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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.

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

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

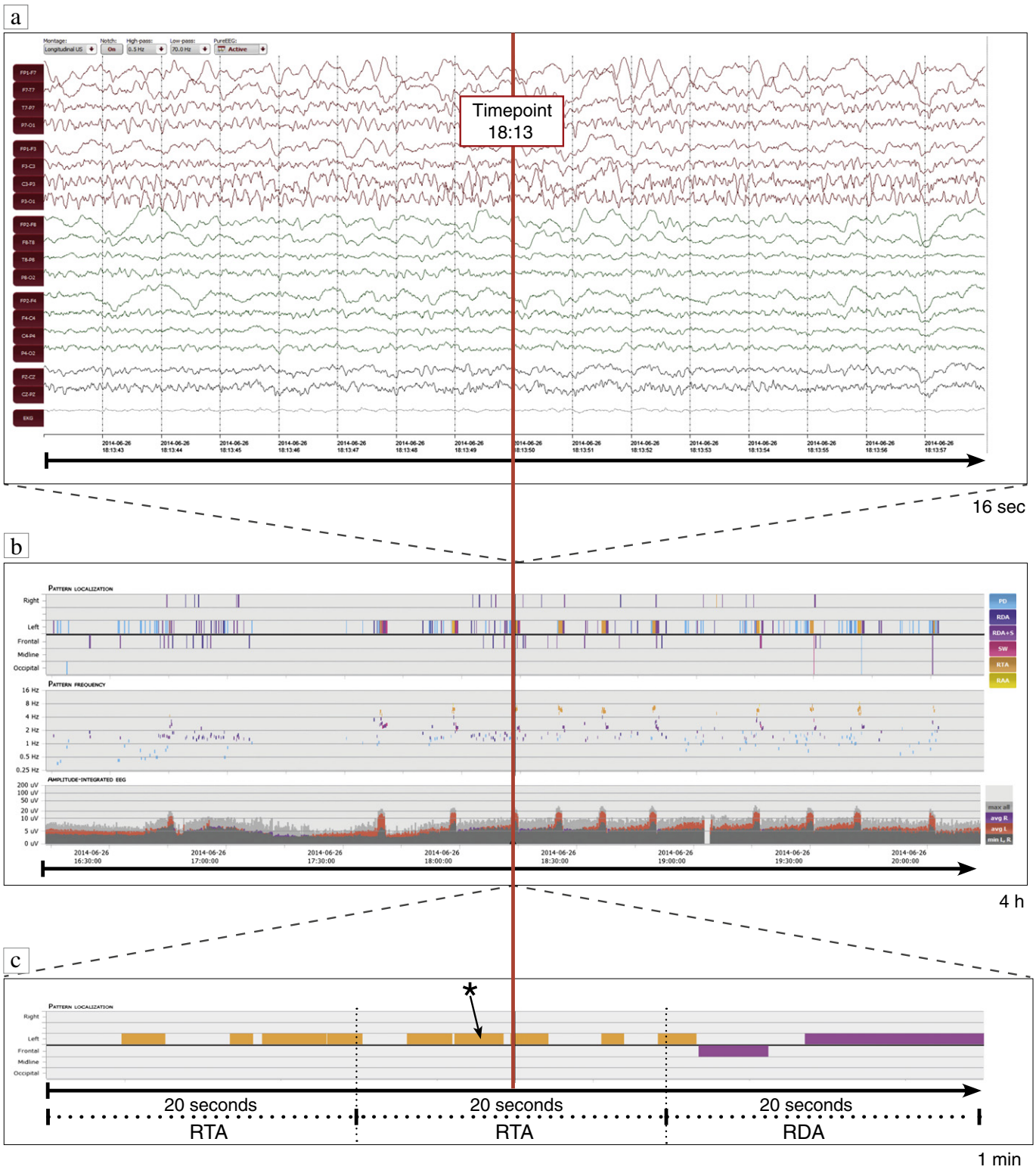

Fig. 1. Explanation of validation strategy: a) shows 16 s of raw EEG with left-sided rhythmic theta activity (RTA). The same EEG at the same time point is represented as a vertical red line in the NeuroTrend data illustration underneath. b) Demonstrates the usage of NeuroTrend as it displays 4 h (variable adjustment of time) of cEEG color-coded on one page. A clear repetition of RTA (orange bars, color code is displayed at the right side) occurring nearly every 15 min can be seen in the left hemisphere. AEEG also shows the 15-minute intervals but not the type of the pattern. c) One minute was extended out to illustrate the assessment process. The whole 1-minute interval shows detections of RTA (orange) and RDA + S (violet) when used for sensitivity and specificity calculation respectively. When divided into 20-second segments, segments 1, 2, and 3 show RTA, but only segment 3 includes RDA detection. For calculation of Cohen's kappa (κ) values, the pattern type and localization with the highest percentage of time coverage are used. The 1-minute segment, therefore, counts as lateralized RTA (*). The 20-second segments are counted twice as lateralized RTA and once as frontal RDA.

