Psychiatry Research 195 (2012) 76–82

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

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

Cheol Seung Yoo [a], Dong Chung Jung [b], Yong Min Ahn [b,c], Yong Sik Kim [a,b,c], Su-Gyeong Kim [c], Hyeri Yoon [b], Young Jin Lim [d], Sang Hoon Yi [e,*]

[a] Institute of Human Behavioral medicine, Seoul National University College of Medicine, 28 Yongon-Dong, Chongno-Gu, Seoul 110–744, Republic of Korea
[b] Department of Neuropsychiatry, Seoul National University Hospital, 28 Yongon-Dong, Chongno-Gu, Seoul 110–744, Republic of Korea
[c] Department of Psychiatry and Behavioral Science, Seoul National University College of Medicine, 28 Yongon-Dong, Chongno-Gu, Seoul 110–744, Republic of Korea
[d] Department of Anesthesiology and Pain Medicine, Seoul National University Hospital, 28 Yongon-Dong, Chongno-Gu, Seoul 110–744, Republic of Korea
[e] Department of Computer Aided Science, Institute of Basic Science, Inje University, 607 Eobang-Dong, Gimhae-Si, Gyeongnam 621–749, Republic of Korea

ARTICLE INFO

Article history:
Received 14 October 2010
Received in revised form 27 May 2011
Accepted 24 June 2011

Keywords:
electroconvulsive therapy
seizure duration
sample entropy
complexity

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,

* Corresponding author at: Department of Computer Aided Science, Inje University, 607 Gimhae-Si, Gyeongnam 621–749, Republic of Korea. Tel.: +82 55 320 3210; fax: +82 55 334 1577.
E-mail address: yish@inje.ac.kr (S.H. Yi).

0165-1781/$ – see front matter © 2011 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.psychres.2011.06.020

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.

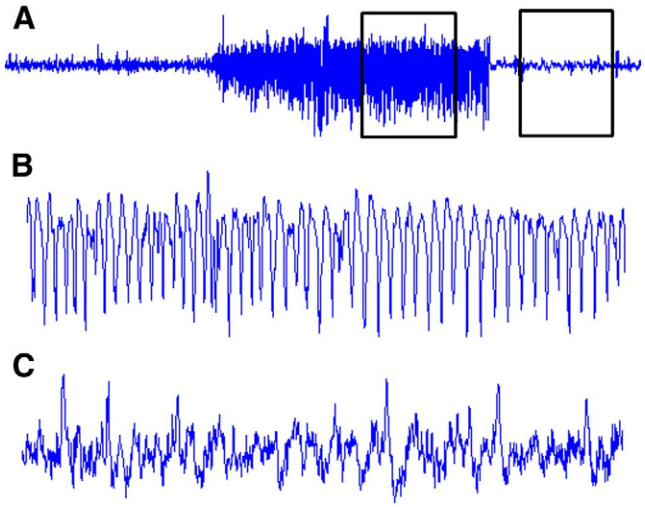

Fig. 1. (A) Original EEG recordings during a seizure. (B) Greater magnification of the EEG trace enclosed by the left box in A. (C) Greater magnification of the EEG trace enclosed by the right box in A.

Understanding the dependency of SampEn on signal amplitude is essential to the interpretation of changing SampEn over the entire EEG recording. According to Koskinen et al., SampEn is mostly unaffected by underlying amplitude changes but is usually influenced by changes in dynamics (Koskinen et al., 2006). To study the applicability of SampEn to the non-stationary signal obtained in this experiment, different EEG recording block sizes were tested with a fixed r value and by varying the length of the different blocks, using 1, 2, 5 and 10 s of data (Fig. 2).

SampEn calculation over various block sizes showed that (1) the values of SampEn are higher during the postictal EEG state compared with the seizure state; (2) SampEn begins to gradually decrease after seizure onset, which may indicate that the dynamical complexity of neural network activity changes from a complex to a simple synchronised state during ECT-induced seizure; (3) SampEn can successfully track dynamical changes across states, from seizure to the post-seizure state; (4) at the boundary of seizure termination, SampEn shows a sharp drop that reflects the characteristics of an attractor made of traces changing from large amplitude to small amplitude; (5) after seizure termination, SampEn recovers to the level observed pre-seizure; and (6) SampEn shows a similar trend in variation with respect to the change of block size from the second panel to the fifth panel in Fig. 2.

