for several reasons. First, the classification becomes a worldwide shorthand form of

communication among clinicians caring for people with epilepsy. Second, the classification allows grouping of patients for therapies. Some regulatory agencies approve drugs or devices indicated for specific seizure types. A new classification should gracefully map to existing indications for drug or device usage. Third, the seizure type grouping might provide a useful link to specific syndromes or etiologies, for example, by noting an association between gelastic seizures and hypothalamic hamartoma or epileptic spasms with tuberous sclerosis. Fourth, the classification allows researchers to better focus their studies on mechanisms of different seizure types. Fifth, a classification provides words to patients to describe their disease. Motivations for revising the 1981 Seizure Classification are listed below.

1 Some seizure types, for example, tonic seizures or epileptic spasms, can have either a focal or generalized onset.
2 Lack of knowledge about the onset makes a seizure unclassifiable and difficult to discuss with the 1981 system.
3 Retrospective seizure descriptions often do not specify a level of consciousness, and altered consciousness, although central to many seizures, is a complicated concept.
4 Some terms in current use do not have high levels of community acceptance or public understanding, such as "psychic," "partial," "simple partial," "complex partial," and "dyscognitive."
5 Some important seizure types are not included.

Results

Classification of seizure types

Figure 1 depicts the basic and Figure 2 depicts the expanded 2017 seizure classification. The two represent the same classification, with collapse of the subcategories to form the basic version. Use of one versus the other depends on the desired degree of detail. Variations on the individual seizure theme can be added for focal seizure types according to level of awareness.

Structure of the classification

The classification chart is columnar, but not hierarchical (meaning that levels can be skipped), so arrows intentionally are omitted. Seizure classification begins with the determination of whether the initial manifestations of the seizure are focal or generalized. The onset may be missed or obscured, in which case the seizure is of unknown onset. The words "focal" and "generalized" at the start of a seizure name are assumed to mean of focal or generalized onset.

For focal seizures, the level of awareness optionally may be included in the seizure type. Awareness is only one potentially important feature of a seizure, but awareness is of sufficient practical importance to justify using it as a seizure classifier. Retained awareness means that the person is aware of self and environment during the seizure, even if immobile. A focal aware seizure (with or without any subsequent classifiers) corresponds to the prior term "simple partial seizure." A focal impaired awareness seizure (with or without any subsequent classifiers) corresponds to the prior term "complex partial seizure." Impaired awareness during any part of the seizure renders it a focal impaired awareness seizure. In addition, focal seizures are subgrouped as those with motor and nonmotor signs and symptoms at the onset. If both motor and nonmotor signs are present at the seizure start, the motor signs will usually dominate, unless non-motor (e.g., sensory) symptoms and signs are prominent.

Focal aware or impaired awareness seizures optionally may be further characterized by one of the listed motor onset or nonmotor onset symptoms, reflecting the first prominent sign or symptom in the seizure, for example, focal impaired awareness automatism seizure. Seizures should be classified by the earliest prominent motor onset or nonmotor onset feature, except that a focal behavior arrest seizure is one for which cessation of activity is the dominant feature throughout the seizure, and any significant impairment of awareness during the course of the seizure causes a focal seizure to be classified as having impaired awareness. Classification according to onset has an anatomic basis, whereas classification by level of awareness has a

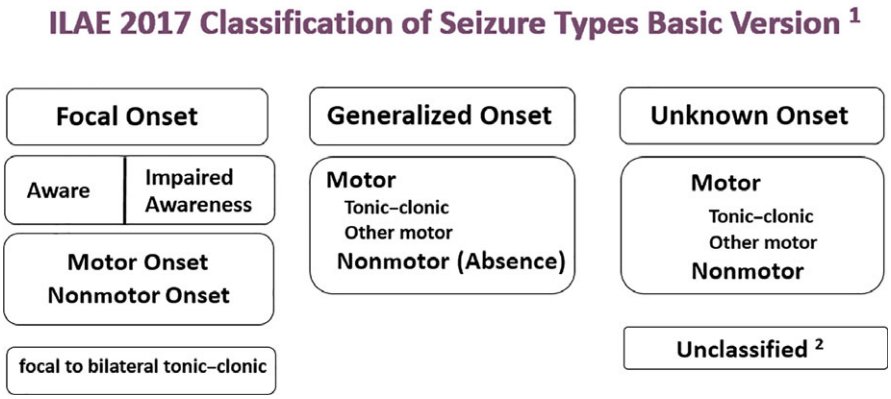

Figure 1.
The basic ILAE 2017 operational classification of seizure types. [1]Definitions, other seizure types and descriptors are listed in the accompanying paper and glossary of terms. [2]Due to inadequate information or inability to place in other categories.
Epilepsia © ILAE

