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Automatic detection of seizure termination during electroconvulsive therapy using sample entropy of the electroencephalogram

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ABSTRACT

Determining the exact duration of seizure activity is an important factor for predicting the efficacy of electroconvulsive therapy (ECT). In most cases, seizure duration is estimated manually by observing the electroencephalogram (EEG) waveform. In this article, we propose a method based on sample entropy (SampEn) that automatically detects the termination time of an ECT-induced seizure. SampEn decreases during seizure activity and has its smallest value at the boundary of seizure termination. SampEn reflects not only different states of regularity and complexity in the EEG but also changes in EEG amplitude before and after seizure activity. Using SampEn, we can more precisely determine seizure termination time and total seizure duration.

1. Introduction

Electroconvulsive therapy (ECT) is a well-established treatment for patients with various psychiatric disorders and conditions, such as major depressive disorder, bipolar disorder, schizophrenia, catatonia and neuroleptic malignant syndrome (Fink, 2001; Shimizu et al., 2007; Chiu, 2009). Generation of a seizure by ECT is essential for its therapeutic effects, and electroencephalogram (EEG) monitoring is recommended to confirm proper seizure duration (Kramer et al., 1989; Lambert, 1992). Reliable monitoring of seizures has become a routine part of the clinical practice of ECT. Practice guidelines suggest that adequate seizure duration should be at least 25–30 s (Ottosson, 1960; Beyer et al., 1998; Swartz, 2001). Although seizure duration itself might not predict the efficacy of ECT alone, it is practically the most important and objective indicator of stimulus dosing, especially in the empirical titration method (Sackeim et al., 1987). To develop a more reliable method of determining EEG seizure duration, computer-automated methods with good correlation with visual determinations were proposed (Swartz et al., 1994; Krystal and Weiner, 1995; Rosenquist et al., 1998). However, the number of studies supporting the validity of the computerised method is too small (Scott, 2007), and the reliability was influenced by the presence of artefact, poor postictal suppression or gradual seizure termination (Krystal and Weiner, 1995). One study reported that the computerised method could not determine seizure end point in 28% of sessions (Rosenquist et al., 1998).

To estimate the duration of seizure, a proper quantifying measure is necessary to discriminate seizure activity from preictal or postictal EEG activity. Some attempts have been made by calculating the correlation or fractal dimension (Gangadhar et al., 1995) and the largest Lyapunov exponent (Chaovalitwongse et al., 2005) of the EEG signal, but the algorithms used to estimate these measures are susceptible to error because of the finite sample size and high sensitivity to noise. These nonlinear techniques usually require stationarity in the time series, as is the case with many linear measures. Moreover, they also require large amounts of data for meaningful results that are typically beyond experimental possibilities for generation of physiological data. However, measures such as approximate entropy (ApEn) or sample entropy (SampEn) do not show these problems, even for relatively small data sets (Radhakrishnan and Gangadhar, 1998).

ApEn is proposed to quantify the regularity and the complexity of physiological signals using the logarithmic likelihood (conditional probability) of pattern reproducibility in the time series (Pincus et al., 1991). A low value of ApEn indicates predictability and regularity in a time series, whereas a high value indicates unpredictable and random variation. ApEn can be used to characterise a wide variety of systems,

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including deterministic, stochastic and composite systems, while also being applicable to noisy, medium-sized time series (Pincus, 1995).

The ApEn algorithm does not exclude self-matches when calculating pairs of similar epochs, introducing bias that reduces the performance of this statistical measure. This limitation of the ApEn method has been noted by many researchers, including Pincus himself (Pincus, 1995). In 2000, Richman and Moorman first introduced sample entropy (SampEn) (Richman and Moorman, 2000) as a novel statistic that measures the irregularity of clinical and experimental time series. SampEn improves upon the performance of ApEn in two respects (Richman and Moorman, 2000): (1) it performs better than ApEn for random data with a known probabilistic character over a wide range of operating conditions and (2) it maintains relative consistency for signals of relatively short length, whereas ApEn does not. Besides these statistical improvements, the SampEn algorithm greatly reduces the computation time of time-series entropy. All of these advantages make SampEn a more promising and practical method than ApEn (Richman and Moorman, 2000; Lake et al., 2002). SampEn has been used for the analysis of EEG data (Ramanand et al., 2004; Abasolo et al., 2006; Chouvarda et al., 2007) and other physiological time series (Lake et al., 2002; Chang et al., 2009). However, this measure of complexity has not been used to evaluate changes in seizure duration during ECT. The present study investigated changes in SampEn of EEG during three stages of ECT-induced seizure (i.e., before, during and after seizure) and attempted to associate these changes with EEG complexity.

Conflicting results have been reported when either ApEn or SampEn is used to quantify the complexity and regularity of seizures, particularly with respect to whether these measures increase or decrease during seizure. Some studies have reported increases in ApEn during epileptic seizures at focal electrodes, possibly due to new oscillations generated by abnormal neuronal synchronisation (Abasolo et al., 2007). Conversely, others have claimed that ApEn is significantly lower during epileptic seizures than during seizure-free periods in absence epilepsy (Burioka et al., 2005). Furthermore, Diambra et al. have shown that the value of ApEn drops abruptly due to the synchronous discharge of large groups of neurons during epileptic activity (Diambra et al., 1999). It has also been reported that the complexity of EEG recordings from an epileptic region is lower than that from normal regions (Liu et al., 2008). A study of EEG activity during ECT-induced seizures found that ApEn had high values at the beginning and the end of the seizure and lower values mid-seizure (Radhakrishnan and Gangadhar, 1998). This sudden drop in ApEn has been used for the automated detection of epilepsy (Srinivasan et al., 2007). ApEn was first used as the input feature in a neural-network-based automated epileptic EEG detection system.