2.4. Detection of seizure termination

Using the changes in SampEn calculated for various EEG block sizes in Fig. 2, we developed an algorithm to automatically determine seizure termination and total seizure duration. Precise determination of seizure termination requires choosing the smallest sized EEG block that guarantees a reliable and precise estimation of SampEn. The accuracy of assessment of termination time depends on the time resolution of the EEG recordings. To determine seizure termination time with a precision of ~1 s, the block size should be at least 1 s. Because the EEG sampling frequency is 100 Hz, the minimum number of data points for calculating SampEn with $m=2$ is 100.

The procedure for estimating the duration of seizure is illustrated in Fig. 3. The first step is to divide the 3-min EEG recordings during seizure into 180 1-s blocks (see the second panel of Fig. 2) and calculate the SampEn of each block with the specified parameters (i.e., $m=2$, $r=0.15$). The next step is to choose the four blocks with the smallest SampEn values from all 180 blocks by sorting blocks in ascending order of SampEn values. In the third step, we take advantage of the property that EEG amplitude during seizure is always larger than that in non-seizure states, as depicted in Fig. 1(A). To confirm whether blocks with the smallest SampEn were recorded during the seizure, we compared the mean absolute amplitudes of a 10-s EEG recording preceding each selected (1-s) block. If the mean amplitude of the 10-s block was <120% of the mean amplitude of entire 3-min EEG recording, that block was excluded as a candidate seizure-termination block. Of the remaining blocks, we identified the block occurring at the latest time. The time of seizure termination is then defined as the time when this last block starts.

An important aspect of the present technique is that we were able to successfully use 1-s blocks of standard EEG recordings to characterise the loss of complexity associated with ECT-induced seizures. Using blocks of short duration is essential, as EEG signals are usually non-stationary, and hence it is difficult to obtain a stationary, long-duration block of EEG signal to reliably estimate SampEn. Thus, by using this method we can avoid the problems associated with non-stationary EEG signals and accurately determine seizure-termination time within 1 s (Diambra et al., 1999). Noise and motion artefacts, such as electrooculography (EOG), electromyography (EMG) and eye blinks, inevitably contaminate scalp EEG signals during ECT. To characterise and quantify EEG signals surrounding seizure, it is necessary to exclude noise and artefacts using *ad hoc* preprocessing procedures (Diambra et al., 1999). However, some preprocessing methods, if not carefully adjusted, corrupt the EEG waveform, often leading to biased SampEn values. Our algorithm does not incorporate any preprocessing when calculating SampEn of EEG. As is well known, the conventional power spectral methods based on fast Fourier transformation (FFT) assumes stationarity of EEG and that the time series has underlying harmonics arising from linear dynamics. Both assumptions may be invalid with the seizure EEG, which has non-stationary spikes and artefacts. Therefore, FFT might not work in the presence of noise or non-stationary artefacts in EEG. Our method estimating the SampEn of a finite block in EEG does not require such assumptions and may be more suitable to quantify the EEG during seizures (Gangadhar et al., 1995).

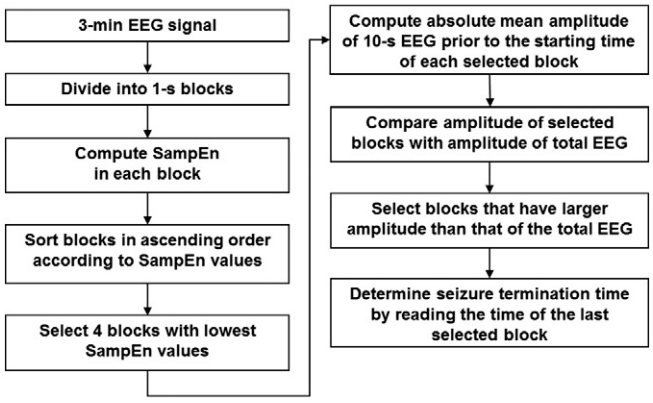

Fig. 3. Schematic diagram of the algorithm for estimating seizure termination.

