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# The Determination of the Duration of Electroconvulsive Therapy-Induced Seizure Using Local Standard Deviation of the Electroencephalogram Signal and the Changes of the RR Interval of Electrocardiogram

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**Objectives** In electroconvulsive therapy (ECT) research and practice, the precise determination of seizure duration is important in the evaluation of clinical relevance of the ECT-induced seizure. In this study, we have developed computerized algorithms to assess the duration of ECT-induced seizure.

**Methods** Subjects included 5 males and 6 females, with the mean age of 33.1 years. Total 55 ECT sessions were included in the analysis. We analyzed the standard deviation of a finite block of electroencephalography (EEG) data and the change in the local slope of RR intervals in electrocardiography (ECG) signals during ECT-induced seizure. And then, we compared the calculated seizure durations from EEG recording (EEG algorithm) and ECG recording (ECG algorithm) with values determined by consensus of clinicians based on the recorded EEG (EEG consensus), as a gold standard criterion, in order to testify the computational validity of our algorithms.

**Results** The mean seizure durations calculated by each method were not significantly different in sessions with abrupt flattened postictal suppression and in sessions with non-abrupt flattened postictal suppression. The intraclass correlation coefficients (95% confidence interval) of the three methods (EEG algorithm, ECG algorithm, EEG consensus) were significant in the total sessions [0.79 (0.70−0.86)], the abrupt flattened postictal suppression sessions [0.84 (0.74−0.91)], and the non-abrupt flattened postictal suppression sessions [0.67 (0.45−0.84)]. Correlations between three methods were also statistically significant, regardless of abruptness of transition.

**Conclusions** Our proposed algorithms could reliably measure the duration of ECT-induced seizure, even in sessions with non-abrupt transitions to flat postictal suppression, in which it is typically difficult to determine the seizure duration.

**Key Words** Electroconvulsive therapy · Electrocardiography · Electroencephalography · Postictal suppression · Seizure duration.

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## Introduction

The elicitation of a generalized seizure and its adequacy is considered to be essential for the therapeutic effects of electroconvulsive therapy (ECT). Recent studies have suggested that a single property of the manifestations of electroencephalography

 

(EEG) elicited by ECT cannot be used as a predictor of response to ECT,[1)2)] but the determination of seizure duration is still a useful part of both clinical practice and research.[1-6)]

EEG recording has been widely used for the determination of ECT-induced seizure duration.[1)6-10)] Computer-automated algorithms are available in most contemporary ECT machines.[11)] In theory, computerized processing of the signals could provide more reliability than manual determination of EEG-based ECT-induced seizure duration.[10)12-15)] Such computer-automated determination is particularly sensitive to artifacts or insufficient postictal suppression, especially when the dose of electrical stimulus is close to the seizure threshold, in which situation it is even more important to be able to assess the adequacy of the ECT session.[1)6)16)] However, according to the literatures including the ECT Handbook of the Royal College,[17)] the predictive accuracy of computer-automated algorithms in ECT machines has not been supported by studies, and was not found to be more reliable than that of experienced ECT practitioners.[2)6)16)18)]

Along with EEG, heart rate changes on electrocardiography (ECG) has been used in seizure detection algorithms especially in epileptic seizures encompassing central autonomic network (CAN) structures.[19)20)] Previous studies suggested that changes in the RR interval, complexity, and variability of ECG appear to be associated with seizures.[21)] Heart rate usually accelerates abruptly with seizure initiation and returns to baseline near the end of ECT-induced seizure, which sometimes makes it easier to determine the termination of seizure than EEG recordings ; the duration of the elevated heart rate has been used for estimating the duration of the cerebral seizure induced by ECT.[22)23)] ECG signal can be a complement or as an alternative to EEG signals due to ECG's lower signal complexity, greater ease and economy of recording and lower processing and computational analysis cost.[24)] Currently, ECG recording has been an essential practice of ECT clinics and is available in most of the contemporary ECT machines.[2)6)8)11)25)] In this context, it is clinically useful approach to develop the ECG signal based computerized algorithm for measuring the end point of ECT-induced seizure, which is potentially applicable in ECT machines.

