SPECIAL REPORT

A definition and classification of status epilepticus – Report of the ILAE Task Force on Classification of Status Epilepticus

*†‡Eugen Trinka, §Hannah Cock, ¶Dale Hesdorffer, #Andrea O. Rossetti, **Ingrid E. Scheffer, ††Shlomo Shinnar, ‡‡Simon Shorvon, and §§Daniel H. Lowenstein

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Eugen Trinka is professor and chairman of Department of Neurology, Paracelsus Medical University Salzburg Austria.

Summary

The Commission on Classification and Terminology and the Commission on Epidemiology of the International League Against Epilepsy (ILAE) have charged a Task Force to revise concepts, definition, and classification of status epilepticus (SE). The proposed new definition of SE is as follows: *Status epilepticus is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms, which lead to abnormally, prolonged seizures (after time point t_1). It is a condition, which can have long-term consequences (after time point t_2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures.* This definition is conceptual, with two operational dimensions: the first is the length of the seizure and the time point (t_1) beyond which the seizure should be regarded as "continuous seizure activity." The second time point (t_2) is the time of ongoing seizure activity after which there is a risk of long-term consequences. In the case of convulsive (tonic–clonic) SE, both time points (t_1 at 5 min and t_2 at 30 min) are based on animal experiments and clinical research. This evidence is incomplete, and there is furthermore considerable variation, so these time points should be considered as the best estimates currently available. Data are not yet available for other forms of SE, but as knowledge and understanding increase, time points can be defined for specific forms of SE based on scientific evidence and incorporated into the definition, without changing the underlying concepts. A *new diagnostic classification system* of SE is proposed, which will provide a framework for clinical diagnosis, investigation, and therapeutic approaches for each patient. There are four axes: (1) semiology; (2) etiology; (3) electroencephalography (EEG) correlates; and (4) age. Axis 1 (semiology) lists different forms of SE divided into those with prominent motor systems, those without prominent motor systems, and currently indeterminate conditions (such as acute confusional states with epileptiform EEG patterns). Axis 2 (etiology) is divided into subcategories of known and unknown causes. Axis 3 (EEG correlates) adopts the latest recommendations by consensus panels to use the following descriptors for the EEG: name of pattern, morphology, location, time-related features, modulation, and effect of intervention. Finally, axis 4 divides age groups into neonatal, infancy, childhood, adolescent and adulthood, and elderly.

KEY WORDS: **Status epilepticus, Seizure, Definition, Classification, Seizure duration.**

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*Department of Neurology, Christian Doppler Klinik, Paracelsus Medical University, Salzburg, Austria; †Center for Cognitive Neuroscience, Salzburg, Austria; ‡Department of Public Health Technology Assessment, UMIT – University for Health Sciences, Medical Informatics and Technology, Hall.i.T., Austria; §Institute of Medical & Biomedical Education, Epilepsy Group, Atkinson Morley Regional Neuroscience Centre, St. Georges University Hospitals NHS Foundation Trust, St George's University of London, London, United Kingdom; ¶GH Sergievsky Center and Department of Epidemiology, Columbia University, New York, New York, U.S.A.; #Department of Clinical Neurosciences, CHUV and University of Lausanne, Lausanne, Switzerland; **Florey Institute of Neuroscience and Mental Health, Austin Health and Royal Children's Hospital, University of Melbourne, Melbourne, Victoria, Australia; ††Departments of Neurology, Pediatrics, and Epidemiology and Population Health Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, New York, U.S.A.; ‡‡National Hospital for Neurology and Neurosurgery, UCL Institute of Neurology, London, United Kingdom; and §§Department of Neurology, University of California, San Francisco, California, U.S.A.

Address correspondence to Eugen Trinka, Department of Neurology, Christian Doppler Klinik, Centre for Cognitive Neuroscience Salzburg, Paracelsus Medical University Salzburg, Ignaz Harrerstrasse 79, A-5020 Salzburg, Austria. E-mail: e.trinka@salk.at

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Key Points

- A new conceptual definition of status epilepticus with two operational dimensions (t_1 and t_2) is proposed
- Time point t_1 indicates when treatment should be initiated, and time point t_2 indicates when long-term consequences may appear
- The Task Force also proposes a new classification of SE that will provide a framework for clinical diagnosis and therapeutic approaches for each patient

Trousseau, 1867: "In the status epilepticus, when the convulsive condition is almost continuous, something special takes place which requires an explanation."

