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Quantitative EEG Analysis for Automated Detection of Nonconvulsive Seizures in Intensive Care Units

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Abstract

Due to increased awareness of the high prevalence of nonconvulsive seizures (NCSs) in critically ill patients, continuous EEG monitoring (cEEG) in ICUs is rapidly increasing in use. However, cEEG monitoring is labor intensive; manual review and interpretation of the EEG are impractical in most ICUs. Effective methods to assist in rapid and accurate detection of NCSs would greatly reduce the cost of cEEG and enhance the quality of patient care. In this study, we report a preliminary investigation of a novel ICU EEG analysis and seizure detection algorithm. Twenty-four prolonged cEEG recordings were included in this study. Seizure detection sensitivity and specificity were assessed for the new algorithm and for the two commercial seizure detection software systems.

The new algorithm performed a mean sensitivity of 90.4% and a mean false detection rate of 0.066/h. The two commercial detection products performed with low sensitivities (12.9% and 10.1%) and false detection rates of 1.036/h and 0.013/h, respectively.

These findings suggest that the novel algorithm has potential to be the basis of clinically useful software that can assist ICU staff in timely identification of NCSs. This study also suggests that

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currently available seizure detection software does not have sufficient performance for the detection of NCSs in critically ill patients.

Keywords

ICU; Nonconvulsive seizures; cEEG monitoring; Seizure detection; Quantitative EEG trending

Introduction

Seizures occur as a consequence of a variety of acute insults to the brain [1-3]. These insults include CNS infections, intracranial hemorrhage, ischemic stroke, traumatic brain injury, and brain tumor. Seizures also occur as a consequence of toxic and metabolic encephalopathies. As a result, seizures are frequently encountered in critical care settings. Some seizures manifest as convulsions and can be easily recognized when a trained observer is nearby. However, 92% of seizures that occur in critically ill patients are nonconvulsive [4-9]. Because nonconvulsive seizures cannot be diagnosed with certainty on the basis of clinical manifestations, continuous EEG (cEEG) monitoring is required for reliable detection [4-9]. The high incidence of discrete nonconvulsive seizures, as well as sustained nonconvulsive status epilepticus, particularly in patients with intracranial hemorrhage and recent convulsive status epilepticus, has been documented by several investigators [3-4, 7, 10-14]. Without timely treatment, nonconvulsive seizures may impair consciousness and may lead to secondary brain injury and worse clinical outcome [3-5, 8-10, 12, 14-18]. As a result, there is growing recognition of the need to monitor the EEG in patients treated in critical care units.

The utility of cEEG monitoring in ICUs has been well established [8, 19-26]. However, most ICUs are not staffed by professionals with expertise in neurology and clinical neurophysiology. As a result, in contrast to other vital organ systems, routine continuous monitoring of brain activity is not performed in most ICUs. Even in hospitals staffed with experts in neurology and electroencephalography, cEEG monitoring is labor-intensive and continuous review and interpretation of raw EEG data are impractical in most clinical settings. Tools that aid rapid and accurate detection of NCSs would greatly improve the efficiency of cEEG monitoring and enhance the quality of patient care. An automated, reliable, and user-friendly system for detecting critical changes in the EEG, such as NCSs, could help make EEG monitoring more practical in ICUs. In addition, a mechanism for simultaneously transmitting the EEG to remote sites for interpretation is highly desirable.

Automated seizure detection software is often used to assist in EEG review. However, in the ICU setting, seizures are caused by a wide range of neurological and systemic disorders. As a result, electrographic seizure patterns can differ substantially from seizures recorded in patients with chronic epilepsy in outpatient and EMU settings. In many instances in the ICU, the electrographic patterns of NCSs differ significantly from patterns that occur in epileptic patients. Some NCS patterns strongly resemble other organized rhythmic patterns in the EEG, such as the triphasic waves seen in metabolic encephalopathies [27]. As a result, use of currently available seizure detection software in ICUs results in either low sensitivity or

high false detections, or both, and therefore does not offer a detection performance that is clinically useful. There are few published articles reporting on the utility of automated algorithms for detecting seizures in acute care settings. A preliminary study by Zhang and colleagues [28] suggests that it is possible to develop automated algorithms that can distinguish between nonconvulsive seizure patterns that occur in acute care settings and other organized rhythmic patterns characteristic of toxic or metabolic encephalopathies. A workshop held by the FDA (Title: Seizure Detection, Cognitive Function, and TBI/Concussion Devices: Issues in Their Evaluation) recently discussed the need of validating seizure detection algorithms intended to be used in ICU patients (<http://www.regonline.com/builder/site/Default.aspx?EventID=960009>).

