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Brief Communication

Salzburg Consensus Criteria for Non-Convulsive Status Epilepticus – approach to clinical application

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ABSTRACT

Background: 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).
Methods: We retrospectively analyzed the EEGs of 50 consecutive nonhypoxic patients with diagnoses of nonconvulsive status epilepticus (NCSE) at discharge and 50 consecutive controls with abnormal EEGs in a large university hospital in Austria. We implemented the American Clinical Neurophysiology Society's Standardized Critical Care EEG Terminology, 2012 version (ACNS criteria) to increase the test performance of SCNC. In patients without preexisting epileptic encephalopathy, the following criteria were applied: (1) more than 25 epileptiform discharges (ED) per 10-second epoch, i.e., >2.5/s and (2) patients with EDs ≤ 2.5/s or rhythmic delta/theta activity (RDT) exceeding 0.5/s AND at least one of the additional criteria: (2a) clinical and EEG improvements from antiepileptic drugs (AEDs), (2b) subtle clinical phenomena, or (2c) typical spatiotemporal evolution. In case of fluctuation without evolution or EEG improvement without clinical improvement, "possible NCSE" was diagnosed. For identification of RDT, the following criteria were compared: (test condition A) continuous delta–theta activity without further rules, (B) ACNS criterion for rhythmic delta activity (RDA), and (C) ACNS criteria for RDA and fluctuation.
Results: False positive rate in controls dropped from 28% (condition A) to 2% (B) ($p = 0.00039$) and finally to 0% (C) ($p = 0.000042$). Application of test condition C in the group with NCSE gives one false negative (2%). Various EEG patterns were found in patients with NCSE: (1) 8.2%, (2a) 2%, (2b) 12.2%, and (2c) 32.7%. Possible NCSE was diagnosed based on fluctuations in 57.1% and EEG improvement without clinical improvement in 14.2%.
Conclusion: The modified SCNC with refined definitions including the ACNS terminology leads to clinically relevant and statistically significant reduction of false positive diagnoses of NCSE and to minimal loss in sensitivity.

This article is part of a Special Issue entitled "Status Epilepticus".

1. Introduction

Status epilepticus (SE) is a potentially life-threatening condition with mortality rates of up to 39% in convulsive SE in population-based studies [1]. However, data for nonconvulsive SE (NCSE) are sparse compared to convulsive forms [2]. Furthermore, clinical and EEG definitions for NCSE have changed over time [3–6]. A consensus panel at the 4th London–Innsbruck Colloquium on status epilepticus and acute seizures held in Salzburg (2013) proposed working criteria for the EEG diagnosis of NCSE (Salzburg Consensus Criteria for Non-Convulsive Status Epilepticus, SCNC) [6]. The American Clinical Neurophysiology Society (ACNS) had published proposals for a Standardized Critical Care EEG Terminology [7,8], which are now widely used and have a high interrater agreement [9]. The ACNS criteria were intended to be used in EEG studies of hypoxic patients [10], but not yet for nonhypoxic patients with NCSE. We performed a single center investigation to test the influence of ACNS criteria on test performance of SCNC regarding specificity and sensitivity in nonhypoxic patients with NCSE. In addition, we used the two currently available outcome scores, Status Epilepticus Severity Score (STESS) [11] and Epidemiology based Mortality Score in SE (EMSE)

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[12] to allow for risk stratification for bad outcome (death) in this patient group.

2. Methods

We investigated fifty consecutive nonhypoxic patients with diagnoses of NCSE (identified by final diagnosis at discharge) from January to October 2014 and 50 consecutive controls without clinical suspicion of NCSE but abnormal EEGs (identified by EEG reports) in the first six days of 2014 at the Department of Neurology, Paracelsus Medical University, Salzburg, Austria. The investigations were done in four steps.