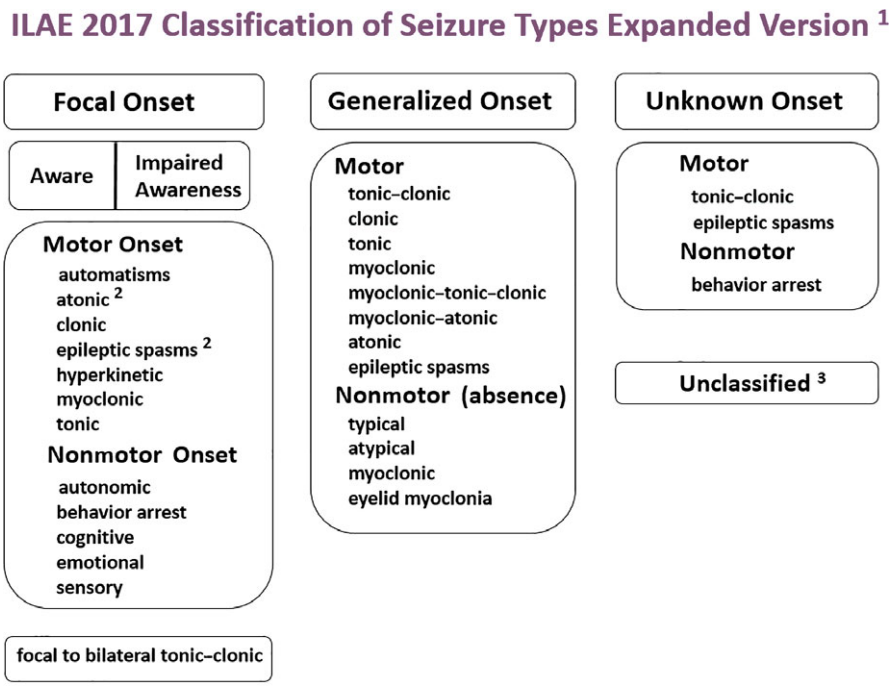

Figure 2.
The expanded ILAE 2017 operational classification of seizure types. The following clarifications should guide the choice of seizure type. For focal seizures, specification of level of awareness is optional. Retained awareness means the person is aware of self and environment during the seizure, even if immobile. A focal aware seizure corresponds to the prior term simple partial seizure. A focal impaired awareness seizure corresponds to the prior term complex partial seizure, and impaired awareness during any part of the seizure renders it a focal impaired awareness seizure. Focal aware or impaired awareness seizures optionally may further be characterized by one of the motor-onset or nonmotor-onset symptoms below, reflecting the first prominent sign or symptom in the seizure. Seizures should be classified by the earliest prominent feature, except that a focal behavior arrest seizure is one for which cessation of activity is the dominant feature throughout the seizure. A focal seizure name also can omit mention of awareness when awareness is not applicable or unknown and thereby classify the seizure directly by motor onset or nonmotor-onset characteristics. Atonic seizures and epileptic spasms would usually not have specified awareness. Cognitive seizures imply impaired language or other cognitive domains or positive features such as déjà vu, hallucinations, illusions, or perceptual distortions. Emotional seizures involve anxiety, fear, joy, other emotions, or appearance of affect without subjective emotions. An absence is atypical because of slow onset or termination or significant changes in tone supported by atypical, slow, generalized spike and wave on the EEG. A seizure may be unclassified due to inadequate information or inability to place the type in other categories. [1]Definitions, other seizure types and descriptors are listed in the accompanying paper and glossary of terms. [2]Degree of awareness usually is not specified. [3]Due to inadequate information or inability to place in other categories.

behavioral basis, justified by the practical importance of impaired awareness. Both methods of classification are available and can be used in concert. Brief behavioral arrest at the start of a seizure often is imperceptible, and so it is not used as a classifier unless dominant throughout the seizure. The earliest (anatomic) classifier will not necessarily be the most significant behavioral feature of a seizure. For example, a seizure might start with fear and progress to vigorous focal clonic activity resulting in falling. This seizure would still be a focal emotional seizure (with or without impairment of awareness), but free text description of the ensuing features would be very useful.