In this paper, we aimed to develop the algorithms for automatic detection of ECT-induced seizure duration based on EEG signal. We applied the method based on local standard deviation (LSD) of EEG data for the determinations of seizure duration which has advantages, fast in calculation, useful for high sampling datasets, and applicable to seizure termination with gradual decrease of EEG amplitude.[6)] And we also developed the algorithms based on local slope of RR intervals data on ECG as a complement or alternatives of EEG for the determination of ECT-induced seizure duration.[26)] Finally, we compared the calculated EEG and ECG seizure durations with values determined by consensus of clinicians based on the recorded EEG, as a gold standard criterion, in order to testify the computational validity of our algorithms.

## Methods

### Subjects

Eleven patients (5 males, 6 females) who underwent ECT from June 2008 to December 2008 were included. As a gold standard criterion against which we hoped to establish the computational validity of our algorithms, we chose the consensus drawn in the termination point of seizure and the change of postictal suppression by three raters ; three psychiatrists blindly and independently determined the endpoint of seizure and the change of postictal suppression manually scoring the EEG and ECG records, and then consensus was built by simultaneous agreement. Among 163 ECT sessions in total administered to the patients, 55 sessions meet the criteria.

### ECT procedures

The ECT procedures were done as previously reported.[10)] In short, most received ECT three times per week, using a MECTA Spectrum 5000Q device (MECTA Corp, Tualatin, OR, USA). In all patients, electrical stimulus was delivered using bifrontotemporal electrodes. EEG and ECG were recorded using frontal and mastoid electrodes, and anterior chest wall electrodes, respectively. Lidocaine, propofol, succinylcholine, and glycopyrrolate were used in the course of general anesthesia, with doses adjusted according to practice guidelines.[27)28)]

The study protocol was reviewed and approved by the Institutional Review Board of Seoul National University Hospital (0807-035-250). Patients and their legal guardians were given the explanation of the procedures and the possible impact on their treatment by their physicians about clinical benefits and safety with the treatment. Written informed consent was obtained from each participant. All procedures in this study were in accordance with the Good Clinical Practices guidelines and the tenets of the Helsinki Declaration.

### Data acquisition and preprocessing of EEG and ECG during ECT-induced seizure

The EEG data obtained during each ECT session included baseline drift and unnecessary noise, which was filtered between 0.1–40 Hz to remove noise and artifacts from the signal. The baseline value was also removed from each EEG signal. The intervals between successive R waves of the ECG were determined with 1 ms accuracy by subtracting the time of each R wave from the time of the previous R wave.

### Duration of ECT-induced seizure estimated by clinician using EEG recording

To date, the duration of ECT-induced seizure in EEG recordings has been determined by clinicians, by referring to the transition to the flattened postictal suppression at the end of a seizure. Because the postictal suppression of EEG is sometimes obscure,[29)30)] the best estimation was used for determining the duration of ECT-induced seizure. The estimation of EEG seizure duration was done after several preliminary sessions and then three raters had a consensus meeting to determine a definite duration of EEG seizure. Their determination was defined as the gold standard of EEG seizure duration in this study.

### Definition of the mode of postictal suppression

We divided ECT sessions into two groups according to the mode of postictal suppression : sessions with good postictal suppression and an abrupt transition to flat EEG suppression (abrupt flattened postictal suppression) and sessions without either abrupt transition to flat EEG or postictal suppression (non-abrupt flattened postictal suppression). Because insufficient postictal suppression often does not lead to a flat EEG tracing after the seizure, making it difficult to detect the end-point of the seizure,[6)] abruptness of the sessions was determined by consensus of the three raters.

