Status Epilepticus (SE)

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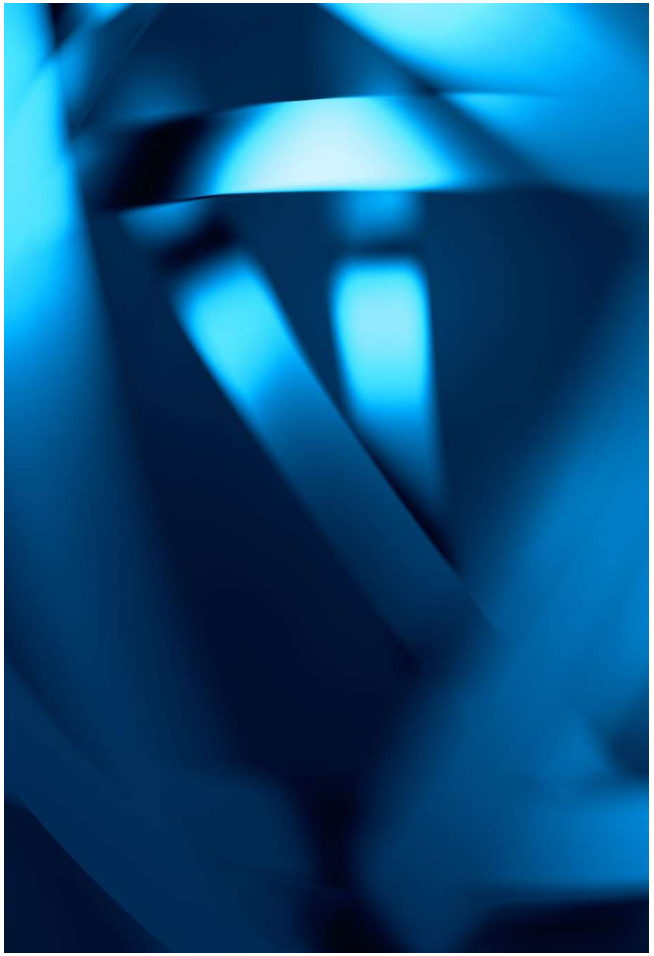


Status epilepticus (SE)

A critical care emergency

- Both convulsive and nonconvulsive status epilepticus (CSE >> NCSE)

Current treatment approaches vary dramatically

Goal

- Rapid termination of the seizure activity
- To reduce neurological injuries and deaths

High mortality esp. refractory status epilepticus

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.

Trinka, et al. ILAE. Epilepsia 2015

Etiologies: acute process

- Metabolic disturbances
  - Electrolyte abnormalities
  - Renal failure
  - Sepsis
- Central nervous system
  - Infection
  - Stroke
  - Head trauma
  - Drug toxicity
  - Hypoxia

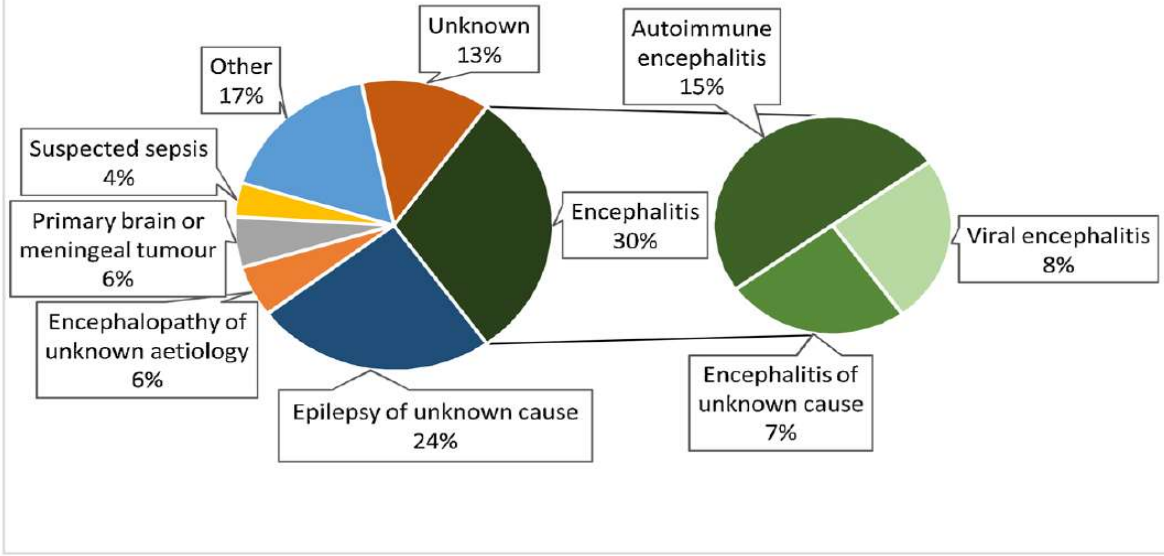
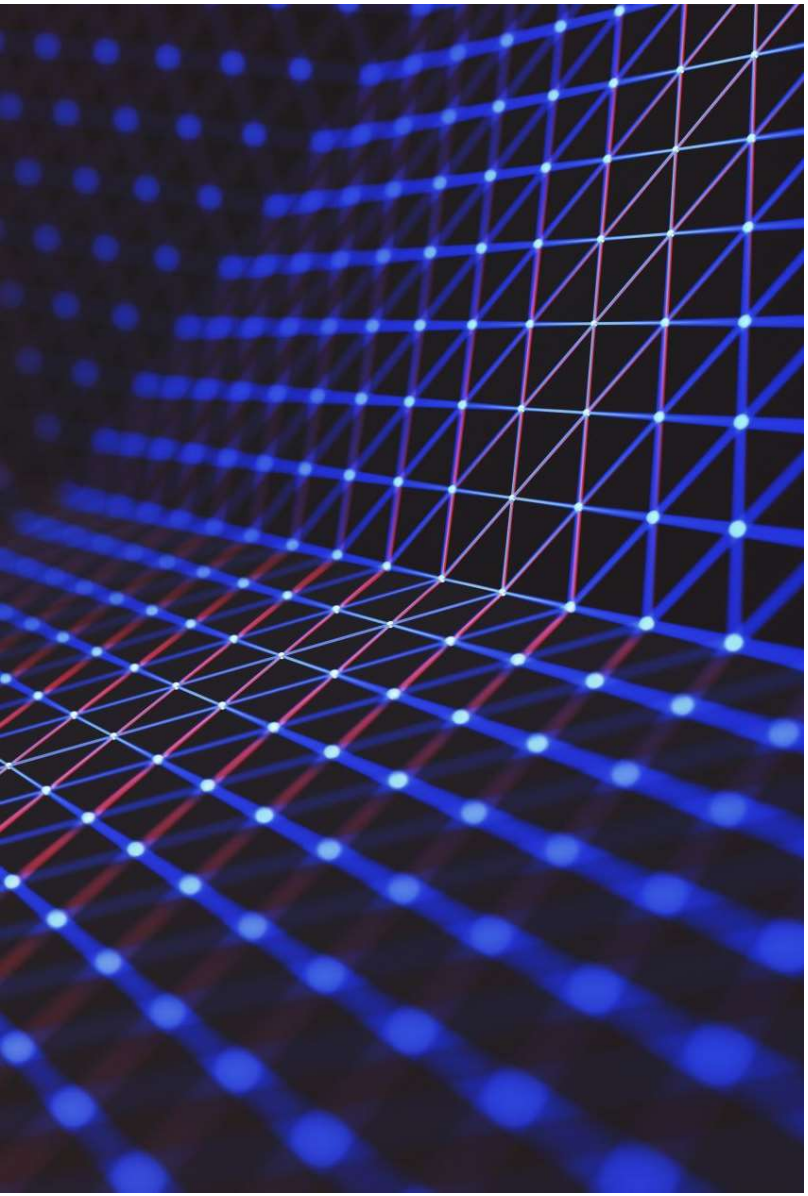


Fig. 1. A pie chart displaying the proportion of aetiologies recorded in the sample.



Cause: chronic process

- Breakthrough seizures
- Discontinuation of antiepileptic drugs
- Chronic ethanol abuse
- CNS tumors or strokes or head injury
- * Respond well to anticonvulsant Rx*

Chin RF, et al. Eur J Neurol. 2004

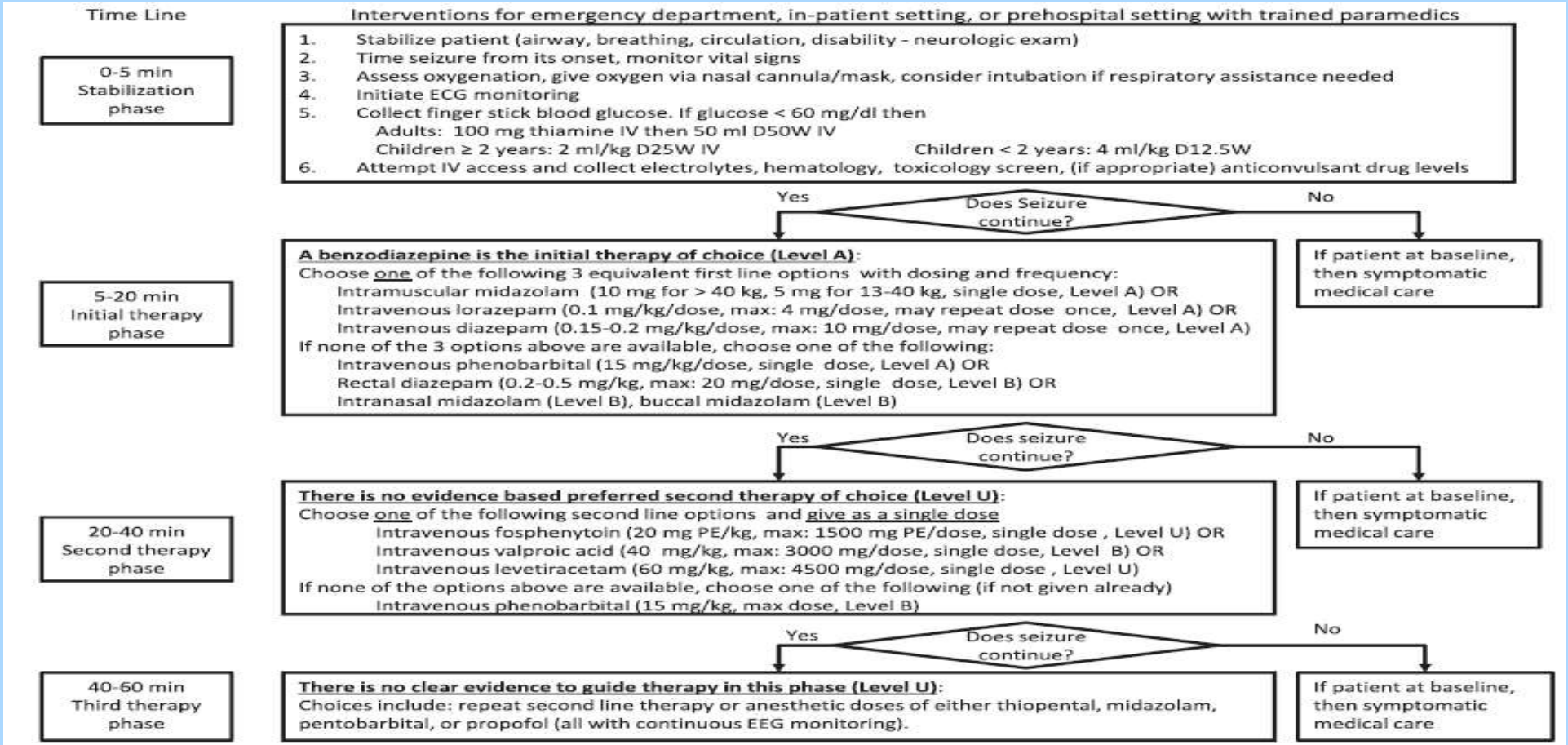
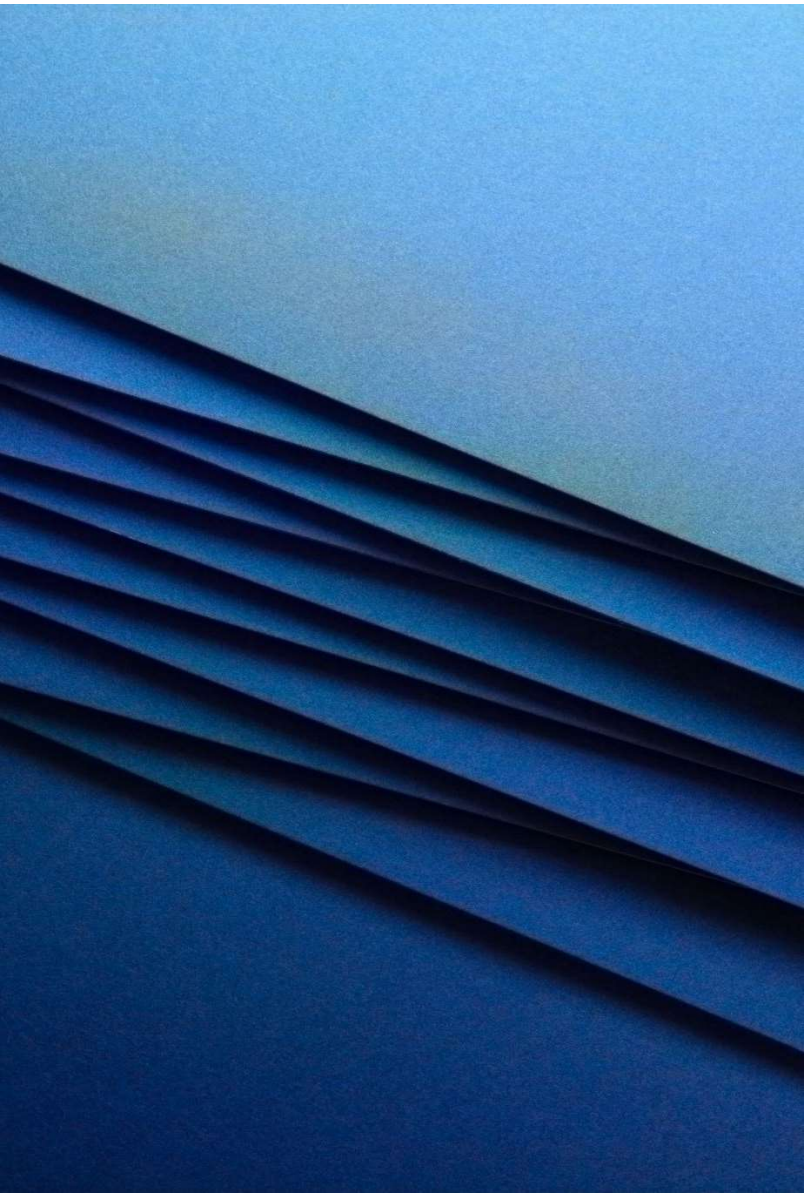


FIGURE 1. Proposed treatment algorithm for status epilepticus.

Disclaimer: This clinical algorithm/guideline is designed to assist clinicians by providing an analytical framework for evaluating and treating patients with status epilepticus. It is not intended to establish a community standard of care, replace a clinician's medical judgment, or establish a protocol for all patients. The clinical conditions contemplated by this algorithm/guideline will not fit or work with all patients. Approaches not covered in this algorithm/guideline may be appropriate.

AES. Epilepsy Currents, Vol. 16, No. 1 (January/February) 2016 pp. 48–61



Status epilepticus

Convulsive status epilepticus

- Consisting of prolonged seizures or repeated generalized tonic–clonic (GTC) seizures with persistent postictal depression of neurologic function between seizures

Repeated partial seizures

- Manifested as focal motor signs, focal sensory symptoms, or focal impairment of function (e.g., aphasia) not associated with altered awareness (so called epilepsia partialis continua)

Nonconvulsive status epilepticus

- Where seizures produce a continuous or fluctuating “epileptic twilight” state

Status epilepticus (SE) in ICU

SE occur in up to 50% of critically ill patients with altered consciousness

More than 80% of SE, they present without movements

Focal status epilepticus (SE)

- Prolonged seizures (or repeated self-limited events without return to baseline clinical conditions) lasting at least 5 min (for tonic-clinic seizures, which may evolve into nonconvulsive SE in coma), or 10 min (for nonconvulsive seizures, or focal SE with or without impaired consciousness or cognitive dysfunction).