In all four parts, the following criteria were applied to EEGs of patients without preexisting epileptic encephalopathy (I) [6]: (1) more than 25 epileptiform discharges (ED) per 10-second epoch, i.e., >2.5/s and (2) patients with EDs 2.5/s or less or rhythmic delta/theta activity (RDT) exceeding 0.5/s AND at least one of the following criteria: (2a) clinical and EEG improvements from intravenous antiepileptic drugs (IV AEDs), (2b) subtle clinical phenomena, or (2c) typical spatiotemporal evolution. Typical spatiotemporal evolution (STE) was defined as "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)" [6]. We implemented ACNS criterion for "evolving" (ACNS-evolving) to provide more detailed, unambiguous instructions as "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)" [8]. In case of fluctuation without evolution, or EEG without clinical improvement, "possible NCSE" was diagnosed [6]. In patients with preexisting encephalopathy (II), in addition to the criteria above (A), these patients had to fulfill one of the following: "Increase in prominence or frequency of the features mentioned above, when compared to baseline with observable change in clinical state" or "Improvement of clinical and EEG features with IV AEDs" [6].

All patterns had to last at least 10 s to qualify for consideration. Other parts of the EEG were also abnormal, but "at least 10 seconds" was the minimal duration in which the abnormalities were severe enough to fulfill the criteria. Frequencies of EDs were counted per 10-second epoch (applied in "worst" epoch) (Supplementary Fig. 1).

In step one, the following test strategies for identification of rhythmical delta/theta activity were compared in the control group to optimize specificity: (test condition A) continuous delta–theta activity without further rules, (test condition B) ACNS criterion for rhythmical delta activity (RDA), and (test condition C) ACNS criteria for RDA and fluctuation. Second, the most specific strategy of step one was applied to 50 patients with NCSE to identify impact on sensitivity, as there is an inverse relationship between sensitivity and specificity. Third, we obtained epidemiological information on how frequent different diagnostic criteria had been applied in patients with NCSE, as this represents a general neurology service in a tertiary care center. Fourth, we tested the performances of STESS [11] and EMSE [12] scores to predict the individual patient's outcome.

In step one of our analysis (test condition B), we applied the 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" [8]. In test condition C, we additionally used 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 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" [8].

Patients with hypoxia, e.g., due to cardiac arrest, were excluded, as these patients need a different treatment protocol including hypothermia. If a patient was transferred to another department or hospital, this was rated as one continuous stay in the hospital. Outcomes of nonsurvival or survival with persistent deficit or with full restitution were rated at discharge from the hospital. If a patient was transferred to a palliative care center (hospice), the outcome was rated as nonsurvival.

Statistical comparison of false positive rates in controls was performed with Fisher's exact test. We compared predictive performance of STESS [11] and EMSE [12] in patients with NCSE to obtain a risk estimate in our patient group for better comparability with other studies. We used either a chi-squared test or Fisher's exact test if requirements for the chi-squared test were not met. All data were collected retrospectively by extraction from patient charts. This is a retrospective non-invasive study, which does not require ethics committee approval according to the Austrian Law on Research.

Table 1
Demographics of patients with diagnosis of NCSE at discharge and controls.

Demographic data	NCSE	Controls with abnormal EEG
Number of patients	50	50
Age, years: median (range)	70.5 (20–94)	69 (14–89)
Females (%)	60	56
Individuals under age 18 years: N (age, years)	0	1 (14)
Vigilance during EEG: N (%) (awake/somnolence/stupor/coma)	18 (36)/12 (24)/13 (26)/7 (14)	45 (90)/4 (8)/0/1 (2)
Preexisting epilepsy/unclassified: N (%)	16 (32)/0	8 (16)/0
Symptomatic (focal)	14	5
Cryptogenic	0	1
Genetic: idiopathic generalized/focal	1 (2)/0	2 (4)/0
Preexisting epileptic encephalopathy: N (%)	1 (2) (LGS, 32 a)	0
Died/survived with decreased function/survived with restitution: N (%)	12 (24)/19 (38)/19 (38)	2 (4)/16 (32)/32 (64)
Etiology: N (%):		
Acute symptomatic	14 (28)	n/a
Remote unprovoked	28 (56)	
Symptomatic seizure/progress disease	7 (14)	
Unprovoked unknown etiology	1 (2)	
First episode of SE	48 (96)	n/a
Recruiting time (criterion)	01–10/2014 (by discharge diagnosis)	first 6 days 2014 (by EEG report)

LGS: Lennox–Gastaut Syndrome. n/a: not applicable.