A focal seizure name can omit mention of awareness when awareness is not applicable or unknown, thereby classifying the seizure directly by motor onset or nonmotor onset characteristics. The terms motor onset and nonmotor onset may be omitted when a subsequent term generates an unambiguous seizure name.

The classification of an individual seizure can stop at any level: a "focal onset" or "generalized onset" seizure, with no other elaboration, or a "focal sensory seizure," "focal motor seizure," "focal tonic seizure," or "focal automatism seizure," and so on. Additional classifiers are encouraged, and their use may depend on the experience and purposes of the person classifying the seizure. The terms focal onset and generalized onset are for purposes of grouping. No inference is made that each seizure type exists in both groups; including absence seizures in the generalized-onset category does not imply existence of "focal absence" seizures.

When the primacy of one versus another key symptom or sign is unclear, the seizure can be classified at a level above the questionably applicable term with additional descriptors

of seizure semiology relevant to the individual seizure. Any signs or symptoms of seizures, suggested descriptor terms as listed in the companion paper or free text descriptions can optionally be appended to the seizure type as descriptions, but they do not alter the seizure type.

The seizure type "focal to bilateral tonic–clonic" is a special seizure type, corresponding to the 1981 phrase "partial onset with secondary generalization." Focal to bilateral tonic–clonic reflects a propagation pattern of a seizure, rather than a unitary seizure type, but it is such a common and important presentation that the separate categorization was continued. The term "to bilateral" rather than "secondary generalized" was used to further distinguish this focal-onset seizure from a generalized-onset seizure. The term "bilateral" is used for propagation patterns and "generalized" for seizures that engage bilateral networks from onset.

Seizure activity propagates through brain networks, sometimes leading to uncertainty about whether an event is a unitary seizure or a series of multiple seizures starting from different networks ("multifocal"). A single unifocal seizure can present with multiple clinical manifestations as a result of propagation. The clinician will need to determine (by observation of a continuous evolution or stereotypy from seizure-to-seizure) whether an event is a single seizure or a series of different seizures. When a single focal seizure presents with a sequence of signs and symptoms, then the seizure is named for the initial prominent sign or symptom, reflecting the usual clinical practice of identifying the seizure onset focus or network. For example, a seizure beginning with sudden inability to understand language followed by impaired awareness and clonic left arm jerks would be classified as a "focal impaired awareness (nonmotor onset) cognitive seizure" (progressing to clonic left arm jerks). The terms in parentheses are optional. The formal seizure type in this example is determined by the cognitive nonmotor onset and presence of altered awareness during any point of the seizure.

Generalized seizures are divided into motor and nonmotor (absence) seizures. Further subdivisions are similar to those of the 1981 classification, with the addition of myoclonic–atonic seizures, common in epilepsy with myoclonic–atonic seizures (Doose syndrome[28]), myoclonic–tonic–clonic seizures common in juvenile myoclonic epilepsy,[29] myoclonic absence,[30] and absence seizures with eyelid myoclonia seen in the syndrome described by Jeavons and elsewhere.[31] Generalized manifestations of seizures can be asymmetrical, rendering difficult the distinction from focal-onset seizures. The word "absence" has a common meaning, but an "absent stare" is not synonymous with an absence seizure, since arrest of activity also occurs in other seizure types.

The 2017 classification allows appending of a limited number of qualifiers to seizures of unknown onset, in order to better characterize the seizure. Seizures of unknown onset may be referred to by the single word "unclassified" or with additional features, including motor, nonmotor, tonic–clonic, epileptic spasms, and behavior arrest. A seizure type of unknown onset may later become classified as either of focal or generalized onset, but any associated behaviors (e.g., tonic–clonic) of the previously unclassified seizure will still apply. In this regard, the term "unknown onset" is a placeholder—not a characteristic of the seizure, but of ignorance.

Reasons for decisions

The terminology for seizure types is designed to be useful for communicating the key characteristics of seizures and to serve as one of the key components of a larger classification for the epilepsies, which is being developed by a separate ILAE Classification Task Force. The basic framework of seizure classification used since 1981 was maintained.

