Original Article

Ictal EEG Non-linear And High Order Spectral Analysis Methods In Electroconvulsive Therapy And Its Clinical Utility

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Abstract

Introduction: Analysis of ictal electroencephalogram (EEG) during electroconvulsive therapy (ECT) early in the course provides information to predict clinical outcome. Previous studies used visual, power spectral and non linear methods to analyze EEG. EEG signals are non stationary, non linear, non Gaussian and chaotic in nature. Such signals can be better characterized by non linear and higher order spectrum analysis. However there is scarcity of data assessing such measurers in predicting clinical outcome. We conducted nonlinear and high order spectrum analyses of ictal EEG recorded during ECT and correlated the measures with clinical outcome.

Methods: Schizophrenia patients receiving ECT were assessed using the brief psychiatric rating scale (BPRS) before and 2 weeks after the start of ECT. EEG was recorded during seizure from left frontal-pole (FP1) channel. In 26 patients, completely artifact-free EEG was available. Approximate entropy (ApEn), Sample entropy (SamEn), Hurst exponent (H), Bispectrum entropy (HOS.En), correlation dimension (CD) and Largest Lyapunov exponent (LLE) were computed for EEG from the earliest ECT session (2nd or 3rd).

Results: HOS.En emerged as a significant measure which predicted outcome at two weeks (HOS.En1: r = -0.434; p = 0.027 & En2: r = -0.414; 0.036) other measures, viz., ApEn (r = -0.001; p = 0.995), SampEn (r = -0.152; p = 0.458), H (r = 0.123; p = 0.549), CD (r = 0.119; p = 0.563) and LLE (r = -0.293; p = 0.146) did not predict the outcome.

Conclusion: In patients with schizophrenia receiving ECT higher bispectrum entropy of ictal EEG early in the ECT course predicts better clinical outcome at the end of two weeks. None of the other non linear measures evaluated in the study predicted clinical outcome.

Key Words: ictal; EEG; non-linear; schizophrenia; outcome

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Introduction

Several authors have investigated various seizure EEG markers to predict the clinical outcome in patients receiving ECT. Previous studies used visual, power spectral and non linear methods to evaluate EEG signal (1). EEG signals are non stationary, non-linear, non Gaussian and chaotic in nature. Researchers have hence used different non linear analysis techniques to quantify EEG signals. In particular, Sample entropy and largest Lyapunov exponent (LLE) of the ictal EEG in ECT are shown to be useful to estimate seizure adequacy and predict clinical improvement (2-5). EEG entropy and high order spectrum analysis (HOS) measures are shown to have seizure detection property in epilepsy patients (6-8). In a recent study we have demonstrated that maximum ictal EEG fractal dimension (FD) predicts clinical outcome at two weeks in schizophrenia patients receiving ECT (9). This measure remains same throughout the course of ECT (10). However it remains unknown whether certain other non-linear and HOS quantification methods also predict clinical outcome. We computed various non linear and high order spectrum measures of ictal EEG during ECT and correlated the same with clinical outcome in schizophrenia patients receiving ECT.

Methods

Material for this analysis was from another study examining the differential efficacy of bifrontal versus bitemporal ECT (11). In this study 122 schizophrenia patients who were prescribed ECT received either bitemporal or bifrontal ECT. ECG and EEG of patients were monitored in all the ECT sessions. For the purpose of this report, we analyzed the EEG records from 2nd or 3rd ECT sessions of these patients.

NIVIQURE machine (India) with EEG monitoring was used to administer ECTs. Anesthetic modification (thiopentone 2-4 mg/kg and succinylcholine 0.5-1 mg/kg) was used for ECTs. Constant current (0.8A) pulses of 1.5 msec width spaced at 125 pulses per second administered for varying train length formed the stimulus that was applied across the chosen sites over the scalp. The threshold during first ECT session was evaluated by titration method (12, 13). During the subsequent sessions, patients obtained 1.5 times of the threshold as ECT stimuli. Duration of seizure (using cuff method), blood pressure and heart rate were monitored.