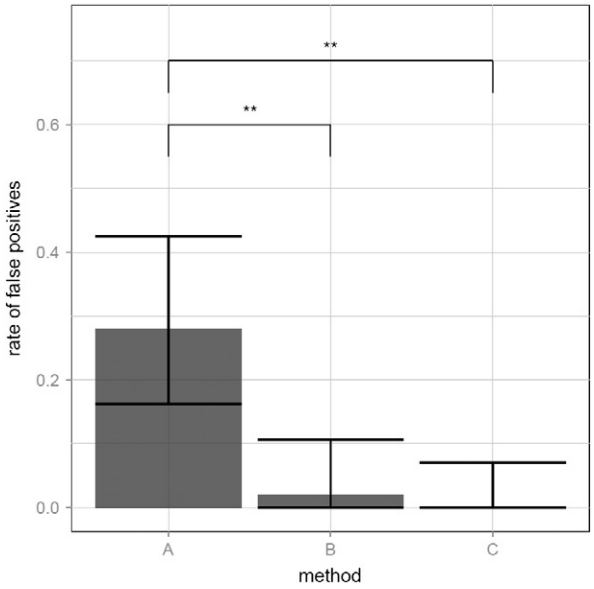

Fig. 1. Influence of EEG reading strategy on specificity. Test condition (A) rhythmic activity as continuous activity without further rules (14 false positives (FP), 28%) was significantly worse than test condition (B) ACNS-RDA (1 FP, 2%) ($p = 0.00039$) or test condition (C) ACNS-RDA and ACNS-fluctuating (0 FP) ($p = 0.000042$). The difference between test conditions (B) and (C) was not significant.

3. Results

Demographics of patients with diagnosis of NCSE at discharge and controls are presented in Table 1.

Strategies of EEG reading had a statistically significant influence on the false positive diagnosis of NCSE in controls (Fig. 1).

The various criteria upon which the diagnosis of NCSE was established are depicted in Table 2.

There were two false negatives (FNs) in 50 patients with NCSE. One patient with absence status had no continuous spike–wave activity for 10 s but many paroxysms filling substantial parts of epochs. This patient was diagnosed as absence status with discontinuous ED. The second FN was a patient with persistent RDT without fluctuations; both had a good outcome. We found no patient with spatiotemporal evolution with a pattern shorter than 10 s in the first consecutive 50 patients with NCSE. Many patients with typical spatiotemporal evolution of rhythmic activity started with a higher frequency (beta- or alpha-range), but finally evolved to RDT. Two-thirds of patients with RDT and spatiotemporal evolution developed sharp waves at the end of the pattern (Table 2). Three out of four patients with epileptiform discharges >2.5/s had frequencies between 2.6/s and 3.0/s.

Anesthesia for treatment of refractory SE was used in two patients with subtle clinical phenomena (33.3%, both survived), one patient with rhythmic delta/theta activity and spatiotemporal evolution (14.3%, deceased), one patient with epileptiform discharges and spatiotemporal evolution (11.1%, deceased), and two patients with fluctuating epileptiform discharges (4.3%, deceased).

In the NCSE group, there were 12 patients fulfilling the ACNS criterion for RDA. Of those, five patients also fulfilled ACNS criterion for fluctuation. In one of them, this was the only diagnostic criterion, while the other four had at least one other criterion for the EEG diagnosis of NCSE. Mortality in comatose patients was higher (nonsignificant) than in noncomatose patients in our group (Table 2). In the group of nonsurvivors, two patients showed improvement of EEG without clinical improvement (16.7%). In survivors, cessation of the culprit EEG pattern was documented in all but one, in whom only progressive clinical improvement was documented.