Because of the inadequacy of seizure detection software in the ICU, “EEG trends” based on quantitative EEG (qEEG) analysis are often used in the ICU setting to facilitate detection of NCS patterns in long-term EEG recordings. To generate EEG trends, EEG waveforms are transformed into multi-channel graphic representation of quantitative EEG measures, such as signal amplitude and/or frequency. The trends are commonly presented in windows of 30 to 120 minutes, making it easier to detect clinically significant transient events, such as seizure discharges, by visual inspection of the trends. Potentially, EEG trending can facilitate the EEG review process. However, EEG trending software is limited because it has difficulty representing brief, focal or slowly evolving, low frequency seizures (Fig. 1) in a form that is easily recognizable. Trends can be a useful aid to experienced electroencephalographers and EEG technicians. However, to our knowledge, there is no published study that evaluates the clinical utility of trending in acute care settings.

While existing EEG-trending software appears to be much more useful than current seizure detection software in the Neuro-Critical Care setting, there are significant technical limitations to existing methods. One of the most useful EEG trends is the “Envelope” trend. The Envelope trend selects waveforms within a specific frequency range and plots the median waveform amplitude over a specified period of time (usually 10 to 20 seconds). However, as shown in Figure 1, this trend often does not facilitate detection of some NCS patterns.

Development of an effective automated seizure detection algorithm for use in acute care settings remains a challenge for two primary reasons. First, the algorithm must detect a wide variety of ictal EEG patterns, many of which are not seen in patients with chronic epilepsy. Second, the algorithm must reject organized rhythmic patterns produced by sleep, anesthesia, and encephalopathies as well as repetitive organized or rhythmic patterns produced by artifacts commonly present in long term recordings in acute care settings.

In this study, we report a preliminary evaluation of a novel ICU automated seizure detection algorithm (ICU-ASDA). ICU-ASDA utilizes novel measures of signal characteristics that can characterize essentially all ictal EEG patterns. Based on these measures, ICU-ASDA incorporates specially designed detection and rejection criteria. The algorithm is illustrated in Figure 2. The performance of ICU-ASDA was compared to that of two commercially available detection programs.

Methods

ICU recordings

The ICU-ASDA was developed and tested in a sample of 24 long-term continuous ICU EEG recordings obtained previously for clinical diagnostic purposes at the Medical University of South Carolina and Emory University Hospital. The total duration of these 24 recordings is approximately 1,500 hours, with a total of 453 NCSs in 11 recordings. Datasets were not preselected before the analysis and therefore included ICU patients with a variety of etiologies and ictal EEG patterns. Seizure events were determined and documented at the clinical sites, with an additional independent review by an additional electroencephalographer (JCS).

The Algorithm

The algorithm introduced here uses signal amplitude variation (AV) for detecting significant changes in amplitude and a regularity statistic (PMRS), based on the repeatability of the signal patterns [29-31] for detecting rhythmicity changes. The algorithm also calculates maximum signal frequency (Fmax) and amplitudes in a high frequency range (>25 Hz; Ahf (amplitude in a high frequency range)), for rejecting unwanted detections (e.g., sleep transients, muscle and chewing artifacts). Although different montages can be applied, analysis was performed using a 16-channel referential montage that included electrodes at Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T3, T4, T5, and T6, referenced to an electrode located between Cz and Pz, as suggested by the American Clinical Neurophysiology Society [32]. The algorithm detects the presence of seizure discharges, and recognizes three onset patterns (i.e., left-unilateral, right-unilateral, or bilateral).

The steps of the algorithm are depicted in Figure 2. Signals are filtered with a 5th order Butterworth filter to reduce unwanted detections due to background activity in the very low and high frequency ranges. After filtering the signals, the algorithm calculates several qEEG measures (PMRS, AV, Fmax, and Ahf) for each of the EEG channels (steps 3a and 3b). Based on these qEEG measurements, step 4 adopts three artifact rejection criteria (ARC) to eliminate false detections. If an EEG window is rejected, the algorithm starts over from step 1 and processes the next EEG epoch. Otherwise, the algorithm goes on to step 6 to determine if the EEG epoch satisfies one of the three detection criteria: (1) left-unilateral ictal pattern, (2) right-unilateral ictal pattern, or (3) bilateral ictal pattern. Figure 3 gives an example of a NCS with a left-unilateral ictal pattern (low-amplitude discharge over the left occipital/parietal region) that was detected by the algorithm.