2.5. Statistical analyses

All statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) software (SPSS, Inc., Chicago, IL, USA). Comparisons of the duration of

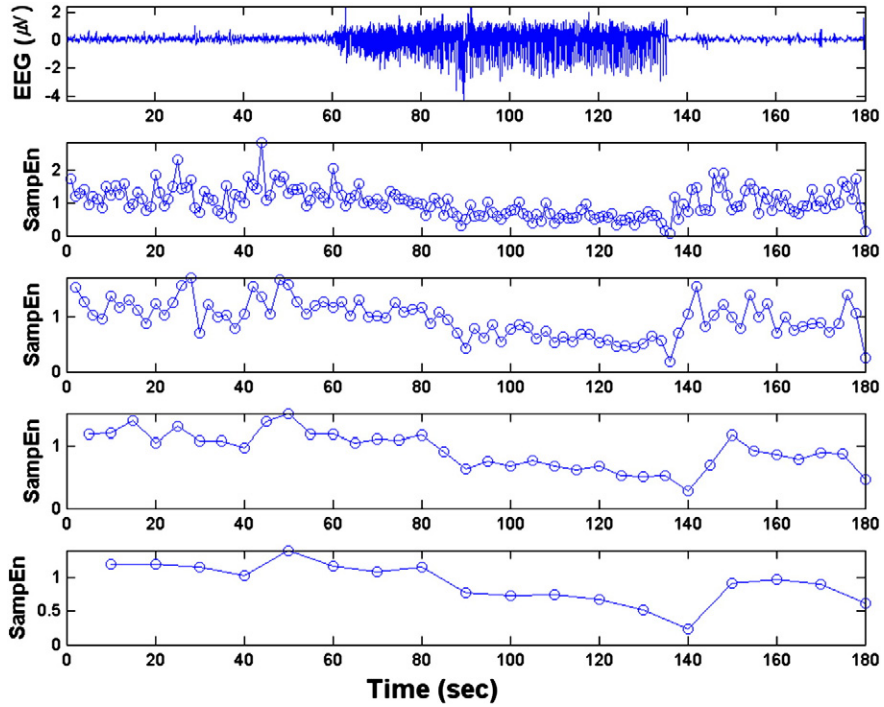

Fig. 2. Top panel: EEG time series with ECT-induced seizure from 60 s to 135 s. Panels 2–5: SampEn over time before, during, and after seizure. SampEn is calculated using blocks of 1-s, 2-s, 5-s, and 10-s duration in panels 2–5, respectively. The seizure begins at 60 s.

ECT-induced seizure between the clinician consensus on EEG recording (EEG consensus) and automatic calculation from EEG recording (EEG auto) were made using independent *t*-tests. Because of the small sample size, assumptions of normality could not be properly imposed. The seizure duration by the automatic detection algorithm was assessed for agreement by the intraclass correlation coefficient (ICC), with a 95% confidence interval. The Pearson correlation coefficient was used to estimate the correlations between EEG consensus and the automatic detection algorithm. A value of $p<0.05$ was deemed to indicate statistical significance.

3. Results

We found our algorithm was able to accurately determine seizure duration even in the presence of motion artefacts and eye blinks (Fig. 4). Although SampEn drops to a smaller value during movement artefacts, our algorithm checks whether these SampEn reductions occur during seizure, and it is therefore able to avoid incorrect identification of seizure termination time. To demonstrate why SampEn shows a sudden decrease at the seizure boundary, we used simulated Gaussian noise of small and large amplitude. A time series as long as 180 s in duration was constructed from small- and large-amplitude Gaussian noise, illustrated in the top panel of Fig. 5. The amplitude in the first 60 s of the time series is small, whereas the amplitude in the middle portion is five times as large, followed by the final section with amplitude similar to the first segment. We calculated SampEn in 10-s blocks of the simulated Gaussian noise based on return maps (Jordan et al., 1960) with small amplitude (left), large amplitude (centre) and varying amplitude (right), as depicted in the middle panel of Fig. 5. Note that the SampEn of a small-amplitude block is not significantly different from that of a large-amplitude block, as signals are normalised to their standard deviation before calculating SampEn (Costa et al., 2002). The return maps in the left and centre of the middle panel of Fig. 5 illustrate that points matching the reference point within a similarity tolerance *r* have nearly the same normalised distribution for both small and large amplitudes. However, SampEn shows a sudden drop at the boundary where the amplitude is greatly reduced. The return map at the right in the middle panel of Fig. 5 shows that points matching the reference point tend to remain clustered in the dense central region more than around the sparse regions. This difference in density distribution is maintained with normalisation and causes the sharp decrease in SampEn. This drop of SampEn at the boundary of amplitude change is central to the algorithmic calculation of seizure duration.

We applied our algorithm for automatic calculation of seizure duration to each ECT session. The results of 24 ECT sessions are shown in Table 1. The table compares the automatically estimated seizure duration with those determined by consensus of three psychiatrists manually scoring the EEG records. In 18 of 24 cases, we obtained values of seizure duration that differed by more than 4% or 2 s between the two forms of estimation (automatic vs. manually scored). The mean durations of ECT-induced seizure as determined by EEG consensus and EEG auto in all sessions are shown in Table 1. The comparison revealed no statistically significant differences.