Comment: Historical Introduction

Status epilepticus (SE), considered the most extreme form of a seizure, was included in the classification of seizures of the International League Against Epilepsy (ILAE) of 1970[1] and 1981.[2] In the first ILAE Classification of Seizures, which was developed in 1964 and approved in 1970,[1] SE was defined in the addendum of the publication as a "seizure that persists for a sufficient length of time or is repeated frequently enough to produce a fixed and enduring condition." SE was divided into partial, generalized, or unilateral types, and basically mirrored the seizure classification.[1,3] In the revision of 1981, the definition was minimally changed into a "seizure" that "persists for a sufficient length of time or is repeated frequently enough that recovery between attacks does not occur."[2] Again, the distinction between partial, generalized, and epilepsia partialis continua (EPC) was mentioned in the addendum of the Classification, without further details.[2] These concepts, although highly valuable, were imprecise, as they did not define the duration of a seizure that was "fixed and enduring" or "sufficient length," nor was there a clinical description (semiology) of the type of SE in the Classification of 1970 and its 1981 revision. These issues were not resolved with the report of the Core Group on Classification.[4]

The ILAE recognized the need to revise the Classification of SE and the Chairs of the Commission of Classification and Terminology (Ingrid Scheffer) and the Commission on Epidemiology (Dale Hesdorffer and Ettore Beghi). Ingrid Scheffer (Australia), Ding Ding (China), Ed Dudek (U.S.A.), Daniel Lowenstein (U.S.A.), Hannah Cock (United Kingdom), Dale Hesdorffer (U.S.A.), Andrea Rossetti (Switzerland), Shlomo Shinnar (U.S.A.), Simon Shorvon (United Kingdom), and Eugen Trinka (Austria).

Purpose of Classification

Classification refers to the way in which items are organized and should be ideally based on the underlying neurobiology to form natural classes or entities.[5] Because current knowledge regarding the pathophysiology and the underlying neurobiology of status epilepticus is far from complete, a proposed classification can be only a compromise between a conceptual, scientific (drawing on what is known) and pragmatic empirical classification.[6]

A classification has to serve several purposes. First, it has to facilitate communication between clinicians by providing them with a common language. The classes should be clinically differentiated. Second, classification should help to improve the treatment of patients, based on current understanding of pathophysiology, prognosis, etiology, and age. Third, classification should permit the conduct of epidemiologic studies of consequences and prevention. Fourth, classification should guide basic research to identify natural classes (i.e., entities or diseases sensu strictu), which in turn will form the basis of a true scientific classification in the future. Therefore, it is important to emphasize that the proposed classification is merely a framework and must not be treated as a doctrine, but reflect our current knowledge on status epilepticus. Future advances in basic, epidemiologic, and clinical research will undoubtedly lead to modifications and major revisions of this proposed classification of SE.

A classification of SE cannot simply reflect the classification of seizure types, since symptoms and signs during the fixed stage of SE frequently are different compared to symptoms during short-lasting seizures. At least half of the patients presenting with SE do not have epilepsy, and acute neurologic disorders and the long duration of status leads to significant variability in its clinical presentation (i.e., semiology). SE is not a disease entity but rather a symptom with a myriad of etiologies.

Definition of Status Epilepticus

A seizure is defined as "*a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. The term transient is used as demarcated in time, with a clear start and finish.*" Classically SE was defined as a "a condition characterized by an epileptic seizure that is sufficiently prolonged or repeated at sufficiently brief intervals so as to produce an unvarying and enduring epileptic condition."[7,8]

Because the ILAE definitions of SE have not provided a precise definition of the duration of SE,[1–5] different opera-

tional definitions have been provided in textbooks, research papers, and clinical trials. The seminal work by Meldrum et al.[9] suggested that 82 min or longer of ongoing seizure activity in baboons can cause irreversible neuronal injury due to excitotoxicity. This observation led to the commonly used definition for SE as seizure duration of 30 min.[10,11] The rationale behind this definition was that irreversible neuronal injury may occur after 30 min of ongoing seizure activity. This definition, therefore, remains useful for epidemiologic studies focused on consequences and prevention of SE. Clinicians have rightfully argued for the need to start treatment earlier, because the prognosis of SE worsens with increasing duration.[12,13] Several suggestions of a shorter timeframe for SE have subsequently been made, but none has been based on scientific evidence provided by prospective studies.