Electrical abnormalities

Rhythmic or periodic EEG alterations with evolution of field, amplitude and frequency

Electrical seizures:

Nonconvulsive seizures
at least 10 seconds

Electrical status epilepticus:

Nonconvulsive status epilepticus
at least 10 minutes

Nonconvulsive SE

- Highly epileptiform patterns
  - Represent as high risk for seizures need to be vigilant
  - Periodic discharges of any location
    (GPDs, LPDs, lateralized rhythmic delta activity [LRDA], and brief potentially ictal rhythmic discharges [BIRDs])
  - Recommend
    - Continuous EEG monitoring
    - Prophylaxis ASMs of cannot perform cEEG

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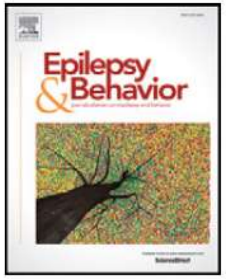


Review

Which EEG patterns in coma are nonconvulsive status epilepticus?

Eugen Trinka [a,b,*], Markus Leitinger [a]

[a] Department of Neurology, Christian Doppler Klinik, Paracelsus Medical University, Salzburg, Austria
[b] Centre for Cognitive Neuroscience, Salzburg, Austria

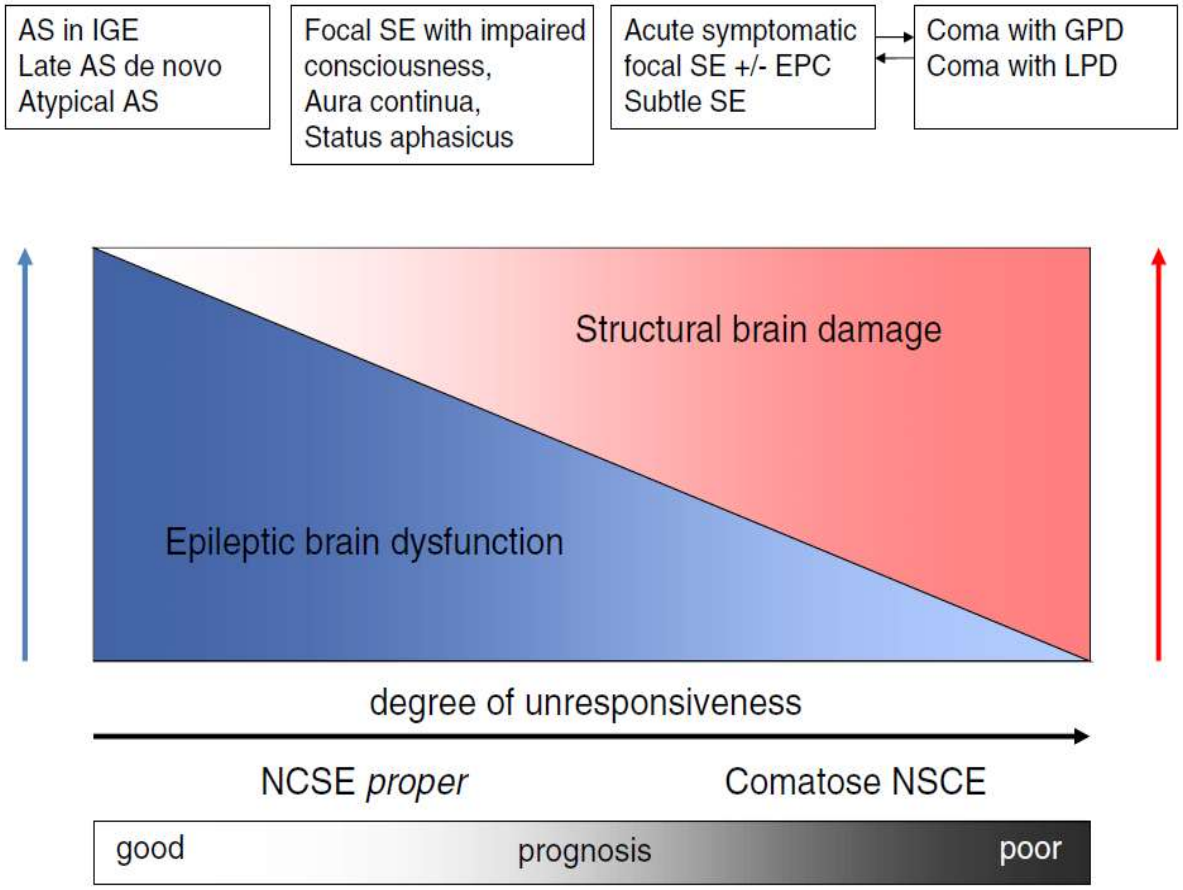


Fig. 2. The relationship of the depth of coma and the contribution of the epileptic activity during nonconvulsive status epilepticus (modified from 14, Fig. 11). Abbreviations: AS: absence status epilepticus, EPC: epilepsia partialis continua, GPDs: generalized periodic discharges, IGE: idiopathic generalized epilepsy, LPDs: lateralized periodic discharges, NCSE: nonconvulsive status epilepticus.

Discharges

The term ictal-interictal continuum encompasses EEG patterns that are potentially harmful and can cause neuronal injury. There are no clear guidelines on how to treat EEG patterns that lie on this continuum.

1) clear electrographic seizures and status epilepticus (SE), i.e., generalized spike-wave discharges at 3/s or faster; and clearly evolving discharges of any type (rhythmic, periodic, fast activity), whether focal or generalized;

2. clear interictal patterns, i.e., spike-wave discharges, periodic discharges, and rhythmic patterns at 1/s or slower with no evolution, unless accompanied by a clear clinical correlate, which would make them ictal regardless of the frequency

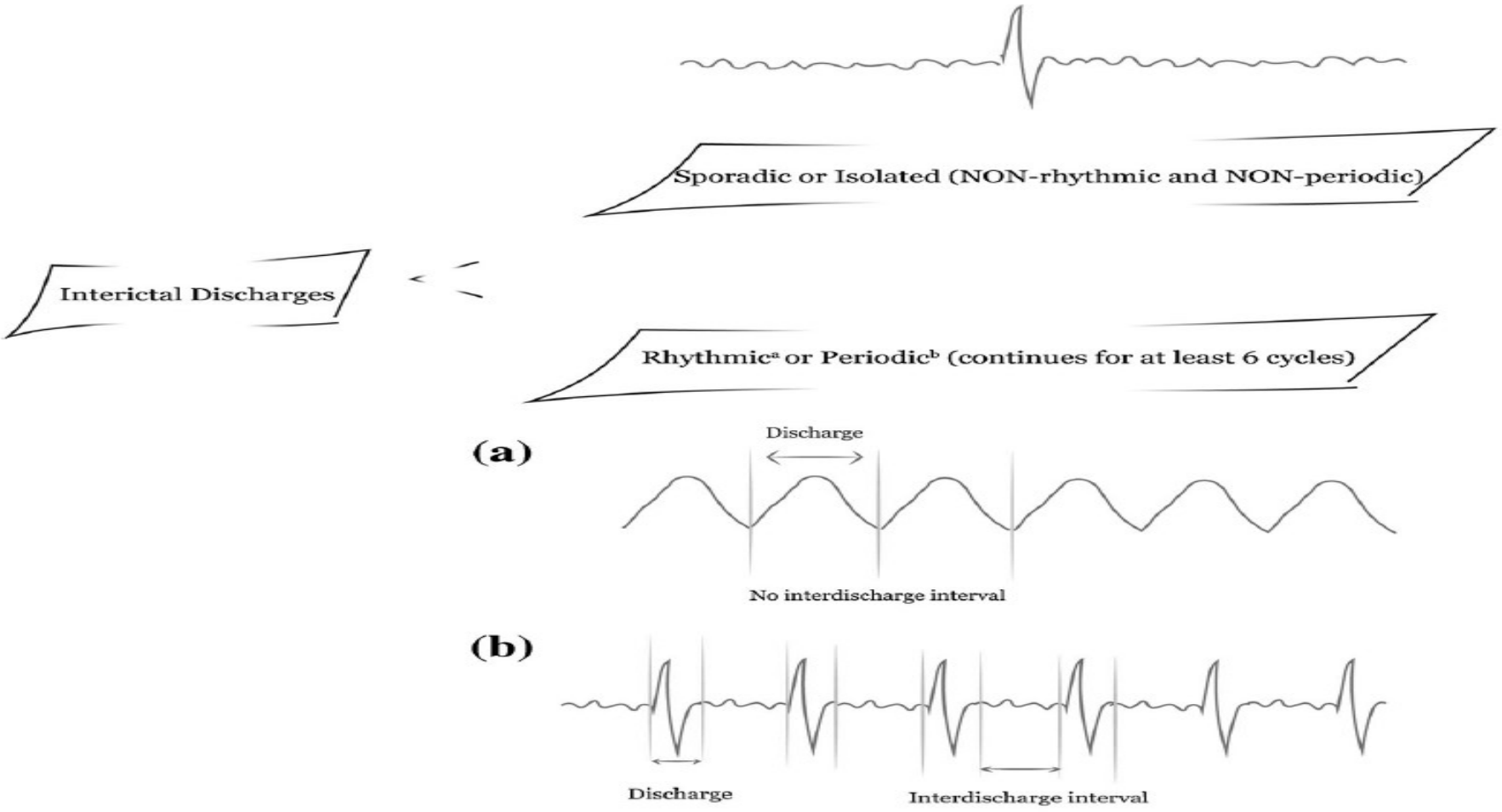
3. any EEG patterns that lie in between the above two categories as being on the ictal-interictal continuum

Periodic discharges (PDs)

"Relatively uniform morphology and duration with a quantifiable

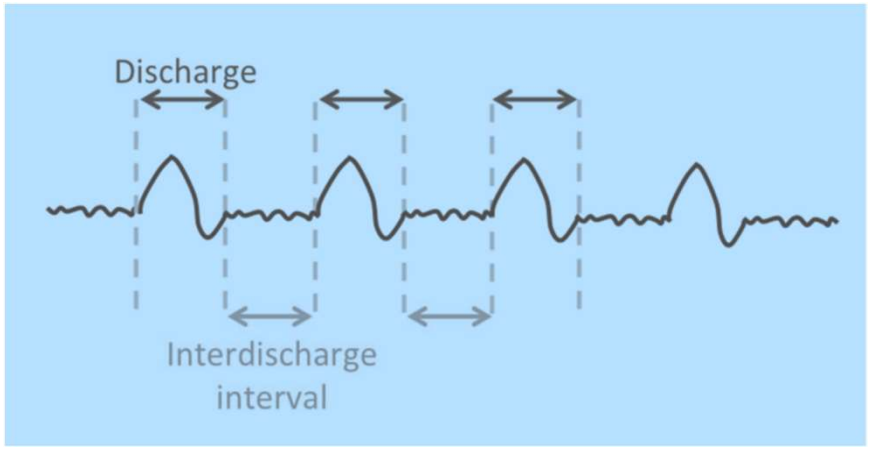
Interdischarge interval between consecutive waveforms and recurrence

Nearly regular intervals


Sporadic or Isolated (NON-rhythmic and NON-periodic)
Interictal Discharges
Rhythmic[a] or Periodic[b] (continues for at least 6 cycles)
(a)
Discharge
No interdischarge interval
(b)
Discharge
Interdischarge interval

Ictal-interictal continuum (IIC EEG pattern)

- **Rhythmic delta activity (RDA):** LRDA, GRDA
- **Periodic discharges (PDs):** LPD, GPD, BiPD, MfPD



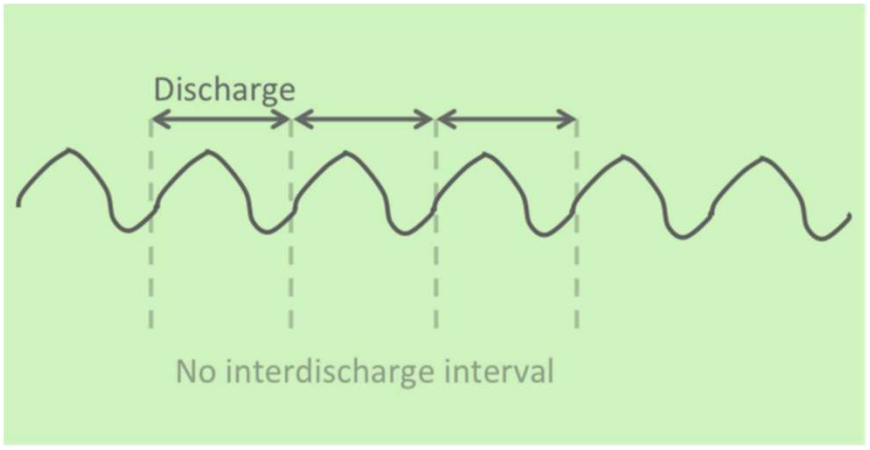
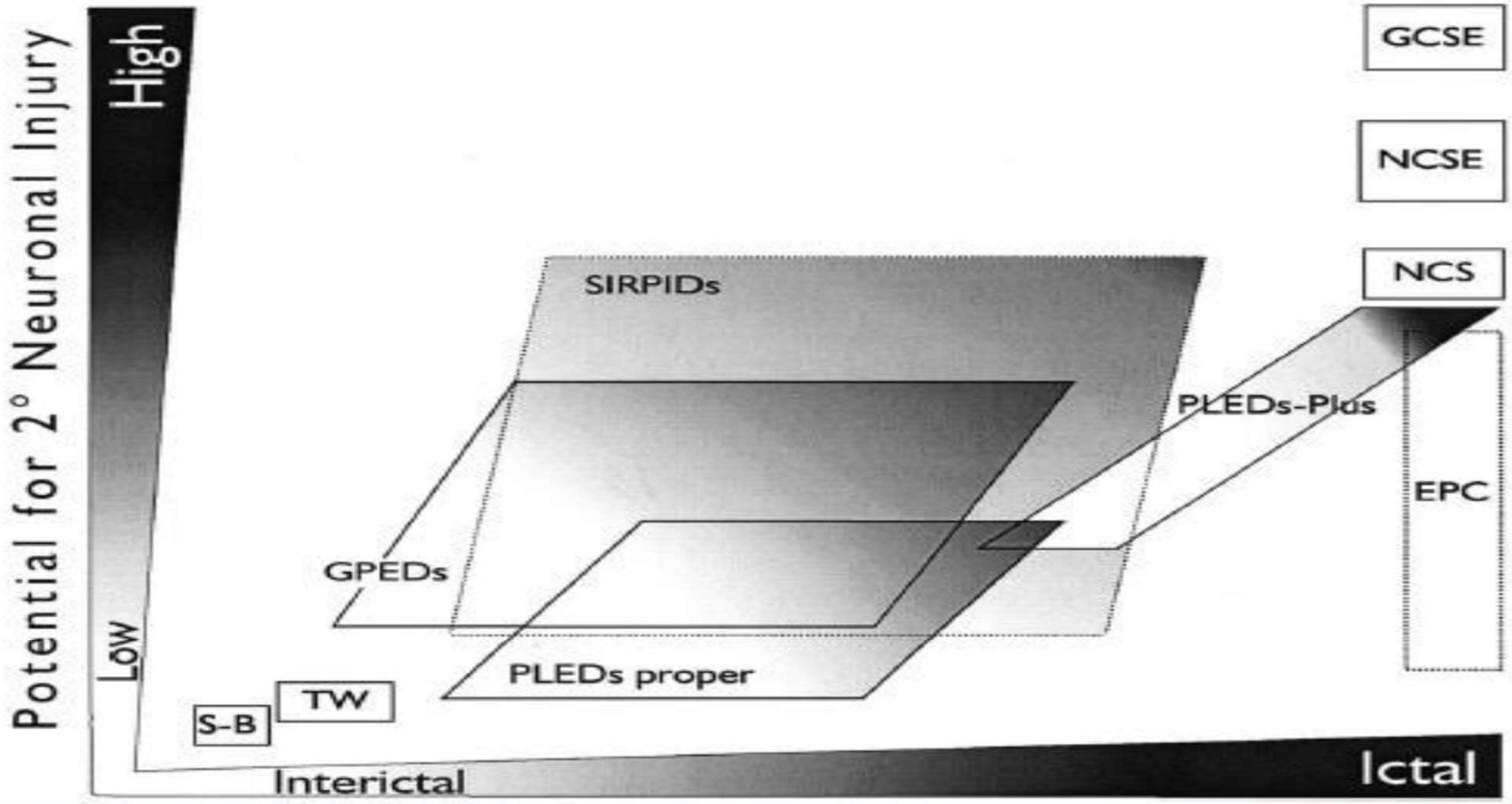


TABLE 1. New Terms for Older Terms

OLD Term		NEW Term
Triphasic waves, most of record	=	continuous 2/s GPDs (with triphasic morphology)
PLEDs	=	LPDs
BIPLEDs	=	BIPDs
GPEDs/PEDs	=	GPDs
FIRDA	=	Occasional frontally predominant brief 2/s GRDA (if 1-10% of record)
PLEDS+	=	LPDs+
SIRPIDs* w/ focal evolving RDA	=	SI-Evolving LRDA
Lateralized seizure, delta frequency	=	Evolving LRDA
Semirhythmic delta	=	Quasi-RDA

*SIRPIDs = stimulus-induced rhythmic, periodic or ictal discharges.