The group diagnosed with "possible NCSE with fluctuation without definite evolution" (with epileptiform discharges or RDT) was further characterized: preexisting epilepsy 25.0% (mortality 16.7%), remote unprovoked 45.8% (mortality 18.2%), acute symptomatic 29.2% (mortality 42.9%), and symptomatic seizures/progressive disease 20.8% (mortality 20.0%). Intravenous AEDs were applied in 26.1% during the EEG in this subgroup, with EEG and clinical improvements in none, and EEG improvement without clinical improvement in two-thirds (mortality 50%). Rate of anesthetics was low (4.3%) in subgroup fluctuation of ED or RDT, but this patient died. Overall mortality in this criterion was 29.2%.

Epidemiology based Mortality Score in SE score identified all nonsurvivors (NPV = 100%) compared to STESS-3 (NPV = 88.9%) ($p = 0.15$) and STESS-4 (NPV = 77.4%) ($p = 0.0117$) scores (Supplementary table). Correctly classified (accuracy) was: EMSE 78.0%, STESS-3 52.0% ($p = 0.012$), and STESS-4 58.0% ($p = 0.054$).

Table 2
EEG results after implementation of ACNS criteria on SCNC; patients with diagnosis of NCSE at discharge.

Criterion	N (%)	Nonsurvivors N (%)
SCNC criterion I (without preexisting epileptic encephalopathy)	49 (98)	12 (24)
SCNC criterion II (with epileptic encephalopathy)	1 (2.0)[a]	0
1. More than 25 epileptiform discharges per 10-second epoch (NCSE-ED>2.5) [13]	4 (8.2)[b]	0
2. Patients with EDs 2.5/s or less, or	15 (30.6)	3 (20.0)
Rhythmic delta/theta activity exceeding 0.5/s AND at least one of the following:	8 (16.3)	2 (25.0)
2a. Clinical and EEG improvement from AEDs		
Epileptiform discharges (NCSE-ECI-ED)	0	n/a
Rhythmic delta–theta activity (NCSE-ECI-RDT)	1 (2.0)[c]	0
2b. Subtle clinical phenomena		
Epileptiform discharges (NCSE-SCP-ED)	6 (12.2)[d]	1 (16.7)
Rhythmic delta–theta activity (NCSE-SCP-RDT)	0	n/a
2c. Typical spatiotemporal evolution		
Epileptiform discharges (NCSE-STE-ED)	9 (18.4)[e]	2 (22.2)
Rhythmic delta–theta activ. (NCSE-STE-RDT)	7 (14.3)[f]	2 (28.6)
"Possible NCSE"		
Only EEG improvement from intravenous (IV) AEDs		
Epileptiform discharges (NCSE-OEI-ED)	6 (12.2)[g]	2 (33.3)
Rhythmic delta–theta activity (NCSE-OEI-RDT)	1 (2.0)[h]	0 (0)
Fluctuation, but no evolution (ED/RDT)		
Epileptiform discharges (NCSE-FED)	23 (46.9)[i]	7 (30.4)
Rhythmic delta–theta activity (NCSE-FRDT)	5 (10.2)[j]	1 (20.0)
Types of NCSE		
NCSE	30 (60)	10 (33.3)
GTCSE→NCSE	9 (18)	1 (11.1)
NCSE→GTCSE→NCSE	2 (4)	0 (0)
FMSE→NCSE	9 (18)	1 (11.1)
Refractory SE	5 (10)	3 (60)
Vigilance		
Awake	18 (36)	3 (16.7)
Somnolent	12 (24)	3 (25.0)
Stuporous	13 (26)	3 (23.1)
Comatose	7 (14)	3 (42.9)

AED: antiepileptic drug, n/a: not applicable; reporting of semiology in standard format [13]. In total, intravenous AEDs were applied to 14 patients (28%) during EEG, with no improvement in 6.

[a] Rhythmical delta–theta activity with spatiotemporal evolution, increase in prominence and frequency with observable change in clinical state.

[b] Two patients with ED > 2.5/s also had ED with typical spatiotemporal evolution (STE), and one had fluctuation of RDT.

