

Original Article

Quantitative electroencephalography as a tool for objective neurophysiological seizure diagnosis: A retrospective study

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ABSTRACT

Objectives: Seizure is the fourth most common neurological disorder in the world; it affects all age groups with equal possibility of occurrence in both males and females. Many antiepileptic drugs are available today, but its diagnosis is challenging. The present study attempted to see if seizure activities could be predicted by analyzing the pre-seizure electrical activities. The prediction may help in taking preventive measures appropriately beforehand in the individuals with seizure proneness.

Material and Methods: We selected 11 generalized seizure patients and 19 control patients out of total 115 patients referred for electro-diagnostics for various reasons. EEG of the subjects recorded, segmented as per protocol, and analyzed using MATLAB and EEGLAB tools.

Results: The mean energy level in alpha and beta band of the study subject was significantly lower ($P = 0.04$ and 0.004 , respectively) as compared to the age matched control subjects. Theta and delta bands did not show any significant difference between the groups. The difference between the pre- and post-electrical seizure energy and entropy was statistically insignificant.

Conclusion: The study shows that the energy level remains low in the seizure patients in the alpha and beta bands. This further goes down when electrophysiological seizure activities starts. The randomness or entropy does not alter significantly among the seizure subjects in comparison to non-seizure subjects.

Keywords: QEEG, Epilepsy, ICA, Alpha waves, Energy, Entropy

INTRODUCTION

Epilepsy is a common neurological disorder worldwide. As per the WHO 60–70 Million people are affected with epilepsy globally (Fergus *et al.*, 2016; Meng *et al.*, 2017).^[1,2] Epileptic seizures are dysfunction of brain characterized clinically by localized or generalized convulsion and electrophysiologically by synchronous discharge of a cluster of neurons placed in the cerebral cortex as evidenced by abnormal patterns in the electroencephalography. The recent classification of epileptic seizures based on the International League Against Epilepsy (Berg *et al.*, 2010, Chang *et al.*, 2017)^[3,4] classifies seizure disorders into three categories: Focal, generalized, and epileptic spasms. Focal seizures usually originate in one cerebral hemisphere of the brain. Generalized seizures affect both the cerebral hemispheres with seizures originating in the cortex or subcortical area. Generalized seizures could be generalized tonic-clonic, absence, atonic, or myoclonic varieties. A third type of seizure is epileptic spasms which manifest by rapid expansion or flexion of extremity and is usually a feature of childhood epileptic syndromes.

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Continuous EEG recording has become an important clinical tool for the assessment and treatment of epilepsy (Gotman, 1989).^[5] The quantitative EEG (QEEG) analysis is one of the proven tools for gauging the effects of substances on the central nervous system in the clinical, experimental, and concerned disciplines (Holler *et al.*, 2018).^[6] Conventionally, frequency parameters are solely used for diagnosis and prediction of seizure activities. After advent of computer based EEG recording and analytical techniques, a lot of advancements have been made in the field of quantitative EEG analytics. Some of the commonly applied newer techniques of quantitative analytics include representation of frequency through wavelet transforms, independent component analysis (ICA), principal component analysis, and non-linear analytics including coherence analysis source localization (Buhimschi *et al.*, 1998; Leman *et al.*, 1999; Maner *et al.*, 2006, and Diab *et al.*, 2010).^[7-10] The energy distribution across various frequency bands has been used recently as one of the sensitive tools for the purpose of seizure detection (Omerhodzic *et al.*, 2010).^[11] EEG offers a real-time assessment of temporal dynamics of brain signals during various activation procedures such as photo-stimulation (flashing of light) and hyperventilation. EEG signals consist of five frequency bands, that is, Gamma (30–60 Hz), Beta (13–30 Hz), Alpha (8–13 Hz), Theta (4–8 Hz), and Delta (0.3–4 Hz).