### Automatic detection of ECT-induced seizure duration using the standard deviation of a finite block in EEG

The recorded EEG signals were low amplitude before seizure, showed an amplitude increase during the seizure, and became low amplitude again after the seizure (Fig. 1). To obtain the filtered signal with the dominant frequency during seizure state, the EEG signals were filtered by band-pass filters with 3.5–8 Hz delta wave regions. Fig. 1A shows the raw EEG signal and Fig. 1B shows the result of applying band pass filtering. And then, each EEG signal was divided into 1 sec blocks and standard deviation (SD) of each block was calculated, as shown in Fig. 1C. To determine the end of the seizure in a postictal state, we calculated the LSD of the EEG amplitude using the average among the SD

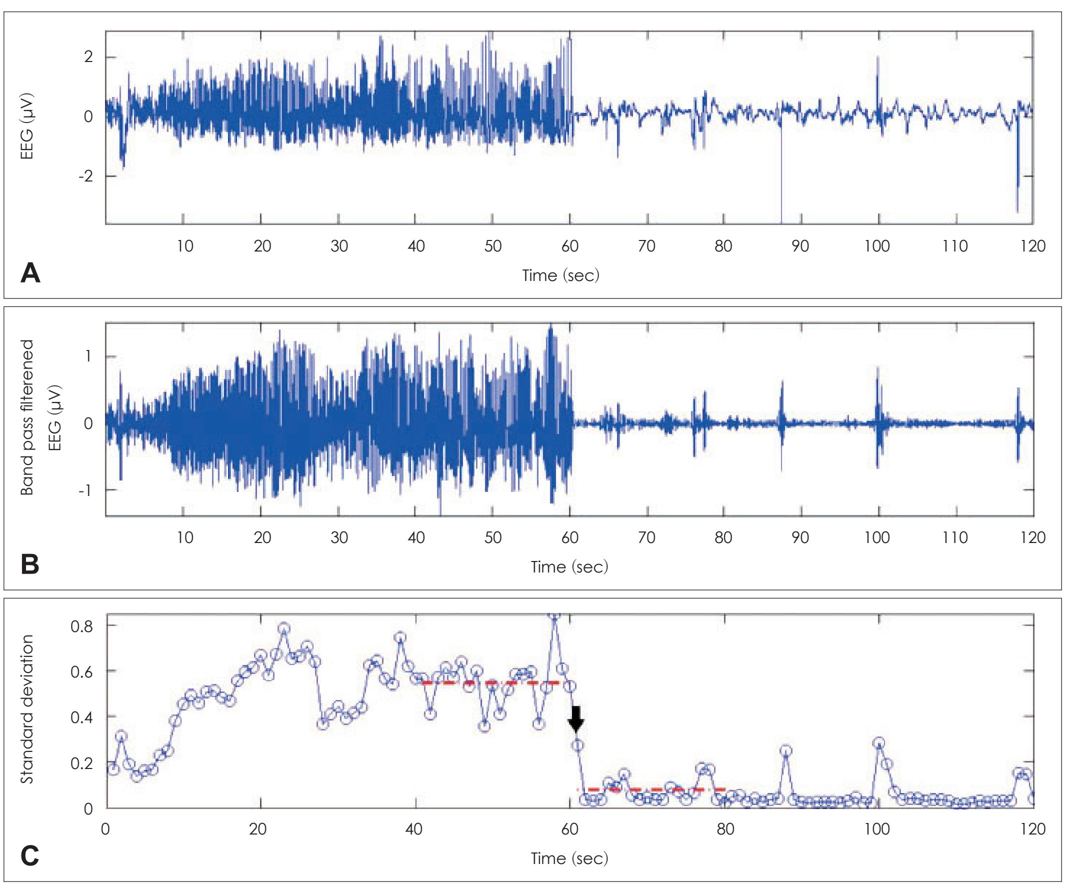


**Fig. 1.** An example of a good detection of the seizure ending point using EEG. (A) Before band pass filtering. (B) After band pass filtering with 3.5–8 Hz. (C) The distribution of LSD of EEG over 1 sec blocks. The dotted lines denote the average of LSD before and after seizure termination. The arrow mark indicates seizure ending point in (C). EEG : Electroencephalography, LSD : Local standard deviation.

