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Detection of interictal epileptiform discharge in focal seizures

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Background: Many factors underlying basic epileptic conditions determine the characteristics of epileptic seizures and the therapeutic outcome. Visual obvious abnormalities in resting baseline EEG are cardinal but incompletely understood like feature of seizure onset zone in focal epilepsy and interictal epileptiform discharge. Present study is an attempt to diagnose that evidence of epileptic discharge in temporal lobe epilepsy (TLE), would persist during interictal period in absence of abnormalities in baseline EEG, which could increase the impact of automatic analysis of EEG waves for clinical relevance.

Materials and Methods: By using 10-20 system, functional connectivity was estimated in the 20 channels of delta, theta, alpha, beta and gamma frequency bands of EEG, from 16 diagnosed focal epileptic seizure patients and 16 age and sex matched controls. To observe the dynamics of the healthy brain, differ from the brain of dynamically focal epileptic patients during interictal period treated with anti-epileptic drugs in the context of resting state during eye close session of EEG. Such differences can be observed by using absolute spectral power from BESS ((Brain Electro Scan Software) of the Axxonet System and statistically measure by applied unpaired student t -test.

Result: The high significance results in slow frequency EEG waves (delta and theta) in power spectral analysis were observed that demonstrates the potential epileptic discharge occurring during interictal period without visible pathological activity for helping in the diagnosis and lateralization of TLE.

Conclusion: The detailed spectral analysis of EEG waves offers novel insight into focal epileptic patients when visually EEG findings were normal. This linear analysis helpful in extracting information from EEG signals in diagnosing specific neuronal correlates for TLE. Present findings concluded that epileptic discharges occur at different topographical regions of brain during interictal period and power spectral analysis plays a new insight in diagnosis of focal discharge.

Key words: Focal seizures, Linear Analysis, Power Spectral Analysis, Temporal Lobe Epilepsy

Introduction

Epilepsy is one of the most common human brain disorders. It is often accompanied by disturbances in behavior, brain dysfunction, and cognitive impairment. According to the World Health Organization, 0.7% to 1% of the world's population suffer from epilepsy and this generally peaks in childhood and advanced age, meaning that a large proportion of patients have this chronic disease for most of their lives. [1] Focal epilepsy originates in the medial or lateral aspect of temporal lobe of brain, mainly from mesial- basal temporal lobe including hippocampus, amygdale and Para hippocampal gyrus. [2] Mesial temporal lobe epilepsy (TLE) is the most common type of pharmaco-resistant epilepsy in adults.

Literature indicates that various parametric [3] and nonparametric [4] techniques have been applied to the analysis of epilepsy. When analysing EEG signals in the time domain, abnormal patterns such as spikes and sharp waves are detected; while in the frequency domain, features from the power spectrum are extracted.[5]

Many studies [6,7,8] used linear and non-linear methods for seizure detection. Tuunainen et al [7] used the absolute and relative power as well as the peak power frequency at left occipital brain lobes as features to identify differences between the patient and the control groups and results

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showed that the occipital peak alpha frequency was significantly lower in patients than in controls. Jerger et al have also focussed on interictal spike patterns to predict and ultimately control seizure activity.[4] A systematic calculation of linear correlation allowed the possibility of extracting information on how the EEG signals across different regions are related. This together with known clinical history can aid in identifying the epileptic focus and provide further insight on seizure dynamics.

Several studies have shown that functional connectivity measures based on intracranial EEG can help to identify the irritative zone and the seizure onset zone. [9,10] High-density scalp EEG revealed interictal network patterns concordant with cognitive deficits in TLE [11] and significant connectivity differences in TLE compared to healthy controls in the absence of interictal spikes. [12] Machine learning algorithms have been used for automatic detection and localization of the epileptogenic zone in TLE using a multitude of imaging modalities. [13,14]

This study is an attempt automatically diagnoses and lateralizes TLE based on EEG without visible pathological activity during interictal period.

Materials and Methods

The present study was conducted to propose the biomedical importance in diagnostic field of complex partial epileptic patients. The study was approved by the Institutional Ethical Committee. The sample size required is 16 in each group (case and control) at 95% confidence and 80% power to verify the expected minimum difference of 0.66 [± 0.64] mean working memory task score of temporal lobe epileptic cases and age and sex matched healthy controls. Sample size of patients is obtained by OPD based random sampling technique. Temporal lobe epileptic (TLE) patients who are seizure free from last one year (interictal period) and are treated by AED (Anti-Epileptic Drugs) were included. The study included confirmed patients of temporal lobe epilepsy that undergo temporal lobe MR Protocol of the brain and Electroencephalography. Detailed clinical and family history of epilepsy and consent was taken.