Statistical Analysis

Each of the test EEG recordings was processed by the test algorithm (with fixed thresholds of detection/rejection criteria) and two currently available seizure detection software systems on the market: Persyst's Reveal and Optima's IdentEvent. Detection performance (sensitivity and the false detection rate per hr) of each detection algorithm was calculated. In order to prevent over-emphasizing overall performance on recordings with longer durations or larger number of seizures, sensitivity and the false detection rate were calculated for each individual recording and the mean values were used as the final overall performance.

Results

Table I provides details of data characteristics as well as the detection performance by the three algorithms. Overall, the ICU-ASDA performed at a mean sensitivity of 90.4% over the 11 recordings that included identified seizure, and a mean false detection rate of 0.066 per hour (i.e., 1.6 per 24 hours) over all 24 studied recordings. This encouraging training performance gives us high confidence to proceed to a formal performance validation study. It is worth noting that, over the same datasets, the two currently commercially available seizure detection software offer clearly sub-par detection performance for detecting NCSs in ICU patients. We believe that this is the reason why the FDA has recently highlighted the importance of independent (from EMU patients) performance validation of seizure detection devices for use in ICU settings, which has not been reported in the literature.

Discussion

There is growing recognition that EEG brain monitoring in acute care settings detects seizures and other acute causes of disturbed brain function that would not be detected otherwise. As a result, EEG monitoring in ICU settings and in Emergency Departments is increasing. This has led to the recognition that seizures are much more common in acutely ill patients than had been suspected, based on clinical examination and routine 20 to 30 minute EEG recordings. Early detection of seizures may lead to interventions that can reduce mortality and morbidity, although further study is needed to establish this. Increasing usage of continuous EEG monitoring can place excessive demands on the time of electroencephalographers - even when assisted by highly trained technicians - to interpret the large quantities of EEG data produced. Thus, there is a need to develop accurate diagnostic tools that will improve accuracy of detection and increase efficiency of record review.

Currently available commercial seizure detection software has been developed for and tested on recordings obtained from patients with uncontrolled epileptic seizures generated in EMUs. Because of major differences in EEG background patterns, artifact sources and ictal EEG patterns, these detectors do not perform well in acute care settings. This study demonstrates the poor performance of currently available commercial seizure detectors in recordings obtained from the ICU. This observation is not surprising, given the fact that the algorithms were not developed for this application. There is a need to develop seizure detection methods specifically designed for use in acute care settings. We report a preliminary study to evaluate a novel seizure detector algorithm developed for such a setting, the ICU-ASDA. These preliminary findings suggest that it is possible to develop algorithms with sufficient sensitivity and specificity for use in acute clinical settings

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- Use of EEG monitoring is increasing in ICUs to identify nonconvulsive seizures.
- No clinically validated seizure detection algorithms exist for ICU patients.
- A new seizure detection algorithm was tested in 24 prolonged EEG recordings.
- The new algorithm performed 90.4% sensitivity and 0.066/h false detection rate.
- This suggests that the algorithm can assist ICU staff in identifying seizures.