The Ictal-Interictal-Injury Continuum



Chong DJ and Hirsch LJ et al; J Clin Neurophysiol 2005

EEG patterns	Do NOT reflect NCSE NOT TREATED	Reflect NCSE Should be TREATED	BORDERLINE Of NCSE in coma One additional criteria is needed to diagnose NCSE
❖ Classical coma patterm - Diffuse polymorphic delta activity - Spindle coma - Alpha/theta coma - Low votage - Burst suppression	× × × × ×		
❖ Ictal patterns with typical spatiotemporal evolution ❖ Epileptiform discharges > 2.5 Hz in comatose patients		× ×	
❖ GPDs or LPDs < 2.5 Hz ❖ Rhythmic discharges (RDs) > 0.5 Hz			× ×

Trinka U, et al. Epilepsy & Behav 2015

Electric seizures causing….

Seizure density over time correlates with increased risk of poor cognitive and neurological outcome, both in children and adults.

Occurrence of electric seizures or periodic discharges has been independently associated to poor outcome in medical and neurological critical care patients and to development of hippocampal atrophy following brain trauma

Payne ET, et al. Brain 2014., DeMarchis GM, et al. Neurology 2016, Hirsch LJ, et al. J Clin Neurophysiol 2012, Vespa P, et al. Ann Neurol 2016

EEG correlates

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.

LPDs

- A variety of etiologies with cortical pathology (e.g., encephalitis, stroke, subarachnoidal bleeding, trauma, tumors, cysticercosis, and intoxication) or subcortical pathology
- A long-lasting debate whether they represent an ictal, interictal, or semiictal pattern
- Comatose patients (coma-LPDs)
- PLED-proper
- PLED-plus, with superimposed faster activity
- Bilateral independent LPDs (or BiPLEDs) or multifocal LPDs

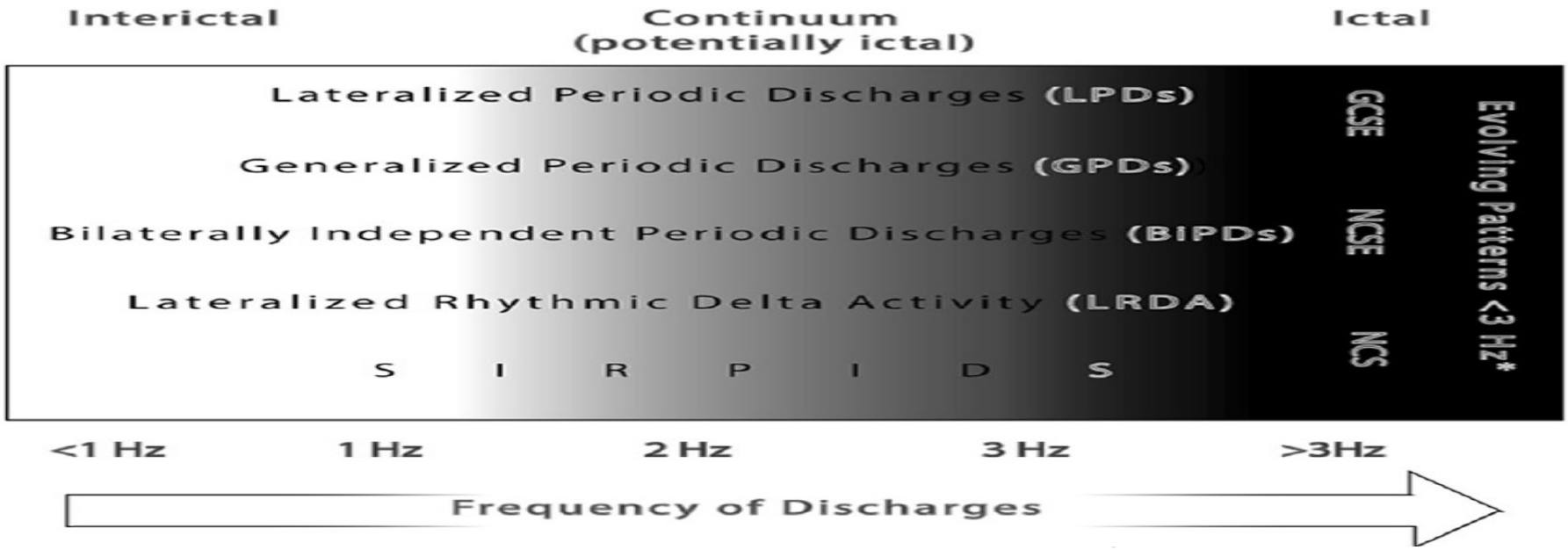


Fig. 3. This figure demonstrates various EEG patterns, primarily based on frequency depicted along the ictal-interictal continuum. The frequency of discharges is shown on the *x*-axis, which has traditionally been the benchmark guiding the aggressiveness of treatment. This frequency based division between intertical, continuum and ictal is arbitrary, conceptual, and does not take evolution of patterns into account. From our experience evolution of EEG patterns can be subtle, especially when observing long epochs in critically ill patients, and if often difficult to reach a consensus. However, the presence of even subtly evolving patterns increases the possibility of them being ictal. If clinical correlate is present with any of these patterns, it has to be considered ictal by definition, regardless of the frequency.*At least 1 Hz with clear (unequivocal) evolution in frequency, morphology, or location is considered to be ictal—see Table 1. *GCSE* generalized convulsive status epilepticus, *NCSE* nonconvulsive status epilepticus, *NCS* nonconvulsive seizure, *SIRPIDs* stimulus-induced rythmic periodic or ictal discharges

Epilepsia, 54(Suppl. 6):28–29, 2013
doi: 10.1111/epi.12270

STATUS EPILEPTICUS 2013

Unified EEG terminology and criteria for nonconvulsive status epilepticus

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Table 1. Working clinical criteria for nonconvulsive status epilepticus

Patients without known epileptic encephalopathy
- EDs > 2.5 Hz, *or*
- EDs ≤ 2.5 Hz or rhythmic delta/theta activity (>0.5 Hz) AND one of the following:
  - EEG and clinical improvement after IV AED[a], *or*
  - Subtle clinical ictal phenomena during the EEG patterns mentioned above, *or*
  - Typical spatiotemporal evolution[b]

Patients with known epileptic encephalopathy
- Increase in prominence or frequency of the features mentioned above, when compared to baseline **with** observable change in clinical state
- Improvement of clinical and EEG[a] features with IV AEDs

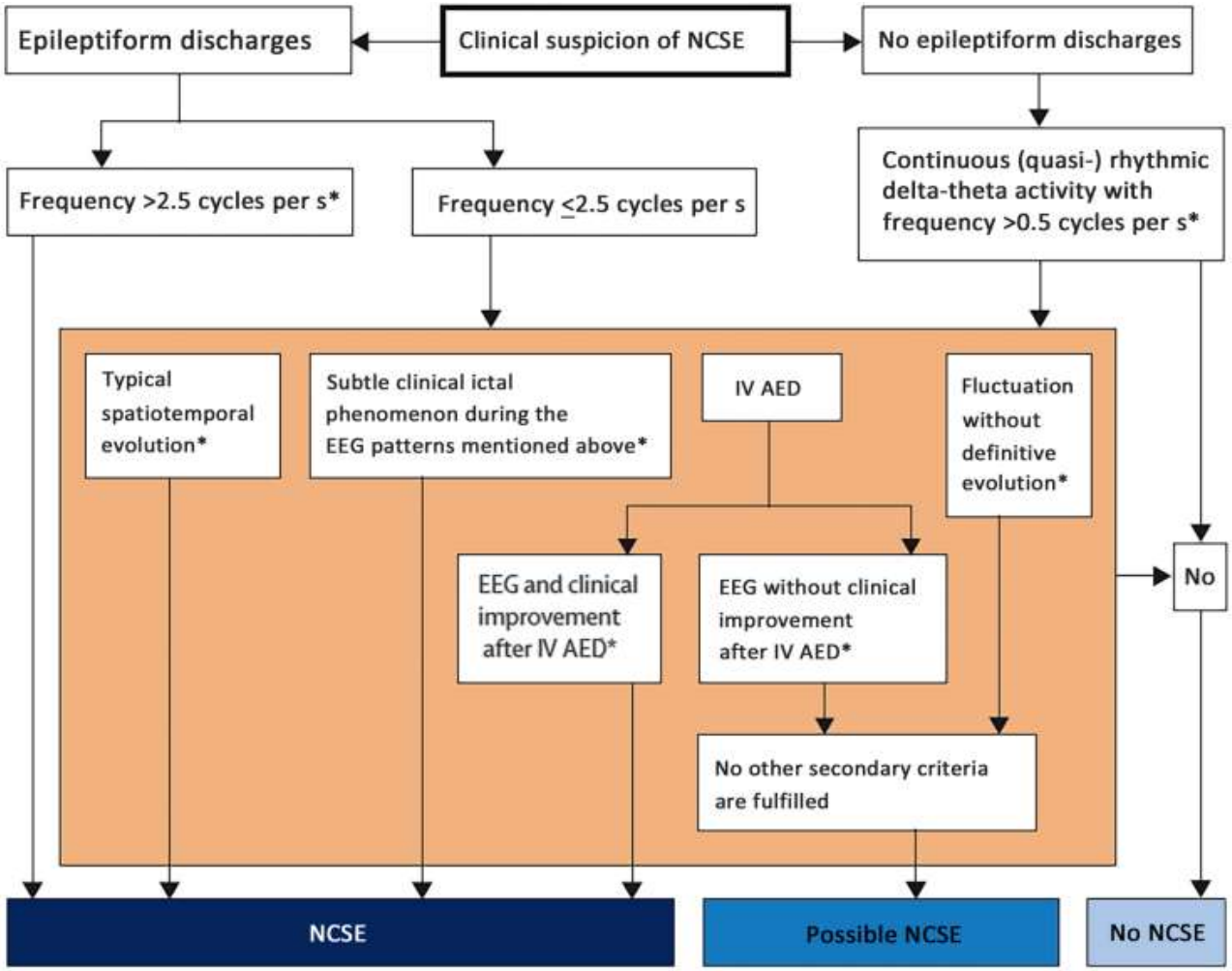
Modified from Kaplan (2007).

EDs, epileptiform discharges (spikes, poly spikes, sharp-waves, sharp-and-slow-wave complexes); IV AEDs: intravenous antiepileptic drugs.

[a]If EEG improvement occurs without clinical improvement, or if fluctuation without definite evolution, this should be considered possible NCSE.

[b]Incrementing onset (increase in voltage and change in frequency), or evolution in pattern (change in frequency >1 Hz or change in location), or decrementing termination (voltage or frequency).

Salzburg Consensus Criteria for diagnosis of Non-Convulsive Status Epilepticus (SCNC) were proposed at the 4th London-Innsbruck Colloquium on status epilepticus in Salzburg (2013)



Validated in three different cohorts, with a sensitivity of 97.2%, a specificity of 95.9%, and a diagnostic accuracy of 96.3% in patients with clinical signs of NCSE

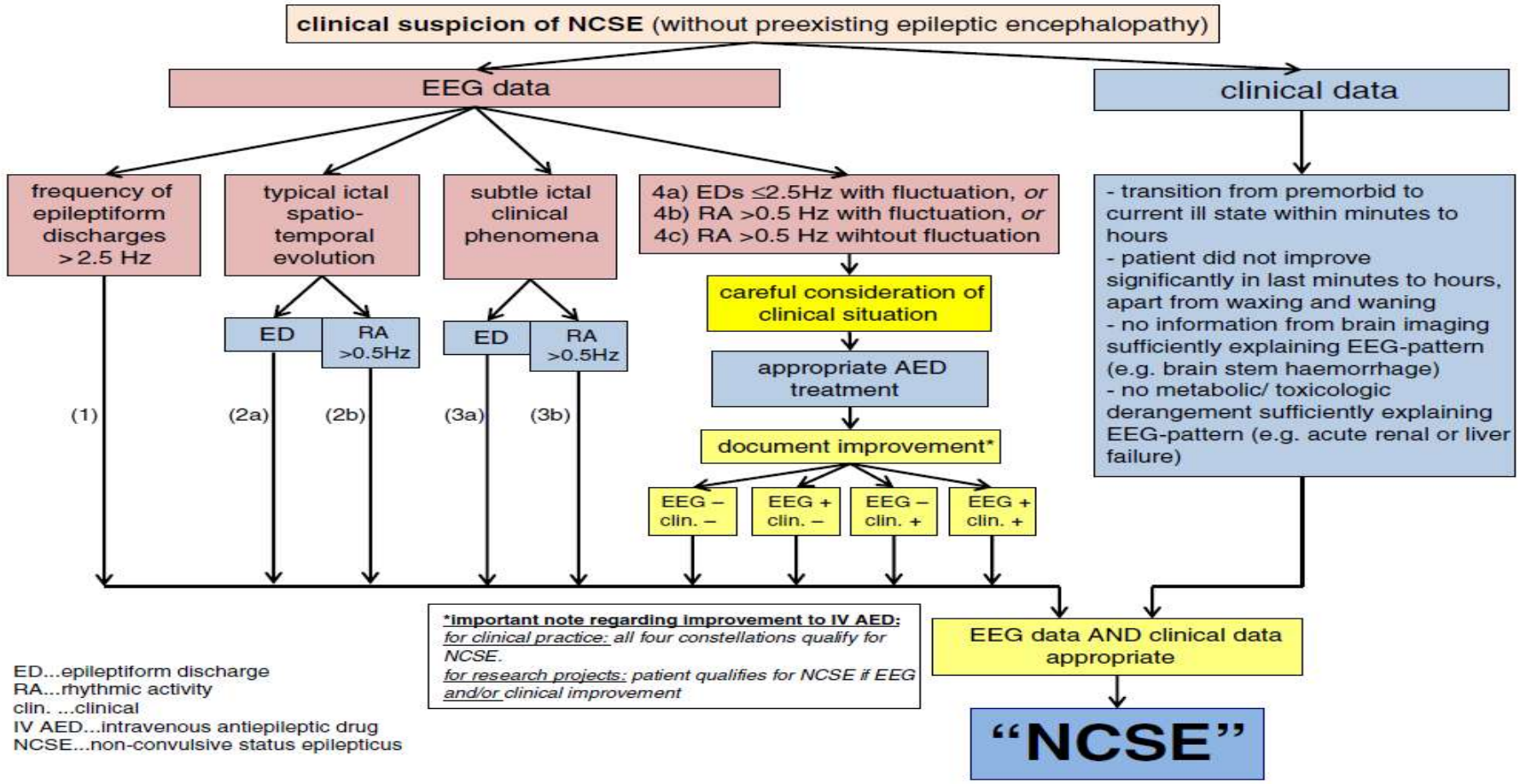


Fig. 12. Algorithm for diagnosis of nonconvulsive status epilepticus with the modified Salzburg Consensus Criteria for NCSE (mSCNC) (see text for further details) [152

Salzburg criteria for nonconvulsive status epilepticus: Details matter,Epilepsia. 2019;60:2334–2336.

