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Prospective assessment and validation of rhythmic and periodic pattern detection in NeuroTrend: A new approach for screening continuous EEG in the intensive care unit

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ABSTRACT

Background: NeuroTrend is a computational method that analyzes long-term scalp EEGs in the ICU according to ACNS standardized critical care EEG terminology (CCET) including electrographic seizures. At present, it attempts to become a screening aid for continuous EEG (cEEG) recordings in the ICU to facilitate the review process and optimize resources.
Methods: A prospective multicenter study was performed in two neurological ICUs including 68 patients who were subjected to video-cEEG. Two reviewers independently annotated the first minute of each hour in the cEEG according to CCET. These segments were also screened for faster patterns with frequencies higher than 4 Hz. The matching annotations (2911 segments) were then used as gold standard condition to test sensitivity and specificity of the rhythmic and periodic pattern detection of NeuroTrend.
Results: Interrater agreement showed substantial agreement for localization (main term 1) and pattern type (main term 2) of the CCET. The overall detection sensitivity of NeuroTrend was 94% with high detection rates for periodic discharges (PD = 80%) and rhythmic delta activity (RDA = 82%). Overall specificity was moderate (67%) mainly because of false positive detections of RDA in cases of general slowing. In contrast, a detection specificity of 88% for PDs was reached. Localization revealed only a slight agreement between reviewers and NeuroTrend.
Conclusions: NeuroTrend might be a suitable screening tool for cEEG in the ICU and has the potential to raise efficiency of long-term EEG monitoring in the ICU. At this stage, pattern localization and differentiation between RDA and general slowing need improvement.

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1. Introduction

The increased use of continuous EEG (cEEG) in the intensive care unit (ICU) for patients with critical illness has been propagated lately by many authors [1–7]. This is due to the fact that nonconvulsive seizures (NCSs) and nonconvulsive status epilepticus (NCSE) occur more often than previously anticipated [8]. Sutter et al. revealed that, after implementing cEEG into clinical practice, the rate of NCS diagnosis increased significantly compared with previous diagnostics. This might be not only due to higher observer awareness and greater availability of EEG but also due to longer observation periods [1]. Incident rates diverge a lot, as the studied patient populations are seldom homogeneous and inclusion criteria for cEEG vary between studies. i.e., 19% of the patients had NCSs in a study from Claassen [5] compared with 34% found in a study of Jordan [9]. Patients who suffered from convulsive status epilepticus often convert to NCSE after their convulsions have stopped [10]. Also, patients with altered state of consciousness and clinical features like subtle motor activity and abnormal eye movements may suffer from NCE or NCSE [11]. Privitera could demonstrate that in 198 patients with altered state of consciousness, 37% had NCSs [12]. In comatose patients, there is nearly no evidence of

Abbreviations: ACNS, American Clinical Neurophysiology Society; AIT, Austrian Institute of Technology; BI, bilateral independent; cEEG, continuous electroencephalography; CCET, critical care EEG terminology; EEG, electroencephalography; FN, false negative; FP, false positive; GHV, General Hospital Vienna; G, generalized; ICU, intensive care unit; κ, kappa; L, lateralized; MF, multifocal; MT1, main term 1; MT2, main term 2; NCR, Neurological Center Rosenhuegel; NCSs, nonconvulsive seizures; NCSE, nonconvulsive status epilepticus; NOPAT, no pattern; NT, NeuroTrend; QEEG, quantitative EEG; PD, periodic discharge; RAA, rhythmic alpha activity; RDA, rhythmic delta activity; RDA + S, rhythmic delta activity plus frequent intermixed sharp waves or spikes; RTA, rhythmic theta activity; SE, sensitivity; SP, specificity; SW, rhythmic spike-and-wave activity; TN, true negative; TP, true positive.

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seizure activity without EEG. Towne showed that in 236 coma patients with unclear genesis, 8% had NCSE [13]. Therefore, cEEG still remains the gold standard for reliable diagnosis of NCSs and NCSE. Whether NCSE is a predictor for bad outcome in patients with critical illness is difficult to assess because treatment effects, causative medical disorder, and complications are difficult to separate. Until now, seizure duration and delayed diagnosis of NCSs and NCSE are the only two independent parameters known to increase morbidity and mortality [14].

Recently, the use of cEEG in patients with critical illness has been reported to be associated with a favorable outcome [15]. Continuous analysis of cEEG by a trained expert reviewing segments of 10 s each is virtually impossible but would enable early and adapted treatment for the patient. Quantitative EEG (QEEG) addressed this important problem by evaluating the EEG in real time and by showing amplitude, power, frequency, and rhythmicity in compressed time scales [16]. The downside of QEEG techniques is the oversimplified approach to extract EEG information. This leads to a predisposition to false positive errors, and seizure activity can be missed in the shadow of high-amplitude artifacts [17].

For a long time period, many authors tried to define and classify NCSs and NCSE including or excluding EEG patterns frequently seen in patients with critical illness such as periodic discharges and fluctuating rhythmic patterns [5,11,14,18–21]. In 2013, the American Clinical Neurophysiology Society (ACNS) developed a standardized critical care EEG terminology (CCET) to facilitate communication between researchers [19].