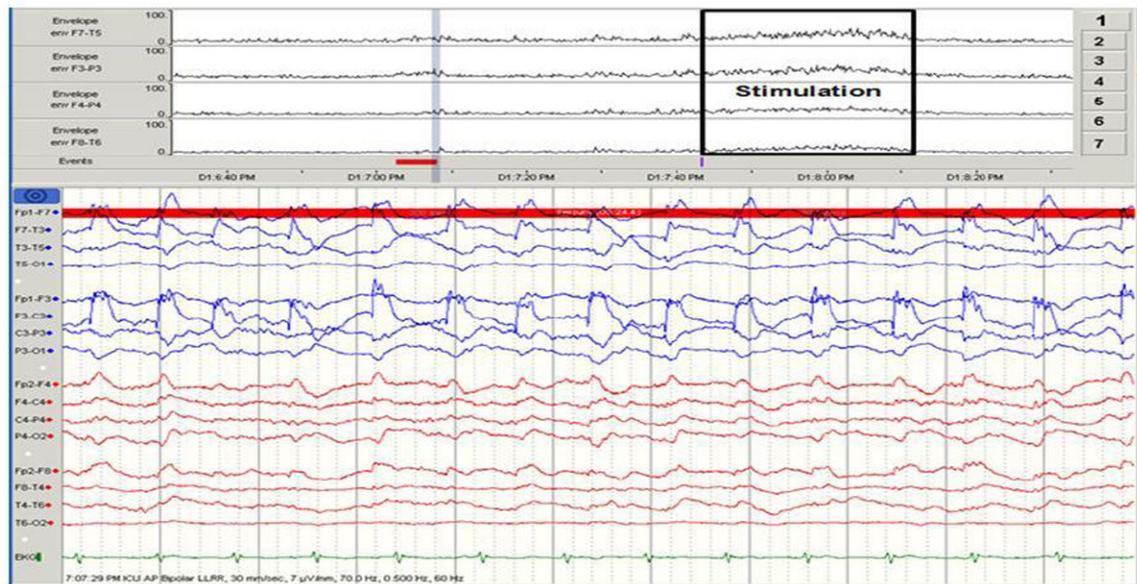


Figure 1.

A 4-channel Envelope trend over a 2-hour period containing a seizure pattern of about 3 minutes (upper trace) shows little change during a low-frequency NCS pattern that is present in the original EEG signal (lower trace shows 11 seconds of the ictal discharge).