[c] One patient diagnosed with clinical and EEG improvements to AED had RDT with STE.

[d] One patient diagnosed with subtle clinical phenomena also showed ED with STE, two RSE.

[e] One also had fluctuation of RDT, one RSE.

[f] Four showed sharp waves at the end of the pattern, one RSE.

[g] In only one patient, this was the diagnostic criterion, two RSE.

[h] In this one patient, this was the diagnostic criterion.

[i] In all of these patients, this was the diagnostic criterion; two also had fluctuation of RDT.

[j] In one of these five patients, this was the diagnostic criterion (out of 12 patients fulfilling ACNS criterion for RDA and fluctuation).

4. Discussion

4.1. Test performance of SCNC

Implementing the ACNS definition of rhythmic delta activity significantly increased the specificity of SCNC. Another mild increase in specificity (not significant) by adding the ACNS criterion of fluctuation was accompanied by a minimal decrease in sensitivity because a patient with RDT without fluctuation with a clinically definite diagnosis of NCSE gave one false negative. As pathological EEGs without suspicion of NCSE (recruiting time for 50 consecutive abnormal EEGs in our center: one week) are much more common than EEGs with definite NCSE (recruiting time: 10 months, i.e., approximately a 40-fold difference), this additional increase in specificity is relevant. This has to be kept in mind when AEDs are given to patients with RDT without fluctuation. We propose a "modified SCNC"; differences compared to SCNC are delineated in Table 3.

It has to be emphasized that we achieved the increased specificity of the modified SCNC mainly by restriction to patterns with "relatively uniform morphology and duration" (ACNS definition of RDA) [8], i.e., excluding continuous *polymorphic* activity, which we found to be quite prevalent in patients with brain pathology without suspicion of NCSE. A second false negative patient with absence status with discontinuous ED failed to fulfill the 10-second criterion of continuous epileptiform discharges. This is communicated as an exception for mSCNC.

4.2. Frequency of diagnostic criteria in nonconvulsive status epilepticus

Fluctuation of graphoelements (epileptiform discharges 46.9%, RDT in 10.2%; Table 2) allowed one route of diagnosing "possible NCSE" and was the most frequently used criterion in this population collected from a general neurology department at a large university hospital. As the clinical measures taken in response to "NCSE" and "possible NCSE" are the same, i.e., administration of AEDs following status epilepticus protocol, we propose to apply the term "NCSE: Fluctuation of ED or RDT" for the former "possible NCSE with fluctuation without definite evolution" (Table 4). We tried to further characterize this criterion but found no correlation of EEG patterns to etiology. Rates of different etiologies and mortalities were in the same range as the whole group (Tables 1 and 2).

The criterion of improvement from IV AED is applied to patients with "EDs ≤ 2.5 Hz or rhythmic delta/theta activity (>0.5 Hz)" [6]. This could encourage physicians to treat patients with Lateralized Periodic Discharges (LPDs) or Generalized Periodic Discharges (GPDs) without evolution or fluctuation or any subtle clinical phenomena. There is a need for better selection of patients with LPDs or GPDs for AED treatment to prevent substantial overtreatment with these frequent EEG patterns. In modified SCNC, LPDs or GPDs should be considered for AED testing or treatment only if they fulfill the ACNS criterion for fluctuation (Table 4). Using the response to AEDs for the diagnosis of NCSE is problematic for two reasons: firstly, diagnostic criteria should be valid ex ante and not ex post. In other words, we should avoid overtreatment in patients with EEG patterns with a low probability of NCSE (e.g., LPDs without any clinical sign or fluctuation), just to know whether it is status or not. Secondly, we cannot assume that all cases of SE respond to AEDs, otherwise we would not have any refractory SE. In modified SCNC, we no longer use response to treatment in the formal process of establishing the diagnosis of NCSE. Instead, documentation of improvement of EEG and/or clinical presentation is recommended (Table 4). Nonresponders to IV AEDs may either be caused by too low a dose or too few AEDs, or by improving (shortly) after the defined testing point, i.e., 10 min after AED fully applied.