The present work aims to address the possibility of using QEEG as an objective diagnostic tool for possibility of prospective seizure attacks among the susceptible individuals. A study of energy and entropy levels among seizure and control subjects both during interictal/normal periods as well as during the actual electrophysiological seizure activities (as evidenced by the typical EEG discharges diagnostic of seizure activities without clinical presentation) could possibly yield an EEG based marker that could be used for prospective seizure prediction among the susceptible individuals.

MATERIAL AND METHODS

Subject selection

With all due ethical considerations and permissions, the EEG records of the subjects referred to the neurodiagnostic facility of the institute for various reasons during the study period has been retrieved. At every level, it has been ensured that patient identity should not get divulged by any means and the data to be exclusively used for the study purpose. Out of a total 115 subjects referred to the facility for EEG study, 11 patients have qualified as per the inclusion and exclusion criteria. Fifteen healthy normal records who did not have any history of seizure and having no seizure specific findings in the EEG records have been taken as control for comparison.

The inclusion criteria for the case group included age of disease onset to be between 5-15 Yrs., duration of the complaint (Seizure) for at least 1 year, EEG ictal discharges should be

generalized and high amplitude. Exclusion criteria included seizure secondary to deep brain stimulation or vagus nerve stimulation or any other specific neurostimulation for epilepsy, cases with focal seizure, cases of known neurological disorders including multiple sclerosis, facial palsy, cerebellar palsy, ADHD, cerebellar ataxia, and Jerky movement, disorders of sleep, history of Drug ediction, smoking, alcohol, etc.

EEG recordings

As per the standard norms of the neurodiagnostic facility of the institute, all recordings were performed during the daytime (9 am–5 pm). EEG recorded using by 21 electrodes with a sampling rate of 256 Hz (RMS EEG-32 Super Spec, India). The EEG signals were collected from Montages of ECG-A2, F4-C4, C4-P4, P4-O2, Fp1-F3, F3-C3, C3-P3, P3-O1, FP2-F8, F8-T4, T4-T6, T6-O2, FP1-F7, F7-T3, T3-T5, and T5-O1 in longitudinal bipolar montages with ground electrode placed at FpZ as per the international 10-20 system of electrode placement. Amplifier of 50 Hz notch filter applied for noise cancellation. Total recording time for all the subjects were 20–25 min as per the standard norms of the lab.

Work plan

Figure 1 shows the flow chart of the work plan for the study.

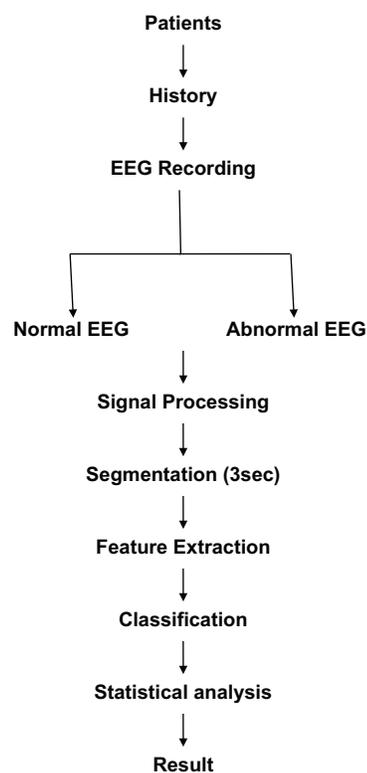


Figure 1: Flow chart of work plan.

