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Prospective multi-center study of an automatic online seizure detection system for epilepsy monitoring units

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HIGHLIGHTS

- Large prospective multi-center study of an automatic seizure detection system including 205 patients.
- Comparison between two automatic seizure detection systems using the same prospectively recorded dataset.
- Performance numbers on the publicly available CHB–MIT dataset and on 310 retrospective patients datasets.

ABSTRACT

Objective: A method for automatic detection of epileptic seizures in long-term scalp-EEG recordings called EpiScan will be presented. EpiScan is used as alarm device to notify medical staff of epilepsy monitoring units (EMUs) in case of a seizure.
Methods: A prospective multi-center study was performed in three EMUs including 205 patients. A comparison between EpiScan and the Persyst seizure detector on the prospective data will be presented. In addition, the detection results of EpiScan on retrospective EEG data of 310 patients and the public available CHB–MIT dataset will be shown.
Results: A detection sensitivity of 81% was reached for unequivocal electrographic seizures with false alarm rate of only 7 per day. No statistical significant differences in the detection sensitivities could be found between the centers. The comparison to the Persyst seizure detector showed a lower false alarm rate of EpiScan but the difference was not of statistical significance.
Conclusions: The automatic seizure detection method EpiScan showed high sensitivity and low false alarm rate in a prospective multi-center study on a large number of patients.
Significance: The application as seizure alarm device in EMUs becomes feasible and will raise the efficiency of video-EEG monitoring and the safety levels of patients.

1. Introduction

Long-term video EEG-monitoring in epilepsy monitoring units (EMUs) plays a central role in pre-surgical evaluation of patients with epilepsy (Smith, 2005). This time-consuming procedure lasting for several days up to weeks requires high effort from staff to ensure patient safety and to evaluate the high amount of data. Safety in EMUs is an on-going discussion. It is generally accepted that precautions have to be in place to promptly detect seizures (Carlson, 2009) and to avoid additional harm to the patients. A study by Atkinson et al. (2012) with $N = 20$ patients showed that only 40% of seizures showed staff response. Changing the safety

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protocol for EMUs can thus lead to a decrease in patient accidents and an increase in detected seizures (Spanaki et al., 2012).

Automatic epileptic seizure detection (ESD) is one method to improve patient safety and efficiency in the EMU. Although these systems have a long history of numerous methodical approaches that proved to be effective in some trials (Gotman and Gloor, 1976; Gotman, 1982, 1990) wide spread clinical application were not accomplished until now. Today, the small number of epilepsy monitoring units using such systems stays in contrast with the increasing awareness of patient security issues during long-term recording and the high costs of this examination method. A low false alarm rate is of major importance for alarm systems to avoid ignorance by staff as found by Lee and Shah (2013). Many epilepsy centers do not use automatic seizure detection systems because of a very high number of false detections.

Several publications proposed patient specific seizure detectors or detectors for certain seizure patterns (Beniczky et al., 2013). These approaches will be of limited value in clinical practice because details of the type of epilepsy or the localization of the seizure onset zone (SOZ) are mostly unknown. Attempts to use the first seizure of a patient for patient specific detectors are limited because of the long time delay to the first seizure. Several studies reported a delay between 2 and 3.7 days in EMUs for pre-surgical evaluation, depending on the type of epilepsy (Todorov et al., 1994). In addition, the average number of seizures that can be recorded in one week of video EEG is rather small (median of 3 in one week in our data). Furthermore, it is important to detect whether or not a patient has one or multiple types of seizures. This implies that detection systems cannot be efficiently trained or configured for patients in the EMU and that only parameter-free detection systems without restriction to seizure types are feasible.

Automatic analysis of the EEG can be done either ad-hoc during the recording of the patient or post hoc after the patient recoding has finished. These situations are also referred to as "online" or "offline" detection, respectively. This article will solely present results of the online seizure detector EpiScan but the major differences to offline detectors are depicted shortly to allow objective comparison to other publications. First of all, because online detection systems may be used as alarm devices whereas offline systems support the EEG evaluation after recording. Furthermore, online detection systems must have a very short time delay to trigger alarms. An artificially delayed alarm allows the collection of information about the trend of the supposed seizure and can avoid false alarms. A system reacting in the range of a few seconds is more close to an alarm device, whereas a system with a detection delay of several minutes or hours behaves like a typical post hoc system. When comparing the performance of ad-hoc to post hoc systems or ad-hoc systems with different delays care has to be taken.