Based on the CCET, the computational encephalography research group of the Austrian Institute of Technology (AIT) developed an automated detection and trending method called NeuroTrend (NT) with the aim to assist and facilitate the review process of cEEG [22]. In this work, we evaluate the performance of NT in terms of sensitivity, specificity, and interrater agreement.

2. Methods

NeuroTrend (NT) is a computational method that automatically detects rhythmic and periodic patterns in surface EEG and visualizes the results graphically. The definition of rhythmic and periodic patterns follows the guidelines of the American Clinical Neurophysiology Society Terminology [19]. Additionally, rhythmic patterns of more than 4 Hz are detected to cover the whole spectrum of electrographic seizure patterns. The aim of this work is to evaluate the sensitivity and specificity of detected patterns compared with manual-annotated EEG segments. The technical methodology used in the rhythmic and periodic pattern detection was described recently by Fürbass [22]. In this work, NeuroTrend version 1.1 was used for the calculation of all detections (NeuroTrend V1.1, www.eeg-vienna.com).

2.1. Data acquisition and patient selection

We prospectively recorded long-term video-EEGs (n = 68) using the international 10–20 electrode system with a sampling rate of 256 Hz. The recording was done at the neurological ICU of the Neurological Center Rosenhuegel (NCR) and the neurosurgical ICU of the General Hospital Vienna (GHV) using a Micromed EEG recording system (SystemPLUS Evolution 1.04.95) between March 1, 2013 and September 1, 2014. Only cEEGs with a recording period longer than 20 h were included. At least nineteen of twenty-one cup electrodes (including reference and ground electrode) had to be functional over the whole recording period. Gold cup electrodes (Genuine Grass Gold Disc electrodes) as well as conductive plastic cup electrodes (Ives EEG Solutions) were used for recordings. Gold cup electrodes were used preferentially. Plastic cup electrodes were used in cases where CT scans had to be carried out regularly.

The treating physician conducted patient selection according to the following criteria:

a) Remote eye movement abnormalities or subtle myoclonus
b) Short time period since patient's admission and neurologic injury
c) Low Glasgow Coma Scale (GCS).

The criteria applied were expected to filter out as many cases of NCSs/NCSE as possible according to Husain et al. [11] and Claassen et al. [5]. Patients younger than 18 years and patients with a high risk of infection (e.g., because of expanded wounds) were excluded from the study.

2.2. Validation strategy

In a first step, two clinical neurophysiologists from the recording centers NCR and GHV were asked to annotate the first minute of each hour in the video-EEG recording of their own center. The reviewers who were naïve to these video-EEGs had to screen for mechanical ventilation artifacts, electrocardiogram artifacts, and rhythmic movements. Electroencephalography pieces including these artifacts were labeled accordingly. Video and sound data were then separated from the EEG, and the EEGs were anonymized. The anonymized EEGs from both sites were then merged, resulting in a dataset of 68 long-term EEG recordings.

In a second step, both evaluators were asked to annotate rhythmic and periodic patterns in the one-minute annotation segments of all 68 EEGs from both centers. The definition of these patterns followed the main term 2 definition (MT2) in the CCET guidelines [19]. The MT2 definition was extended to include rhythmic pattern of more than 4 Hz. Both reviewers were firm with the recent version of CCET and had used ACNS training slides several times. The reviewers could use the EEG viewer without any restriction in relation to montage or filters. Several nonoverlapping annotations were allowed. Each annotation may have an arbitrary start and an end position but has to be fully included in the annotation minute. For each annotation, the reviewer was allowed to choose between one of the following pattern types: periodic discharges (PDs), rhythmic delta activity (RDA), rhythmic theta activity (RTA), rhythmic alpha activity (RAA), and rhythmic spike-and-wave activity (SW). If the reviewer did not insert any annotation in the one-minute interval, it was counted as no pattern (NOPAT).

In addition to the pattern type, a localization property had to be defined. This property was defined according to the CCET [19] as main term 1 (MT1): generalized (G), lateralized (L), multifocal (MF), and bilateral independent (BI).

The annotations from the two reviewers were then used as gold standard condition to test the sensitivity and specificity of the rhythmic and periodic pattern detection of NT. Evaluation scripts were used to automatically read the reviewer annotations and to calculate the detection performance numbers. Artifact annotations from the first annotation step were only assessed if no other markers were placed in the annotation segment.

2.3. Statistical methods

The detection performance was defined by assigning one of four possible test conditions to each annotation minute: true positive (TP), false positive (FP), true negative (TN), and false negative (FN). A pattern was counted as TP if one of the detected patterns in the annotation minute matched the gold standard annotation. A gold standard annotation was defined as an agreement between both reviewers. If no agreement between the two reviewers was met, the annotation interval was excluded from the calculation. A gold standard annotation without a matching detection in the annotation minute was counted as FN. An annotation segment with one or several detections that do not match the