This problem was addressed in an article by Lowenstein et al.[14] The obvious discrepancy between the limited knowledge of the pathophysiology and the need to treat patients rapidly led to the concept of an *operational* and a *conceptual* definition. *Generalized convulsive SE* in adults and children older than 5 years was operationally defined as *"...≥5 min of (1) continuous seizure or (2) two or more discrete seizures between which there is incomplete recovery of consciousness,"*[14] This time frame has been generally accepted by the clinical community and used to guide when emergency treatment of generalized convulsive SE should commence. As a basic research (or conceptual) definition, the ILAE Core Group on Classification group suggested the following: *"Generalized, convulsive status epilepticus refers to a condition in which there is failure of the "normal" factors that serve to terminate a typical GTCS [generalized tonic–clonic seizures]."*[15] Although this distinction between a pragmatic, operational definition and a basic research definition of generalized convulsive status has guided the treatment of generalized convulsive SE, other forms of SE have not been addressed.

The ILAE Task Force on Classification of Status Epilepticus proposes a *definition* that encompasses all types of SE, and takes into consideration current knowledge regarding the pathophysiology of SE and the need to address clinical treatment decision making time points, as well as the conduct of epidemiologic and clinical studies:

> SE is a condition resulting either from the failure of the mechanisms responsible for seizure termination or from the initiation of mechanisms which lead to abnormally prolonged seizures (after time point t_1). It is a condition that can have long-term consequences (after time point t_2), including neuronal death, neuronal injury, and alteration of neuronal networks, depending on the type and duration of seizures.

This definition is conceptual, with two *operational dimensions*: the first is the length of the seizure and the time point (t_1) at which the seizure should be regarded as an *"abnormally prolonged seizure."* The second time point (t_2) is the time of ongoing seizure activity beyond which there is a risk of long-term consequences. In the case of convulsive (tonic–clonic) SE, both time points are based on animal experiments and clinical research. This evidence is incomplete; there is furthermore considerable variation, so these time points should be considered as the best estimates currently available. Data are not yet available for other forms of SE, but as knowledge and understanding increases, time points can be defined for specific forms of SE based on scientific evidence and incorporated into the definition, without changing the underlying concepts. This division into two time points has clear clinical implications: The time point of operational dimension 1 determines the time at which treatment should be considered or started, whereas the time point of operational dimension 2 determines how aggressively treatment should be implemented to prevent long-term consequences. The time domain may vary considerably between different forms of SE.

Data from select populations with refractory epilepsy undergoing video–electroencephalography (EEG) monitoring indicate that most convulsive seizures last <5 min.[16–20] In unselected community-based populations, the data suggest that the estimated duration of seizures >5 min is much more common than suggested by inpatient monitoring and that ≥10% of first unprovoked seizures last longer than 30 min.[20,21] Observations from a less selected pediatric population show that there are two subgroups of patients, one with a tendency to brief seizures (<5 min) and the other subgroup that represents a significant minority of patients with a propensity to more prolonged seizures.[20] In this study, a seizure that lasted >7 min was likely to be prolonged and therefore required acute treatment. Taken together, these findings led the Task Force to reach a consensus opinion that treatment of convulsive seizures should be initiated at around 5 min.

Given the experimental evidence indicating irreversible brain damage after prolonged seizures[9] and the potential threat of brain damage in humans, we suggest the time of t_2 at 30 min in convulsive SE, in line with previous definitions of SE.[10,11] As in the animal experimentation, considerable variation in the duration of prolonged seizures that result in damage has been found, but this time point is chosen on the basis of providing a practical safe guideline for clinical purposes. There is limited information to define t_1 and t_2 in focal SE,[19, 22] and no information for absence SE (see Table 1). Furthermore, the likelihood of damage is dependent on the location of the epileptic focus (also true in experimental animals), the intensity of the status, the age of the patient, and other factors, and research is needed to define these aspects further. It must be emphasized that the time limits given in Table 1 are meant primarily for operational purposes. They are

Table 1. Operational dimensions with t_1 indicating the time that emergency treatment of SE should be started and t_2 indicating the time at which long-term consequences may be expected

Type of SE	Operational dimension 1 Time (t_1), when a seizure is likely to be prolonged leading to continuous seizure activity	Operational dimension 2 Time (t_2), when a seizure may cause long term consequences (including neuronal injury, neuronal death, alteration of neuronal networks and functional deficits)
Tonic–clonic SE	5 min	30 min
Focal SE with impaired consciousness	10 min	>60 min
Absence status epilepticus	10–15 min[a]	Unknown

[a]Evidence for the time frame is currently limited and future data may lead to modifications.

general approximations only, and the timing of onset of cerebral damage will vary considerably in different clinical circumstances.

