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Automatic multimodal detection for long-term seizure documentation in epilepsy

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HIGHLIGHTS

- Automatic seizure detection assessing efficacy of EEG/ECG/EMG signals for seizure documentation.
- Multi-center evaluation including 92 patients with 494 seizures comparing full to reduced montages.
- Using 8 frontal and temporal electrodes will significantly improve conventional seizure reporting.

ABSTRACT

Objective: This study investigated sensitivity and false detection rate of a multimodal automatic seizure detection algorithm and the applicability to reduced electrode montages for long-term seizure documentation in epilepsy patients.
Methods: An automatic seizure detection algorithm based on EEG, EMG, and ECG signals was developed. EEG/ECG recordings of 92 patients from two epilepsy monitoring units including 494 seizures were used to assess detection performance. EMG data were extracted by bandpass filtering of EEG signals. Sensitivity and false detection rate were evaluated for each signal modality and for reduced electrode montages.
Results: All focal seizures evolving to bilateral tonic-clonic (BTCS, $n = 50$) and 89% of focal seizures (FS, $n = 139$) were detected. Average sensitivity in temporal lobe epilepsy (TLE) patients was 94% and 74% in extratemporal lobe epilepsy (XTLE) patients. Overall detection sensitivity was 86%. Average false detection rate was 12.8 false detections in 24 h (FD/24 h) for TLE and 22 FD/24 h in XTLE patients. Utilization of 8 frontal and temporal electrodes reduced average sensitivity from 86% to 81%.
Conclusion: Our automatic multimodal seizure detection algorithm shows high sensitivity with full and reduced electrode montages.
Significance: Evaluation of different signal modalities and electrode montages paces the way for semi-automatic seizure documentation systems.

1. Introduction

Seizure documentation and quantification represents the primary outcome measure of epilepsy therapy including antiepileptic drug treatment, epilepsy surgery, and neurostimulation. Presently, patients document their seizures using seizure diaries without systematic and objective validation approach by physicians. Recent publications showed that manual seizure counting suffers from underreporting with sensitivities of 50% during day and as low as 30% during night and can therefore be considered as highly unreliable (Blachut et al., 2015). This inaccuracy represents a major issue for the assessment of treatment efficacy including drug trials.

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We propose a semi-automatic system for seizure documentation and quantification based on computer methods to scan biomedical signals for epileptic seizures followed by a manual evaluation of these detections by trained staff. For this application a low number of sensors should be used to assure patient compliance and to simplify hardware design. On the other hand, data from ictal events needs to be recorded with a reasonable number of sensors to allow post-hoc analysis for correct seizure identification. A prerequisite for this approach is a wearable electrophysiological hardware setup that can be utilized over long time periods. Secondly, and with utterly importance, a clinically validated computer based detection method has to be used. This method has to ensure high sensitivity and low false detection rates, to pay off additional efforts of neurophysiological measurements with numerous EEG electrodes and other sensors.

EEG represents the gold standard in epilepsy diagnosis and to prove the epileptic nature of seizures which makes it the primary modality for automatic seizure documentation. Automatic seizure detection methods based on surface EEG recorded during inpatient epilepsy monitoring showed high sensitivity in multi-center studies (Fürbass et al., 2015a; Hopfengärtner et al., 2014). Reduced EEG electrode sets showed a rapid drop in detection sensitivity for rhythmic patterns (Herta et al., 2017) which has to be considered for wearable documentation devices.

ECG can be utilized as another modality for seizure detection. Epileptic seizures cause an activation of the central autonomic network (CAN) resulting in changes in heart rhythm at seizure onset. Ictal tachycardia (ITC) represents the most frequent change in heart rhythm and can be observed in 65–86% of seizures (Eggleston et al., 2014; Leutmezer et al., 2003). Furthermore, a larger affected brain area was reported to define the degree and rate of ITC (Stefanidou et al., 2015). ITC occurs early during seizure evolution and often even precedes EEG changes visible on scalp-EEG (Leutmezer et al., 2003). The high sensitivity of ITC, its early occurrence, and the easy technical setup for ECG measurement makes this biomarker highly promising for automatic seizure detection devices.