of N blocks (n = 20) (Fig. 1C). The LSD of the blocks was calculated by the root-sum-square of the standard deviations of the n successive blocks. The LSD of EEG signals begins to abruptly increase after seizure onset and sharply decreases at the boundary of seizure termination. The difference between the two dotted lines in Fig. 1C shows the difference between the LSD at the boundary of seizure termination.

Using the changes in LSD calculated for the EEG blocks in Fig. 1C, we developed an algorithm to automatically determine seizure termination and total seizure duration. First, two LSDs adjacent to the reference block were calculated. Second, the first process is iterated over all reference blocks and every difference between two LSDs is obtained along all reference blocks. Finally, the time of seizure termination is determined by a reference block that has the largest difference in two adjacent LSDs. Precise determination of seizure termination requires choosing the smallest block size that guarantees a reliable and precise estimation. Accuracy of the assessment of the termination time depends on the time resolution of the EEG recordings. To determine seizure termination time with a precision of about 1 sec, the block size should be at most 1 sec.

### Automatic detection of ECT-induced seizure duration using the local slope of RR intervals

Each data set was divided into segments of 2-min duration. The heart rate usually accelerates abruptly (i.e., decreased RR intervals) with seizure initiation and returns to baseline near seizure end (Fig. 2A). The RR interval data was 5-point moving average filter which removed high frequency noise or artifacts along with out-of-band noise. Fig. 2A shows the raw RR interval data and Fig. 2B shows the result of moving average filtering.

To quantify the changes of the filtered RR interval data in the postictal state, 2 min RR interval data were divided into 5 sec windows. Within each window, the local slope by the 1st difference was calculated by 1 sec overlapping windows. Fig. 2C shows the distribution of the local slope over each 5 sec window during seizure. The local slope in the seizure ending point increased abruptly. Thus, the seizure duration was calculated by determining the point at which the local slope abruptly increased, as depicted in Fig. 2C.