Comment: Axes

The purpose of the diagnostic axes is to provide a framework for clinical diagnosis, investigation, and therapeutic approaches for each patient.[1,4] Previously, in 1970, the axes encompassed (1) clinical seizure type, (2) electroencephalographic ictal and interictal expression, (3) anatomic substrate, (4) etiology, and (5) age. In the 1981 revision, the axes were limited to the seizure type and EEG expression (ictal and interictal) (Classification 1981).

At least half of the patients with SE do not have epilepsy or specific epilepsy syndromes—they have SE due to acute or remote central nervous system or systemic illness. Therefore, the axes used previously in seizure classification need to be modified for the classification of status epilepticus.

Classification of Status Epilepticus

For classification of SE we propose the following four axes:

1 Semiology
2 Etiology
3 EEG correlates
4 Age

Ideally, every patient should be categorized according to each of the four axes. However, it is acknowledged that this will not always be possible. At initial presentation, the approximate age of the patient and the semiology will be immediately assessable. The etiology will be apparent less frequently and may take time to identify. It is also recognized that EEG recordings will not be available in many settings, particularly at presentation. However, the EEG will affect choice and aggressiveness of treatment, prognosis, and clinical approaches, so an EEG should be sought where possible and as early as possible. In fact, some forms of SE may only be reliably diagnosed by EEG.[23] Like in other acute neurologic conditions, the semiology (symptoms and signs) and the EEG pattern in SE are highly dynamic and may change over short time periods in a given patient. Thus, repeated neurologic examinations and EEG investigations in a patient with SE may lead to a different classification. For example, SE may start with focal motor symptoms evolving into bilateral convulsive SE (A.1.b) and may present a few hours later as nonconvulsive SE (NCSE) with coma and minor motor phenomena resembling so called "subtle status" (B.1). Likewise, the EEG may show lateralized periodic discharges at the beginning and a bilateral synchronous pattern at the second investigation.

Axis 1: Semiology

This axis refers to the clinical presentation of SE and is therefore the backbone of this classification. The two main taxonomic criteria are:

1. The presence or absence of prominent motor symptoms
2 The degree (qualitative or quantitative) of impaired consciousness

Those forms with prominent motor symptoms and impairment of consciousness may be summarized as *convulsive SE* as opposed to the *nonconvulsive forms of SE* (NCSE). Although the term *convulsion* is sometimes disregarded as a lay term, it reflects the clinician′s ordinary language. In fact "status epilepticus" is also a lay term, as it is the English translation of *état de mal*, which was used in the 19th century by patients in the Salpêtrière.[24] Thus, it was decided to keep the well-accepted term "convulsive." It designates "*episodes of excessive abnormal muscle contractions, usually bilateral, which may be sustained, or interrupted*"[25] (Table 2).

Table 2. Axis 1: Classification of status epilepticus (SE)

(A) With prominent motor symptoms
A.1 Convulsive SE (CSE, synonym: tonic–clonic SE)
A.1.a. Generalized convulsive
A.1.b. Focal onset evolving into bilateral convulsive SE
A.1.c. Unknown whether focal or generalized
A.2 Myoclonic SE (prominent epileptic myoclonic jerks)
A.2.a. With coma
A.2.b. Without coma
A.3 Focal motor
A.3.a. Repeated focal motor seizures (Jacksonian)
A.3.b. Epilepsia partialis continua (EPC)
A.3.c. Adversive status
A.3.d. Oculoclonic status
A.3.e. Ictal paresis (i.e., focal inhibitory SE)
A.4 Tonic status
A.5 Hyperkinetic SE
(B) Without prominent motor symptoms (i.e., nonconvulsive SE, NCSE)
B.1 NCSE with coma (including so-called "subtle" SE)
B.2 NCSE without coma
B.2.a. Generalized
B.2.a.a Typical absence status
B.2.a.b Atypical absence status
B.2.a.c Myoclonic absence status
B.2.b. Focal
B.2.b.a Without impairment of consciousness (aura continua, with autonomic, sensory, visual, olfactory, gustatory, emotional/psychic/experiential, or auditory symptoms)
B.2.b.b Aphasic status
B.2.b.c With impaired consciousness
B.2.c Unknown whether focal or generalized
B.2.c.a Autonomic SE

Axis 2: Etiology

The underlying cause (etiology) of SE is categorized in a manner that is consistent with the concepts of the ILAE Commission for Classification proposal 2010,[5] but acknowledges the well-established terms that are used by epileptologists, emergency doctors, neurologists, pediatric neurologists, neurosurgeons, family doctors, and other clinicians looking after patients with SE (Table 3).