Rhythmic delta activity:

- Rhythmic = repetition of a waveform with relatively uniform morphology and duration and without an interval Ibetween consecutive waveforms.
- RDA = rhythmic activity 4 Hz. The duration of one cycle (i.e., the period) of the rhythmic pattern should vary by 50% from the duration of the subsequent cycle for the majority (N50%) of cycle pairs to qualify as rhythmic."

Fluctuation:

- Follows: 3 changes, not more than 1 min apart
  - changes in frequency (by at least 0.5/s)
  - changes in morphology
  - changes in location (by at least 1 standard interelectrode distance) but not qualifying as evolving.
- This includes patterns fluctuating from 1 to 1.5 to 1 to 1.5/s; spreading in and out of a single electrode repeatedly; or alternating between 2 morphologies repeatedly.

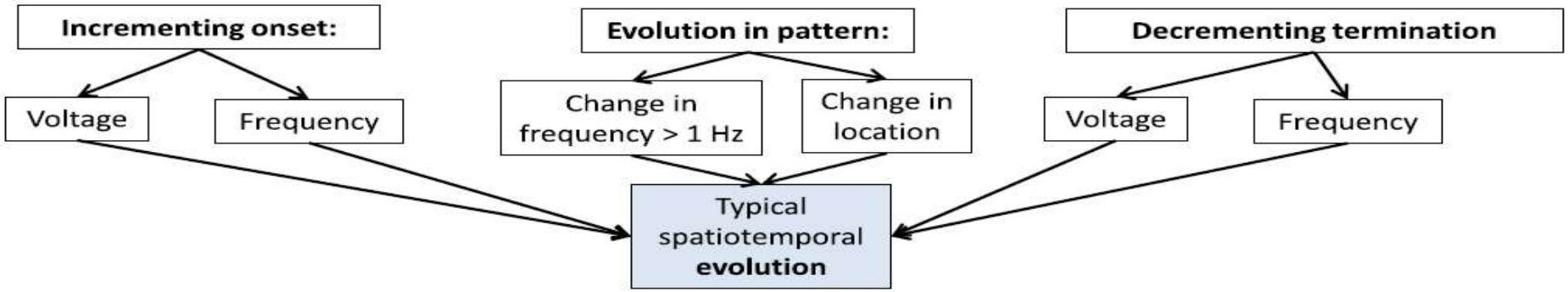
Evolution

- At least 2 unequivocal, sequential changes in frequency, morphology, or location defined as follows
  - evolution in frequency is defined as at least 2 consecutive changes in the same direction by at least 0.5/s, e.g., from 2 to 2.5to 3/s or from 3 to 2 to 1.5/s
  - evolution in morphology is defined as at least 2 consecutive changes to a novel morphology
  - evolution in location is defined as sequentially spreading into or sequentially out of at least two different standard 10–20 electrode locations.

Response to IV AEDs

- Reactivity to IV AEDs within 10 min after AED was fully applied and tested clinically
- Improvement is defined a s better performance in one of the following three domains:
  - (i)"say your surname"
  - (ii)"repeat 1, 2, 3"
  - (iii) "raise your arms"(document the response which can be no response, patient opens eyes to i–iii, and patient looks at the examiner in response to i–iii.
  - If no response repeat procedure after strong tactile stimuli on both sides of the body.
- Electroencephalographic response: improvement is defined as reduction to "occasional occurrence", i.e., 1–9% of epoch).

Which EEG patterns in coma are nonconvulsive status epilepticus?Eugen Trinkaa,b,*,MarkusLeitingeraaDepartment of Neurology, Christian Doppler Klinik, Paracelsus Med University, Salzburg, AustriabCentre for Cognitive Neuroscience, Salzburg, Austria



Evolution: *Incrementing onset (increase in voltage and change in frequency), or evolution in pattern (change in frequency >1 Hz and change in location), or decrementing termination (voltage and frequency).* ***AND ACNS criterion for "evolving" (ACNS-evolving)*** *"at least 2 unequivocal, sequential changes in frequency, morphology or location defined as follows: Evolution in frequency is defined as at least 2 consecutive changes in the same direction by at least 0.5/s, e.g. from 2 to 2.5 to 3/s, or from 3 to 2 to 1.5/s; Evolution in morphology is defined as at least 2 consecutive changes to a novel morphology; Evolution in location is defined as sequentially spreading into or sequentially out of at least two different standard 10-20 electrode locations. In order to qualify as present, a single frequency or location must persist at least 3 cycles (e.g. 1/s for 3 seconds, or 3/s for 1 second)"[2].*

ACNS-criterion for Rhythmic Delta Activity (ACNS-RDA) *"Rhythmic = repetition of a waveform with relatively uniform morphology and duration, and without an interval between consecutive waveforms. RDA = rhythmic activity < 4 Hz. The duration of one cycle (i.e., the period) of the rhythmic pattern should vary by <50% from the duration of the subsequent cycle for the majority (>50%) of cycle pairs to qualify as rhythmic." [2].*

Subtle ictal clinical phenomena: *minor twitching of mouth, periorbital region or extremities should appear in close temporal relation to EEG-pattern (be cautious concerning non-epileptic involuntary movements as mimicks, e.g. Parkinsonian tremor, drug induced myoclonus (e.g. opioids), serotonin syndrome,...),*

Reactivity to IV AEDs*: within 10 minutes after AED fully applied; clinical presentation tested: improvement is defined as better performance in one of five domains (i) "say your surname", (ii) "repeat 1,2,3", (iii) "raise your arms"(first tell, if no response demonstrate), (iv) patient opens eyes to i - iii, (v) patient looks at the examiner in response to i - iii. If no response repeat procedure after strong tactile stimuli on both sides of the body.*

EEG tested: improvement is defined as reduction to "occasional", i.e. 1-9% of epoch.

ACNS criterion for fluctuation (ACNS-fluctuation) *" >3 changes, not more than one minute apart, in frequency (by at least 0.5/s), >3 changes in morphology, or >3 changes in location (by at least 1 standard inter-electrode distance), but not qualifying as evolving. This includes patterns fluctuating from 1 to 1.5 to 1 to 1.5/s; spreading in and out of a single electrode repeatedly; or alternating between 2 morphologies repeatedly." [2]).*

Fig. 13. Algorithm for EEG definition of typical spatiotemporal evolution (see text for further details) and definitions required for mSCNC.

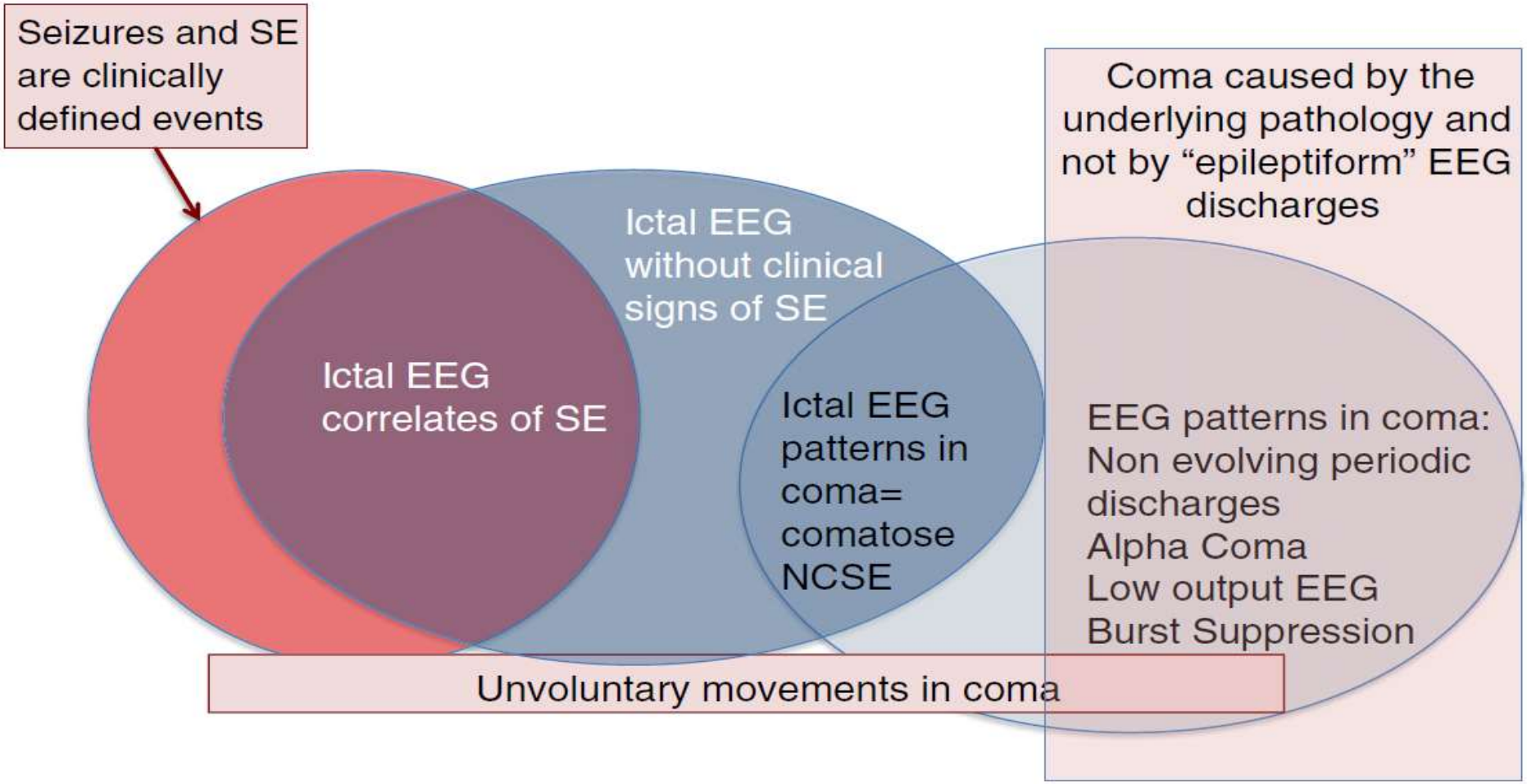


Fig. 14. The relationship of seizures/status epilepticus, ictal EEG patterns, and EEG patterns

Seizures but EEG-non epileptiform

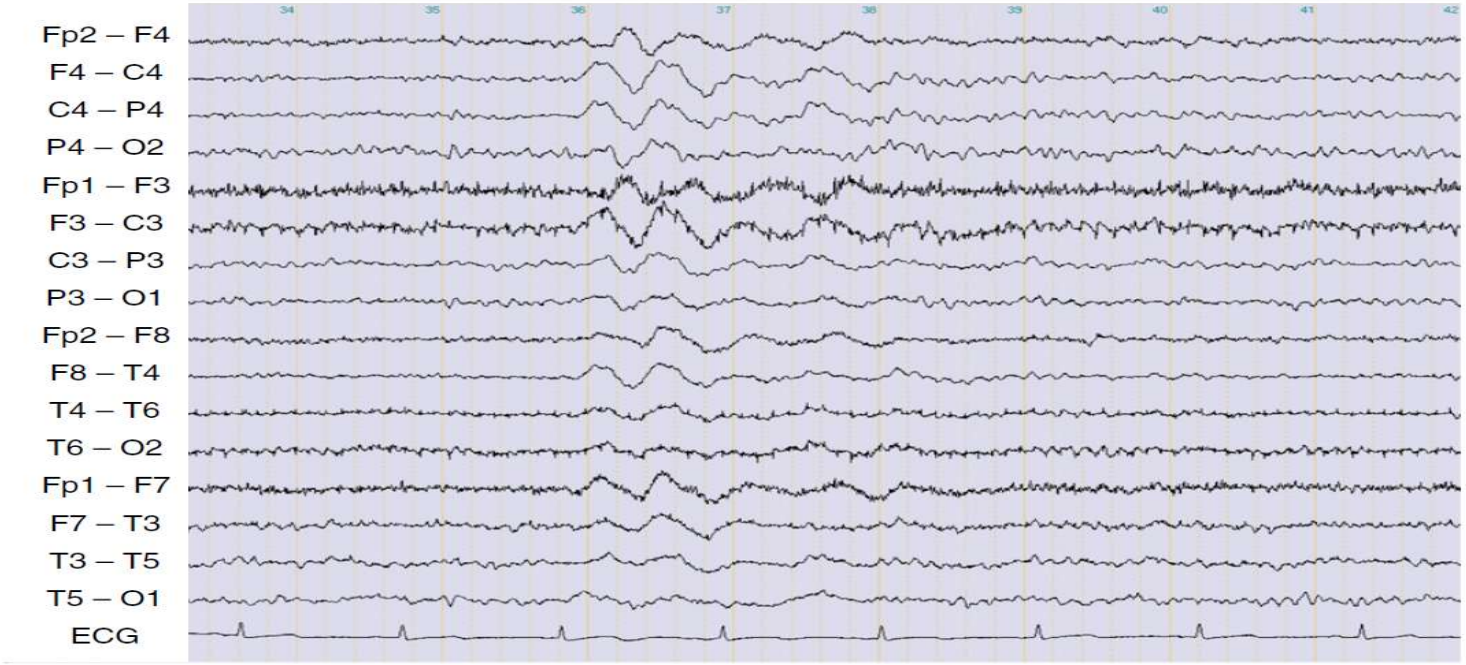


Fig. 3. Woman, 54 years of age; mild drowsiness; posterior reversible encephalopathy syndrome; TC 01, HF 70: frontal intermittent rhythmic delta activity.