The present study is a hospital based, observational comparative case control study that included 16 patients of temporal lobe epilepsy (diagnosed on the basis of Magnetic Resonance (MR) Protocol and Electroencephalography findings) taken from the outdoor of Departments of Neurology and Medicine.

Inclusion Criteria adopted for the present study would be: Age between 20 – 30 years, with epilepsy satisfying the guidelines lay down by the International League Epilepsy Society, during the interictal period of epilepsy. In the present study 12 out of 16 patients suffering from complex partial seizures, no significant changes were found in MRI.

Exclusion Criteria for the study was with known contraindications to Temporal Lobe MR Protocol epilepsy or any previously diagnosed non central nervous system disorders liable to cause seizures, syncope and hypoglycemic attacks, pseudo- seizures or drug induced seizures. Patients with malignancy, previous craniotomy or cervical spine surgery or head injury

EEG recording

In the present study, 21 channels scalp electroencephalography times series at tracing was acquired as further norms of International 10-20 system with biauricular reference.[15] Electrode impedance was kept <5kΩ electrical activities, amplified with a band pass filter of 0.1-30.0 Hz, digitalized at sampling rate 256 Hz. QEEG (Quantitative Electroencephalography) was done for all the subjects and controls using **BESS** (Brain Electro Scan Software) of the **Axxonet System**. EEG was recorded using a Stretchable cap and positioned on the subject's head according to the known anatomical landmarks.[16]

EEG was recorded from frontal (Fz/ Fp1/ Fp2, F3/ F4, F7/F8), temporal (T3/T4/T5, T6), central (C3/C4/ Cz), parietal (P3/P4/Pz) and occipital (O1/O2/Oz) regions of brain for detection of any epileptic discharge in brain during eye close session of EEG.

Data Acquisition. The following parameters were observed and evaluated: Absolute power of delta (0.2-3.9 Hz), theta (4.0-7.9 Hz), alpha (8.0-12.9 Hz), beta (13.0-30.0 Hz) and gamma bands (30.1-80 Hz) of EEG wave‟s frequency was calculated. The EEG recordings were run for 5 minutes during interictal period in complex partial seizure patients and in healthy controls with the subjects at rest with eye closed session. EEG data were offline re-referenced to common average reference and filtered between 0.5 to 30 Hz to remove possible high frequency noise.

Absolute Power

This is a frequency domain measure obtained after applying Fast Fourier Trasnsform (Linear Transform) to time series EEG signals. The algorithm for above linear transformation is inbuilt in the **BESS** (Brain Electro Scan Software) of the **Axxonet System** in Neurophysiology Lab of Department of Physiology.

Statistical Analysis

The Microsoft excel 2010 was used for statistically analysis of recorded data. The unpaired t-test was used for the mean comparison of all parameters between patients and control subjects and considered two-sided p values < 0.05 to be significant.

Results

During eye closed session of EEG in delta band the significant difference of mean absolute power was observed in FP1 (p =0.007), FP2 (p= 0.019), O2 (p=0.44), F8 (p= 0.048), FZ (p=0.008) and CZ (p=0.05) channels of EEG in patients of temporal lobe epilepsy when compare with that of healthy control population.

Channels	Patients Mean (SD)	Controls Mean (SD)	p value
FP1	23.59 (4.767)	15.68 (9.79)	0.007*
FP2	31.66 (14.53)	20.43 (10.93)	0.019*
F3	22.96375(8.07)	19.573(8.41)	0.254
F4	20.392(8.488)	21.948(32.68)	0.855
C3	20.773(9.37)	19.74(13.26)	0.802
C4	23.786(9.569)	17.169(10.789)	0.076
P3	22.016(8.139)	23.93(18.480)	0.706
P4	24.586(9.332)	19.89(9.525)	0.17
O1	23.6(8.839)	18.09(7.158)	0.062
O2	24.49 (9.363)	18.30 (7.173)	0.044*
F7	16.68(8.891)	24.54(30.813)	0.335
F8	26.88 (7.726)	20.67 (9.225)	0.048*
T3	18.59(9.98)	16.99(9.371)	0.645
T4	22.684(8.925)	17.223(8.069)	0.079
T5	11.106(3.484)	12.693(4.467)	0.271
T6	11.94(3.118)	11.165(4.469)	0.57
Fz	21.98 (6.791)	14.06 (8.7.7)	0.008*
Cz	23.98(9.917)	17.191(8.99)	0.05*
Pz	22.050(8.554)	18.135(6.680)	0.159
Oz	10.118(3.851)	15.080(10.525)	0.087