The amount and kind of data to evaluate an automatic seizure detection system is an important and frequently discussed issue. A sufficient number of long-term patient recordings are needed in order to draw reliable conclusions about sensitivity, specificity or the differentiation between two competing systems or datasets. One critical point in assessment of seizure detectors is the estimation of the sensitivity. Seizures are rare events with high inter- and intra-patient variability. The detection sensitivity of an automatic system represents a random variable with high variance and unknown distribution. In statistics the central limit theorem states that a sampling distribution approaches the normal distribution if the sample size is sufficient, no matter how the population distribution was shaped. A sample size of $N = 30$ is considered as appropriate for moderately skewed population distributions and will give a rough estimate of the performance. Population distributions far from normal need a sample size of $N = 500$ or more. For the sensitivity and false alarm rate of a seizure detection system we cannot assume a distribution close to normal and thus have to carefully determine the amount of data necessary to get significant results.

However, sensitivity based on a high number of patients alone does not validate a clinical application if only parts of the recordings are used. Only complete and uncut datasets reflect the real clinical situation and can prove sensitivity and specificity at the same time. A detection system may easily be able to detect 100% of the seizures in a dataset when only ictal EEG fragments are used but will show an excessive false alarm rate when evaluated on full long-term recordings. In addition, changes of the EEG during the day/night cycle need to be included in the evaluation leading to a necessary continuous recording length of more than 24 h.

The Computational Encephalography research group (www.eeg-vienna.com) of the Austrian Institute of Technology (AIT) has developed an automatic seizure detection system for long-term scalp EEG recordings called EpiScan. The detection algorithm of EpiScan works as an alarm device which allows notification of medical staff in case of a seizure. The system does not require parameters or patients specific settings. In this article the results of a prospective multi-center study will be presented. The results of EpiScan will be compared to the results of the Persyst seizure detector using the same prospective dataset. A comparison to the EpiScan performance on the development dataset and the MIT–CHB dataset will be carried out.

2. Methods

2.1. Data analysis

EpiScan is based on a computational method, which automatically detects epileptic seizures in digitized EEG. This method was developed over several years by a team of physicians, mathematicians and medical experts (Schachinger et al., 2006; Perko et al., 2007; Kluge et al., 2009; Hartmann et al., 2011; Fürbass et al., 2012). It is intended to analyze the EEG ad-hoc and to act as an online detection system. The EpiScan method analyses the digital EEG during recording in intervals of a quarter-second. Frequencies below 0.7 Hz and above 99 Hz are removed by finite impulse response filters. Line noise is removed with notch filters at 50 and 60 Hz. EEG segments with artifacts like i.e. excessive amplitudes or artifacts from loose electrodes are removed automatically (Skupch et al., 2013) and are not used for detection. This will avoid false alarms based on measurement problems. The EEG is then scanned for rhythmic patterns in the time and frequency domain by algorithms called Epileptiform Wave Sequence Analysis (EWS) and Periodic Waveform Analysis (PWA), respectively (Hartmann et al., 2011; Fürbass et al., 2012). An energy detector scans for tonic or tonic–clonic seizures with strong muscle artifacts. All extracted features are normalized by a spatio-spectral model of the brain activity that is continuously updated by past information from the EEG. A set of classifiers is used to remove events with physiological origin. The use of these adaption and classification algorithms avoids repeated detections of physiological or pathological patterns that are no seizures and is therefore another important mechanism to avoid excessive false alarms. The parameters of the classifiers were optimized using an automatic parameter optimization method (Dollfuss et al., 2013).

2.2. Quantity and quality of data needed for evaluation

The amount of data in a study is a critical parameter for the reliability of the results. Standard measures in statistics like i.e. the mean or confidence intervals of a result assume a sufficient high number of replicates in order to be valid estimates. An objective estimate of the number of participants for a seizure detector study