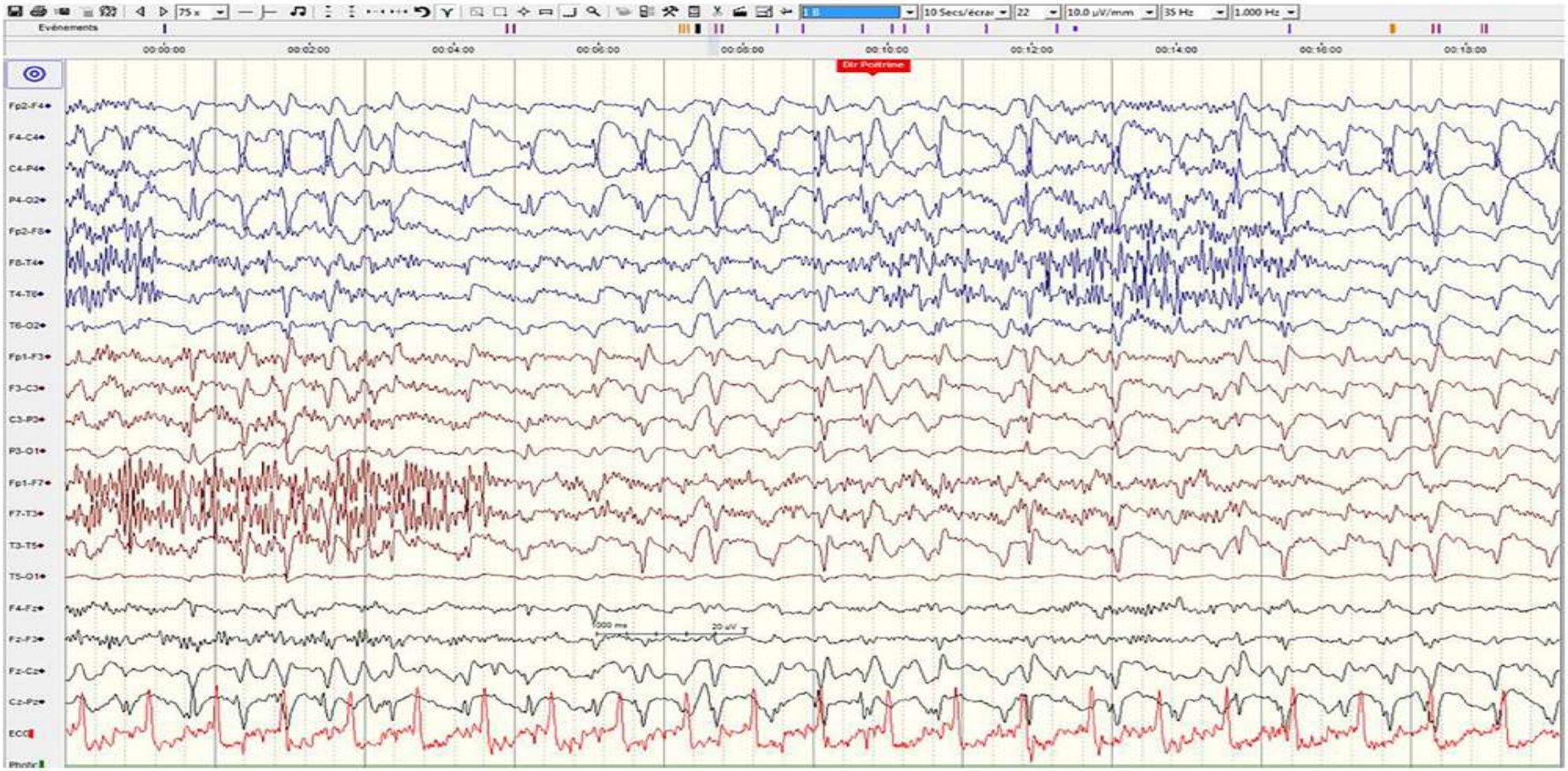


Fig. 2. 42 year old woman with cardiac arrest. The EEG 27 h later (bipolar longitudinal montage, 30 mm/sec) shows periodic sharp waves (GPDs) somewhat more prominent or the right, superimposed on an irregular theta background that appears reactive upon pain stimulation (red mark). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

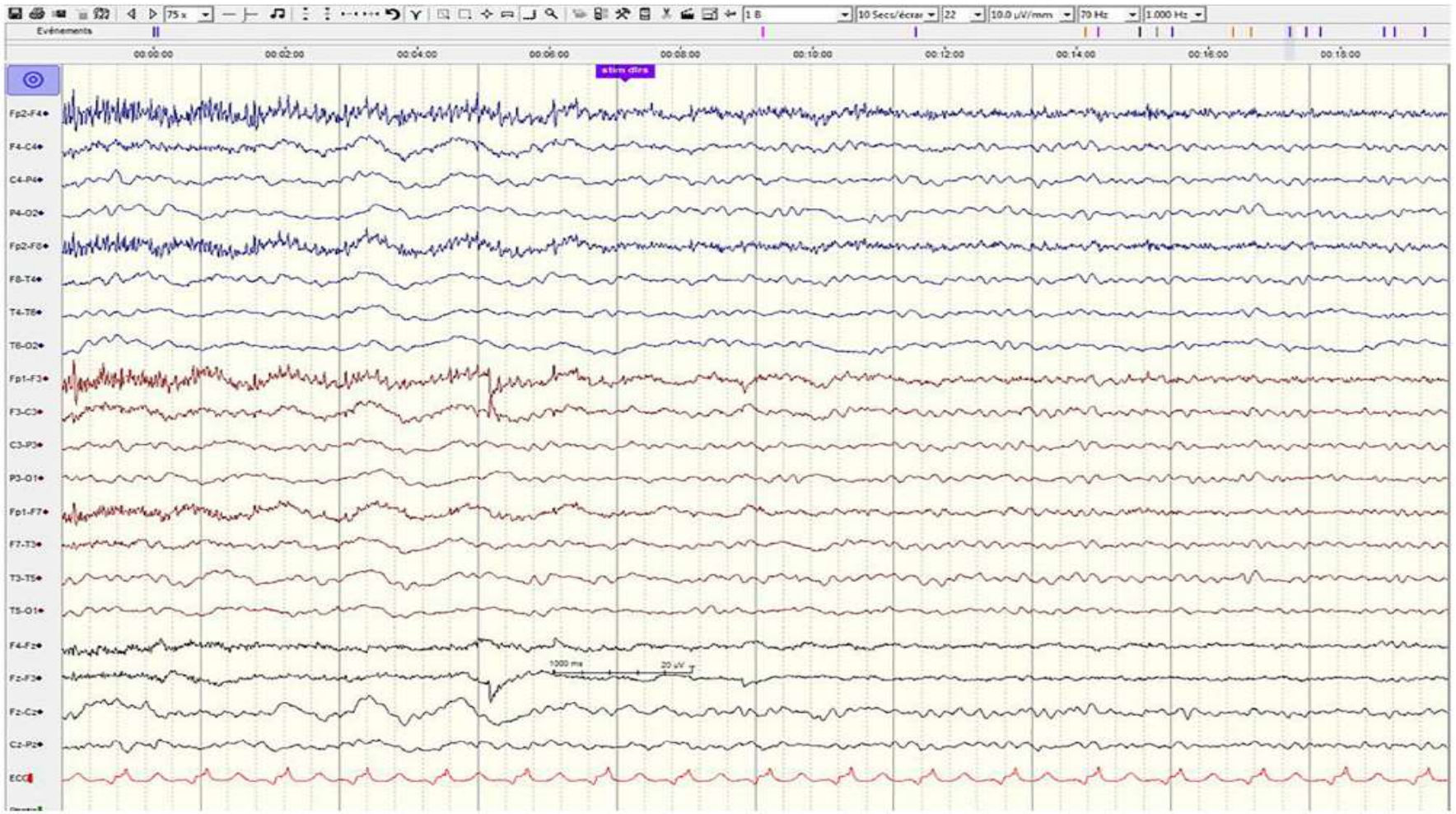
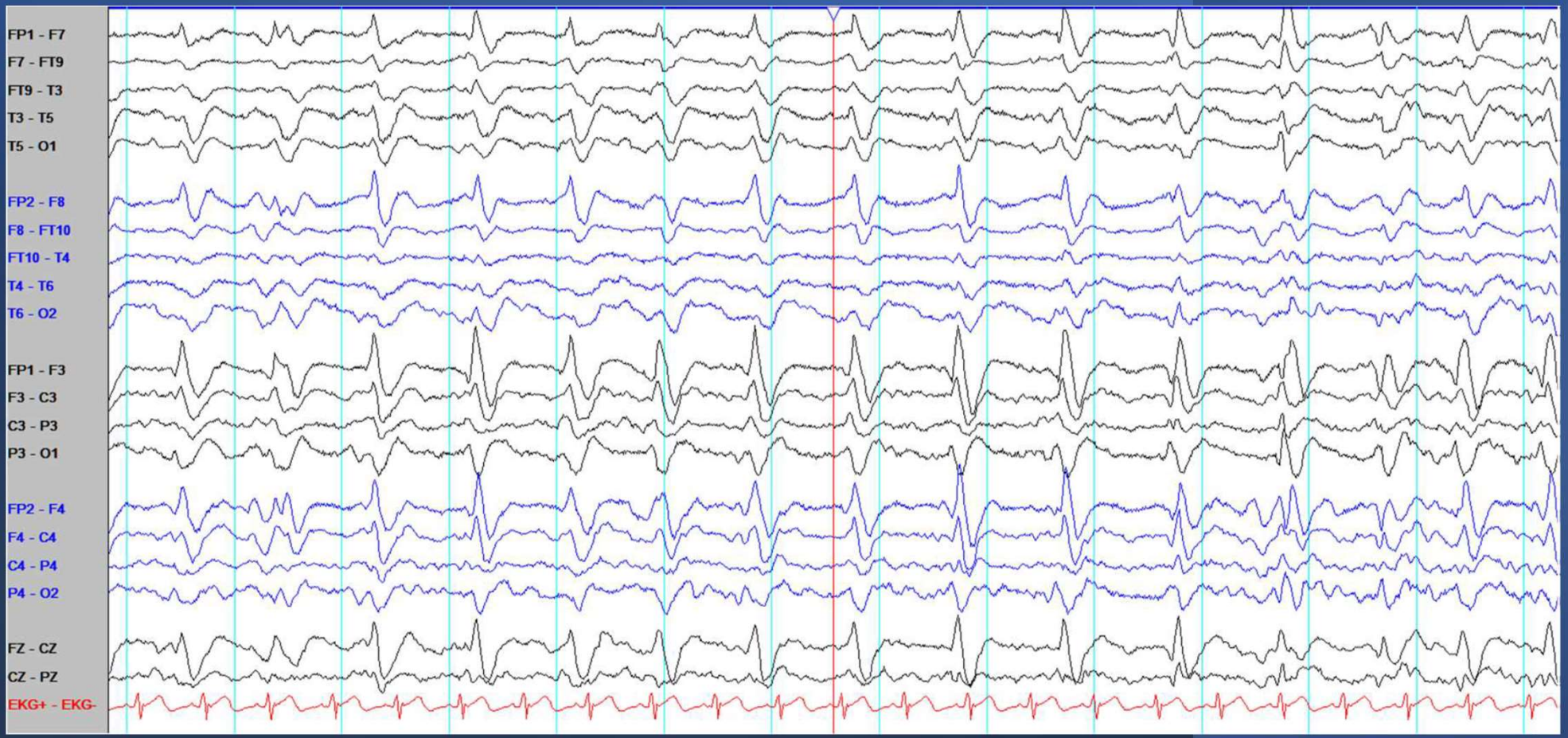


Fig. 3. (Same patient as in Fig. 2) 17 days after cardiac arrest, treated with levetiracetam and valproate, she interacts with the environment; her EEG shows a poorly developed diffuse theta activity that reacts promptly upon stimulation, accelerating towards alpha frequencies.


FP1 - F7
F7 - FT9
FT9 - T3
T3 - T5
T5 - O1
FP2 - F8
F8 - FT10
FT10 - T4
T4 - T6
T6 - O2
FP1 - F3
F3 - C3
C3 - P3
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CZ - PZ
EKG+ - EKG-

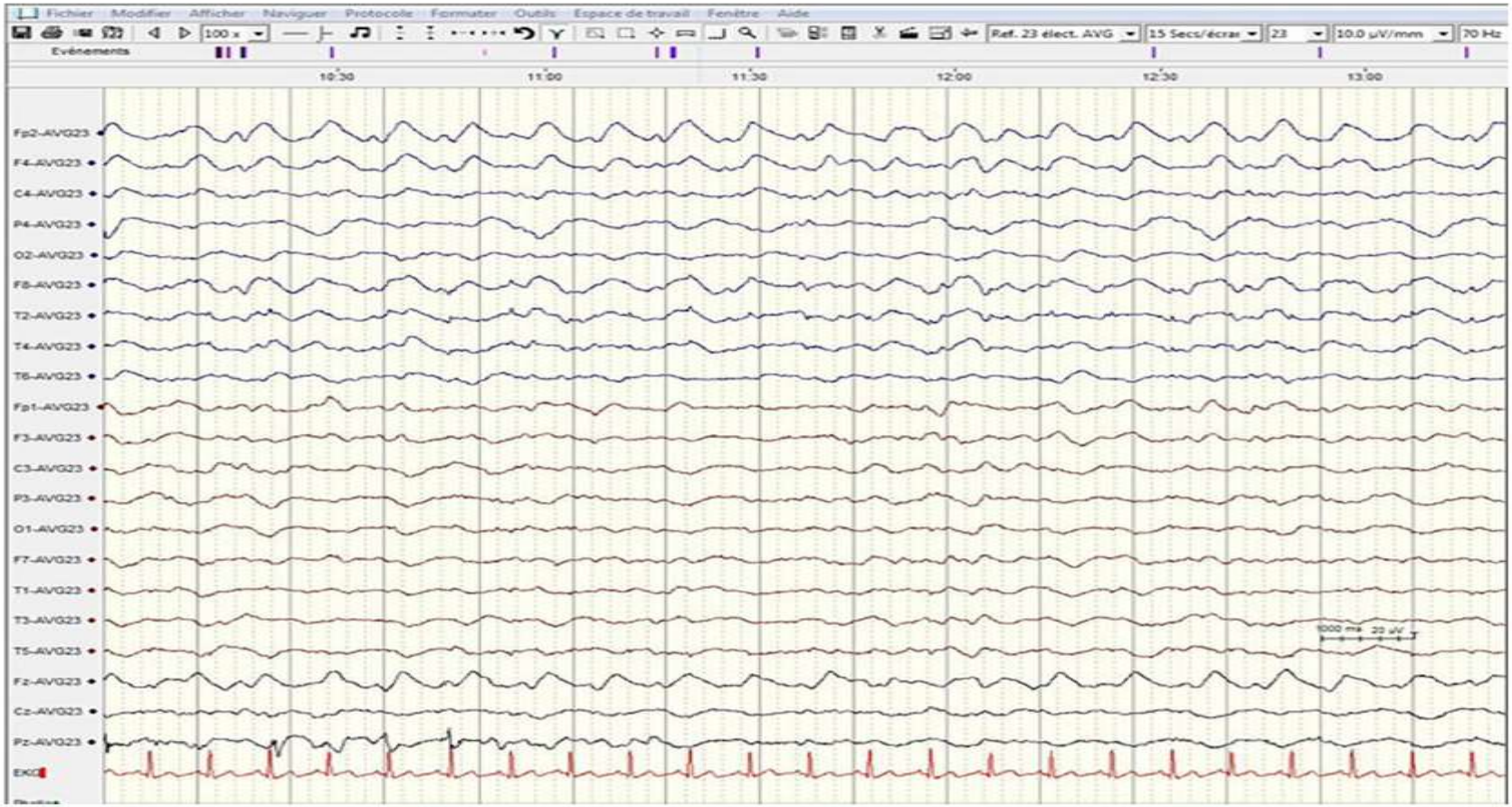


Fig. 1. 48 year old woman with subarachnoid bleeding and coma persisting after 6 days. The EEG (average referential montage, 20 mm/sec) shows intermittent right-sided lateralized rhythmic delta activity with superimposed sharp elements (LRDA + S). [In these figures, right-sided channels are displayed on the top, in red lines; left, on bottom, in blue.] (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Modulation: (SIRPIDs)
Stimulus-induced rhythmic, periodic, or ictal discharges

- Induced by alerting stimuli such as auditory stimuli, sternal rub, examination, suctioning, turning, and other patient-care activities
- Commonly elicited by stimulation in critically ill (stuporous or comatose), encephalopathic patients
- Pathophysiology of SIRPIDs is unknown
- The relationship between clinical seizures and SIRPIDs is unclear, although some association is found between SIRPIDs and clinical status epilepticus