Table I: Mean absolute spectralpower during eye close session in Delta band in EEG

Channels	Patients Mean (SD)	Controls Mean (SD)	p value
FP 1	13.34 (3.963)	6.878(5.065)	0.000*
FP2	15.01(4.571)	8.709(4.27)	0.000*
F3	12.85(4.464)	9.24(3.451)	0.016*
F4	10.63(5.572)	9.145(4.636)	0.638
C3	12.36(5.183)	9.28(3.211)	0.086
C4	13.78(5.596)	6.939(3.212)	0.000*
P3	12.59(4.125)	9.393(4.346)	0.035*
P4	14.62(4.6333)	9.556(3.857)	0.002*
O1	15.21(4.709)	9.456(3.37)	0.000*
O2	14.96(6.243)	10.04(3.53)	0.01*
F7	6.77(3.681)	10.25(8.61)	0.148
F8	13.07(4.079)	9.841(3.256)	0.006*
T3	10.75(4.400)	7.995(2.484)	0.037*
T4	13.05(3.744)	8.242(3.067)	0.000*
T5	3.788(1.349)	6.348(3.073)	0.005*
T6	4.074(1.423)	4.24(2.25)	0.798
Fz	13.33(3.77)	6.727(4.942)	0.000*
Cz	13.98(5.969)	9.409(5.117)	0.027*
Pz	13.43(5.179)	9.682(3.536)	0.023*
Oz	3.229(1.349)	5.943(2.947)	0.002*

Table II: Mean absolute spectral power during eye close session in theta band of EEG

Channels	Patients Mean (SD)	Controls Mean (SD)	p value
FP 1	7.967(2.116)	4.904(4.064)	0.012*
FP2	8.870(2.251)	6.765(3.936)	0.081
F3	7.948(3.080)	7.386(3.541)	0.635
F4	6.210(2.819)	6.707(7.051)	0.795
C3	8.085(3.772)	6.741(4.372)	0.359
C4	8.595(4.122)	5.294(2.87)	0.013*
P3	8.971(3.953)	8.219(5.24)	0.650
P4	10.455(3.16)	8.093(5.3114)	0.136
O1	13.198(5.04)	11.24(7.032)	0.374
O2	13.059(6.39)	13.425(7.10)	0.879
F7	4.57 (2.77)	8.551(5.653)	0.017*
F8	8.025(1.91)	7.474(3.322)	0.569
T3	6.60(2.47)	5.785(2.234)	0.331
T4	8.307(2.109)	6.208(3.198)	0.036*
T5	2.756(1.713)	5.868(4.447)	0.013*
T6	3.11(2.42)	3.923.307)	0.432
Fz	8.118(2.299)	5.16(4.894)	0.036*
Cz	8.96(4.53)	7.442(5.29)	0.388
Pz	9.853(4.59)	8.330(5.053)	0.379
Oz	1.907(0.862)	4.869(3.988)	0.006*

***Table III:* Mean absolute spectral power during eye close session in alpha band of EEG**

Channels	Patients Mean (SD)	Controls Mean (SD)	p value
FP 1	8.811(2.695)	4.458(2.476)	0.000*
FP2	10.73(3.727)	5.948(2.71)	0.000*
F3	9.458(3.871)	6.146(2.132)	0.005*
F4	7.814(0.333)	5.963(6.460)	0.334
C3	8.945(3.965)	5.989(2.702)	0.020*
C4	9.384(4.055)	5.104(2.522)	0.001*
P3	8.62(3.293)	6.485(3.113)	0.069
P4	9.578(3.384)	6.254(2.502)	0.004*
O1	10.24(3.088)	6.593(2.05)	0.000*
O2	10.05(3.747)	7.071(2.18)	0.010*
F7	5.918(3.364)	7.45(6.846)	0.428
F8	9.795(3.264)	6.467(2.17)	0.002*
T3	8.291(3.902)	5.766(2.313)	0.034*
T4	9.954(3.604)	6.083(1.964)	0.001*
T5	3.578(0.803)	4.521(1.868)	0.073
T6	3.9059(0.874)	3.425(1.551)	0.286
Fz	9.2(2.999)	4.388(2.575)	0.000*
Cz	9.918(4.368)	5.686(2.527)	0.002*
Pz	9.248(3.294)	5.934(1.885)	0.002*
Oz	3.248(1.451)	4.315(1.451)	0.143

Table IV: Mean absolute spectral power during eye close session of EEG in beta band