The term "*known*" or "*symptomatic*" is used—consistent with the common neurologic terminology—for SE caused by a known disorder, which can be structural, metabolic, inflammatory, infectious, toxic, or genetic. Based on its temporal relationship, the subdivisions acute, remote, and progressive can be applied.

Table 3. Currently indeterminate conditions (or "boundary syndromes")

Epileptic encephalopathies
Coma with non evolving epileptiform EEG pattern[a]
Behavioral disturbance (e.g., psychosis) in patients with epilepsy
Acute confusional states, (e.g., delirium) with epileptiform EEG patterns

[a]Lateralized and generalized periodic discharges with monotonous appearance are not considered as evolving EEG patterns.[26,27]

Table 4. Etiology of status epilepticus

Known (i.e., symptomatic)
Acute (e.g., stroke, intoxication, malaria, encephalitis, etc.)
Remote (e.g., posttraumatic, postencephalitic, poststroke, etc.)
Progressive (e.g., brain tumor, Lafora's disease and other PMEs, dementias)
SE in defined electroclinical syndromes
Unknown (i.e., cryptogenic)

The term "idiopathic" or "genetic" is not applicable to the underlying etiology of SE. In idiopathic or genetic epilepsy syndromes, the cause of status is not the same as for the disease, but some metabolic, toxic, or intrinsic factors (like sleep deprivation) may trigger SE in these syndromes. Therefore, the term "idiopathic"[28] or "genetic"[5] is not used here. SE in a patient with juvenile myoclonic epilepsy (which itself is "idiopathic" or "genetic") can be symptomatic, due to inappropriate antiepileptic drug (AED) treatment, abrupt drug withdrawal, or drug intoxication.

The term "*unknown*" or "*cryptogenic*" (Greek: κρύπτος, hidden or unknown, τὸ γένος, family, class, descent, origin) is used in its strict original meaning: *unknown cause*. The assumption that it is "presumably" symptomatic or genetic is inappropriate. Synonymously and consistent with the proposal 2010,[5] the term "unknown" or appropriate translations in different languages can be used (Table 4).

SE in its varied forms has a plethora of causes; a list is attached (Appendix 1). The list will be updated periodically and will provide a database for clinicians.

Axis 3: Electroencephalographic correlates

None of the ictal EEG patterns of any type of SE is specific. Epileptiform discharges are regarded as the hallmark, but with increasing duration of SE, the EEG changes and rhythmic nonepileptiform patterns may prevail. Similar EEG patterns, such as triphasic waves, can be recorded in various pathologic conditions, leading to substantial confusion in the literature. Although the EEG is overloaded with movement and muscle artifact in the convulsive forms of SE and thus of limited clinical value, it is indispensable in the diagnosis of NCSE, as the clinical signs (if any) are often subtle and nonspecific.[23,29] Advances in electrophysiologic techniques may provide us with increased capability to utilize EEG in the emergency setting and allow better delineation of the highly dynamic changes of EEG patterns in the near future.

Currently there are no evidence-based EEG criteria for SE. Based on large descriptive series and consensus panels,[26,27,30–32] we propose the following terminology to describe EEG patterns in SE:

1 *Location:* generalized (including bilateral synchronous patterns), lateralized, bilateral independent, multifocal.
2 *Name of the pattern:* Periodic discharges, rhythmic delta activity or spike-and-wave/sharp-and-wave plus subtypes.
3 *Morphology:* sharpness, number of phases (e.g., triphasic morphology), absolute and relative amplitude, polarity.

4 *Time-related features*: prevalence, frequency, duration, daily pattern duration and index, onset (sudden vs. gradual), and dynamics (evolving, fluctuating, or static).
5 *Modulation:* stimulus-induced vs. spontaneous.
6 *Effect of intervention (medication) on EEG.*

Axis 4: Age

1 Neonatal (0 to 30 days).
2 Infancy (1 month to 2 years).
3 Childhood (> 2 to 12 years).
4 Adolescence and adulthood (> 12 to 59 years).
5 Elderly (≥ 60 years).