Application of IV AEDs was the only criterion for diagnosis of NCSE in two patients. Both had EEG improvement without clinical improvement, and both survived. One of the abovementioned false negatives had rhythmic delta activity without evolution or fluctuation.

Table 3
Differences between Salzburg Consensus Criteria for Non-Convulsive Status Epilepticus (SCNC) and modified SCNC (mSCNC).

	SCNC	mSCNC	Impact of modification
Duration of pattern to qualify for NCSE	10 s	10 s, exception: discontinuous absence SE	Discontinuous absence SE needs further studies
Counting epileptiform discharges (ED)	Not specified	All EDs in "worst" 10-second epoch	Clear instructions
Evolution	Various options	Same options as SCNC, but ACNS criterion for evolving	Clear instructions
Rhythmical delta/theta activity (RDT)	"Rhythmical" delta and theta	ACNS criterion for rhythmical delta activity	Clear instructions, significantly fewer false positives compared to "continuous" activity
Fluctuation of ED or RDT	Not specified	ACNS criterion for fluctuation	Clear instructions
Patterns to apply IV AED	ED ≤ 2.5/s *or* rhythmic delta/theta activity > 0.5/s	ED ≤ 2.5/s with fluctuation *or* rhythmic delta/theta activity > 0.5/s with fluctuation, *or* rhythmic delta/theta activity > 0.5/s without fluctuation;	LPDs and GPDs without fluctuations or subtle ictal clinical signs are no longer "tested" with AEDs; this avoids overtreatment.
How and when to test clinical improvement from IV AED	Not specified	Within 10 min after AED fully applied, improvement is defined as better performance in one of five domains: (i) "say your surname", (ii) "repeat 1,2,3", (iii) "raise your arms", (iv) opens eyes, (v) looks at examiner.	Clear instructions
How and when to test EEG improvement from IV AED	Not specified	Within 10 min after AED fully applied, improvement is defined as reduction of culprit graphoelements to "occasional", i.e., 1–9% of epoch.	Clear instructions
Improvement from IV AED relevant for diagnosis of NCSE	YES: depending on improvement diagnosis of "NCSE" *or* "possible NCSE" *or* no NCSE (if no other criterion fulfilled)	NO: IV AED is applied in criterion 4 (Table 4), but response/nonresponse has no impact on diagnosis.	Patients with treatment-refractory NCSE no longer missed for diagnosis of NCSE, allowing adequate treatment and scientific investigation.

IV AED: intravenously applied antiepileptic drug.

Table 4
The modified Salzburg Consensus Criteria for Non-Convulsive Status Epilepticus (mSCNC), which is suggested for all patients with qualitative or quantitative disturbance of consciousness and suspicion of NCSE. The diagnosis of NCSE is the result of combining EEG and clinical data. Clinical symptoms/signs raising suspicion of NCSE have to last at least 10 min [14,15].

EEG data:

EEG changes fulfilling the criteria have to be continuously present for ≥10 s. Criteria not applicable to physiological graphoelements.
A: Patients without known epileptic encephalopathy (at least ONE of the criteria 1–3 should be fulfilled for diagnosis of NCSE)
1. EDs > 2.5 Hz (i.e., >25 EDs in "worst" 10-second epoch)
2. Typical ictal spatiotemporal evolution* of:
   –(2a) EDs OR
   –(2b) Rhythmic activity** (>0.5 Hz)
3. Subtle ictal clinical phenomena*** with:
   –(3a) EDs OR
   –(3b) Rhythmic activity** (>0.5 Hz)
4. If criteria 1–3 are not fulfilled, but one of the following patterns is present, apply appropriate AED(s) after careful consideration of clinical situation and document response****:
   –(4a) EDs ≤ 2.5 Hz with fluctuation***** OR
   –(4b) Rhythmic activity** (>0.5 Hz) with fluctuation***** OR
   –(4c) Rhythmic activity** (>0.5 Hz) without fluctuation*****

B: Patients with known epileptic encephalopathy
In addition to the criteria above (A), these patients have to fulfill one of the following:
–Increase in prominence or frequency when compared to baseline *with* observable change in clinical state
–Improvement of clinical and EEG features with IV AEDs (see A.4.)