Channels	Patients Mean (SD)	Controls Mean (SD)	p value
FP 1	6.57(2.74)	3.978(2.111)	0.005*
FP2	9.214(4.689)	5.437(2.995)	0.011*
F3	7.391(4.320)	5.425(2.584)	0.129
F4	6.642(4.392)	5.652(6.714)	0.625
C3	6.964(4.551)	5.571(3.090)	0.319
C4	7.526(4.665)	4.669(2.956)	0.047*
P3	7.045(4.195)	6.10(3.811)	0.513
P4	7.64(4.562)	5.663(3.134)	0.163
O1	7.681(4.351)	5.34(2.034)	0.061
O2	7.925(4.583)	5.58(1.962)	0.071
F7	5.43(3.712)	6.747(7.753)	0.545
F8	8.300(4.156)	5.86(2.745)	0.060
T3	6.633(4.547)	5.038(2.639)	0.234
T4	7.641(4.464)	4.857(2.285)	0.034*
T5	3.261(1.335)	3.75(1.449)	0.329
T6	3.470(1.397)	3.313(1.436)	0.756
Fz	7.064(3.736)	3.961(2.265)	0.008*
Cz	7.584(4.621)	4.752(2.435)	0.038*
Pz	7.238(4.147)	4.979(1.952)	0.058
Oz	3.233(1.912)	4.250(2..623)	0.220

Table V: Mean absolute spectral power during eye closed session of EEG in gamma band

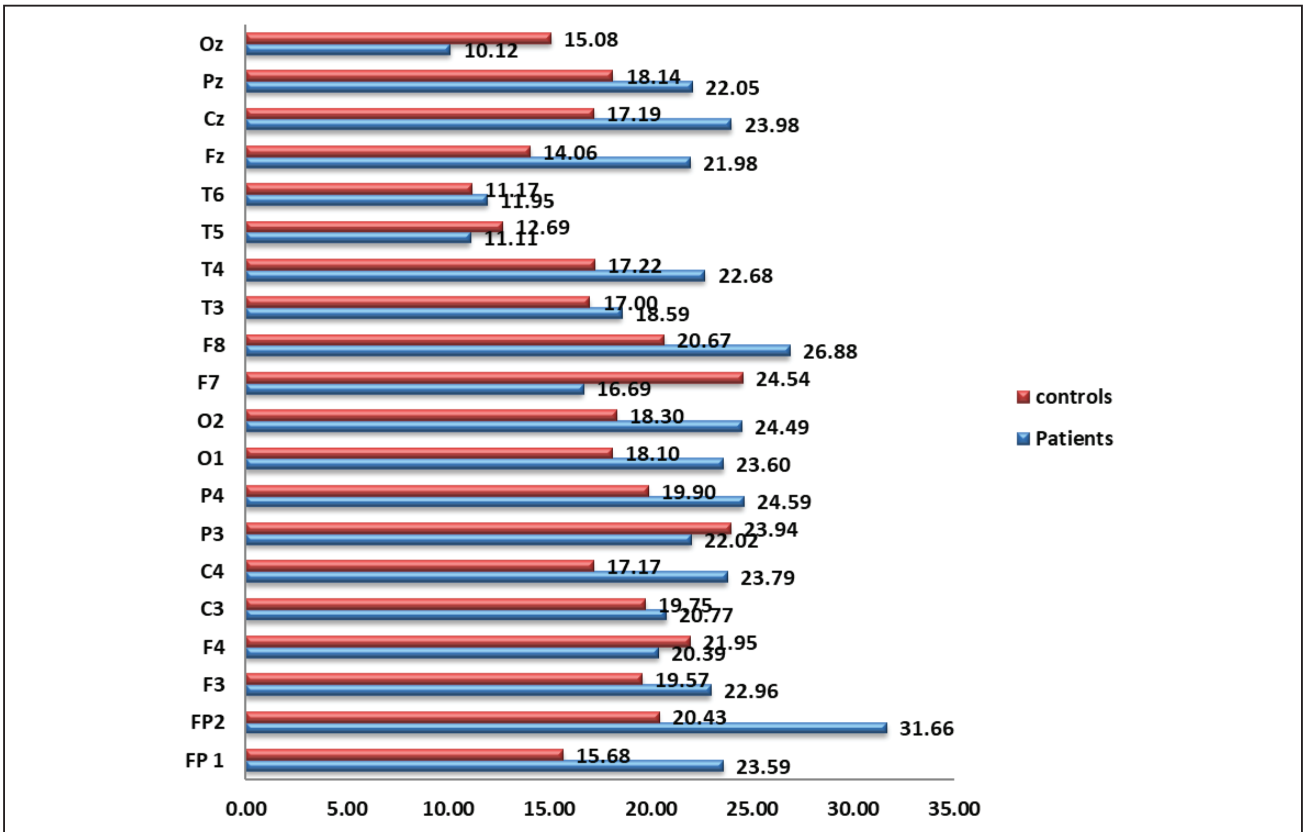

Figure 1: Mean absolute spectral power during eye close session in Delta band in EEG.