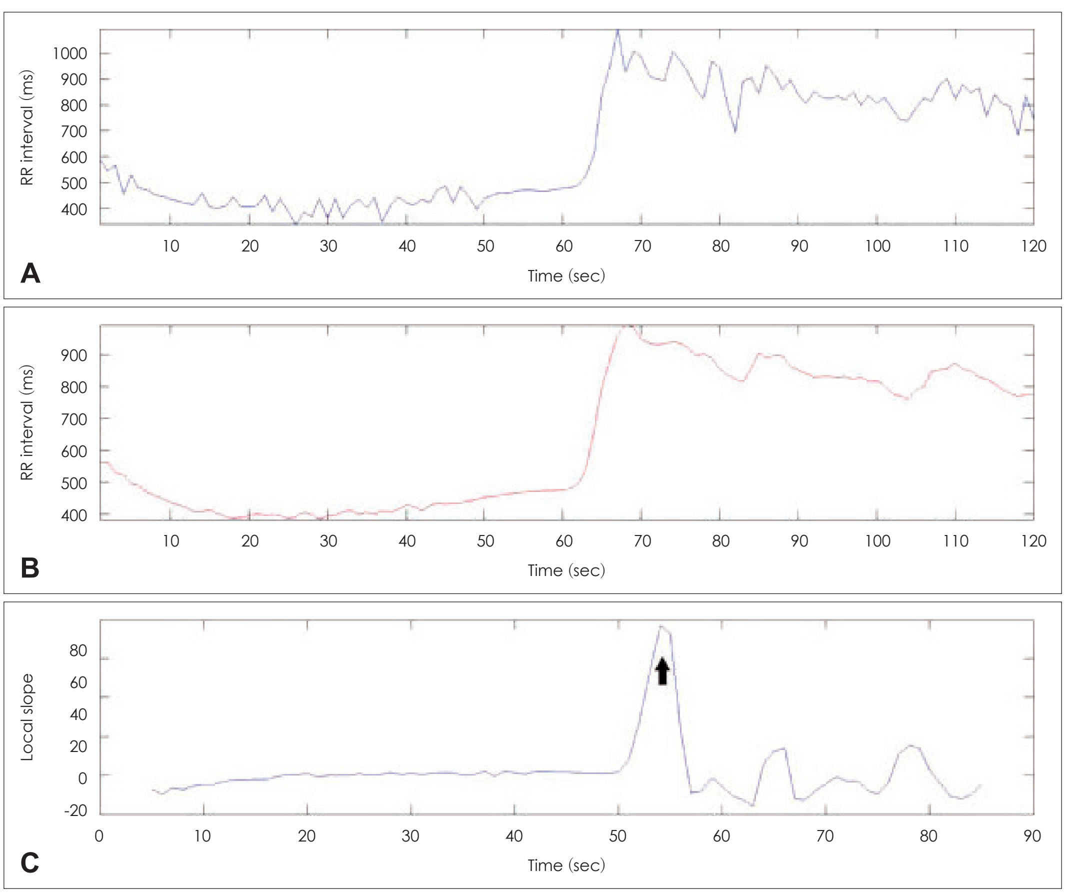


**Fig. 2.** An example of a good detection for the seizure ending point using the first difference of the RR interval. (A) Before moving average filter. (B) After moving average filter. (C) The distribution of the local slope over each 5 sec window during seizure. The arrow mark indicates seizure ending point in (C).

### Statistical analyses

All statistical analysis was conducted using the SPSS software (ver. 19.0 ; IBM Corp., Armonk, NY, USA). Analysis of variance (ANOVA) was conducted on the three measurements for the seizure duration. Where overall differences were significant, comparisons between sessions with abrupt and non-abrupt flattened postictal suppression were made for each method using independent t-tests. Similarly, comparisons of the duration of ECT-induced seizure between the clinician consensus on EEG recording (EEG consensus), automatic calculation from EEG recording (EEG auto), and automatic calculation from ECG recording (heart rate variability auto, HRV auto) were made using ANOVA. Because of the small sample size, assumptions of normality could not be judged. The seizure duration by the two detection algorithms was assessed for agreement by intraclass correlation coefficient (ICC), with a 95% confidence interval. The Pearson correlation coefficient was used to estimate the correlations between EEG consensus and the two detection algorithms. A value of $p < 0.05$ was deemed to indicate statistical significance.

## Results

### Participants characteristics

The mean (SD) age of 11 patients was 33.1 (10.2) years. The patients were diagnosed with schizophrenia (n = 7), schizoaffective disorder (n = 2), bipolar disorder (n = 1), and major depressive disorder (n = 1), respectively. Ten patients were prescribed with antipsychotic agents, 7 of them taking clozapine, and 4 patients were taking antidepressants. The number of patients taking benzodiazepine, propranolol, and trihexyphenidyl was 3, 4, and 4, respectively.

### ICC of seizure duration among the clinician visual rating, the EEG algorithm and ECG algorithm

The mean durations of ECT-induced seizure, which were calculated with the determination of end-point of ECT-induced seizure in three ways of EEG consensus, EEG auto, and HRV auto in total 55 sessions, were 48.20 (19.11), 48.53 (19.64), and 45.71 (19.85), respectively. There were no statistical differences. In the comparison of sessions between abrupt and non-abrupt flattened postictal suppression, the seizure durations of abrupt flattened postictal suppression sessions were longer than those of nonabrupt flattened postictal suppression sessions in EEG consensus and HRV auto, but not in EEG auto (data not shown).