Intraclass correlation (ICC) was calculated to test the consistency of seizure termination time obtained by clinician rating and the SampEn method. A high level of consistency between the two methods was observed in this sample data set ($r=0.99$, 95% confidence interval = 0.98–0.99).

The correlation between durations determined by EEG consensus and by EEG auto was also estimated to check the consistency of the SampEn method. Seizure durations using the automatic algorithm correlated statistically significantly with EEG consensus in all sessions (Pearson's correlation coefficient $r=0.99$, $p<0.01$).

4. Discussion

We found a strong statistical agreement between seizure durations calculated manually by psychiatrists and automatically using SampEn, as reflected by the ICC of $r=0.99$ ((0.98–0.99), 95% confidence interval). ICCs between 0.60 and 0.80 are taken to represent substantial agreement (Pinna et al., 2007). In this study, ICC was 0.99, as previously mentioned, showing substantial agreement (Pinna et al., 2007). Thus, the method described here supports the reliability of automatic detection of seizure termination using the SampEn of EEG data. The mean seizure durations calculated by the two methods did not differ statistically across whole sessions. The correlation ($r=0.99$) between seizure durations from EEG consensus and EEG auto using SampEn in this study was also consistent with the previous result.

We should note that if an electrical stimulation artefact due to ECT resulted in EEG amplitude similar to that during a seizure, the EEG SampEn decreased correspondingly. As such, abnormally large-amplitude EEG signals should be excluded to prevent misidentification as a seizure. In this study, seizure duration was determined with a precision of about 1 s, as the calculation of SampEn with $m=2$ requires a minimal block length of 100 data points. As this in turn relies on the EEG sampling frequency, if time resolution higher than 1 s is desired, it is necessary to sample the EEG at >100 Hz.

The revised edition of the ECT Handbook of the Royal College no longer mentions 15–25-s duration as criteria for motor and EEG seizures (Scott, 2005). Rattehalli et al. claimed that a generalised

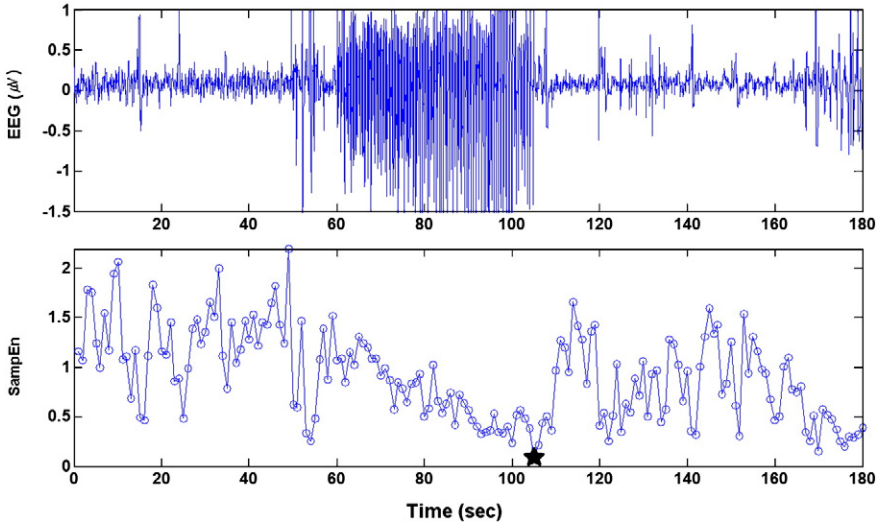

Fig. 4. Example of movement artifacts in the EEG signal after seizure. Top panel: EEG time series before, during, and after ECT. Bottom panel: SampEn over 1-s blocks before, during, and after seizure. The seizure begins at 60 s, and its termination time is determined by the minimum calculated value of SampEn during the seizure (indicated by the star).

