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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.