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Maximum Fractal Dimension of Cerebral Seizure Remains Constant Through the Course of Electroconvulsive Therapy

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Abstract

Electroconvulsive therapy (ECT), in which electrical current is used to induce seizures, is an effective treatment in psychiatry. Different methods of analyzing the electroencephalogram (EEG) changes during ECT have been studied for predicting clinical outcome. Analysis of the fractal dimension (FD) is one such method. Mid-seizure and post-seizure FD has been shown to correlate with antidepressant effect. In this study, we examined whether the highest fractal dimension achieved during each ECT session changed over the course of 6 ECTs. The sample for this study came from a randomized controlled trial, comparing the efficacy of bifrontal and bitemporal electrode placements in schizophrenia. EEG was recorded using bilateral frontal pole leads during all ECT sessions. In 40 of the 114 randomized patients, we could obtain artifact-free EEGs for the first 6 ECT sessions. FD was calculated using standardized algorithms. For each session, the average of 5 highest FDs was calculated. The change in this value over a course of 6 ECTs was analyzed using repeated-measures analysis of variance. The average highest FD remained virtually unchanged across the 6 ECT sessions. Means (standard deviations) average maximum FDs over the 6 sessions were 1.57 (0.075), 1.57 (0.064), 1.56 (0.064), 1.57 (0.062), 1.55 (0.07), and 1.56 (0.067); occasion effect, F = 0.5, P = .75. Group effect (F = 0.01, P = .92) and group × occasion interaction effect (F = 1.88, P = .1) were not significant, suggesting no influence of electrode placement on maximum FD. Seizure duration, however, showed significant decline over the course of ECT. Maximum FD of ECT-induced EEG seizure remains fairly constant over frontal poles across the first 6 ECT sessions, which is true irrespective of ECT electrode placements.

Keywords

electroencephalogram (EEG), ictal, fractal dimension, course, electroconvulsive therapy (ECT)

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Introduction

As seizure is essential during ECT, researchers have explored whether seizure characteristics have any association with clinical outcome. Duration of seizure has no consistent relation with clinical outcome.[1] However, morphology of EEG during seizure shows promise in this direction. In a related development, the Royal College of Psychiatrists' guidelines have excluded duration criteria for defining effective seizure; rather, importance is given to the architecture of EEG seizure and its motor manifestation.[2]

The extent of post-ictal EEG suppression and intensity of mid-seizure EEG seem to correlate with antidepressant effect.[3] FD is a geometric method of analysis of EEG, which has advantage of simplicity of calculation. Seizure EEG FD during early course of ECT predicts clinical outcome after 2 weeks of ECT course.[4,5] In a recent study, we found maximum ictal FD during early course predicts 2 weeks outcome in schizophrenia.[6]

Little research has been conducted on the changes in EEG characteristics through the course of ECT. Krystal et al[7] found that ictal EEG at first session was characterized by a greater mid-ictal amplitude and post-ictal suppression than subsequent sessions for barely suprathreshold unilateral ECT, but not for barely suprathreshold bilateral or moderately suprathreshold unilateral ECT.[7] McCall et al[8] reported regularity of ictal EEG decline over the course of ECT in patients receiving right unilateral ECT.

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Whether FD varies through the course of ECT has not been studied. Hence, in this study, we evaluated ictal EEG FD across 6 ECT sessions in schizophrenic patients receiving bilateral ECT, bifrontal (BF ECT) or bitemporal (BT ECT).

Method

Material for this analysis was obtained from a clinical trial examining the differential efficacy of BF versus BT ECT in schizophrenia patients. In this study, 122 schizophrenic patients, who were prescribed ECT, were randomized to receive either BF or BT ECT.[9] In all ECT sessions, patients had EEG and electrocardiography monitoring. For the purpose of this report, we analyzed the EEG records of the first to sixth ECT sessions.

In all cases, ECT was prescribed by the treating clinical teams. No patient was prescribed ECT solely for the purpose of this study; antipsychotic and other medications prescribed by the clinical team were noted, but were not controlled. The standard practice in the institute is to evaluate all ECT patients with detailed history, mental status and neurological examination, complete blood picture, metabolic workup, and electrocardiogram. Any change in psychotropic medication is usually avoided unless there is a pressing need. Pre-anesthetic evaluation is obtained for all patients before starting ECT. These were followed in this study.

ECTs were administered using the Niviqure machine (Niviqure Meditech, Bengaluru, India) with EEG monitoring. Brief-pulse stimulation with constant current at 800 mA, 125 pulses per second with pulse width of 1.5 milliseconds was used; duration of train was altered to adjust the stimulus dose. All ECTs were administered under anesthetic modification (thiopentone 2-4 mg/kg and succinylcholine 0.5-1 mg/kg). During the first ECT session, threshold was determined by the titration method.[10,11] From the second session onward, patients received ECTs of stimuli at 1.5 times their threshold. Seizure duration, both EEG and motor (using the cuff method), as well as heart rate and blood pressure were monitored.