ICC (95% confidence interval) of seizure durations measured by EEG consensus, EEG auto, and HRV auto in all sessions (n = 55) was 0.79 (0.70–0.86), which was statistically significant ($p < 0.001$). ICC of those by EEG consensus, EEG auto, and HRV auto in abrupt flattened postictal suppression sessions (n = 35), was 0.84 (0.74–0.91, $p < 0.001$) and in non-abrupt flattened postictal suppression sessions (n = 20) was 0.67 (0.45–0.84, $p < 0.001$).

**Table 1.** The correlation coefficients between EEG consensus, EEG auto and HRV auto

| | EEG consensus | EEG auto |
|---|---|---|
| Total sessions (n = 55) | | |
| EEG auto | 0.81* | |
| HRV auto | 0.76* | 0.80* |
| Abrupt suppression sessions (n = 35) | | |
| EEG auto | 0.85* | |
| HRV auto | 0.76* | 0.93* |
| Non-abrupt suppression sessions (n = 20) | | |
| EEG auto | 0.80* | |
| HRV auto | 0.69* | 0.59* |

* : $p < 0.01$ significance level. EEG : Electroencephalography, HRV : Heart rate variability

The correlations of seizure durations between EEG consensus and EEG auto, EEG consensus and HRV auto, and EEG auto and HRV auto were statistically significant in all sessions, abrupt flattened postictal suppression sessions, and non-abrupt flattened postictal suppression sessions (Table 1). All of the correlations were large except the correlations of HRV auto with EEG consensus and EEG auto in non-abrupt flattened postictal suppression sessions, which were moderate in degree.

## Discussion

In this study, we developed the algorithm to define the duration of ECT-induced seizure using LSD of the EEG signal and the local slope of the RR interval of ECG. Both computerized algorithms showed statistically significant ICC of EEG consensus duration, EEG auto duration, and ECG auto duration, even in cases with no abrupt transition to flat EEG or poor postictal suppression, in which it is difficult to determine the seizure duration by direct observation. Our proposed method provided a useful framework for enhancing its applicability in ECT practice and research field.

Previously reported durations of ECT-induced tachycardia correlated highly with EEG seizure estimates (r = 0.75).[31] In this study, the correlations between EEG consensus, EEG auto, and ECG auto were also above 0.76, except the correlations between HRV auto and EEG consensus and ECG auto and EEG auto in non-abrupt flattened postictal suppression sessions. Although there is no rule of thumb, correlation coefficients of 0.40–0.69, 0.70–0.89, and 0.90–1.00 are generally considered to be moderate, strong, and very strong, respectively.[32)33)] In non-abrupt suppression sessions, the correlation coefficient between EEG consensus and EEG auto was 0.80, indicating a strong correlation, but that between EEG auto and ECG auto was 0.59 indicating only a moderate correlation. In abrupt flattened postictal suppression sessions, the correlation between EEG consensus and EEG auto was strong (r = 0.85), and correlation between EEG auto and ECG auto was very strong (r = 0.93).[32)33)] This suggests that the relatively poor correlation between EEG auto and ECG auto in non-abrupt flattened postictal suppression sessions are not primarily due to the algorithms used in the study, but is at least partly due to poor postictal suppression or gradual transition to the end of an EEG-induced seizure.