Epilepsia . 2004

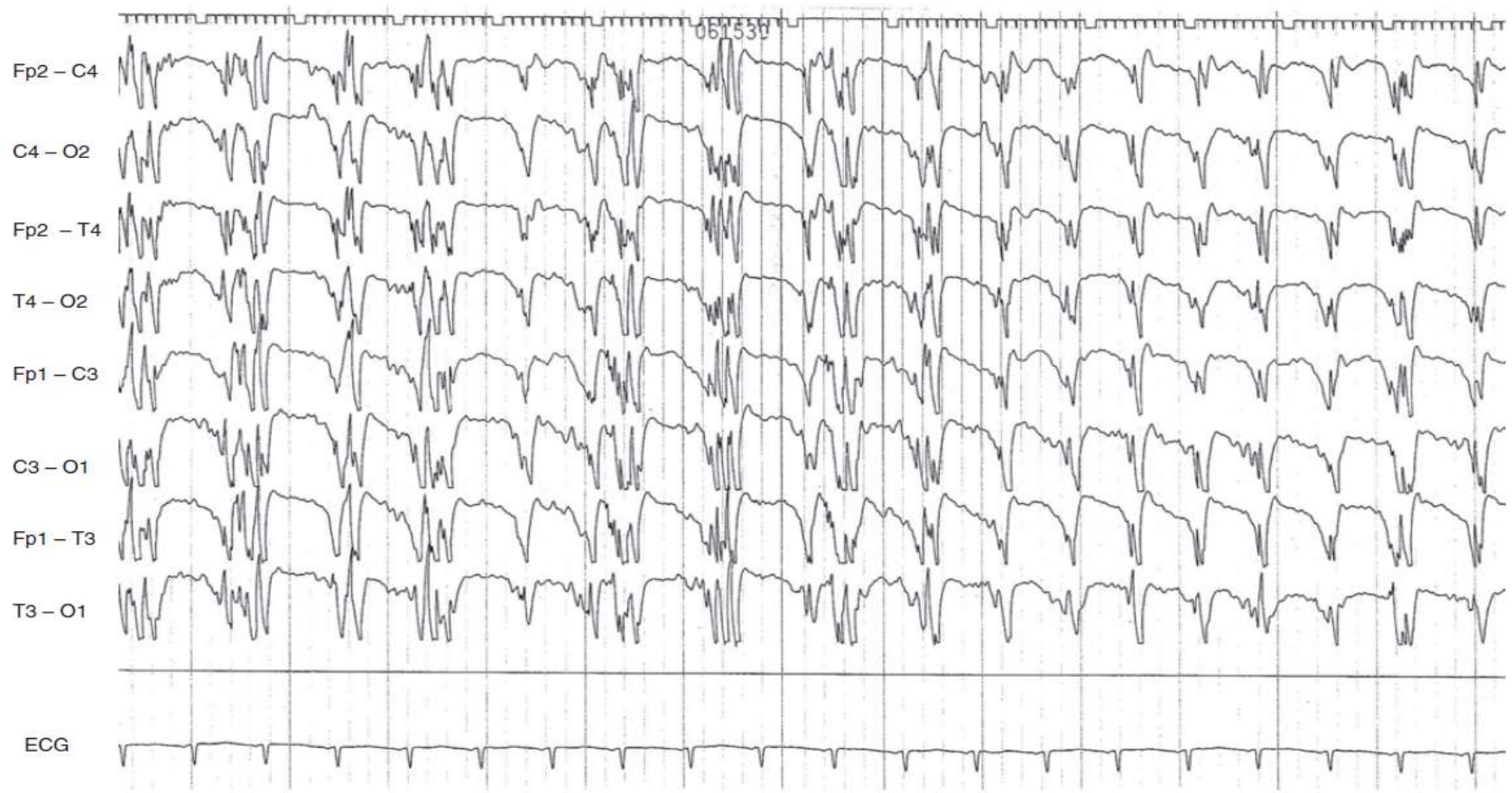
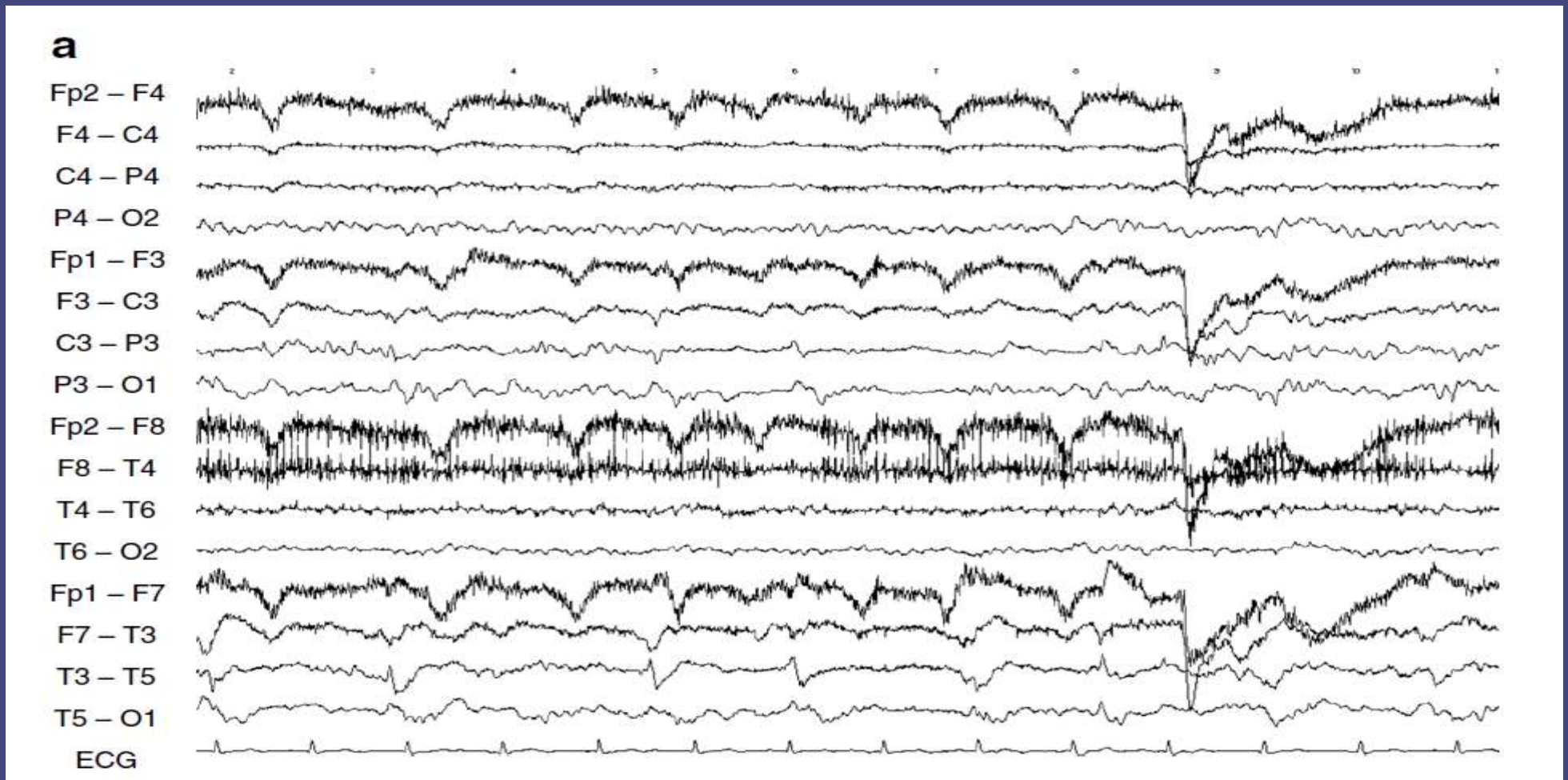
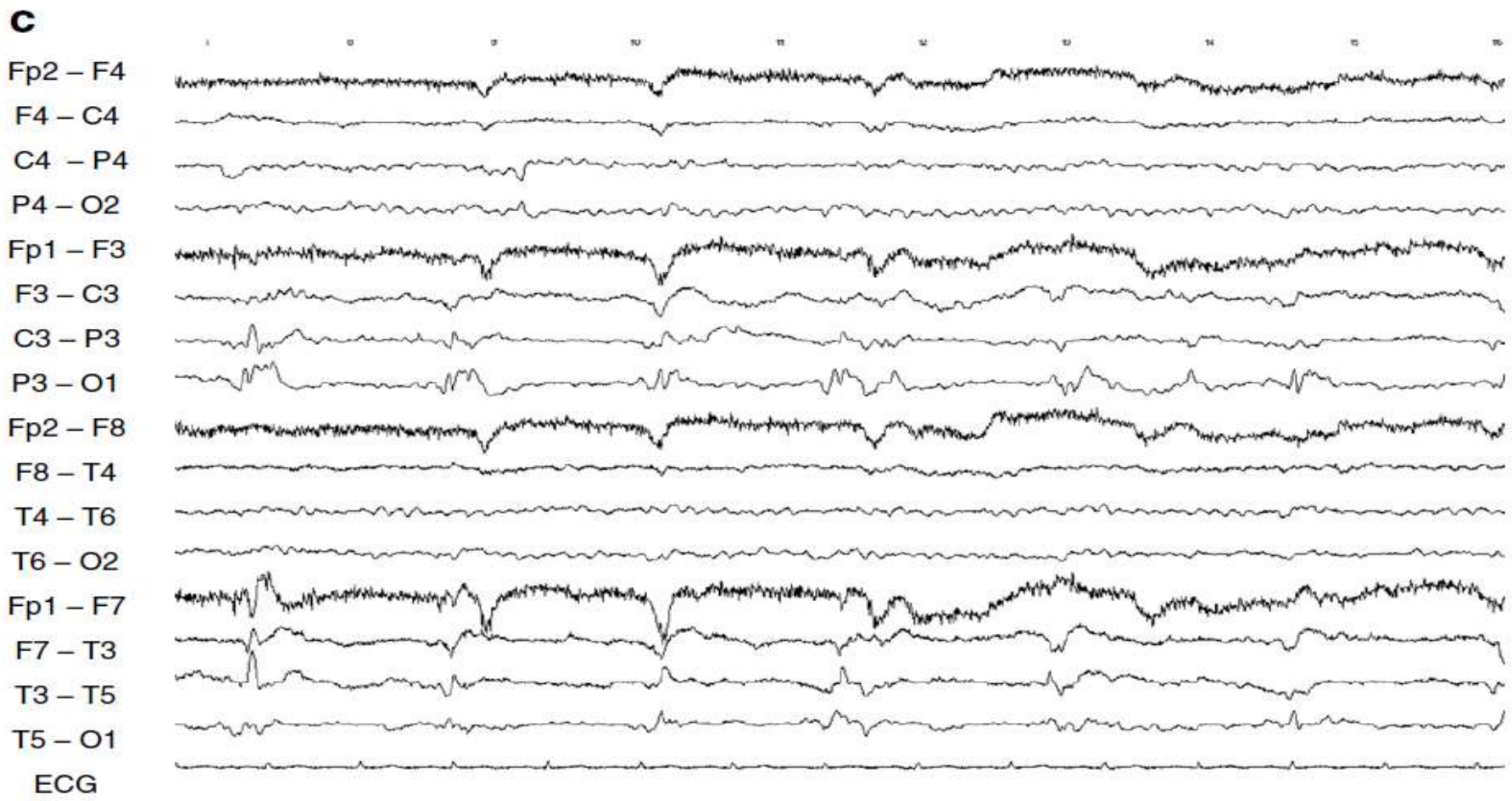
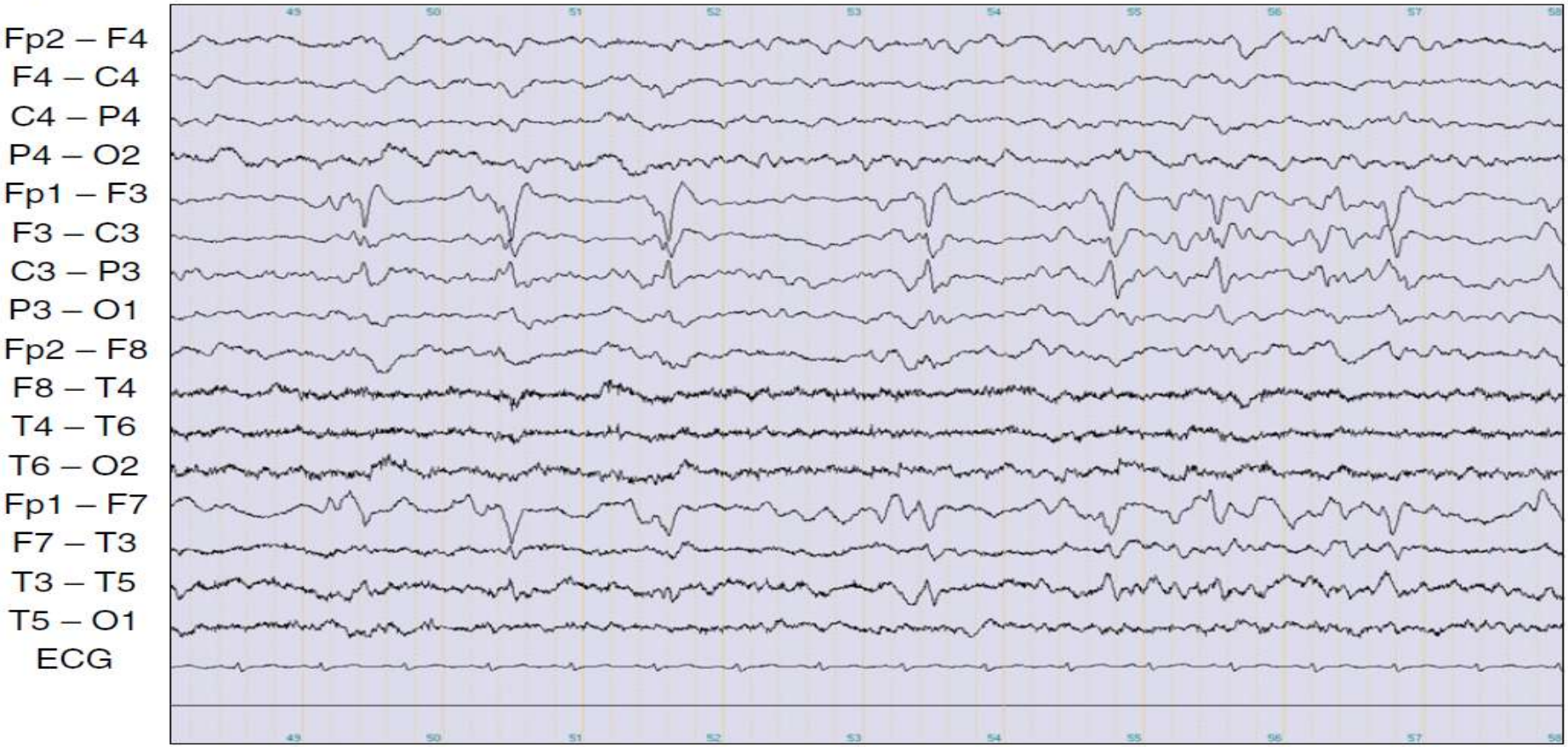


Fig. 4. Man, 66 years of age. Coma after cardiorespiratory arrest; TC 1.0, HF 70. Machine-like generalized 1/s (poly)spikes and waves. Outcome: died.


a
Fp2 – F4
F4 – C4
C4 – P4
P4 – O2
Fp1 – F3
F3 – C3
C3 – P3
P3 – O1
Fp2 – F8
F8 – T4
T4 – T6
T6 – O2
Fp1 – F7
F7 – T3
T3 – T5
T5 – O1
ECG