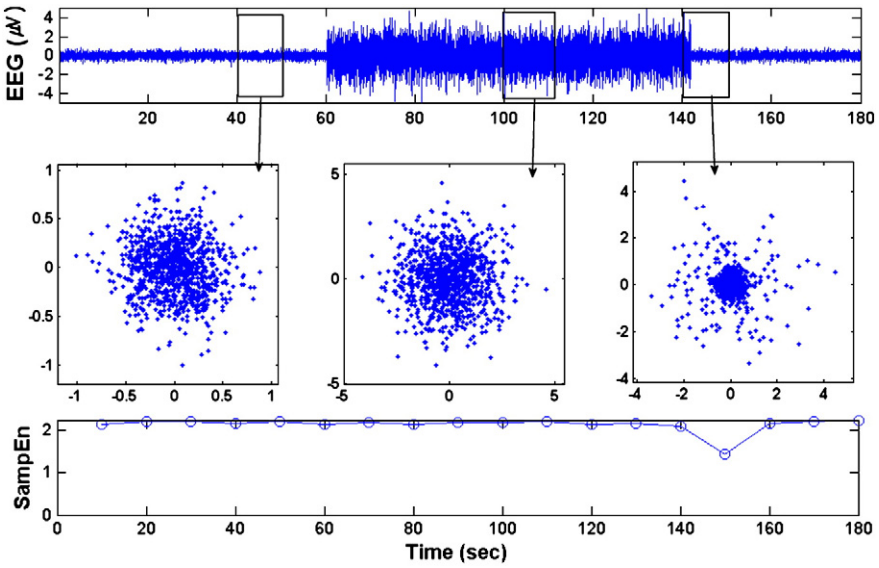

Fig. 5. Calculation of SampEn over blocks of a simulated time series with varying amplitude. Top panel: Simulated Gaussian noise with varying amplitudes. Center panel: Time series return maps of with small (left), large (center), and variable (right) amplitudes. SampEn is calculated from the return map. Bottom panel: SampEn calculated over 10-s blocks shows a sudden drop at the boundary where the amplitude becomes much smaller.

seizure activity with widespread polyspike activity and subsequent slower (3 Hz) spike–wave complexes is now considered more important in assessing EEG-seizure adequacy (Rattehalli et al., 2009). However, determination of the pattern of EEG seizure may not be easy for clinicians, especially for those with less expertise. Thus, reliable automatic measurement of ECT-induced seizure duration can still be helpful in the determination of adequacy of the ECT-induced cerebral seizure (Swartz and Manly, 1999; Ranganath et al., 2003; Scott, 2007; Rattehalli et al., 2009).

Because EEG monitoring is vulnerable to a variety of technical problems, it is recommended that ECT clinics continue to monitor seizure activity and the timing of generalised convulsions (Scott, 2007). Thus, measurement of seizure duration with ECG could compensate for problems caused during recording EEG, such as artefacts or gradual postictal suppression (Swartz and Manly, 1999; Ranganath et al., 2003; Scott, 2007). In this study, we confirmed that the duration of ECT-induced seizure, based on the SampEn algorithm we developed, reliably indicated seizure duration, calculated based on the EEG recording.

In this report, we have estimated the duration of seizure produced through ECT by determining the seizure termination time using the SampEn of the EEG. SampEn decreases during seizure activity and reaches its smallest values at the boundary of seizure termination. After seizure termination, SampEn rapidly reverts to pre-seizure values. Using the dependence of SampEn on the dynamical state and amplitude of the EEG at the boundary of seizure, we have proposed a method to determine the time of seizure termination with a precision of 1 s. Automating the process to determine seizure termination presents many advantages; it can help clinicians with faster decision making on restimulation, especially in case of barely suprathreshold stimulus. Considering that current psychiatry training often lacks sufficient ECT education (Akinsola et al., 2011; Dinwiddie and Spitz, 2010), this will make ECT practice easier for clinicians with less experience. It can also provide an automated alarm about prolonged seizure. Although some ECT devices currently provide quantitative information regarding the EEG changes accompanying seizure, none of these methods has been rigorously validated (Weiner et al., 2001). As the number of patients and ECT sessions are relatively small, further studies will be required to generalise the result of this study. However, our method using SampEn has the potential to be developed into a widely used, reliable and real-time method to automatically estimate seizure duration and quantify other seizure properties, such as regularity and postictal suppression, which could be used in clinical application.

Table 1
Comparison of seizure duration calculated by clinicians and by the SampEn algorithm using data from seven patients over 24 ECT sessions.

Patient no.-ECT no.	Seizure duration by SampEn (s)	Seizure duration by consensus (s)
1-1	66*	63
1-2	76	77
1-3	55	56
1-4	66	66
2-1	74	73
3-1	54	54
3-2	83	83
3-3	73*	77
3-4	61	61
4-1	61	60
4-2	76	77
4-3	77	78
5-1	74*	77
5-2	46*	48
5-3	47	47
6-1	75	75
6-2	56	56
6-3	87	87
6-4	80*	84
6-5	55	55
6-6	38	38
6-7	38	38
6-8	31*	37
7-1	59	59
Mean ± SD	63.58 ± 15.25	62.96 ± 15.43

*: cases in which automatic detections differed by more than 4% or 2 sec from the consensus of manual detections.