EEG signal analysis

EEG raw signal pre-processing in MATLAB included artifact removal, frequency division, and segmentation. A 50 Hz notch filter has been used to remove interference on the power line from the raw signals. In this study, we have used ICA for the removal of the artifacts and we reconstructed brain waves of alpha, beta, theta, and delta. Usually, two classical wavelet functions are often used to analyze the EEG. One is Daubechies (Db) wavelet and another biorthogonal wavelet; here, we have used Db4 for the waves decomposition (Kalayci and Özdamar, 1995; Petrosian *et al.*, 2000).^[12,13]

ICA uses for the rejection of artifacts

ICA has been used to remove artifacts from electroencephalography data. The signals recorded from the scalp were obtained by a mixture of various other signals such as an eye blink and muscle artifacts. ICA is used to filter all the artifacts that may be originating from those bio-signals originating from eye blink and neuromuscular sources. The raw signal, which was allowed to go through ICA, was made to pass through a notch filter to remove the artifacts caused due to interference of 50 Hz line frequency in the EEG dataset. This was followed by a Bandpass filter (band of 0.3–45 Hz) to get the desired signal in the band of 0.3–45 Hz.

Using ICA the signal has been decomposed into various independent components. Every independent component represented a source of activity. Depending on the source which may be signal or noise, the component has been accepted or rejected.

Let the signal recorded at the scalp is X (x_1, x_2, x_3, \dots). The number of sources lets be S ($s_1, s_2, s_3, s_4, s_5, \dots$) and each source is mixed by factors let A (a, b, c, \dots). Hence, this can be represented mathematically: $X=A*S$.

ICA Implementation in EEGLAB

EEGLAB allows various file formats to be imported into the lab, we have used edf format. Data were first filtered and then the direct current component was removed from the signal. ICA

algorithm was implemented. Noisy component was removed from the signal based on the scalp map. Figure 2 describes the process of artifact removal by ICA in MATLAB through the scalp map. The signal is now ready for feature extraction.

Feature extraction

Feature extraction is the process of extracting useful information from the signal.

Energy

Energy is defined as the strength of a signal. It is defined mathematically as follows:

$$ED_i = \sum_{j=1}^N |D_{ij}|^2, \quad i = 1, \dots, l \quad (1)$$

$$EA_l = \sum_{j=1}^N |A_{lj}|^2 \quad (2)$$

As per Parseval's theorem, the energy of the distorted signal can be partitioned at different resolution levels. Signal energy can be defined in the above equation.

$i = 1, 2, \dots$ Where $i = 1, 2, \dots$ is the wavelet decomposition level from level 1 to level. N is the number of the coefficients of detail or approximates at each disintegration level. is the energy of the particulars at disintegration level I and EA_l is the energy of the approximate at decomposition level l (Omerhodzic *et al.*, 2010; Kumar *et al.*, 2017).^[11,14]

Statistical analyses

IBM SPSS Statistics software has been used for the analysis of EEG data. A significance level of 0.05 has been taken with a confidence limit of 95% to delignate the statistical significance of any parameter.

RESULTS

A total of 115 subject's EEG data have been recorded during the period of reference, out of which 19 subjects with

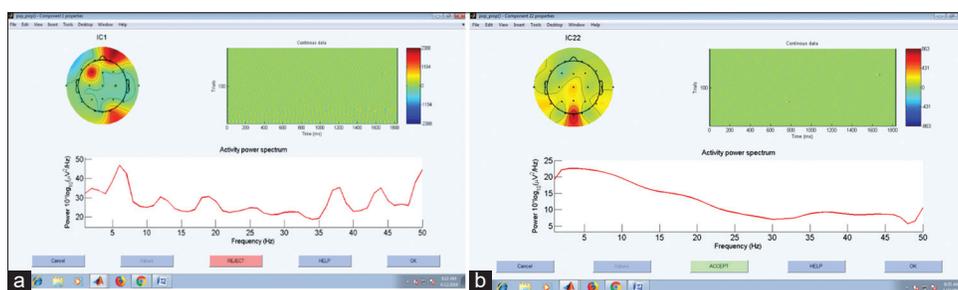


Figure 2: Scalp map with (a) and without (b) eye blink artifact.

generalized seizure have been taken as control and 11 subjects have been taken as study subject following inclusion and exclusion criteria. The mean age of experimental group was 10.1 years whereas that of control group subjects were 11 years [Figure 3]. Rest of the data have been discarded due to presence of one or more biases.