EEG recording:

EEG was recorded with the Nivique ECT-EEG machine using left and right frontal pole leads (FP1 and FP2), referenced to ipsilateral mastoids. For each session, EEG recording started after stimulus through the ictal phase until after 5 or more seconds following the cessation of EEG seizures. The sampling rate for EEG was 128 Hz. We included records that were artifact-free (i.e., free of movement and electromyogram artifacts) for the entire length of recording with respect to both EEG and ECG at the 2nd or 3rd ECT session. We obtained such artifact-free records in 26 patients.

Computation of non linear measures:

Approximate entropy (ApEn), Sample entropy (SamEn), Hurst exponent (H), Bispectrum entropy (HOS.En), correlation dimension (CD) and Largest Lyapunov exponent (LLE) were computed for the ictal EEG. All measures were computed using customized software by a rater blinded to clinical data. Details of the algorithm are described elsewhere (6, 7, 14).

Clinical Assessments:

The clinical status of all patients was assessed by one of the authors (VHP) using the Brief Psychiatric Rating Scale (BPRS\textsuperscript{15}) and Clinical Global Impression (CGI) (16).

Statistical analysis:

Pearson’s correlation coefficient was used to assess relationship between BPRS total scores at the end of 2 weeks of ECT (i.e., following 6th ECT) and non linear EEG measures of seizure of 2\textsuperscript{nd} or 3\textsuperscript{rd} ECT. Demographic and clinical variables of the 26 patients, whose EEG were analyzed, were compared with that of the remaining 88 patients using chi-square test (for categorical variables) and Student’s t-test (for
Results

Mean (SD) age of 26 patients was 29.4 (7.9) years and 8 (30.8%) were females. All of them were on antipsychotic medications; none were on antiepileptic medications. Fifteen (57.7%) had received bifrontal ECT. The mean (SD) number of ECT sessions received by the patients was 7.84 (2.8). In all patients, the reason for stopping ECT course was observation of substantial improvement in the clinical status. At the time of stopping ECT, their mean (range) CGI was 1.61 (1-3).

There was no significant correlation between baseline BPRS and EEG measures (Table I). HOS.En emerged as a significant measure which negatively correlated with BPRS score at end of two weeks. (En1: \( r = -0.434; \ p = 0.027 \) & En2: \( r = -0.414; \ p = 0.036 \) (Fig. 1). Other measures, viz., ApEn \( r = -0.001; \ p = 0.995 \), SampEn \( r = -0.152; \ p = 0.458 \), H \( r = 0.123; \ p = 0.549 \), CD \( r = 0.119; \ p = 0.563 \) and LLE \( r = -0.293; \ p = 0.146 \) did not predict the clinical outcome (Table II).

![Fig. 1: Scatterplot showing non linear measures HOS entropy on x-axis and BPRS scores on y-axis.](image)

Discussion

To our knowledge this is first study investigating various non-linear and high order spectrum measures during ictal EEG induced by ECT. Our results showed that HOS is useful measure which predicted the clinical outcome. HOS is a non-linear method...
which captures subtle changes in the signal very effectively. It is a 3rd order statistical analysis and has property of high signal to noise ratio (SNR). It was shown to capture interaction among its frequency components and phase coupling (17). It is a very robust tool to differentiate various non-Gaussian signals for accurate identification of changes in the time series. Thus this novel measure was also sensitive in predicting clinical outcome (6, 7, 14).

It is interesting to note that correlation coefficient noted with HOS and clinical outcome is comparable to our previous study which assessed higher FD and clinical outcome (9) in the same sample of ECT patients (actually same data). However, we could not replicate previous findings on usefulness of ictal EEG ApEn and LLE measures as predictors of therapeutic improvement after ECT (3, 4).

Neurobiological explanation for this association remains elusive. Few lines of investigations demonstrated greater seizure intensity is associated with higher intrinsic GABAergic activity which might influence clinical outcome (18). There is scarcity of literature on association between non-linear EEG quantification and biological phenomenon. Further studies are needed to elucidate possible link between EEG markers and specific neuronal activity.

Major limitation of the study was small sample size. We could not get artifact free recording in all the patients. We adhered to strict selection criteria of absolutely artifact free ictal EEG. However it should be noted that these patients with artifact-free EEG were not significantly different from the rest in many clinical and demographic variables (9).

In conclusion, we provide evidence for the utility of high order spectrum analysis of ictal EEG during early in the course of ECT in predicting clinical outcome at two weeks. Further studies are required to confirm this finding.

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References