EEG Recording

EEG was recorded with the Niviqure ECT-EEG machine using left and right frontal pole leads (FP1 and FP2), referenced to ipsilateral mastoid processes. For each session, EEG recording started after stimulus through the ictal phase until 5 seconds after the cessation of EEG seizures. The sampling rate for EEG was 128 per second and the left frontal channel EEG was used for analysis. Two researchers (GR and HAA) viewed the EEGs recorded during the first 6 ECT sessions of all patients. EEG records with artifacts (ie, movement and electromyogram artifacts) were discarded. Artifacts were minimized, as succinylcholine was used during ECT and all voluntary muscles (including the ocular and facial) except for those in the cuffed limb, were paralyzed. However, manipulations during ventilation of the patients during ECT produced movement artifacts in a substantial proportion of patients. Hence, we had artifact-free EEGs for 6 ECT sessions (240 EEG records in total), in only 40 patients. Twenty-one of these patients had received BT and 19 had received BT ECT (see below).

EEG Analysis

EEG Analysis Using FD

FD was calculated based on the principles described by Katz[12]:

$$\mathrm{FD} = \frac{\ln(L)}{\ln(d)},$$

where L refers to the total length of the waveform and d refers to the maximum distance of the waveform, namely, the distance between the first and the last data on the 2-dimensional, unidirectional waveform. We have further simplified the FD estimation by taking the number of pixels used to display EEG segment. We estimated FD for the visually displayed EEG epochs of 4 seconds, which correspond to 512 pixels (d) on the X-axis. Each pixel on the Y-axis corresponded to 15 µV of EEG signal. The height (y_i, i = 1, 2, 3, . . ., 512) of the EEG wave (pixels used by the EEG wave on the Y-axis) corresponding to a pixel x_i on the X-axis was counted. The length segment of the wave m_i can be calculated using the Pythagoras theorem, that is,

$$m_i = \sqrt{x_i^2 + y_i^2} = \sqrt{1 + y_i^2},$$

which was approximated for ease of computation as $m_i \approx (1 + y_i)$. The total length of the wave form L is then obtained as

$$L = \sum_{i=1}^{i=512} m_i \approx \sum_{i=1}^{i=512} (1 + y_i).$$

Clearly, the maximum distance of the waveform d = 512 pixels. This enables the evaluation of

$$\mathrm{FD} = \frac{\ln(L)}{\ln(d)}$$

of successive 4-second EEG segments.

The FD value provides a quick geometrical measure of EEG seizure in ECT. FD was calculated for a 4-second EEG epoch as seen on the screen. The zoom value for visual display was fixed for all analyses. The customized software provides a line graph plotting the consecutive FD values of the entire EEG record of the seizure (Figure 1). For each EEG recording maximum FD was noted by a rater blind to the ECT session and clinical details of the patients.

For each session, the 5 highest FDs were noted by visually scanning the FD graph. The average of these 5 for each seizure EEG was used for comparison across ECT sessions and between 2 ECT electrode placements. In 16 randomly chosen EEGs, 2 researchers (GR and HAA) calculated this average

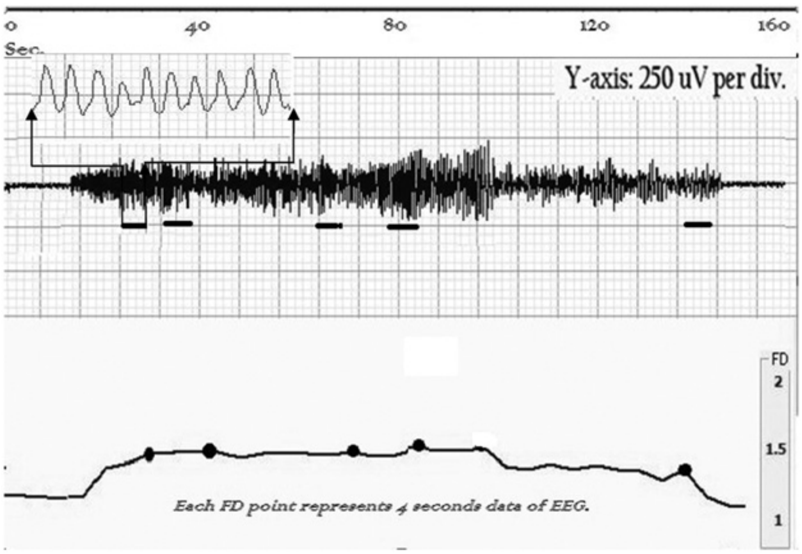

Figure 1. Typical electroencephalogram (EEG) and fractal dimension (FD) graphs recorded during an electroconvulsive therapy (ECT)–induced seizure as well as the points chosen as ictal FD. The insert on the left-top corner displays a 4-second EEG epoch with the same *Y*-axis scale.

independently. The interrater reliability was excellent (intraclass correlation coefficient = 0.87; $P < .001$).