Acknowledgements

This work was supported by the Inje Research and Scholarship Foundation in 2007. For Yong Min Ahn, this study was supported by Grant No. A090828 from the Research and Development Projects in Health and Medical Technology funded by the Korea Health Industry Development Institute. For Yong Sik Kim, this study was supported by an unrestricted research grant (No. 06-2006-0210) from Norvatis Korea. All the authors

declare that they have no commercial associations that might pose a conflict of interest with respect to this article.

Appendix A. Sample entropy algorithm

Consider the time series $x(i)$, $i = 1, 2, 3,\ldots, N$. Let us choose the two input parameters m and r, where m is the dimension of the reconstructed vector in phase space, and r specifies the filtering level. Let the m samples beginning at sample $x(i)$ be denoted by the vector $v_m(i) = [x(i), x(i+1),\ldots, x(i+m-1)]$ and consider the set of all vectors of length m within $x(n)$, such that $[v_m(1), v_m(2),\ldots, v_m(N-m)]$. Let us define a correlation density function $C_{i,m}(r)$ (Pincus and Goldberger, 1994)

$$C_{i,m}(r) = \frac{n_{i,m}(r)}{N-m+1},$$

where $n_m(r)$ is the number of vectors that are similar to $v_m(i)$, given the similarity criterion r, excluding self-matching. Similar calculations are carried out for each i, with $i = 1, 2,\ldots N-m$. The function $C_m(r)$ is then defined as the average of the function $C_{i,m}(r)$,

$$C_m(r) = \frac{\sum_{i=1}^{N-m} C_{i,m}(r)}{N-m}.$$

Similarly, let $C_{i,(m+1)}(r)$ be defined as

$$C_{i,(m+1)}(r) = \frac{n_{i,(m+1)}(r)}{N-m-1},$$

where $n_{i,(m+1)}(r)$ is the number of vectors in the sequence $[v_{m+1}(1), v_{m+1}(2),\ldots, v_{m+1}(N-m)]$ that is similar to $v_{m+1}(i)$, given the similarity criterion r, excluding self-matching. Similar calculations are carried out for each i, with $i = 1, 2,\ldots, N-m$. The function $C_{m+1}(r)$ is then defined as the average of the function $C_{i,(m+1)}(r)$. The statistic $SampEn(m, r, N)$ is then defined by,

$$SampEn(m, r, N) = -\ln\left(C_{m+1}(r) / C_m(r)\right).$$

This represents the negative natural logarithm of the conditional probability that two sequences similar for m points remain similar at the next point when self-matches are not included. A lower value of SampEn indicates more self-similarity and regularity in the time series. This study used open source software from PhysioNet developed for SampEn analysis (Goldberger et al., 2000).

References

Abasolo, D., Hornero, R., Espino, P., Alvarez, D., Poza, J., 2006. Entropy analysis of the EEG background activity in Alzheimer's disease patients. Physiological Measurement 27, 241–253.

Abasolo, D., James, C.J., Hornero, R., 2007. Non-linear analysis of intracranial electroencephalogram recordings with approximate entropy and Lempel-Ziv complexity for epileptic seizure detection. Conference Proceedings - IEEE Engineering in Medicine and Biology Society 2007, 1953–1956.

Abrams, R., 2002. Electroconvulsive Therapy, 4th. Oxford University Press, New York.

Akinsola, O., Sundram, F., Bangaru, R., 2011. Electroconvulsive Therapy Training and Confidence in Administration: A National Survey of Psychiatric Trainees in Ireland. The Journal of ECT 27, 127–130.

Beyer, J., Weiner, R., Glenn, M.D., 1998. Electroconvulsive Therapy: A Programmed Text, 2nd. American Psychiatric Press, Inc, Washington, DC.

Burioka, N., Cornelissen, G., Maegaki, Y., Halberg, F., Kaplan, D.T., Miyata, M., Fukuoka, Y., Endo, M., Suyama, H., Tomita, Y., Shimizu, E., 2005. Approximate entropy of the electroencephalogram in healthy awake subjects and absence epilepsy patients. Clinical EEG and Neuroscience 36, 188–193.