C
Fp2 – F4
F4 – C4
C4 – P4
P4 – O2
Fp1 – F3
F3 – C3
C3 – P3
P3 – O1
Fp2 – F8
F8 – T4
T4 – T6
T6 – O2
Fp1 – F7
F7 – T3
T3 – T5
T5 – O1
ECG

a


Fp2 – F4
F4 – C4
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P4 – O2
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F3 – C3
C3 – P3
P3 – O1
Fp2 – F8
F8 – T4
T4 – T6
T6 – O2
Fp1 – F7
F7 – T3
T3 – T5
T5 – O1
ECG
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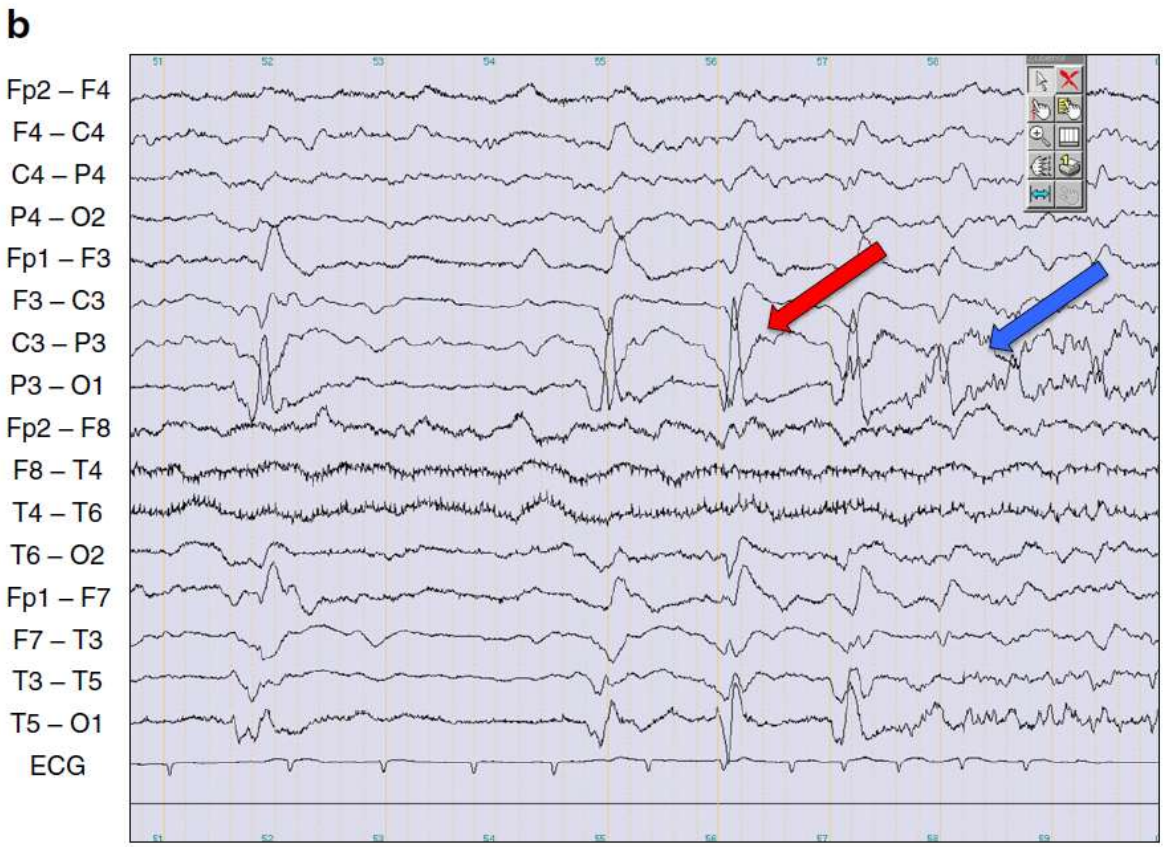


Fig. 9. (a) Man, 88 years of age, postictal coma after acute symptomatic generalized tonic–clonic seizure with left medial cerebral artery occlusion; TC 1.0, HF 70; lateralized periodic discharges over left frontocentral with fluctuation of interburst interval; (b) the same trace with increase in interburst frequency, decrease in amplitude, and superposition of faster frequencies (red arrow; old term: "periodic lateralized epileptiform discharges (PLED)-plus") merging into an ictal activity (= begin of electrographic seizure; blue arrow). Note also the longer periods of suppressed background over the left hemisphere. (c, d) The same trace as before with polyspikes over left temporoparietal (= electrographic seizure).

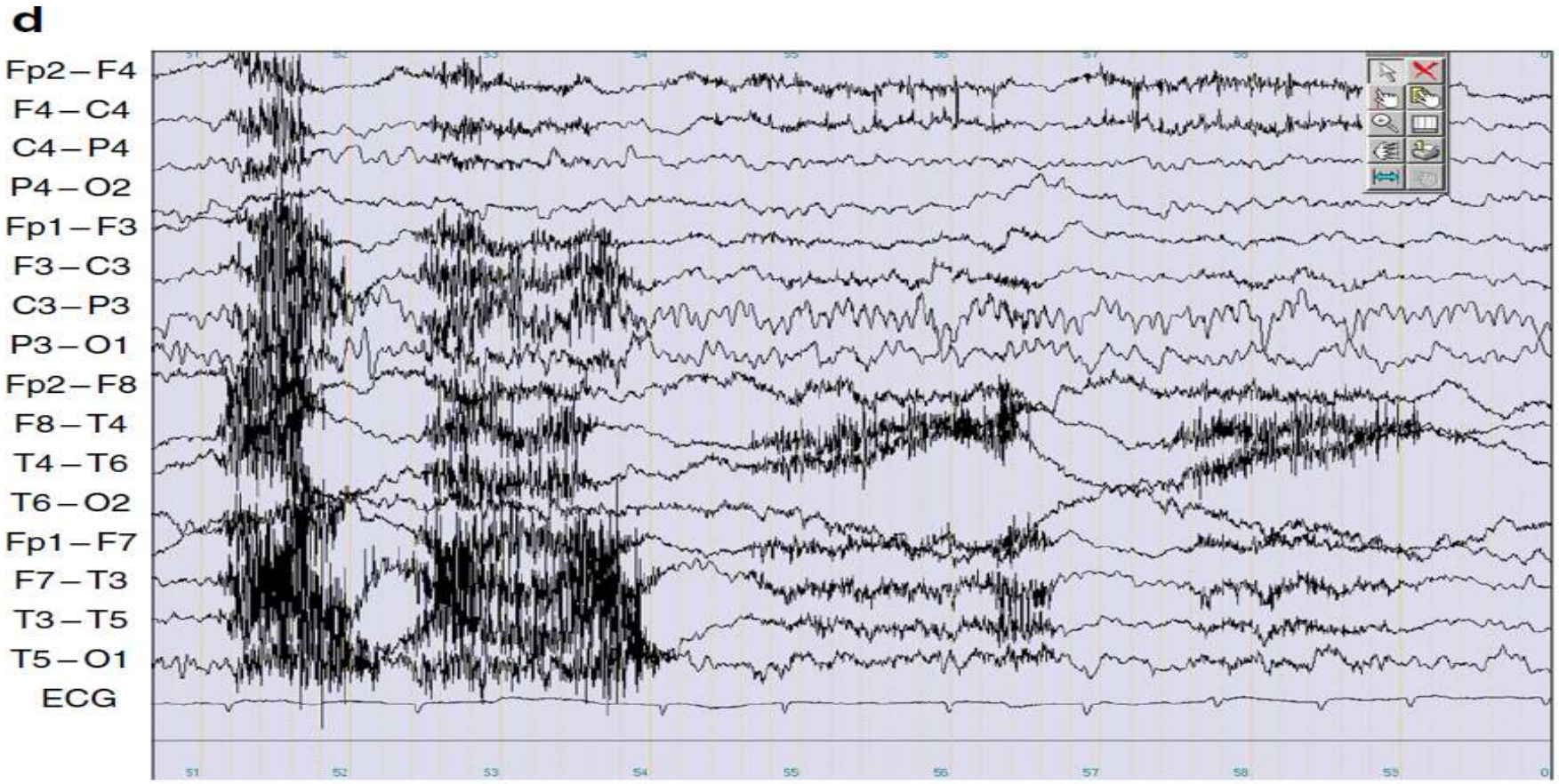


Fig. 9 (*continued*).

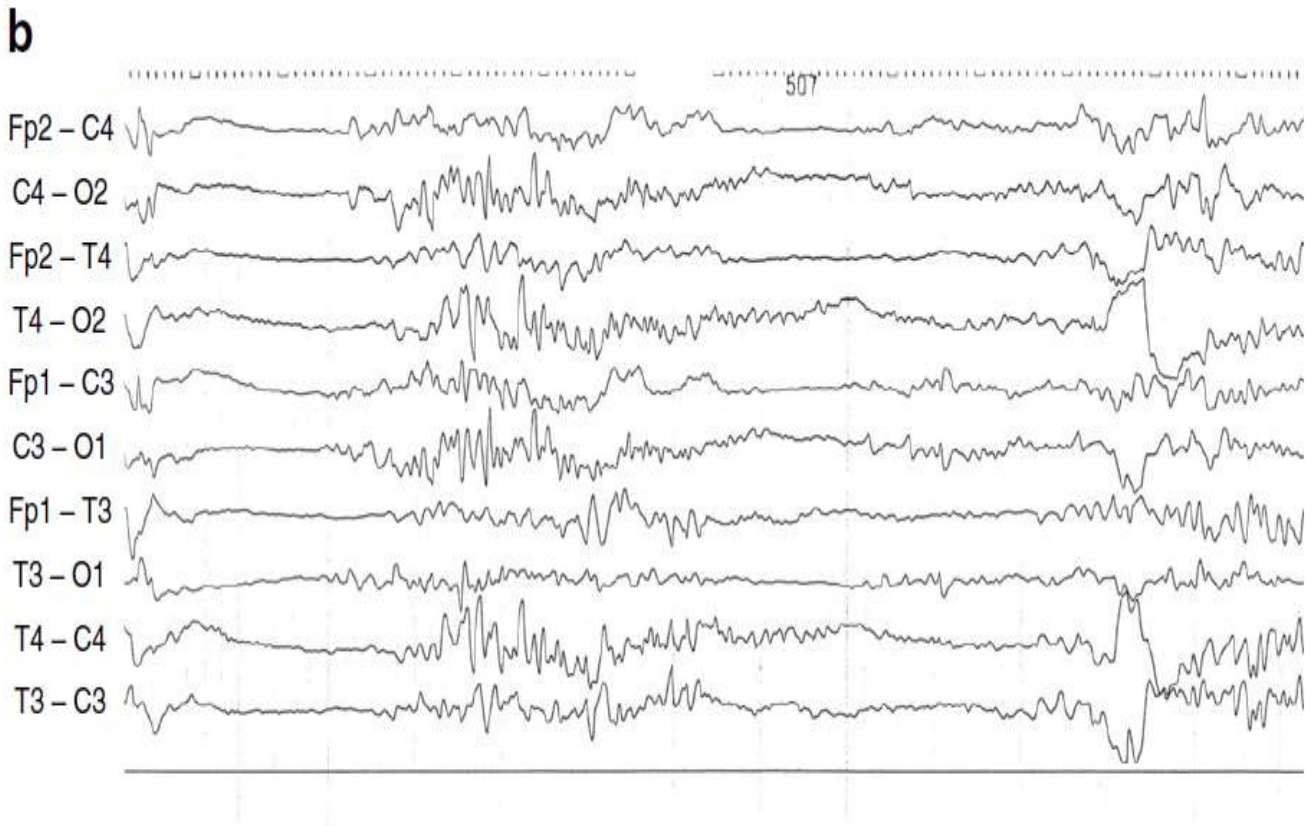


Fig. 11. (a) Man, 77 years of age; TC 1.0, HF 70; deep coma after cardiopulmonary arrest. Burst suppression pattern with bursts of mixed frequencies and interposed spikes and sharp waves. Despite the buildup within the bursts in amplitude, there is no spatiotemporal evolution suggestive of an ictal activity. Severe suppression of activity between the bursts. Outcome: died within days. (b) Boy, 2 weeks, Ohtahara syndrome due to olivary–dentate dysplasia and agenesis of mammillary bodies [151]; TC 1.0, HF 70; bursts with mixed frequencies (fast and slow waves) with less severe suppression between the bursts than in hypoxic encephalopathy. Later, a hypsarrhythmic EEG pattern developed. Outcome: died at the age of 3 years.

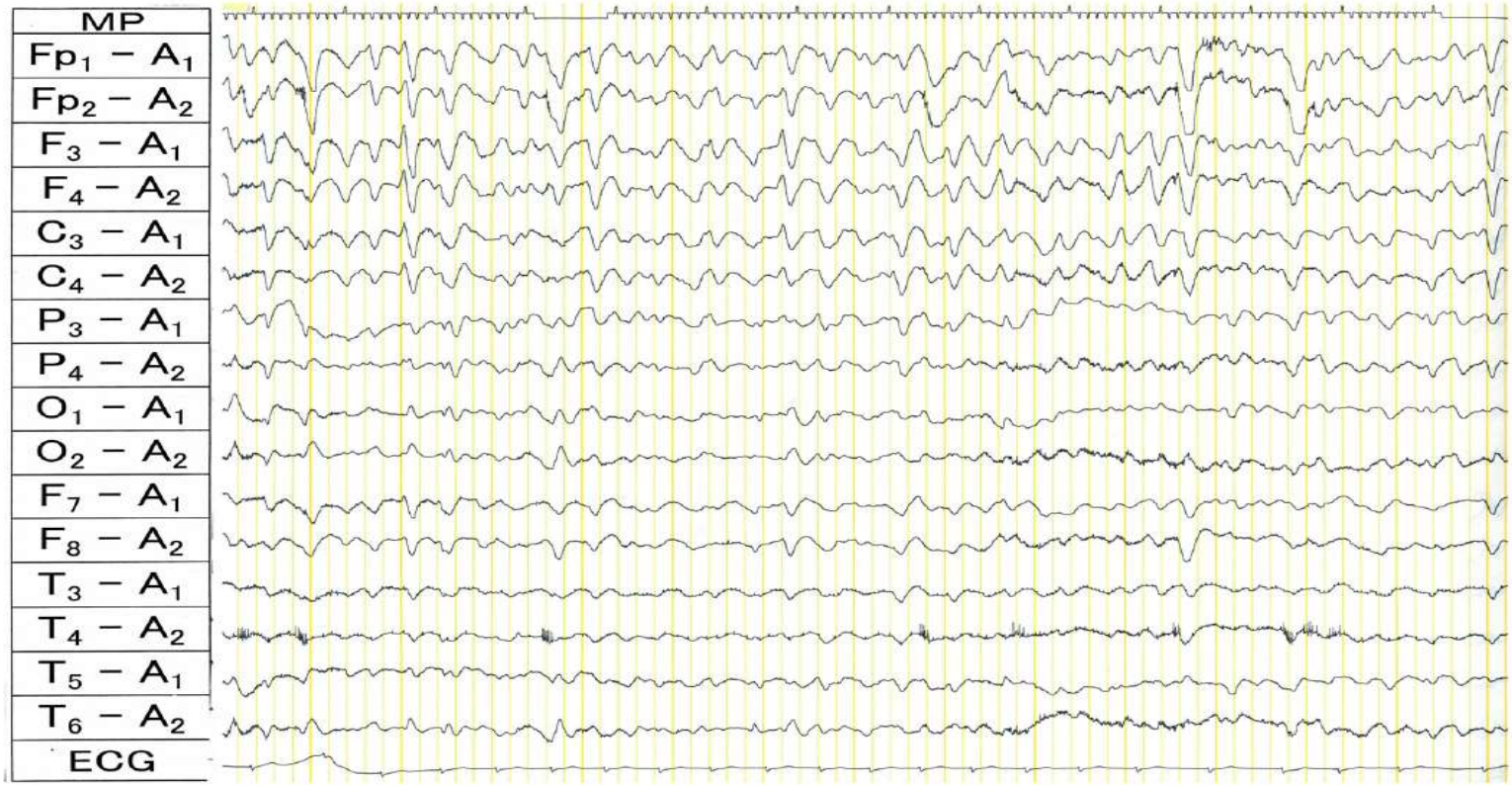


Figure 1. Ictal electroencephalogram (EEG) in a patient with nonconvulsive status epilepticus (NCSE). Ictal EEG of patient #8 in Table 1. This EEG was taken from an 83-year-old female with acute hyperammonemic encephalopathy resulting from Osler–Weber–Rendu disease. During the episode of NCSE with total aphasia, triphasic wave-like waves were observed with spatiotemporal evolution. Five minutes after starting phenytoin, aphasia started to improve, which completely disappeared 15 minutes after starting phenytoin.