Other modalities for automatic seizure detection were investigated recently, including methods based on surface EMG (Beniczky et al., 2016) and motion sensors (Conradsen et al., 2012) as well as gyroscopic sensors and dermal skin conductance sensors (Banks et al., 2014).

In this study we present a multimodal automatic seizure detection method using information from EEG, ECG assessing ictal tachycardia and EMG measuring ictal tonic muscle activity. We investigated this method both with a full 10–20 electrode set as well as a reduced number of EEG electrodes suitable for ambulatory settings. We assessed strengths and weaknesses of this approach in patients with specific seizure and epilepsy types.

2. Methods

2.1. Data

We retrospectively analyzed 92 long-term EEG/ECG/EMG recordings from two epilepsy monitoring units including at least 21 EEG electrodes and at least one ECG channel. Signed informed consent was obtained from all patients. We included all available EEG recordings with one or more epileptic seizure during the recording period resulting in a total of 11,978 h of data with 494 epileptic seizures of various types (min per patient = 23 h, max per patient = 547 h). From 92 patients included in our study 55 patients had temporal lobe epilepsy (TLE) and 37 patients had extratemporal lobe epilepsy (XTLE). Data were recorded with a Micromed (Veneto, SpA) and an ITmed (Natus Medical Incorporated) system at a 256 Hz sampling rate using gold-disc electrodes placed according to the international 10–20 system with additional temporal electrodes. To mimic the behaviour of prospective data, digital EEGs were analyzed without manual pre-processing, data selection or data cutting.

The effect of reduced scalp electrode montages was simulated by removing electrodes from the digital EEG file before further analysis. Two different montages with reduced number of electrodes were assessed: the **8 electrode forehead montage** including electrodes FP1, F7, T7, FP2, F8, T8, FZ, ECG and the **7 electrode posterior montage** including electrodes T7, P7, O1, T8, P8, O2, ECG. Fig. 1 shows standard electrode positions (circles) as well as electrodes of forehead montage (dashed circles) and electrodes of posterior montage (shaded circles).

2.2. Performance evaluation methodology

Seizures were annotated following standard protocols of the two epilepsy monitoring units using both clinical and EEG information. The first three seizures of each patient were categorized according to the ILAE operational seizure classification (http://www.ilae.org/Visitors/Centre/documents/ClassificationSeizureILAE-2016.pdf) in order to facilitate performance evaluation according to seizure type. Seizure markers were set based on standard EMU review procedure using video, EEG, and other clinical information including manual validation of seizures by an experienced clinical epileptologists (HS, SP, or CB). Only validated seizure markers were used to define seizure epochs as basis for assessing detected and undetected seizures. Each seizure epoch ranged from 30 s before the clinical seizure marker to 180 s after this marker resulting in a total 210 s intervals of single seizure epochs.

Our seizure detection algorithm provided both time points and modality of detection. Time points of detected events were compared to the visually identified seizure epochs. Seizure epochs were defined as true positive (TP) if at least one detection occurred within the epoch time range. Detections outside of seizure epochs were defined as false positives (FP). Seizure epochs without a matching detection were defined as false negative (FN). For assessment of detection performance according to seizure types we distinguished between focal seizures (FS group) and focal seizures evolving to bilateral tonic-clonic (BTCS group). The first three seizure epochs including seizure type annotations in each patient were evaluated, consecutive seizure epochs and detections overlapping these epochs were ignored. Patients with at least one seizure of a certain type were included in the corresponding seizure type group. Patients having two different seizure types were included in both seizure type groups.

Sensitivity (**SE**) was defined as the ratio between the number of true positives (#TP) and the number of all seizures (#TP + #FN) and was calculated for each patient. False detection rate was defined as the number of false detections per 24 h (**FD/24 h**).

A paired *t*-test was used as test statistic between performance results of two detector types or electrode sets.

2.3. Computer algorithm

The computer algorithm detects seizures using EEG, surface EMG, and ECG signals that were recorded using scalp EEG and chest ECG electrodes. Fig. 1 gives an overview of the detection system.

EEG is able to pick up pathologic brain activity by showing rhythmic signal components, but patient movements and loose electrode contacts can cause signal artefacts with similar morphology. Before applying the EEG seizure detection algorithm artefacts were removed applying PureEEG, a fully automatic artefact