gold standard annotation was counted as FP. An annotation segment without gold standard annotation (NOPAT) and without any detection was counted as TN. Sensitivity (SE) and specificity (SP) were calculated according to the following formulas:

$$SE[\%] = \frac{TP}{TP + FN} * 100$$
$$SP[\%] = \frac{TN}{TN + FP} * 100.$$

To verify the interrater agreement between both reviewers, kappa (κ) values were calculated for each annotation interval. The same approach was used for the comparison between reviewers and NT for the categorical parameters MT1 and MT2. Both κ-statistics were calculated in two passes. First, the standard annotation interval of 60 s was used. Second, the same segment was divided into three shorter segments of 20 s, each offering a more detailed analysis. In each annotated segment, the annotation with the longest duration time was used to calculate κ-statistics. The rationale behind having two different evaluation intervals lies in NT's intentional usage as trending software and is demonstrated in Fig. 1. While we hypothesize that the 20-second time interval gives us a statement about the actual hit rate, the 60-second time interval should reflect the progression of EEG patterns and their trend.

The following qualitative classifications are used to categorize κ values into different ranges: poor agreement: ≤0; slight agreement: 0.01–0.20; fair agreement: 0.20–0.40; moderate agreement: 0.40–0.60; substantial agreement: 0.60–0.80; and almost perfect agreement: 0.80–1.00 [23].

3. Results

3.1. Patient characteristics

In the study period, 80 patients were monitored with continuous video-EEG. Five patients were excluded from the study because of insufficient data quality, long time periods with detached electrodes, or less than 17 electrodes at the beginning of recording. Another 7 patients were excluded because of a recording duration of less than 20 h. The mean age was 58 (±16.5) years with a female to male ratio of 35:33. Plastic cup electrodes were used in 27 cases, while the majority of patients (n = 41) were monitored with gold cup electrodes. Continuous Electroencephalography (cEEG) of 4813 h were recorded in total with a median length of 48 h. This led to 2911 segments of 1 min each available for evaluation purposes.

3.2. Interrater agreement

Interrater agreement of main term 1 (MT1) as well as main term 2 (MT2) according to standardized critical care EEG terminology (CCET) as well as electrographic seizures was performed between the two reviewers [19]. Main term 1 showed a substantial agreement in both short (20-second) and long (60-second) annotation intervals. The same Cohen's kappa (κ) values could be found for MT2 and are presented in Table 1. A good agreement between reviewers was crucial to enable further validation between reviewers and automated pattern detection. Looking at each MT2 pattern separately, rhythmic delta activity (RDA) was the pattern with the highest disagreement between reviewers and deteriorated further in the more detailed 20-second analysis (Fig. 2). Rhythmic alpha activity (RAA), spike-and-wave activity (SW), and rhythmic theta activity (RTA) showed a good agreement but occurred in very low numbers.

3.3. Validation of main term 2 (MT2)

Sensitivity and specificity of NeuroTrend (NT) for MT2 patterns are shown in Fig. 3. While sensitivity for the detection of any MT2 pattern is high (0.94), specificity is low (0.67) for 60-second annotations with a positive predictive value of 0.2 and a negative predictive value of 0.99. In the shorter 20-second time interval, sensitivity declines to 0.84, while specificity rises to 0.78. The same can be seen for periodic discharges (PDs) and RDA. Sensitivity declines from 0.8 to 0.59 for PD and 0.82 to 0.71 for RDA if compared between the 60-second annotation interval and the shorter 20-second annotation interval. Specificity inversely rises from 0.88 to 0.93 for PD and from 0.72 to 0.83 for RDA. Rhythmic theta activity and rhythmic spike-and-wave activity showed high specificity and sensitivity, while RTA was detected with a high specificity solely. Because of the low number of RTA, SW, and RAA in our study, no serious conclusions can be drawn for these patterns.