Chang, J.S., Yoo, C.S., Yi, S.H., Hong, K.H., Oh, H.S., Hwang, J.Y., Kim, S.G., Ahn, Y.M., Kim, Y.S., 2009. Differential pattern of heart rate variability in patients with schizophrenia. Progress in Neuro-Psychopharmacology & Biological Psychiatry 33, 991–995.

Chaovalitwongse, W., Iasemidis, L.D., Pardalos, P.M., Carney, P.R., Shiau, D.S., Sackellares, J.C., 2005. Performance of a seizure warning algorithm based on the dynamics of intracranial EEG. Epilepsy Research 64, 93–113.

Chiu, N.M., 2009. Repeated electroconvulsive therapy for a patient with Capgras syndrome and Parkinsonism. Progress in Neuro-Psychopharmacology & Biological Psychiatry 33, 1084–1085.

Chouvarda, I., Papadelis, C., Kourtidou-Papadeli, C., Bamidis, P.D., Koufogiannis, D., Bekiaris, E., Maglaveras, N., 2007. Non-linear analysis for the sleepy drivers problem. Studies in Health Technology and Informatics 129, 1294–1298.

Costa, M., Goldberger, A.L., Peng, C.K., 2002. Multiscale entropy analysis of complex physiologic time series. Physical Review Letters 89, 068102.

Diambra, L., de Figueiredo, J.C.B., Malta, C.P., 1999. Epileptic activity recognition in EEG recording. Physica A: Statistical Mechanics and its Applications 273, 495–505.

Dinwiddie, S.H., Spitz, D., 2010. Resident education in electroconvulsive therapy. The Journal of ECT 26, 310–316.

Fink, M., 2001. Convulsive therapy: a review of the first 55 years. Journal of Affective Disorders 63, 1–15.

Gangadhar, B.N., Dutt, D.N., Janakiramaiah, N., Sadasivan, P.K., 1995. Automation of seizure duration estimation during ECT; use of fractal dimension. Engineering in Medicine and Biology Society, 1995 and 14th Conference of the Biomedical Engineering Society of India. An International Meeting, Proceedings of the First Regional Conference., IEEE. 3/37-33/38.

Goldberger, A.L., Amaral, L.A., Glass, L., Hausdorff, J.M., Ivanov, P.C., Mark, R.G., Mietus, J.E., Moody, G.B., Peng, C.K., Stanley, H.E., 2000. PhysioBank, PhysioToolkit, and PhysioNet: components of a new research resource for complex physiologic signals. Circulation 101, E215–E220.

Jordan, F.T., Sanford, J., Wright, A., 1960. Anaesthesia in the fowl. Journal of Comparative Pathology 70, 437–449.

Koskinen, M., Seppanen, T., Shanbao, T., Mustola, S., Thakor, N.V., 2006. Monotonicity of approximate entropy during transition from awareness to unresponsiveness due to propofol anesthetic induction. Biomedical Engineering, IEEE Transactions on 53, 669–675.

Kramer, B.A., Pollock, V.E., Schneider, L.S., Gray, G.E., 1989. Interrater reliability of MECTA SR-1 seizure duration. Biological Psychiatry 25, 642–644.

Krystal, A.D., Weiner, R.D., 1995. ECT seizure duration: reliability of manual and computer-automated determinations. Convulsive Therapy 11, 158–169.

Lake, D.E., Richman, J.S., Griffin, M.P., Moorman, J.R., 2002. Sample entropy analysis of neonatal heart rate variability. American Journal of Physiology. Regulatory, Integrative and Comparative Physiology 283, R789–R797.

Lambert, M., 1992. Interrater reliability of seizure duration in ECT. Biological Psychiatry 31, 102–103.

Liu, C.C., Pardalos, P.M., Chaovalitwongse, W.A., Shiau, D.S., Ghacibeh, G., Suharitdamrong, W., Sackellares, J.C., 2008. Quantitative complexity analysis in multi-channel intracranial EEG recordings form epilepsy brains. Journal of Combinatorial Optimization 15, 276–286.

MECTA-Corporation, 1997. MECTA Instruction Manual SpECTrum 5000Q® SpECTrum 4000Q® SpECTrum 5000M® SpECTrum 4000M® July 14, 2004. Revision 03 100/200 Joule International. MECTA Corporation, Tualatin, OR.

Ottosson, J.O., 1960. Experimental studies of the mode of action of electroconvulsive therapy: Introduction. Acta Psychiatrica Scandinavica 35, 5–6.