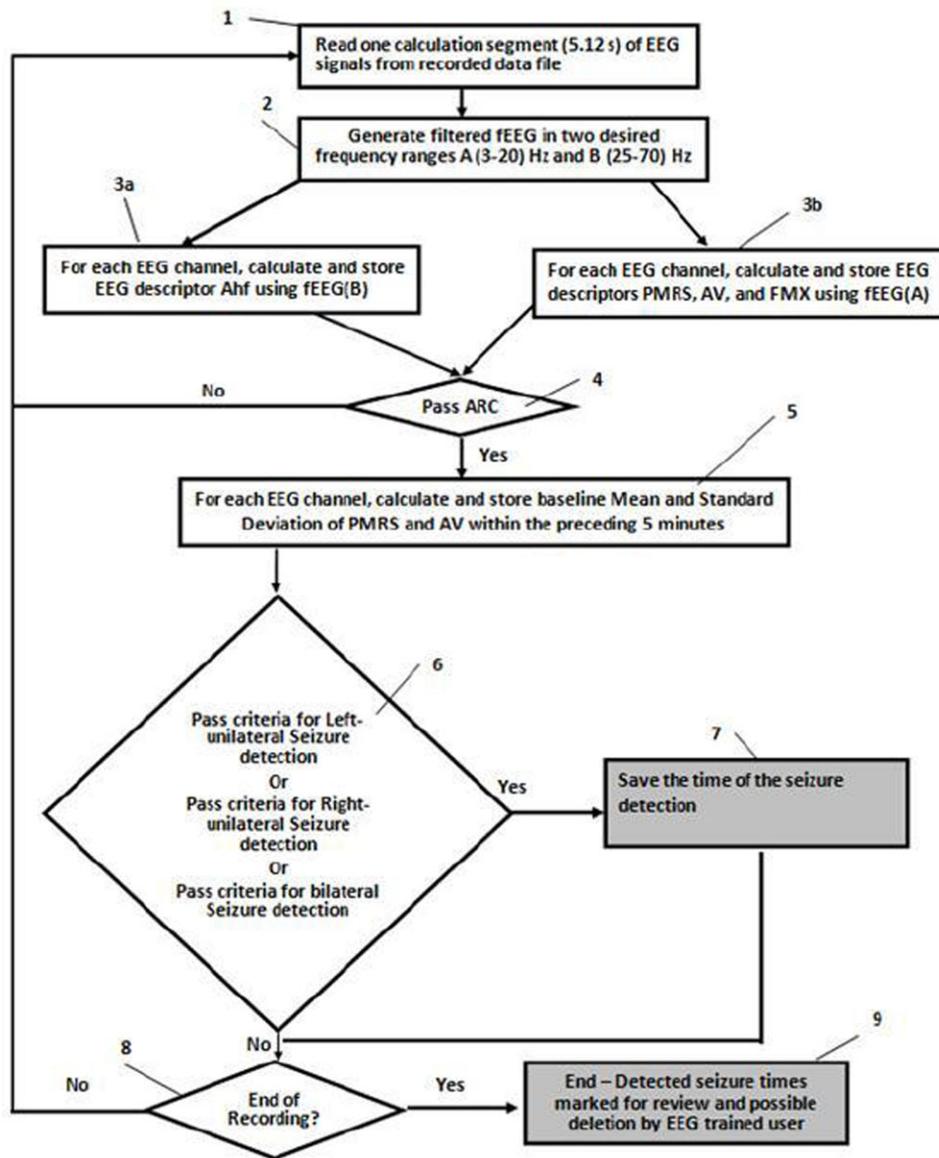


Figure 2.
Flow chart of the proposed ICU seizure detection algorithm

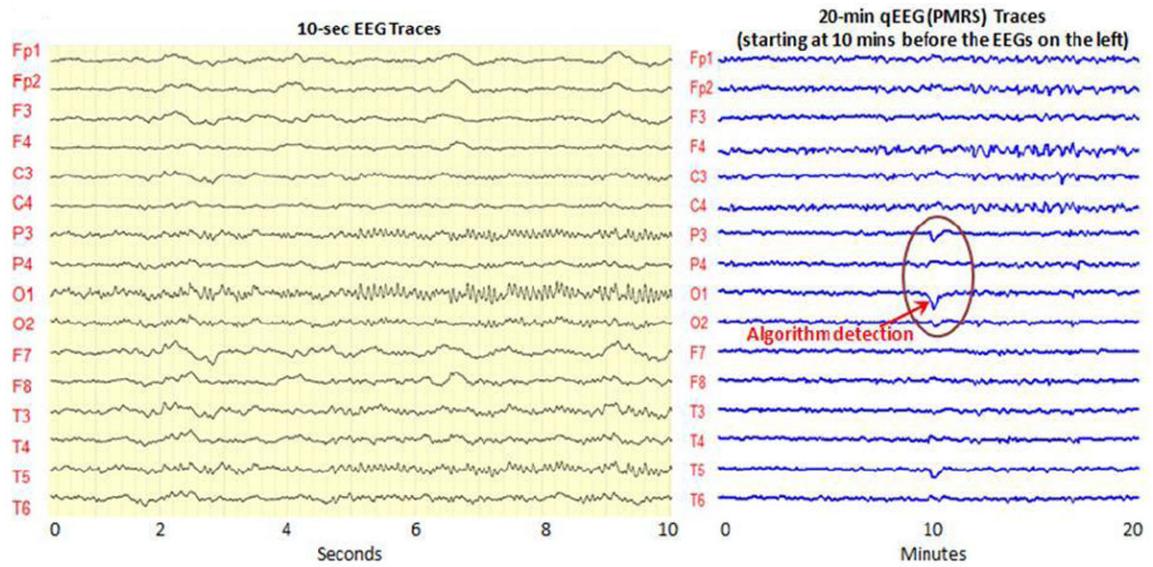


Figure 3.
 Demonstration of a low-amplitude ICU nonconvulsive seizure (left occipital/parietal) detected by the test ICU seizure detection algorithm

Table 1

Data characteristics and detection performance statistics

Recording	Duration (h)	# of Seizures	Detection Performance Statistics					
			ICU-ASDA		Reveal		IdentEvent	
			Sensitivity	FDR / hr	Sensitivity	FDR / hr	Sensitivity	FDR / hr
01	12.29	10	1.000	0.000	0.300	1.058	0.000	0.000
02	8.19	25	0.800	0.000	0.004	0.611	0.000	0.000
03	6.82	28	0.929	0.147	0.107	3.079	0.000	0.000
04	3.40	26	0.923	0.000	0.000	0.294	0.000	0.000
05	23.39	0		0.171		2.095		0.000
06	42.06	0		0.048		0.143		0.000
07	55.53	0		0.072		1.765		0.018
08	44.58	0		0.067		0.606		0.000
09	28.73	0		0.070		0.070		0.000
10	311.05	0		0.100		0.884		0.003
11	63.95	0		0.000		3.018		0.016
12	44.37	0		0.000		0.135		0.000
13	19.84	0		0.000		0.000		0.050
14	278.17	50	0.940	0.151	0.200	0.417	0.360	0.007
15	25.67	0		0.078		0.156		0.000
16	21.93	0		0.091		0.365		0.000
17	27.06	5	0.800	0.037	0.000	0.222	0.000	0.000
18	27.46	0		0.146		6.664		0.000
19	138.55	18	1.000	0.007	0.111	0.144	0.222	0.000
20	47.42	16	0.750	0.148	0.000	0.042	0.063	0.021
21	15.27	217	0.876	0.000	0.055	0.000	0.028	0.000
22	49.11	5	1.000	0.020	0.400	0.224	0.000	0.000
23	162.14	0		0.148		0.703		0.074
24	43.55	53	0.925	0.092	0.208	2.158	0.434	0.115
Total/Overall	1,500.53	453	90.4%	0.066 / h = 1.6 / day	12.9%	1.036 / h = 24.9 / day	10.1%	0.013 / h = 0.3 / day