In the present study, we sought to address the conflicting data regarding the variation of ApEn in the presence of seizure. To do this, we calculated SampEn of the EEG, an improved measure of complexity, during the ECT-induced seizure. We found that SampEn decreased during seizure activity and dropped abruptly at the boundary of seizure termination. We propose a new method for computer-automated detection of seizure termination using SampEn.

2. Materials and Methods

2.1. ECT data

We conducted our analysis using data from 24 sessions of electroconvulsive therapy (ECT) under general anaesthesia with seven patients, three male and four female. In total, 87 ECT sessions were administered to the patients and of these, we chose to focus on 24 sessions, which had a consensus to determine the termination point of EEG seizure by three raters. Six patients were diagnosed with schizophrenia and the other patient with schizoaffective disorder. All the patients were administered bilateral ECT using an MECTA Spectrum 5000Q device (MECTA Corp, Tualatin, OR, USA). ECT was done on a three-times-per-week schedule. Bifrontotemporal electrodes were used to deliver the electrical stimulus, and the EEG was recorded through frontal and mastoid electrodes. ECG signals were recorded using three electrodes placed on the anterior chest wall. Lidocaine, propofol, succinylcholine and glycopyrrolate were used as anaesthetic medications, with doses determined by practice guidelines (Beyer et al., 1998; Abrams, 2002). In one patient, whose seizure duration was shorter than 25 s at the maximum stimulus level, etomidate and remifentanil were used instead of propofol.

The electrical stimulus dose was determined using an empirical titration procedure (Sackeim et al., 1987). The usual initial stimulus dose was 48.0 mC, delivered at 20 Hz for 1.5 s with a pulse width of 1.0 ms. If the resulting seizure duration was <25 s, the stimulus was delivered again using an increased dose. Subsequent stimulus doses were 96.0, 192.0, 384.0, 768.0 and 1152.0 mC, according to the titration table offered by the manufacturer (MECTA-Corporation, 1997).

Three psychiatrists independently determined end points manually scoring the EEG records, and then consensus was built by simultaneous agreement among them. The consensus drawn by three raters served as our gold-standard criterion against which we hoped to establish the computational validity of SampEn. Seizure end point was defined as the point when the evidence of EEG seizure disappears (Tiller and Lyndon, 2003).

The study protocol was reviewed and approved by the local ethics committee of Seoul National University Hospital, and written informed consent was obtained from each participant before enrolment. Patients and their legal guardians were assured that there would be no impact on treatment decisions or plans, regardless of whether they agreed to participate in the study. All procedures used in the study were based on the Good Clinical Practices guidelines and were in accordance with the tenets of the Helsinki Declaration.

2.2. SampEn

To assess the complexity of a system, two related measures that can be used effectively for short-duration and noisy time series, ApEn (Pincus and Goldberger, 1994) and SampEn (Richman and Moorman, 2000), have been introduced. These measures estimate the irregularity and complexity of an attractor reconstructed from a time series using an embedding process. SampEn eliminates self-matches and has the advantage of being less dependent on time-series length and more consistent than ApEn when comparisons are made over a broad range of conditions (Richman and Moorman, 2000). Thus, we used SampEn to assess EEG complexity. Appendix A is a brief description of the procedure for the evaluation of SampEn.

2.3. Estimating SampEn of a finite block in EEG

According to Pincus and Goldberger, the selection of parameters m, r and N has a significant effect on outcome reliability (Pincus and Goldberger, 1994). The parameter value for N should be at least 10^m to gain valid estimates. For a general stochastic process, a choice of $m=2$ is better than $m=1$. Values $m>2$ require a large N and, thus, long time series, which cause problems of stationarity. The filtering fraction r should be larger than the noise level in a signal, but too large a value for r leads to loss of detailed system information. Here, r is set to be 0.15 times the standard deviation of the original data.

In this article, these parameters were treated as fixed across the population. SampEn was calculated using the finite data points within each block of data. Although SampEn is in essence a regularity statistic unrelated to signal magnitude, amplitude variations might affect the outcome through r. The recorded EEG signals were low amplitude before seizure, showed an amplitude increase during the seizure and became low amplitude again after the seizure, as illustrated in Fig. 1.

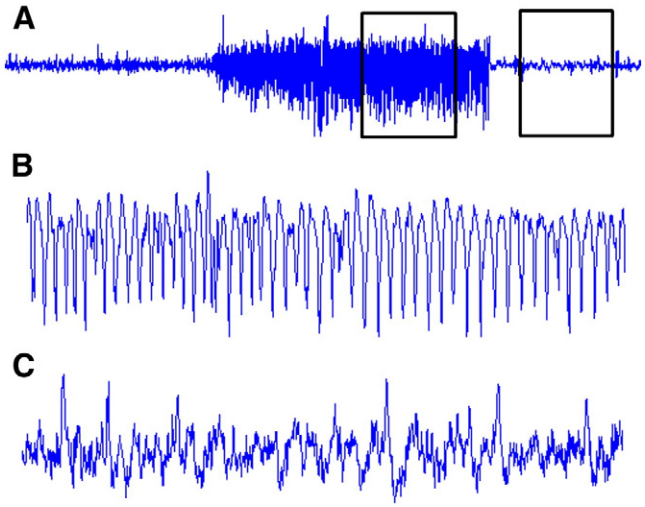

Fig. 1. (A) Original EEG recordings during a seizure. (B) Greater magnification of the EEG trace enclosed by the left box in A. (C) Greater magnification of the EEG trace enclosed by the right box in A.