Examples of SE that occur in different age groups, are listed in Table 5 and Figure 1. SE in neonates may be subtle and difficult to recognize. Some forms of SE are seen as an integral part of the electroclinical syndrome; others can occur in patients within a certain electroclinical syndrome, or when trigger factors or precipitating causes are present, such as sleep deprivation, intoxication, or inappropriate medication. Examples are phenytoin in some forms of progressive myoclonic epilepsies,[33] carbamazepine in juvenile myoclonic epilepsy,[34,35] or absence epilepsies.[36]

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Table 5. SE in selected electroclinical syndromes according to age

SE occurring in neonatal and infantile-onset epilepsy syndromes
Tonic status (e.g., in Ohtahara syndrome or West syndrome)
Myoclonic status in Dravet syndrome
Focal status
Febrile SE
SE occurring mainly in childhood and adolescence
Autonomic SE in early-onset benign childhood occipital epilepsy (Panayiotopoulos syndrome)
NCSE in specific childhood epilepsy syndromes and etiologies (e.g., Ring chromosome 20 and other karyotype abnormalities, Angelman syndrome, epilepsy with myoclonic-atonic seizures, other childhood myoclonic encephalopathies; see Appendices 1–3)
Tonic status in Lennox-Gastaut syndrome
Myoclonic status in progressive myoclonus epilepsies
Electrical status epilepticus in slow wave sleep (ESES)
Aphasic status in Landau-Kleffner syndrome
SE occurring mainly in adolescence and adulthood
Myoclonic status in juvenile myoclonic epilepsy
Absence status in juvenile absence epilepsy
Myoclonic status in Down syndrome
SE occurring mainly in the elderly
Myoclonic status in Alzheimer's disease
Nonconvulsive status epilepticus in Creutzfeldt-Jakob disease
De novo (or relapsing) absence status of later life

These forms of SE may be encountered prevalently in some age groups, but not exclusively.

Conflict of Interest

Dr. Trinka has received research funding from UCB Pharma, Biogen-Idec, Red Bull, Merck, the European Union, FWF Österreichischer Fond zur Wissenschaftsförderung, and Bundesministerium für Wissenschaft und Forschung and has acted as a paid consultant to Eisai, Takeda, Ever Neuropharma, Biogen Idec, Medtronics, Bial, and UCB and has received speakers' honoraria from Bial, Eisai, GL Lannacher, GlaxoSmithKline, Boehringer, Viropharma, Actavis, and UCB Pharma. He has no specific conflicts relevant to this work. Dr. Cock has served as a paid consultant for Special Products Ltd and Eisai Europe Ltd, and received support from UCB pharma, GlaxoSmithKline, and Lupin pharmaceuticals. Details at www.whopaysthisdoctor.org. She has no specific conflicts relevant to this work. Dr. Hesdorffer serves on Advisory Boards for Upsher-Smith and Acorda; is a consultant to Cyberonics, The Department of Rehabilitation Medicine at Mount Sinai Medical Center, and the Comprehensive Epilepsy Center at NYU Langone Medical Center; and is an Associate Editor of *Epilepsia*. She has no specific conflicts relevant to this work. Dr. Rossetti received research support from UCB Pharma and Sage Pharmaceuticals. He has no specific conflicts relevant to this work. Dr. Scheffer has no specific conflicts relevant to this work. Dr. Shinnar has served as consultant to Accorda, AstraZeneca, Questcor, and Upsher-Smith. He serves on a Daqta Safety Monitoring Board for UCB pharma. He has no specific conflicts relevant to this work. Dr. Shorvon has received research grants, or speakers or consultancy fees from Eisai, Viropharma, Sage, and Takeda. He has no specific conflicts relevant to this work. Dr. Lowenstein has served in the past as a paid consultant for Upsher-Smith, and his current work with the Human Epilepsy Project, a research project administered through the Epilepsy Study Consortium, is supported by UCB Pharma, Pfizer, Lundbeck, and Eisai, as well as various foundations. He has no specific conflicts relevant to this work. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guideline.

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Appendix 1: List of Etiologies That May Cause Status Epilepticus (Not Exhaustive)

1 Cerebrovascular diseases
- a Ischemic stroke
- b Intracerebral bleeding
- c Subarachnoid bleeding
- d Subdural hematoma
- e Epidural hematoma
- f Sinus venous thrombosis and cortical venous thrombosis
- g Posterior reversible leukoencephalopathy syndrome
- h Vascular dementia