Focal versus partial

In 1981, the Commission declined to designate as "focal" a seizure that might involve an entire hemisphere, so the term "partial" was preferred. The 1981 terminology was in a way prescient of the modern emphasis on networks, but "partial" conveys a sense of part of a seizure, rather than a location or anatomic system. The term "focal" is more understandable in terms of seizure-onset location.

Focal versus generalized

In 2010[1] the ILAE defined focal as "originating within networks limited to one hemisphere. They may be discretely localized or more widely distributed. Focal seizures may originate in subcortical structures." Generalized from onset seizures were defined as "originating at some point within, and rapidly engaging, bilaterally distributed networks." Classifying a seizure as having apparently generalized onset does not rule out a focal onset obscured by limitations of our current clinical methods, but this is more an issue of correct diagnosis than of classification. Furthermore, focal seizures may rapidly engage bilateral networks, whereas classification is based on unilateral onset. For some seizure types, for example, epileptic spasms, the distinction of a focal versus generalized onset may require careful study of a video-EEG recording or the type of onset may be unknown. A distinction between focal and generalized onset is a practical one, and may change with advances in ability to characterize the onset of seizures.

Focality of seizure onset can be inferred by pattern matching to known focal-onset seizures, even when the focality is not clear strictly in terms of observable behavior. A seizure is focal, for example, when it starts with déjà vu and then progresses to loss of awareness and responsiveness, lip-smacking, and hand-rubbing for a minute. There is nothing intrinsically "focal" in the description, but video-EEG recordings of countless similar seizures have previously shown focal onsets. If the epilepsy type is known, the

onset can be presumed even if it is unwitnessed; for example, an absence seizure in a person with known juvenile absence epilepsy.

Clinicians have long been aware that so-called generalized seizures, for example, absence seizures with EEG generalized spike-waves, do not manifest equally in all parts of the brain. The Task Force emphasized the concept of bilateral, rather than generalized, involvement of some seizures, since seizures can be bilateral without involving every brain network. The bilateral manifestations need not be symmetric. The term "focal to bilateral tonic–clonic" was substituted for "secondarily generalized." The term "generalized" was maintained for seizures generalized from onset.

Unknown onset

Clinicians commonly hear about tonic–clonic seizures for which the onset was unobserved. Perhaps, the patient was asleep, alone, or observers were too distracted by the manifestations of the seizure to notice the presence of focal features. There should be an opportunity to provisionally classify this seizure, even in the absence of knowledge about its origin. The Task Force therefore allowed further description of seizures of unknown onset when key characteristics, such as tonic–clonic activity or behavior arrest are observed during the course of the seizure. The Task Force recommends classifying a seizure as having focal or generalized onset only when there is a high degree of confidence (e.g., ≥80%, arbitrarily chosen to parallel the usual allowable beta error) in the accuracy of the determination; otherwise, the seizure should remain unclassified until more information is available.

It may be impossible to classify a seizure at all, either because of incomplete information or because of the unusual nature of the seizure, in which case it is called an unclassified seizure. Categorization as unclassified should be used only for the exceptional situation in which the clinician is confident that the event is a seizure but cannot further classify the event.

Consciousness and awareness

The 1981 classification and the revision in 2010[1,10,32] suggested a fundamental distinction between seizures with loss or impairment of consciousness and those with no impairment of consciousness. Basing a classification on consciousness (or one of its allied functions) reflects a practical choice that seizures with impaired consciousness should often be approached differently from those with unimpaired consciousness, for example, with respect to allowing driving in adults or interfering with learning. The ILAE chose to retain impairment of consciousness as a key concept in the grouping of focal seizures. However, consciousness is a complex phenomenon, with both subjective and objective components.[33] Multiple different types of consciousness have been described for seizures.[34] Surrogate markers[35–37] for consciousness usually comprise measurements of awareness, responsiveness, memory, and a sense of self as distinct from others. The 1981 classification specifically mentioned awareness and responsiveness, but not memory for the event.