Further, data have been analyzed for energy of alpha, beta, theta, and delta waves. Mean energy level for alpha waves

among control subjects was 9.78 ± 7.65 and that of study subject was 3.65 ± 2.38 . Similarly, mean beta energy was 8.77 ± 6.10 for control and 4.83 ± 1.66 for test subjects. A significant reduction of alpha ($P = 0.04$) and beta waves ($P = 0.004$) was observed in the seizure group. The mean theta activity has been found slightly increased in the experimental group in comparison to the control group, whereas the mean delta energy level showed slight decreased level, but both are statistically not significant [Table 1 and Figure 4].

DISCUSSION

Electroencephalography is one of the most important tools for seizure detection used across the globe. Despite of lots of technological advancements, the EEG interpretation is largely subjective and diagnosis of seizure is mostly based on the subjective observations and clinical acumen of the clinician. The present study aimed to investigate the possibility of objective diagnosis of seizure possibly from the background electroencephalographic characteristics of the prospective seizure patients even before actual seizure events.

The pre-recorded EEG data and subject's clinical information have been analyzed following due protocol to make a comparison between the electroencephalographic patterns

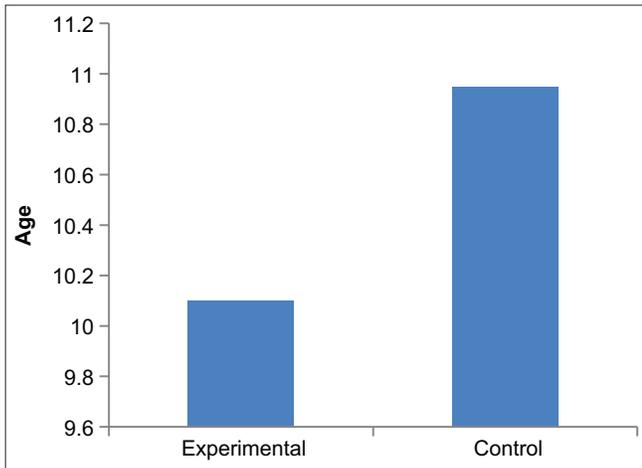


Figure 3: Average age of experimental and control.