Pincus, S., 1995. Approximate entropy (ApEn) as a complexity measure. Chaos 5, 110–117.

Pincus, S.M., Goldberger, A.L., 1994. Physiological time-series analysis: what does regularity quantify? The American Journal of Physiology 266, H1643–H1656.

Pincus, S.M., Gladstone, I.M., Ehrenkranz, R.A., 1991. A regularity statistic for medical data analysis. Journal of Clinical Monitoring and Computing 7, 335–345.

Pinna, G.D., Maestri, R., Torunski, A., Danilowicz-Szymanowicz, L., Szwoch, M., La Rovere, M.T., Raczak, G., 2007. Heart rate variability measures: a fresh look at reliability. Clinical Science (Lond) 113, 131–140.

Radhakrishnan, N., Gangadhar, B.N., 1998. Estimating regularity in epileptic seizure time-series data. A complexity-measure approach. IEEE Engineering in Medicine and Biology Magazine 17, 89–94.

Ramanand, P., Nampoori, V.P., Sreenivasan, R., 2004. Complexity quantification of dense array EEG using sample entropy analysis. Journal of Integrative Neuroscience 3, 343–358.

Ranganath, R.D., Jagadisha, Gangadhar, B.N., Tomar, M., Candade, V.S., Hemalatha, K.R., 2003. ECT and heart rate changes: An alternative to EEG monitoring for seizure confirmation during modified ECT. German Journal of Psychiatry 6, 60–63.

Rattehalli, R.D., Thirthalli, J., Rawat, V., Gangadhar, B.N., Adams, C.E., 2009. Measuring electroencephalographic seizure adequacy during electroconvulsive therapy: a comparison of 2 definitions. The Journal of ECT 25, 243–245.

Richman, J.S., Moorman, J.R., 2000. Physiological time-series analysis using approximate entropy and sample entropy. American Journal of Physiology. Heart and Circulatory Physiology 278, H2039–H2049.

Rosenquist, P.B., McCall, W.V., Colenda, C.C., Melton, B.A., 1998. A comparison of visual and computer-generated measures of "seizure quality". The Journal of ECT 14, 76–82.

Sackeim, H.A., Decina, P., Kanzler, M., Kerr, B., Malitz, S., 1987. Effects of electrode placement on the efficacy of titrated, low-dose ECT. The American Journal of Psychiatry 144, 1449–1455.

Scott, A.I.F., 2005. The ECT handbook : the third report of the Royal College of Psychiatrists' Special Committee on ECT, 2nd ed. Royal College of Psychiatrists, London.

Scott, A.I.F., 2007. Monitoring electroconvulsive therapy by electroencephalogram: an update for ECT practitioners. Advances in Psychiatric Treatment 13, 298–304.

Shimizu, E., Imai, M., Fujisaki, M., Shinoda, N., Handa, S., Watanabe, H., Nakazato, M., Hashimoto, K., Iyo, M., 2007. Maintenance electroconvulsive therapy (ECT) for treatment-resistant disorganized schizophrenia. Progress in Neuro-Psychopharmacology & Biological Psychiatry 31, 571–573.

Srinivasan, V., Eswaran, C., Sriraam, N., 2007. Approximate entropy-based epileptic EEG detection using artificial neural networks. IEEE Transactions on Information Technology in Biomedicine 11, 288–295.

Swartz, C.M., 2001. Stimulus Dosing in Electroconvulsive Therapy and the Threshold Multiple Method. The Journal of ECT 17, 87–90.
Swartz, C.M., Manly, D.T., 1999. Endpoint of ECT-induced elevation in heart rate. The Journal of ECT 15, 125–128.
Swartz, C.M., Abrams, R., Rasmussen, K., Pavel, J., Zorumski, C.F., Srinivasaraghavan, J., 1994. Computer automated versus visually determined electroencephalographic and electromyographic seizure duration. Convulsive Therapy 10, 165–170.
Tiller, J.W.G., Lyndon, R.W., 2003. Electroconvulsive therapy: An Australasian guide. Australian Postgraduate Medicine, Melbourne.
Weiner, R.D., Coffey, C.E., Fochtmann, L.J., Greenberg, R.M., Isenberg, K.E., Kellner, C.H., Sackeim, H.A., Moench, L., 2001. The Practice of Electroconvulsive Therapy by American Psychiatric Association Committee on Electroconvulsive Therapy: Recommendations for Treatment, Training and Privileging, 2nd ed. A Task Force Report of the American Psychiatric Association, Washington, DC.