Retrospective determination of state of consciousness can be difficult. An untrained classifier might assume that a person must be on the ground, immobile, unaware, and unresponsive (e.g., "passed out") for a seizure to show impaired consciousness. The Task Force adopted state of awareness as a relatively simple surrogate marker for consciousness. "Retained awareness" is considered to be an abbreviation for "seizures with no impairment of consciousness during the event." We employ an operational definition of awareness as knowledge of self and environment. In this context, awareness refers to perception or knowledge of events occurring during a seizure, not to knowledge of whether a seizure occurred. In several languages, "unaware" translates as "unconscious," in which case changing the seizure designation from "complex partial" to "impaired awareness" will emphasize the importance of consciousness by putting its surrogate directly in the seizure title. In English, "focal aware seizure" is shorter than is "focal seizure without impairment of consciousness" and possibly better understood by patients. As a practical issue, retained awareness usually includes the presumption that the person having the seizure later can recall and validate having retained awareness; otherwise, impaired awareness may be assumed. Exceptional seizures present with isolated transient epileptic amnesia in clear awareness,[38] but classification of an amnestic seizure as a focal aware seizure would require clear documentation by meticulous observers. Awareness may be left unspecified when the extent of awareness cannot be ascertained.

Responsiveness may or may not be compromised during a focal seizure.[39] Responsiveness does not equate to awareness or consciousness, since some people are immobilized and consequently unresponsive during a seizure, but still able to observe and recall their environment. In addition, responsiveness often is not tested during seizures. For these reasons, responsiveness was not chosen as a primary feature for seizure classification, although responsiveness can be helpful in classifying the seizure when it can be tested, and degree of responsiveness may be relevant to the impact of a seizure. The term "dyscognitive" was not carried into the current classification as a synonym for "complex partial" because of lack of clarity and negative public and professional feedback.

Awareness is not a classifier for generalized-onset seizures, because the large majority of generalized seizures present with impaired awareness or full loss of consciousness. However, it is recognized that awareness and responsiveness can be at least partially retained during some generalized seizures, for example, with brief absence seizures,[40] including absence seizures with eyelid myoclonias or myoclonic seizures.

Etiology

A classification of seizure types can be applied to seizures of different etiologies. A posttraumatic seizure or a reflex seizure may be focal with or without impairment of awareness. Knowledge of the etiology, for instance, presence of a focal cortical dysplasia, can aid in classification of the seizure type. Any seizure can become prolonged, leading to status epilepticus of that seizure type.

Supportive information

As part of the diagnostic process, a clinician will commonly use supportive evidence to help classify a seizure, even though that evidence is not part of the classification. Such evidence may include videos brought in by family, EEG patterns, lesions detected by neuroimaging, laboratory results such as detection of antineuronal antibodies, gene mutations, or an epilepsy syndrome diagnosis known to be associated with either focal or generalized seizures or both, such as Dravet syndrome. The seizures usually can be classified on the basis of symptoms and behavior, provided that good subjective and objective descriptions are available. Use of any available supportive information to classify the seizure is encouraged. Availability of supportive information may not exist in the resource-poor parts of the world, which may lead to a less specific, but still correct classification.

ICD-9, ICD-10, ICD-11, and ICD-12

The World Health Organization International Classification of Diseases (ICD) is used for inpatient and outpatient diagnoses, billing, research, and many other purposes.[41,42] Concordance between ICD epilepsy diagnoses and ILAE seizure types is desirable for clarity and consistency. This is possible only to a limited extent with existing ICD terms, since ICD-9, ICD-10, and ICD-11 are already formulated. The ILAE proposals will always lead ICD standards. ICD-9 and ICD-10 make use of old seizure terminology, including terms such as petit mal and grand mal. ICD-11 does not name seizure types at all, but focuses on epilepsy etiologies and syndromes, as do ILAE epilepsy classifications.[1] For this reason, there is no conflict between our proposed seizure type classification and ICD-11. Efforts can be made to incorporate new classifications of seizure types and syndromes into the development of ICD-12.

Discussion

Discontinued terms

Simple/complex partial

After approximately 35 years of use, the terms "simple partial seizure" and "complex partial seizure" may be missed by some clinicians. There are several reasons for changing. First, a decision was previously made[1] to globally change partial to focal. Second, "complex partial" has no intrinsic meaning to the public. The phrase "focal impaired awareness" can convey meaning to a lay person with no knowledge of seizure classification. Third, the words "complex" and "simple" can be misleading in some contexts. Complex seems to imply that this seizure type is more complicated or difficult to understand than other seizure types. Calling a seizure "simple" may trivialize its impact to a patient who does not find the manifestations and consequences of the seizures to be at all simple.