κ-Statistic showed similar results in regard to the agreement between NT and the reviewer gold standard (Table 2). Included segments in which no patterns were found (NOPAT) κ-statistic revealed a fair agreement between NT and the gold standard with a decline of agreement from 0.38 for 60-second annotations to 0.24 for 20-second annotations. This decline cannot be reproduced if no patterns (NOPATs) are

Table 1
Interrater agreement of main term 2 according to standardized critical care EEG terminology including electrographic seizures between two independent reviewers. The results of the longer sixty-second evaluation intervals are shown as opposed to the shorter twenty-second intervals. Overall, there is substantial agreement between the two reviewers regardless of the chosen evaluation interval. It is evident that rhythmic slowing of the EEG is often difficult to differentiate from RDA. Numbers of RAA and RTA are too low to make a reasonable statement. NOPAT = no pattern, PD = periodic discharge, RAA = rhythmic alpha activity, RDA = rhythmic delta activity, RTA = rhythmic theta activity, SW = rhythmic spike-and-wave activity.

		Reviewer 2											
		NOPA		PD		RAA		RDA		RTA		SW	
		60 sec.	20 sec.	60 sec.	20 sec.	60 sec.	20 sec.	60 sec.	20 sec.	60 sec.	20 sec.	60 sec.	20 sec.
Reviewer 1	NOPA	**1489**	**7149**	38	168	0	3	24	57	1	3	0	2
	PD	21	105	**242**	**393**	0	0	4	9	1	2	0	0
	RAA	0	0	0	0	**2**	**3**	0	0	1	2	0	0
	RDA	43	103	6	5	0	0	**74**	**109**	0	0	1	2
	RTA	0	1	2	2	0	0	1	2	**5**	**10**	0	0
	SW	2	4	0	0	1	2	0	0	1	0	**8**	**13**
Cohens Kappa:		**0.79**	**0.67**										

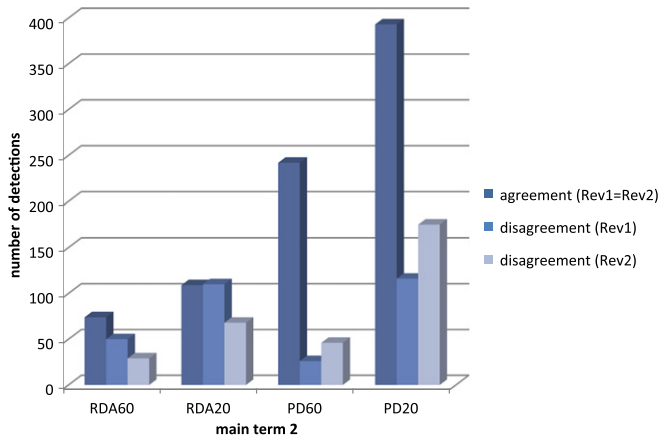

Fig. 2. The number of interrater agreements (Rev1 = Rev2) as well as disagreements (Rev1, Rev2) is shown for rhythmic delta activity (RDA) and periodic discharges (PDs) separately for 20- and 60-second annotation intervals. PDs show a substantial agreement with an even rise in agreements and disagreements in both annotation intervals. Agreement for RDA on the contrary deteriorates with more detailed analysis.

excluded from the calculation. This is mainly due to the fact that NT often detected RDA falsely when NOPAT was assigned. This observation was getting worse if a higher time resolution was used for calculation.

3.4. Validation of main term 1 (MT1)

While MT1 showed a substantial agreement (0.79) between reviewers, κ between reviewers and NT is poor (0.16) if NOPATs are not included in the statistic.

3.5. Artifacts

Artifacts in cEEG play a major role in the ICU and can disturb automatic pattern detection heavily. NeuroTrend, therefore, uses an artifact rejection module called "PureEEG" which has been described recently [24]. During the review process, cEEGs were reviewed for artifacts in the annotation segments with the help of video and sound recordings. Artifacts were marked but not excluded in NT analysis. During evaluation of these segments, it could be seen that NT was relatively stable for artifacts with 664 (60.3%) detections as NOPAT out of 1102 artifact markers resulting in 438 (39.7%) falsely labeled segments. In terms of pattern, mainly NT's RDA detection was triggered by artifacts and reached 295 (67.3%) false detections. False detection rate of an artifact as a rhythmic or periodic pattern was 108 (24.7%) for PD, 32 (7.3%) for RTA, and 3 (0.7%) for SW. Artifacts were never detected falsely as RAA.