Clinical data:

Add clinical information for establishing the diagnosis of NCSE:
–Transition from premorbid to current ill state within minutes to hours
–Patient did not improve significantly in last minutes to hours, apart from waxing and waning.
–No information from brain imaging sufficiently explaining EEG pattern (e.g., brain stem hemorrhage)
–No metabolic/toxicological derangement sufficiently explaining EEG pattern (e.g., acute renal or liver failure)

Explaining remarks and specifications:
*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)*" [8].
**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*" [8].
***Minor twitching of mouth, periorbital region, or extremities should appear in close temporal relation to EEG pattern (be cautious concerning nonepileptic involuntary movements as mimics, e.g., Parkinsonian tremor, drug-induced myoclonus (e.g., opioids), serotonin syndrome,…).
****Reactivity to IV AEDs within 10 min 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, and (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.
Document response: –No EEG improvement and no clinical improvement
–Only EEG improvement but no clinical improvement
–Only clinical improvement but no EEG improvement
–EEG AND clinical improvements
For clinical practice: all four constellations qualify for NCSE.
For research projects: patient qualifies for NCSE if EEG and/or clinical improvement is documented, provided the clinical context is also in concordance with that.
*****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 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*" [8].
EDs: epileptiform discharges (spikes, polyspikes, sharp waves, sharp-and-slow-wave complexes) IV AED: intravenous antiepileptic drug

4.3. Other diagnostic criteria for NCSE

Taking the threshold of ED > 2.5/s allowed sensitive detection of NCSE [5,6]. Three patients (75% of subgroup NCSE-ED > 2.5, i.e., six percent of total group) would have been missed by using the threshold of 3.0/s, which had been previously proposed [3,4]. Differences in criteria (for NCSE, EEG AND clinical improvements; for "possible NCSE", only EEG improvement [6] versus EEG improvement OR clinical improvement [3–5]) were not detected. Appearance of subtle clinical phenomena in addition to certain patterns [6] allowed diagnosis in 12% of patients with definitive NCSE compared to schemes without this criterion [3–5]. The criteria of "post-discharge slowing or voltage attenuation" [3] or "post-PEDs background slowing or attenuation" [5] were not evaluated in the current study, as PEDs (i.e., LPDs and GPDs) were taken as ictal if accompanied by subtle clinical phenomena or if there was fluctuation of EDs. However, PEDs without these options were not regarded to represent NCSE but rather reflected brain damage [16].

4.4. Scores for outcome prediction

In addition to validation of SCNC criteria, we also assessed SE outcome scores for better patient characterization and comparability of our results. In this population, EMSE score was superior to STESS-3 score and STESS-4 score in NPV, PPV, and correctly classified (CC) scores. This was concordant to recent findings in another retrospective population [12], where CC in NCSE was 81.4% [12] compared to 78.0% in the current study. False positives for EMSE can be considered survivors with significant burden of age, etiology, comorbidity, and EEG. These were mainly found in the group of epileptiform discharges, whereas this was rare in NCSE diagnosed by RDT (Supplementary table). False positive rates were higher in comatose patients. False positives of EMSE were almost evenly distributed independent from semiology, with the exception of patients who followed the sequence of NCSE→GTCSE→NCSE, but in this group, numbers were too small to draw firm conclusions.

5. Conclusion

Salzburg Consensus Criteria for Non-Convulsive Status Epilepticus implementing the ACNS definitions for rhythmic delta activity avoid numerous false positives. The ACNS criterion for fluctuation further reduces false positives marginally but, in turn, leads to small loss of sensitivity. Further studies are needed to identify correct procedure. Epidemiology based Mortality Score in SE was superior to STESS-3 and STESS-4 in this cohort. We propose a modified SCNC (mSCNC) for further research and prospective validation studies.

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.yebeh.2015.05.007.

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Conflict of interests

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