Convulsion

The term "convulsion" is a popular, ambiguous, and unofficial term used to mean substantial motor activity during a seizure. Such activity might be tonic, clonic, myoclonic, or tonic–clonic. In some languages, convulsions and seizures are considered synonyms and the motor component is not clear. The word "convulsion" is not part of the 2017 seizure classification, but will undoubtedly persist in popular usage.

Added terms

Aware/impaired awareness

As discussed earlier, these terms designate knowledge of self and environment during a seizure.

Hyperkinetic

Hyperkinetic seizures have been added to the focal seizure category. Hyperkinetic activity comprises agitated thrashing or leg pedaling movements. Hypermotor is an earlier term introduced as part of a different proposed classification by Lüders and colleagues in 1993.[43] The term hypermotor, which contains both Greek and Roman roots, was supplanted in the 2001 ILAE glossary[44] and 2006 report[2] by "hyperkinetic," and to be both etymologically and historically consistent, "hyperkinetic" was chosen for the 2017 classification.

Cognitive

This term replaces "psychic" and refers to specific cognitive impairments during the seizure, for example, aphasia, apraxia, or neglect. The word "impairment" is implied because seizures never enhance cognition. A cognitive seizure can also comprise positive cognitive phenomena, such as déjà vu, jamais vu, illusions, or hallucinations.

Emotional

A focal nonmotor seizure can have emotional manifestations, such as fear or joy. The term also encompasses affective manifestations with the appearance of emotions occurring without subjective emotionality, such as may occur with some gelastic or dacrystic seizures.

New focal seizure types

Some seizure types that were described previously as only generalized seizures now appear under seizures of

focal, generalized and unknown onset. These include epileptic spasms, tonic, clonic, atonic, and myoclonic seizures. The list of motor behaviors constituting seizure types comprises the most common focal motor seizures, but other less common types, for example, focal tonic–clonic, may be encountered. Focal automatisms, autonomic, behavior arrest, cognitive, emotional, and hyperkinetic are new seizure types. Focal to bilateral tonic–clonic seizure is a new type as the renamed secondarily generalized seizure.

New generalized seizure types

Relative to the 1981 classification, new generalized seizure types include absence with eyelid myoclonia, myoclonic–atonic, and myoclonic–tonic–clonic (although clonic onset of tonic–clonic seizures was mentioned in the 1981 publication). Seizures with eyelid myoclonia could logically have been placed under the motor category, but since eyelid myoclonia are most significant as features of absence seizures, seizures with eyelid myoclonia were placed in the nonmotor/absence category. Seizures with eyelid myoclonia may even rarely display focal features.[45] Similarly, myoclonic absence seizures potentially have features of both absence and motor seizures, and could have been placed in either group. Epileptic spasms are seizures represented in focal, generalized, and unknown onset categories, and the distinction may require video-EEG recording. The term "epileptic" is implied for every seizure type, but explicitly stated for epileptic spasms, because of the ambiguity of the single word "spasms" in neurologic use.

What is different from the 1981 classification?

Table 1 summarizes the changes in the ILAE 2017 seizure type classification from the 1981 classification. Note that several of these changes were already incorporated into the 2010 revision of terminology and subsequent revisions.[1,32]

Table 1. Changes in seizure type classification from 1981 to 2017

1. Change of "partial" to "focal"
2. Certain seizure types can be either of focal, generalized, or unknown onset
3. Seizures of unknown onset may have features that can still be classified
4. Awareness is used as a classifier of focal seizures
5. The terms dyscognitive, simple partial, complex partial, psychic, and secondarily generalized were eliminated
6. New focal seizure types include automatisms, autonomic, behavior arrest, cognitive, emotional, hyperkinetic, sensory, and focal to bilateral tonic–clonic seizures. Atonic, clonic, epileptic spasms, myoclonic, and tonic seizures can be either focal or generalized
7. New generalized seizure types include absence with eyelid myoclonia, myoclonic absence, myoclonic–tonic–clonic, myoclonic–atonic, and epileptic spasms

Compared to the 1981 classification, certain seizure types now appear in multiple categories. Epileptic spasms can be of focal, generalized, or unknown onset. Represented both in focal and generalized columns are atonic, clonic, myoclonic, and tonic seizures, although the pathophysiology of these seizure types may differ for the focal onset versus generalized-onset seizure type of that name.

A companion paper provides guidance on how to apply the 2017 classification. Employment of the 2017 classification in the field for a few years likely will motivate minor revisions and clarifications.

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