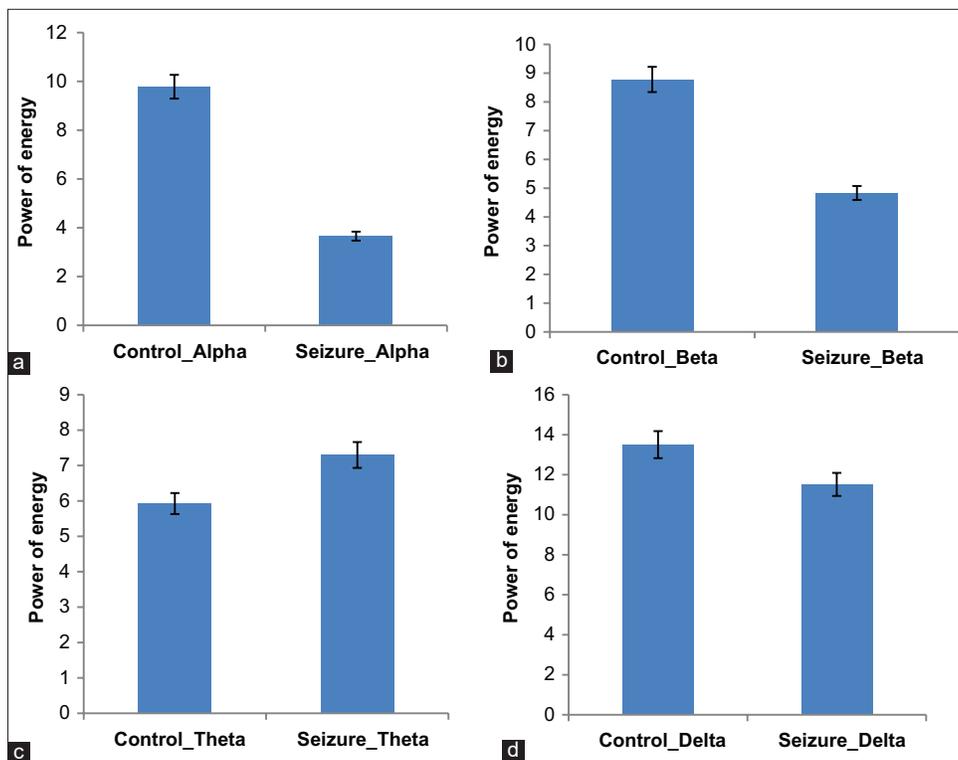


Figure 4: Mean energy of α showing in figure (a), β showing in figure (b), θ showing in figure (c), and δ showing in figure (d), between normal and seizure with SD.

Table 1: Statistical analysis of the experimental and control group.

Waves	Mean of control	Mean of experimental	SD of control	SD of experimental	Significant value
Alpha	9.78	3.65	7.65	2.38	0.047
Beta	8.77	4.83	6.10	1.66	0.004
Theta	5.92	7.29	4.22	5.33	0.133
Delta	13.50	11.51	13.21	9.16	0.715

of non-seizure subjects and EEG of subjects with history of recent seizure. From the results of the study, the following observations could be figured out.

- The mean energy level of control subjects was higher than that of seizure patient even during non-electrophysiological seizure, but it was statistically insignificant
- There was no statistically significant difference between the energy levels during pre-seizure and post-seizure electrical activity in the study subjects
- Energy level in theta and delta band of control and study subject did not had statistically significant difference
- The energy level for alpha and beta frequency band in seizure group subjects was much lower in comparison to the control group subjects when the EEG segments taken for analysis was from the period of electrical seizure activities
- Entropy, which signifies randomness of the brain electrical activity, did not show any significant difference between the control subject and study subjects.

From the above observations, it is apparent that out of the two important parameters of the electroencephalographic signals studied, that is, energy and entropy, energy has come out as most important discriminator between the seizure and non-seizure categories. The energy of the filtered EEG signals has the optimal discriminative capability under the extreme energy difference (EED) criterion, and thus, EED can be considered as a feature extractor (Li and Sun., 2008).^[15] The previous study reported that seizure EEG changes are indicative of increased excitability, distorted synchrony, and decreased signal complexity for the period of a pre-seizure (Mormann *et al.*, 2006 and Zaveri *et al.*, 2009).^[16,17] As the EEG signal is a kind of non-linear signal, its dispersion characteristics are complex and difficult to estimate.^[18] The seizure subset of the data has shown a decreased mean level of energy in comparison to the non-seizure subset of individuals which were contrary to the common expectation and scientific believes. This may be attributed to the complex neural behaviors related to dispersion. The other parameter, the entropy, which is a measure of complexity did not show any significant difference between seizure and non-seizure individuals. This indicates that there is no any significant change in the signal characteristics of the background electrical activities among seizure patients in comparison to normal individuals. Another interesting and rather robust methodology for objective tool for seizure detection could be the multichannel surface EEG-based patient non-specific seizure detection approach. This approach includes

DMD power, power spectral density, variance, and KFD extracted from WPD coefficients measurement for detecting seizure. In any continuous EEG signal seizure, event may be observed for seconds as compared to many minutes of non-seizure EEG signals (Dash *et al.*, 2019).^[19] Hence, cluster-based seizure classification is preferred. Based on the observation, a future study with bigger database could be attempted with combined approach.

CONCLUSION

This a small retrospective study on the pre-recorded data to find if the normal background characteristics of an EEG signal be used for seizure detection and prediction. The study indicated changes in the energy level between the EEG characteristics of non-seizure subjects and that of seizure individuals. Further, a study will be required for better understanding the underlying mechanism.

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Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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