2 CNS infections
- a Acute bacterial meningitis
- b Chronic bacterial meningitis
- c Acute viral encephalitis (including Japanese B encephalitis, herpes simplex encephalitis, human herpesvirus 6)
- d Progressive multifocal leukoencephalopathy (PML)
- e Cerebral toxoplasmosis
- f Tuberculosis
- g Neurocysticercosis
- h Cerebral malaria
- i Atypical bacterial infections
- j HIV-related diseases
- k Prion diseases (Creutzfeldt-Jakob disease, CJD)
- l Protozoal infections
- m Fungal diseases
- n Subacute sclerosing panencephalitis
- o Progressive Rubella encephalitis

3 Neurodegenerative diseases
- a Alzheimer's disease
- b Corticobasal degeneration
- c Frontotemporal dementia

4 Intracranial tumors
- a Glial tumors
- b Meningioma
- c Metastases
- d Lymphoma
- e Meningeosis neoplastica
- f Ependymoma
- g Primitive neuroectodermal tumor (PNET)

5 Cortical dysplasias
- a Focal cortical dysplasia (FCD) II, tuberous sclerosis complex (TSC), hemimegalencephaly, hemi-hemimegalencephaly
- b Ganglioglioma, gangliocytoma, dysembryoplastic neuroepithelial tumor (DNET)
- c Periventricular nodular heterotopia (PNH) and other nodular heterotopias
- d Subcortical band heterotopia spectrum
- e Lissencephaly
- f Familial and sporadic polymicrogyria
- g Familial and sporadic schizencephaly
- h Infratentorial malformations (e.g., dentate dysplasia, mamillary dysplasia, etc.)

6 Head trauma
- a Closed head injury
- b Open head injury
- c Penetrating head injury

7 Alcohol related
- a Intoxication
- b Alcohol withdrawal
- c Late alcohol encephalopathy with seizures
- d Wernicke encephalopathy

8 Intoxication
- a Drugs
- b Neurotoxins
- c Heavy metals

9 Withdrawal of or low levels of antiepileptic drugs

10 Cerebral hypoxia or anoxia

11 Metabolic disturbances (e.g., electrolyte imbalances, glucose imbalance, organ failure, acidosis, renal failure, hepatic encephalopathy, radiation encephalopathy, etc.)

12 Autoimmune disorders causing SE
- a Multiple sclerosis
- b Paraneoplastic encephalitis
- c Hashimoto's encephalopathy
- d Anti-NMDA (*N*-methyl-D-aspartate) receptor encephalitis
- e Anti–voltage–gated potassium channel receptor encephalitis (including anti–leucine–rich glioma inactivated 1 encephalitis)
- f Anti-glutamic acid decarboxylase antibody associated encephalitis
- g Anti–alpha–amino–3–hydroxy–5–methylisoxazole–4–propionic acid receptor encephalitis
- h Seronegative autoimmune encephalitis
- i Rasmussen encephalitis
- j Cerebral lupus (systemic lupus erythematosus)
- k CREST (calcinosis, Raynaud phenomenon, esophageal dysmotility, sclerodactyly, telangiectasia) syndrome
- l Adult-onset Still's disease
- m Goodpasture syndrome
- n Thrombotic thrombocytopenic purpura (Moschcowitz syndrome, Henoch Schönlein purpura)

13 Mitochondrial diseases causing SE
- a Alpers disease
- b Mitochondrial encephalopathy, lactic acidosis, and stroke-like episodes (MELAS)
- c Leigh syndrome
- d Myoclonic encephalopathy with ragged red fibers (MERRF)
- e Neuropathy, ataxia, and retinitis pigmentosa (NARP)

14 Chromosomal aberrations and genetic anomalies
- a Ring chromosome 20
- b Angelman syndrome
- c Wolf-Hirshhorn syndrome
- d Fragile X syndrome
- e X-linked mental retardation syndrome
- f Ring chromosome 17
- g Rett syndrome
- h Down syndrome (trisomy 21)

15 Neurocutaneous syndromes
- a Sturge-Weber syndrome

16 Metabolic disorders
- a Porphyria
- b Menkes disease
- c Wilson disease
- d Adrenoleukodystrophy
- e Alexander disease
- f Cobalamin C/D deficiency
- g Ornithine transcarbamylase deficiency
- h Hyperprolinemia
- i Maple syrup urine disease
- j 3-Methylcrotonyl Coenzyme A carboxylase deficiency
- k Lysinuric protein intolerance
- l Hydroxyglutaric aciduria
- m Metachromatic leukodystrophy
- n Neuronal ceroid lipofuscinosis (types I, II, III, including Kufs disease)
- o Lafora disease
- p Unverricht-Lundborg disease
- q Sialidosis (type I and II)
- r Morbus Gaucher
- s Beta ureidopropionase deficiency
- t 3-Hydroxyacyl Coenzyme A dehydrogenase deficiency
- u Carnitine palmitoyltransferase deficiency
- v Succinic semialdehyde dehydrogenase deficiency