4. Discussion

In this article, we assessed and validated the rhythmic and periodic pattern detection performance of an automated computer algorithm called NeuroTrend (NT) [22]. The aim of NT is the quick visualization of several hours of cEEG recordings based on ACNS standardized critical care EEG terminology (CCET) including rhythmic patterns with frequencies higher than 4 Hz [19].

While conventional QEEG displays compressed raw EEG in terms of technical measurements, NT transcribes automatic detections into neurophysiological established wording [24]. Another big difference between QEEG and NT consists in the prior usage of artifact rejection. Therefore, QEEG may facilitate the review process of larger cEEG files but comprises the risk of false interpretation due to processed artifacts. Both methods have got a strong data compression property. NeuroTrend allows the graphical representation of large cEEG files, giving the reviewer the possibility to screen several hours to days of cEEG on a few pages. It is important to stress that NT's focus lies in displaying trend data. It should depict changes in EEG over longer time periods and not exact values at a certain time point. That is why an unconventional approach to assess correct pattern analysis has been chosen. While most studies assess monitoring devices by interrater agreement at preselected time points, we tried to approach real cEEG testing conditions by using unselected time intervals [25,26]. Furthermore, final calculations of agreement were automated to minimize confounders. A time interval of 1 min every hour was randomly chosen regardless of recording quality, presence or absence of artifact, and EEG pattern. To enable the evaluation of correct EEG pattern detection during this minute, we separately analyzed a segment of 60-second as well as three 20-second fragments. It might seem that the detection of shorter segments

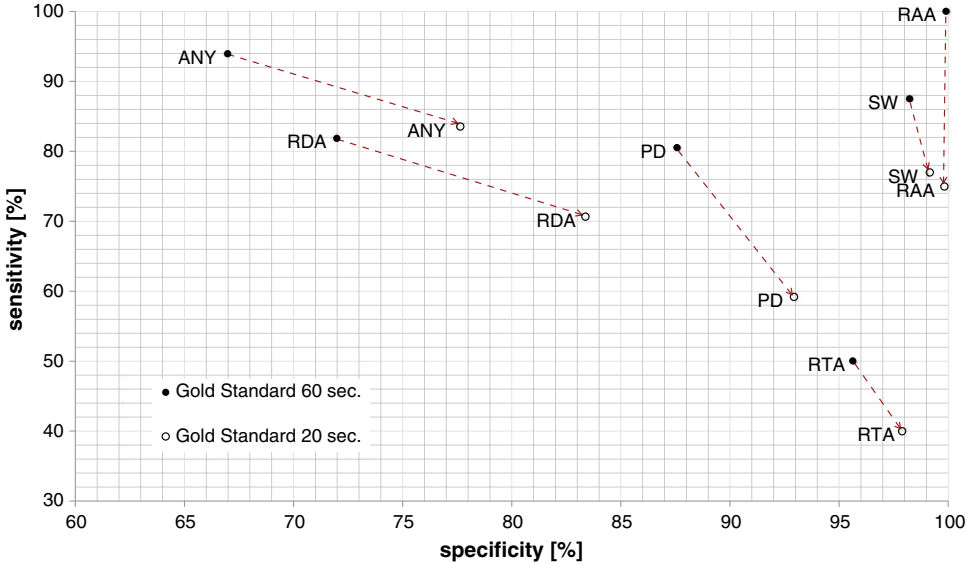

Fig. 3. Detection performance of NeuroTrend. NeuroTrend has a high sensitivity compared with the gold standard of two reviewers (60 s) for PD, RDA, and ANY patterns. Therefore, it is suitable as a screening tool. Specificity for PD is high, while specificity for RDA and, therefore, also for ANY is moderate. The shorter 20-second annotation interval showed us a shift towards a higher specificity at the cost of a lower sensitivity. For the patterns SW, RTA, and RAA, not enough data were collected to be significant. PD = periodic discharge, RAA = rhythmic alpha activity, RDA = rhythmic delta activity, RTA = rhythmic theta activity, SW = rhythmic spike-and-wave activity, ANY = all patterns previously mentioned together.

Table 2
Kappa statistic of main term 2 according to standardized critical care EEG terminology including electrographic seizures between reviewers (gold standard) and NeuroTrend. The results of the longer sixty-second evaluation intervals are shown as opposed to the shorter twenty-second intervals. Overall, there is a fair agreement with a considerable drawback in the shorter evaluation interval. This is due to the increased number of false positive detections, especially for RDA. Excluding NOPAT and considering only intervals where reviewers and NeuroTrend found a pattern highlight this finding. No difference can be found in Cohen's kappa between the sixty-second evaluation and the twenty-second evaluation anymore. NOPAT = no pattern, PD = periodic discharge, RAA = rhythmic alpha activity, RDA = rhythmic delta activity, RTA = rhythmic theta activity, SW = rhythmic spike-and-wave activity.