Statistical Analysis

T test and χ^2 tests were used to compare patient's BF and BT groups. The change in this value over a course of 6 ECTs was analyzed using repeated-measures analysis of variance.

Results

The mean (standard deviation [SD]) age of patients receiving BF ECT and BT ECT was 26.3 (5.9) and 25.9 (7.4) years, respectively ($t = 0.163$, $P = .87$). There were 9 females in the BF ECT group and 10 in the BT ECT group ($\chi^2 = 0.96$, $P = .51$). The mean (SD) baseline brief psychiatric rating scale score of the BF ECT group was 58.9 (6.6) and of the BT ECT group was 55.1 (7.2); $t = 1.6$, $P = .11$. The average highest FD remained virtually unchanged across the 6 ECT sessions. Mean (SD) average maximum FDs over the 6 sessions were 1.57 (0.075), 1.57 (0.064), 1.56 (0.064), 1.57 (0.062), 1.55 (0.07), and 1.56 (0.067); occasion effect: $F = 0.5$, $P = .75$. There was no group effect ($F = 0.01$, $P = .92$; nor was there a group × occasion interaction ($F = 1.88$; $P = .1$; Table 1). In contrast, the duration had significant decline over the course of ECT. Mean (SD) EEG seizure durations (in seconds) over the 6 sessions were 78.9 (40.6), 71.1 (31.5), 63.6 (28.4), 61.2 (26.2), 61.9 (32.2), and 58.6 (25.7); occasion effect: $F = 2.9$, $P = .015$.

Table 1. Mean and Standard Deviation of Average Highest FD of Each Session for Different Electrode Placements.

	BF (n = 21)		BT (n = 19)	
Session	Mean	SD	Mean	SD
1	1.5777	0.08846	1.5767	0.06075
2	1.558	0.06741	1.5538	0.07091
3	1.5615	0.06055	1.5527	0.07016
4	1.56	0.05411	1.5732	0.05412
5	1.5361	0.08062	1.5391	0.07089
6	1.5734	0.06131	1.5634	0.05895

Abbreviations: FD, fractal dimension; BF, bifrontal; BT, bitemporal; SD, standard deviation.

Discussion

Earlier studies have shown a relationship between FD during the early course and therapeutic effect after 2 weeks.[4-6] The result of the current analysis suggests that the highest FD achieved during early course is maintained through the course of ECT. This may be because once generalized, the seizures follow a pattern that shows little variation within that individual, suggesting "all-or-none" behavior of seizures with regard to their morphology. This suggests that the highest FD obtained during the early course is actually an index of the behavior of seizure through the course of ECT. Stated in another way, higher FD during the early course also indicates higher FD through the course of ECT, which in turn is associated with greater clinical improvement.

Overall, the morphology of EEG seizure shows little variation through a course of bilateral ECT. This is consistent with the finding by Krystal et al,[7] who reported no variation in the EEG seizure spectral power in successive bilateral ECTs. However, this does not appear to be the case with unilateral ECT. Mid-ictal amplitude and post-ictal suppression were found to be greater during the first ECT session than during the subsequent sessions for barely suprathreshold unilateral ECT, but not for moderately suprathreshold unilateral ECT and for barely suprathreshold bilateral ECT.[7] Likewise, regularity of ictal EEG was found to decline over the course of the ECT in patients receiving right unilateral ECT.[8]

This analysis also highlights the fact that the morphology of EEG measures remains unchanged, in contrast to the duration of seizure that shortens over ECT sessions given thrice weekly.[13]

We had expected that the maximum FD would be greater in patients receiving BF ECT, because use of BF ECT is associated with superior outcome in the larger data set of the same study.[9] However, contrary to our expectation, we did not find a significant difference between BF ECT and BT ECT. The therapeutic advantage of BF ECT over BT ECT is relatively small (though statistically significant)—we believe that the maximum FD during seizure may not be sensitive to be robustly associated with this small difference.

In conclusion, this study shows that the maximum FD remains virtually constant through a course of ECT irrespective of the ECT electrode placement and contrary to the duration of seizures.

Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article:

Vittal S. Candade is the Director of Niviqure Meditech Pvt Ltd, which manufactures ECT machines and related software.

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