The both EEG and ECG based computerized algorithms we proposed have practical advantages in terms of their low computational cost due to simplicity and their complementarities, facilitating the possibility of clinical and research application. Compared to the previously reported method using the SampEn of the EEG[10)] for estimating the duration of ECT-induced seizure by determining the seizure termination time, the method based on LSD of EEG amplitude has advantages ; fast in calculation, useful for high sampling datasets, and applicable to seizure termination with gradual decrease of EEG amplitude.[6)] ECG signal has been considered as a valuable complement or as an alternative to cortical electrical signals due to their higher signal-to-noise ratio, greater ease of implementation into extra-cranial devices and cost-effectiveness of recording and lower processing and computational analysis cost due to ECG's lower signal complexity than EEG signal.[24)] ECG recording is also less vulnerable to technical problems and is less frequently indeterminate than EEG recording.[6)22)34)] Thus, ECG analyses of ECT-induced seizure has greater means than any known alternative to detect seizures.[8)] For example, it has been reported that the signs of high EEG amplitude, sharp EEG endpoint, distinct postictal suppression, and tonic-clonic activity can appear in seizures of questionable quality and weak generalization throughout the brain, suggesting that none of these characteristics by themselves indicate good quality or seizure generalization. However, including the findings of magnitude and length of ECT-induced tachycardia has been suggested to add the significance of clinically relevant ECT-induced seizure evaluation.[35)] In this study, our algorithms based on the local slope of the RR interval of ECG have a reliable correlation with that based on the EEG recording even in the non-abrupt transition to flat postictal suppression, which is difficult to determine the end-point of seizure by EEG based direct observation. These results suggests that measurement of seizure duration with ECG could compensate for problems related with EEG recording, such as artifacts or gradual postictal suppression.[6)8)23)]

Reliable estimation of the seizure duration induced by ECT is used as the reference for stimulus dosage adjustment.[36)] It can be one of essential parameters in the evaluation of clinical relevance of the ECT-induced seizure in order to identify the characteristics of the seizures, regardless of the continued debate over whether seizure duration is important in the efficacy of ECT.[37)] For clinical and research purposes, it is necessary to objectively determine ECT-induced seizure duration with partially independent physiological variables (i.e., EEG and ECG). We developed reliable and simple EEG algorithm and ECG algorithm in measuring the duration of ECT-induced cerebral seizures. Furthermore, our method can be applicable for the determination of termination of epilepsy.[26)] Further study is necessary in order to understand the clinical meaning of the discrepancy between EEG auto and HRV auto in non-abrupt flattened postictal suppression sessions, and to explore whether the correlations can be improved through development of the algorithm combining EEG and ECG signals which could provide rich information compared to individual information from either only EEG or ECG signals,[2)8)13)38-40)] because the combining the signals from EEG, neurological events and from ECG, autonomic behaviors provides superior seizure detection efficiency.[26)]

This study has several limitations. The study population is relatively young. Therefore, it may be necessary to evaluate the applicability of these algorithms for elderly population. In this study, we only examined the single channel EEG recording but it may be necessary to examine the results in multichannel EEG recordings which are equipped in most ECT machines. Although this study was intended to develop and verify the automated and consistent methods in determining the end-point of ECT-induced seizure, further study with a larger sample size is necessary to examine whether anesthetics, concomitant medications, age, electrode placement, and so on, affect the applicability of these algorithms.[41)]

We have developed computerized algorithms to assess the duration of ECT-induced seizure, analyzing the standard deviation of a finite block of EEG data and the change in local slope of RR intervals in ECG signals. The seizure duration could be reliably measured with the algorithms, which showed statistically significant ICC even in sessions with non-abrupt flattened postictal suppression. Further study with a larger sample size may provide an improved algorithm or more meaningful characteristics of ECT-induced seizure.

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**Conflicts of interest**

The authors have no financial conflicts of interest.

## Author Contributions

Conceptualization: Yong Sik Kim, Yong Min Ahn, Sang Hoon Yi. Data curation: Cheol Seung Yoo, Dong Chung Jung, Yong Sik Kim, Yong Min Ahn. Formal analysis: Cheol Seung Yoo, Dong Chung Jung, Yong Sik Kim. Funding acquisition: Yong Sik Kim, Yong Min Ahn. Writing—original draft: Eun Young Kim, Cheol Seung Yoo, Yong Sik Kim, Yong Min Ahn, In-Won Chung. Writing—review & editing: Eun Young Kim.

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