		NeuroTrend											
		NOPA		PD		RAA		RDA		RTA		SW	
		60 sec.	20 sec.	60 sec.	20 sec.	60 sec.	20 sec.	60 sec.	20 sec.	60 sec.	20 sec.	60 sec.	20 sec.
Gold standard	NOPA	**1052**	**5607**	130	438	0	10	300	999	7	77	0	18
	PD	18	73	**155**	**216**	0	0	58	85	0	0	12	21
	RAA	0	0	0	0	**0**	**1**	0	0	3	3	0	0
	RDA	3	15	17	19	0	0	**58**	**74**	2	1	0	0
	RTA	0	0	5	6	0	0	2	6	**1**	**2**	0	0
	SW	0	0	2	4	0	0	2	4	0	0	**4**	**5**
	Cohens Kappa (NOPA included):			**0.38**	**0.24**								
	Cohens Kappa (NOPA excluded):			**0.38**	**0.36**								

is more precise to predict the hit rate and, therefore, sensitivity and specificity. However, in contrast to spike detection and other alarm devices, the detection of a single measurement by the algorithm is not its primary purpose. Similar to a human EEG reviewer who has the ability to focus on relevant EEG changes, NT should display the progression of predominant ongoing patterns. That is why our primary study outcome was measured by the longest pattern available during 60 s as presented in Fig. 1.

Because the validation process should be as close to real screening conditions as possible, all cEEG data were recorded prospectively, no cEEG file was used for preceding algorithm development, and artifacts were not removed.

Interrater agreement between both reviewers showed a substantial agreement (0.6–0.8) in MT1 and MT2. A good agreement was essentially required to establish a gold standard condition against which NT could be tested. Our findings of a high interrater agreement correspond to previous interobserver studies that tested the 2012 version of the ACNS nomenclature [27,28].

Because EEG segments were not preselected, the marker NOPAT for EEG segments without rhythmic or periodic pattern was introduced.

The assessment of NT showed that it might be a useful screening tool for cEEG. On the one hand, NT revealed a high overall sensitivity (0.94) for MT2 patterns and a low rate of false negative detections. On the other hand, overall specificity (0.67) was low with only one true hit out of five detections. It should not be overlooked that sensitivity declines and specificity rises when the shorter 20-second interval is used for evaluation. Specificity for PD is good (0.88) while specificity for any pattern and RDA is moderate. Table 2 illustrates nicely the large number of false positive RDA detections in segments where the reviewers assigned NOPAT. Likewise to moderate results in specificity for RDA in our study and poor raw percentage of positive agreement for RDA (57%), a recent study showed that RDA is often difficult to distinguish from general slowing [29].

Evaluation of MT1 revealed that NT has a tendency to detect patterns as lateralized. Patterns with anterior - posterior lag and hemispheric differences are the cause of this behavior.

Electroencephalography is prone to artifacts, and many forms of artifacts in cEEG at the ICU have been described [30]. Like already outlined above NT can distinguish itself from other screening tools by an artifact rejection property called "PureEEG" [24]. Artifacts can falsely trigger pattern detections of NT in 39.7% of all prior labeled artifacts. Especially RDA was triggered by artifacts, which lead to a high false positive detection of RDA.

Limitations of the study can be seen in a small number of patients and the unequal distribution of patterns. These issues had to be condoned to enable a prospective study. Furthermore, it could be argued that including only segments where solely two reviewers gave an agreement may exclude potential difficult patterns from evaluation. Once again, it has to be stressed that interrater agreement for CCET has been proven high in our as well as in previous studies [27,28].

5. Conclusion

NeuroTrend might become a suitable screening tool for cEEG and has the potential to raise the efficiency of long-term EEG monitoring in the ICU. As it still offers the possibility to switch between trend data and raw EEG, it does not interfere the review process and can be used complementary to raw EEG, which remains gold standard for EEG interpretation. At this stage, pattern localization and differentiation between RDA and general slowing need further improvement.

Disclosure

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Algorithm development was conducted by the "Austrian Institute of Technology" including the authors Franz Fürbass, Manfred Hartmann, and Tilman Kluge. The Austrian Institute of Technology is the manufacturer of the EEG software package "Encevis", which will include the NeuroTrend algorithms.

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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