Duration for EEG monitor

Critically ill patients at least 48 h of continuous EEG are needed in order to capture more than 90% of epileptic events (Classen et al, 2004)

A useful seizure-risk predicting tool (using the eponym of ‘‘2HELPS2B”)

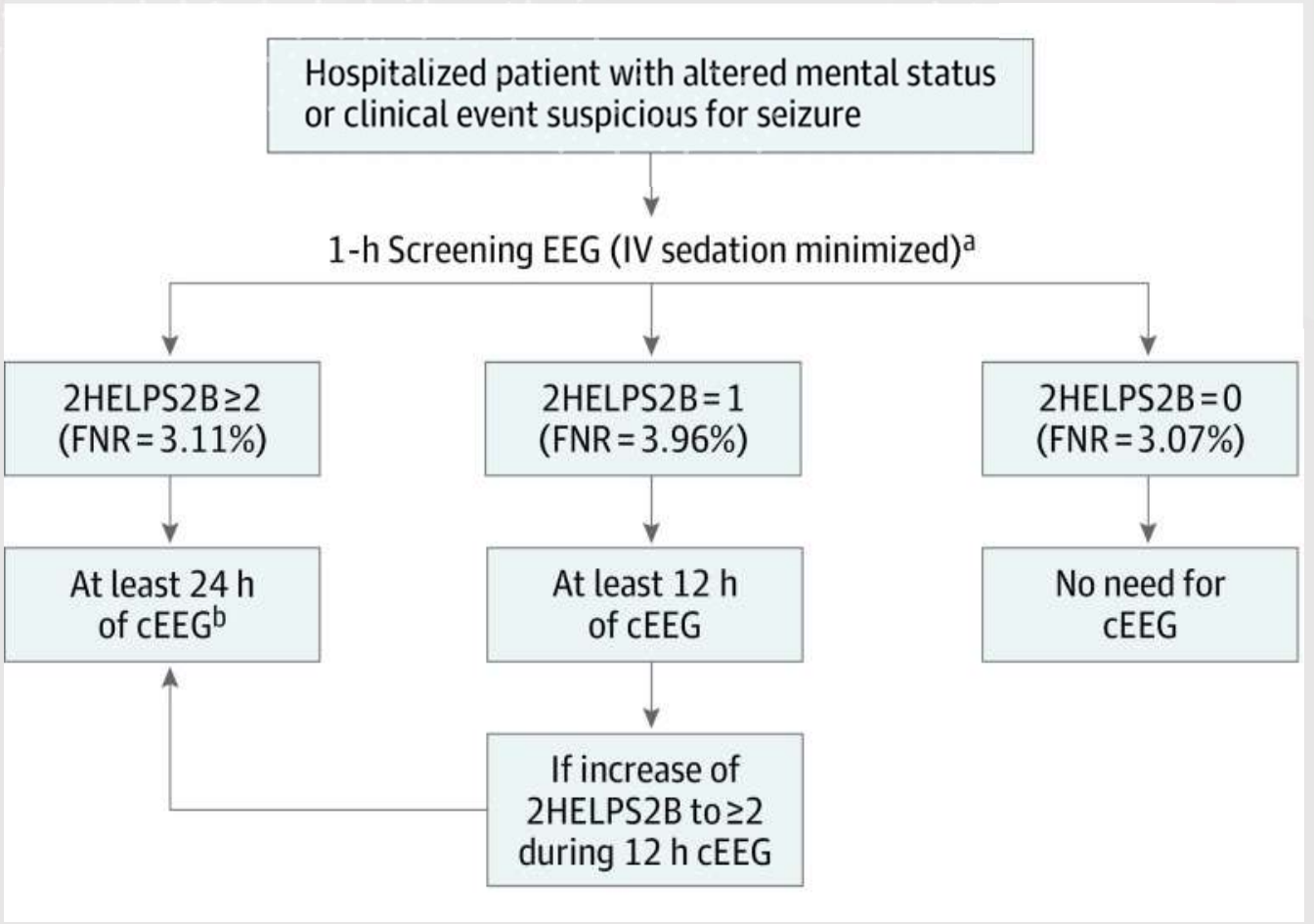
Claassen et al., 2004, Struck et al., 2017b

"2HELPS2B"

- The score was created in 2017, and validated in 2020
- To stratify seizure risk in hospital inpatients
- It does not apply to patients admitted for elective epilepsy monitoring and post-cardiac arrest patients
- To improve cost-effectiveness of continuous EEG (cEEG)
- By doing an initial 1 hour-long EEG and applying the score, patients can be stratified to stop EEG monitoring at that point, or continue to 12 hour or 24-hour cEEG monitoring

Claassen et al., 2004, Struck et al., 2017, Mofet EW, et al. Neurocrit Care 2020

2HELPS2B Score



2HELPS2B: Estimate duration of EEG monitoring needed to detect 95% of seizures

Risk Factor	Points
Frequency > **2Hz** [a]	1
Sporadic **E**pileptiform Discharges	1
LPD/BIPD/LRDA	1
Plus Features [b]	1
Prior **S**eizure	1
Brief Ictal Rhythmic Discharge	2
	Total Score

Total Score:	0	1	2	3	4	5	>6
Seizure Risk:	<5%	12%	27%	50%	73%	88%	>95%

Fig. 1 Illustration of factors used to calculate the 2HELPS2B score. The total score represents the sum of points, which is associated with a particular seizure risk. *BIPD* brief independent periodic discharge, *cEEG* continuous EEG, *GPD* generalized periodic discharge, *LPD* lateralized periodic discharge, *LRDA* lateralized rhythmic delta activity. [a]Frequency > 2 Hz applies to GRDA, LRDA, BIPDs, LPDs, or GPDs. [b]Plus features are defined as superimposed rhythmic, fast, or sharp activity for GRDA, LRDA, BIPDs, LPDs, or GPDs

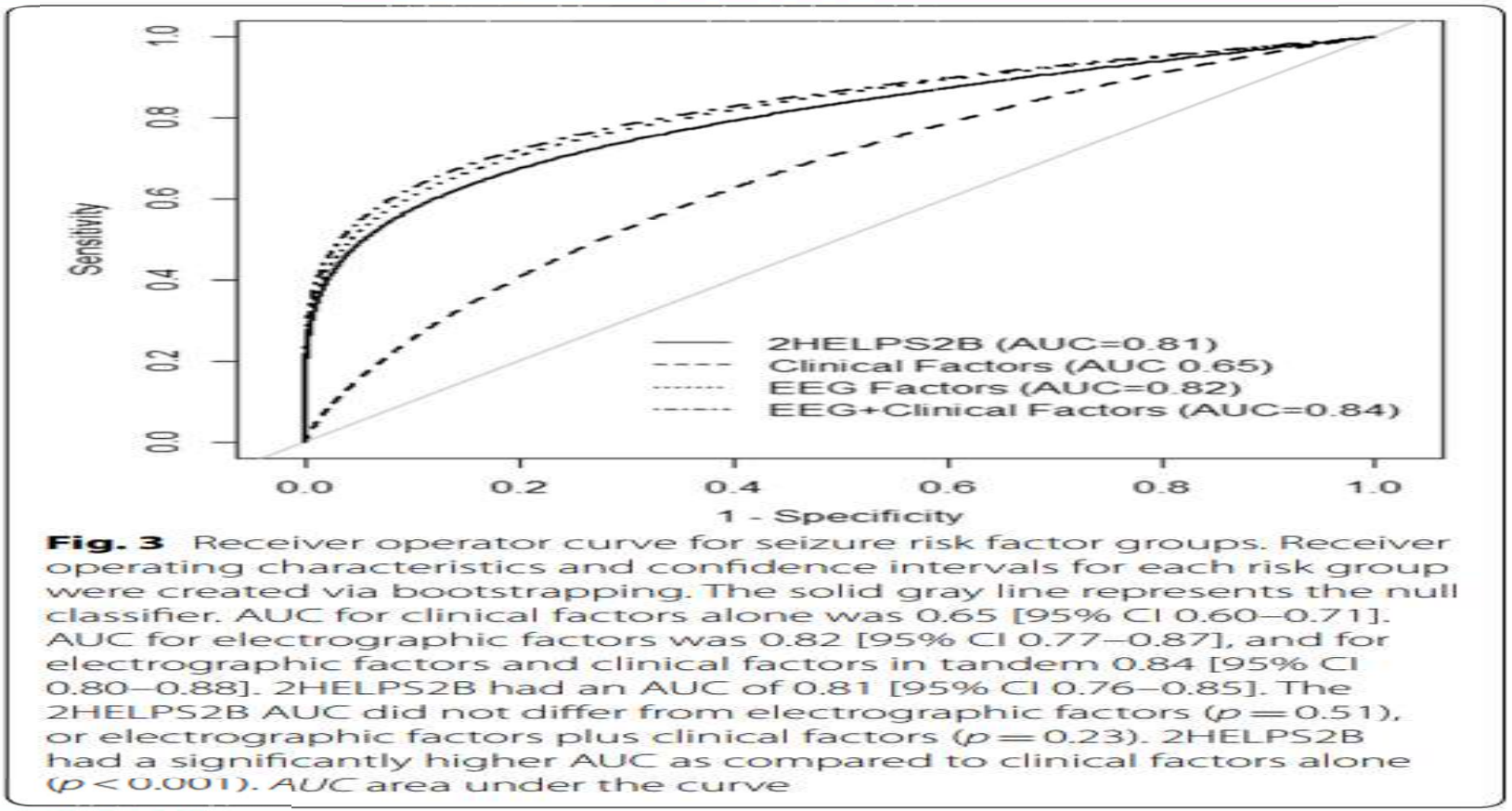


Fig. 3 Receiver operator curve for seizure risk factor groups. Receiver operating characteristics and confidence intervals for each risk group were created via bootstrapping. The solid gray line represents the null classifier. AUC for clinical factors alone was 0.65 [95% CI 0.60–0.71]. AUC for electrographic factors was 0.82 [95% CI 0.77–0.87], and for electrographic factors and clinical factors in tandem 0.84 [95% CI 0.80–0.88]. 2HELPS2B had an AUC of 0.81 [95% CI 0.76–0.85]. The 2HELPS2B AUC did not differ from electrographic factors ($p = 0.51$), or electrographic factors plus clinical factors ($p = 0.23$). 2HELPS2B had a significantly higher AUC as compared to clinical factors alone ($p < 0.001$). *AUC* area under the curve

F1000Research F1000Research 2017, 6(F1000 Faculty Rev):1690 Last updated: 15 SEP 2017

REVIEW

Novel clinical features of nonconvulsive status epilepticus [version 1; referees: 2 approved]

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Table 2. Expanded spectrum of manifestations of nonconvulsive status epilepticus (NCSE).

Classical clinical features
- Complex partial seizures type
  - Staring, repetitive blinking, chewing, swallowing, or automatism
  - Clouding of consciousness generally characterized by
    - alteration of mental function
    - consciousness with concurrent language disturbances
- Simple partial seizures type
  - Symptoms linked to the anatomical and functional locations of the CNS foci
  - Temporal lobe epilepsy, amygdalar and hippocampal lesions
    - epigastric discomfort and uncinate fits
      - such as autonomic seizures, psychic seizures, and parosmia
  - Lateral temporal lesions
    - auditory hallucinations and language disturbance
  - Frontal lobe epilepsy
    - motor seizures
      - not only tonic seizures and seizures with fencing postures
      - but also those with complex gesticulation
  - Parietal lobe epilepsy
    - somatosensory abnormalities such as numbness
  - Occipital lobe epilepsy
    - visual seizures

Nagayama M, et al. F1000Research 2017.

Consciousness disturbance Acute consciousness disturbance Comatose state Mental alteration Fluctuation of consciousness level Prolonged consciousness disturbance Protracted coma Fluctuation of consciousness level Recurrent loss of consciousness attack
Transient neurological attack (TNA) including isolated vertigo, dizziness, and headache
Higher brain dysfunction Wernicke's aphasia, Broca's aphasia, Klüver–Bucy syndrome Amnesia, indifference Confabulation, hallucinatory delusion, delirium Body schema disturbances (e.g. abnormal proprioception and supernumerary phantom limbs) Neglect, auditory and visual hallucinations, cortical blindness
Cognitive impairment and psychiatric manifestations Dementia, including acute dementia Abnormal behavior and/or speech Persistent laughing (status gelasticus)

Nagayama M, et al. F1000Research 2017.

Automatism	Licking chops, nose wiping, facial pantomime
Abnormal eye position and movement	Conjugate deviation of eyes, spontaneous nystagmus
Myoclonus of the face and extremities	Especially interictal small myoclonus of the face and extremities
Autonomic dysfunction	Gastrointestinal or cardiovascular autonomic events Panayiotopoulos syndrome
Acute organ dysfunction (epilepsy-related organ dysfunction [Epi-ROD])	Acute apnea, including prolonged post-hyperventilation apnea Acute cardiac arrest, acute dysfunction of other organs May cause sudden unexpected death in epilepsy (SUDEP)

In general, neurological deficits of an unexplained, episodic, fluctuating, or recurrent nature should arouse suspicion of NCSE. We need to consider convulsive SE and especially NCSE in the differential diagnosis of various acute organ dysfunctions, even in the absence of overt seizures.

Nagayama M, et al. F1000Research 2017.

Table 3. Epilepsy-related organ dysfunction (Epi-ROD).

Features	Frequent in both convulsive status epilepticus (SE) and nonconvulsive status epilepticus (NCSE) Convulsive SE 60%, NCSE 40%, both 60% Life-threatening/high mortality (33.3%) with acute encephalopathy, stroke, and central nervous system infection, and so on Heterogeneous in nature
Implication	Differentiate SE in acute OD, even without overt seizure

OD: organ dysfunction

- 60% of NCSE: multiple organ failure, arrhythmia, and liver dysfunction
- 40.0%: acute respiratory failure, alveolar hypoventilation, acute cardiopulmonary arrest, acute takotsubo cardiomyopathy, renal dysfunction, and QT interval prolongation
- 60%: renal dysfunction, multiple organ failure, and disseminated intravascular coagulation with neurogenic diabetes insipidus

Nagayama M, et al. F1000Research 2017.

Prognosis of refractory status epilepticus

- Refractory status epilepticus
  - A risk of physiological compromise
  - Neuronal damage
  - Progressive drug resistance
- Rx
  - ICU for early anesthesia
- Prognosis
  - Poor
  - Mortality 17-48% ((Approximately 3 times > non-refractory SE)
  - No morbidity only 29%

Prognosis of NCSE

NCSE -- Harmful to neurons, especially in the setting of acute brain injury

- Early treatment leading to shorter hospital stays and better outcome

Some studies disagree…….

- Isolated seizures are not harmful
- Neither seizures nor NCSE were significant predictors of outcome
- The use of IV benzodiazepines was associated with an increased risk of death ($p = 0.03$).
- IV anesthetic drips used for treatment of refractory SE (RSE) are associated with worse outcomes
- The use of continuous IV anesthetic-dose anti-seizure medications was associated with higher mortality, intubation, hypotension and poor function with long-term outcome
- therapeutic coma was associated with worse outcome at hospital discharge, new disability (with a relative risk, RR of 4.6), mortality (RR 5.5), more infections, and longer hospital stays

Claassen et al., 2007, Sutter et al., 2014, Marchi et al., 2015

Predictive value of the Status Epilepticus Severity Score (STESS)

	Features	STESS
Consciousness	Alert or somnolent/confused	0
	Stuporous or comatose	1
Worst seizure type	Simple-partial, complex-partial, absence, myoclonic*	0
	Generalized-convulsive	1
	Nonconvulsive status epilepticus in coma	2
Age	< 65 years	0
	≥ 65 years	2
History of previous seizures	Yes	0
	No or unknown	1
Total		0–6

* complicating idiopathic generalized epilepsy

- **In-hospital mortality correlated highly significantly with STESS, the optimal cut-off was 4**

BMC Neurology 2016

Long-term anticonvulsant therapy

- Must be given
- The choice of drug depends on
  - Previous Rx
  - The type of epilepsy
  - The clinical setting
- Other maintenance can be started also by giving oral loading doses

Conclusion: Status epilepticus

Persistent seizure, causing neuronal damage

Type

- Convulsive, Nonconvulsive, Focal status
- SE, refractory SE, super-refractory SE, NORSE, FIRES

High morbidity & mortality

- Overall mortality ~ 20% (SE) → up to 80%
  (super-refractory SE with unproper Rx or most severe etiologies)

EEG for diagnosis and guide for Rx

Requiring prompt treatment

- ABC, initial anticonvulsant, anesthetic agent, supportive care in ICU
- Consider: autoimmune encephalitis and Rx without delays

Thank you