17 Others
- a Familial hemiplegic migraine
- b Infantile onset spinocerebellar ataxia (SCA)
- c Wrinkly skin syndrome
- d Neurocutaneous melanomatosis
- e Neuroserpin mutation
- f Wolfram syndrome
- g Autosomal recessive hyperekplexia
- h Cockayne syndrome
- i Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)
- j Robinow syndrome
- k Malignant hyperpyrexia

l Juvenile Huntington's disease (Westphal variant)

Appendix 2: List of Specific Associations in Which SE Is an Integral Part of the Syndrome, the Entity, or Is a Symptom with Strong Clinical Implications (List Is Incomplete and Will Be Elaborated)

Absence status in Ring chromosome 20 syndrome.
Angelman syndrome.
Absence status epilepsy.[37]

Appendix 3: Previous Definitions and Classifications of Status Epilepticus by ILAE-Affiliated Groups

1 Classification of Seizures 1970 (endorsed by the ILAE general assembly):
- a Definition of SE: *" . . . a seizure persists for a sufficient length of time or is repeated frequently enough to produce a fixed and enduring epileptic condition ("status" implies a fixed or enduring state)."*
- b Classification of SE: *"Status may be divided into partial (e.g., Jacksonian), or generalized (e.g., absence status or tonic–clonic status), or unilateral (e.g., hemiclonic) types."*

2 Classification of Seizures Revised 1981 (endorsed by the ILAE general assembly):
- a Definition: *" . . . a seizure persists for a sufficient length of time or is repeated frequently enough that recovery between attacks does not occur."*
- b Classification: *"Status may be divided into partial (e.g., Jacksonian), or generalized (e.g., absence status or tonic–clonic status). When very localized motor status occurs, it is referred to as epilepsia partialis continua."*

3 Glossary of descriptive terms 2001:
- a Definition of status epilepticus: *"A seizure that shows no clinical signs of arresting after a duration encompassing the great majority of seizures of that type in most patients or recurrent seizures without interictal resumption of baseline central nervous system function."*

4 Diagnostic scheme for people with epileptic seizures and with epilepsy 2001:
- a Classification: Continuous seizure types:
  - i Generalized status epilepticus
    - 1 Generalized tonic–clonic status epilepticus
    - 2 Clonic status epilepticus
    - 3 Absence status epilepticus
    - 4 Tonic status epilepticus
    - 5 Myoclonic status epilepticus
  - ii Focal status epilepticus
    - 1 Epilepsia partialis continua (EPC) of Kojevnikov
    - 2 Aura continua
    - 3 Limbic status epilepticus (psychomotor status)
    - 4 Hemiconvulsive status epilepticus with hemiparesis

5 Definition of epileptic seizures and epilepsy 2005:
- a Definition of seizure: *"An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain. The term transient is used as demarcated in time, with a clear start and finish."*
- b Definition of status epilepticus: Though there is no formal definition in the Report, SE is defined as *"a special circumstance with prolonged or recurrent seizures."*

6 Report of the ILAE Classification Core Group 2006:
- a Definition: There is no formal definition of SE in the 2006 report, instead SE is described as *"the failure of natural homeostatic seizure-suppressing mechanisms responsible for seizure termination . . . . Regardless of the specific operationalized definition, however, the mechanisms involved in initiation and spread of the various types of status epilepticus are, in general, similar to those of self limited ictal events, but additional factors that need to be considered in determining criteria for classification include:*
  - *Different mechanisms that can prevent seizure termination, for example, mechanisms that prevent active inhibition, desynchronization of hypersynchronous discharges, and depolarization block.*
  - *Progressive features that contribute to subsequent functional and structural brain disturbances.*
  - *Maturational factors*"
- b Classification: The proposal of the core group recognizes nine types of SE
  - i Epilepsia partialis continua (EPC) of Kojevnikov
  - ii Supplementary motor area (SMA) status epilepticus
  - iii Aura continua
  - iv Dyscognitive focal (psychomotor, complex partial) status epilepticus
  - v Tonic–clonic status epilepticus
  - vi Absence status epilepticus
  - vii Myoclonic status epilepticus
  - viii Tonic status epilepticus
  - ix Subtle status epilepticus