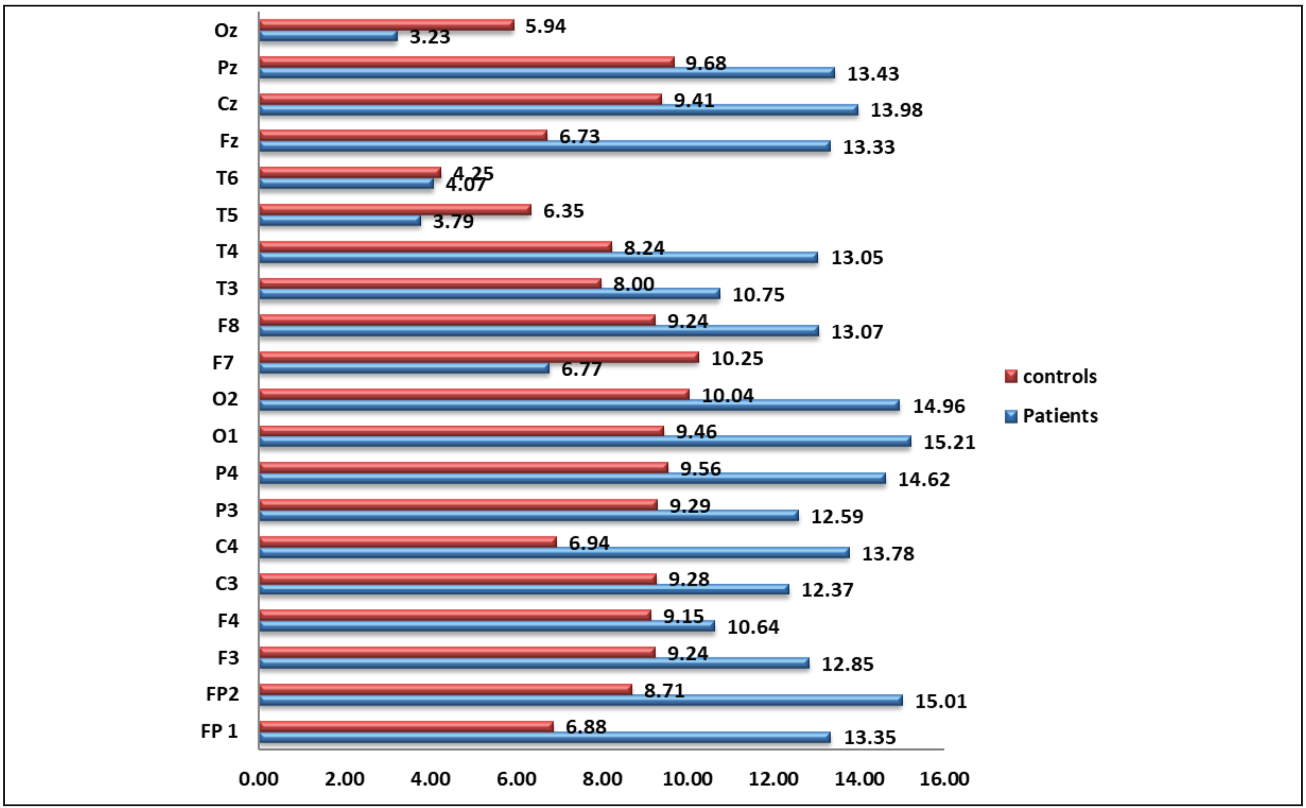

Figure 2: Absolute power of theta band in EEG during eye close session was significant observed in FP1 (p= 0.0004), FP2 (p= 0.0004), F3 (p= 0.016), C4 (p= 0.0002), P3 (p= 0.035), P4 (p= 0.0021), O1 (p= 0.0004), O2 (p= 0.0102), F8 (p= 0.006), T3 (p= 0.037), T4 (p= 0.0004), T5 (p=0.005), FZ(p= 0.0002), CZ (p= 0.0231), PZ (p= 0.02) and OZ (p= 0.002) channels of EEG in patients of temporal lobe epilepsy when compare with that of healthy control population (Table II; Figure 2)

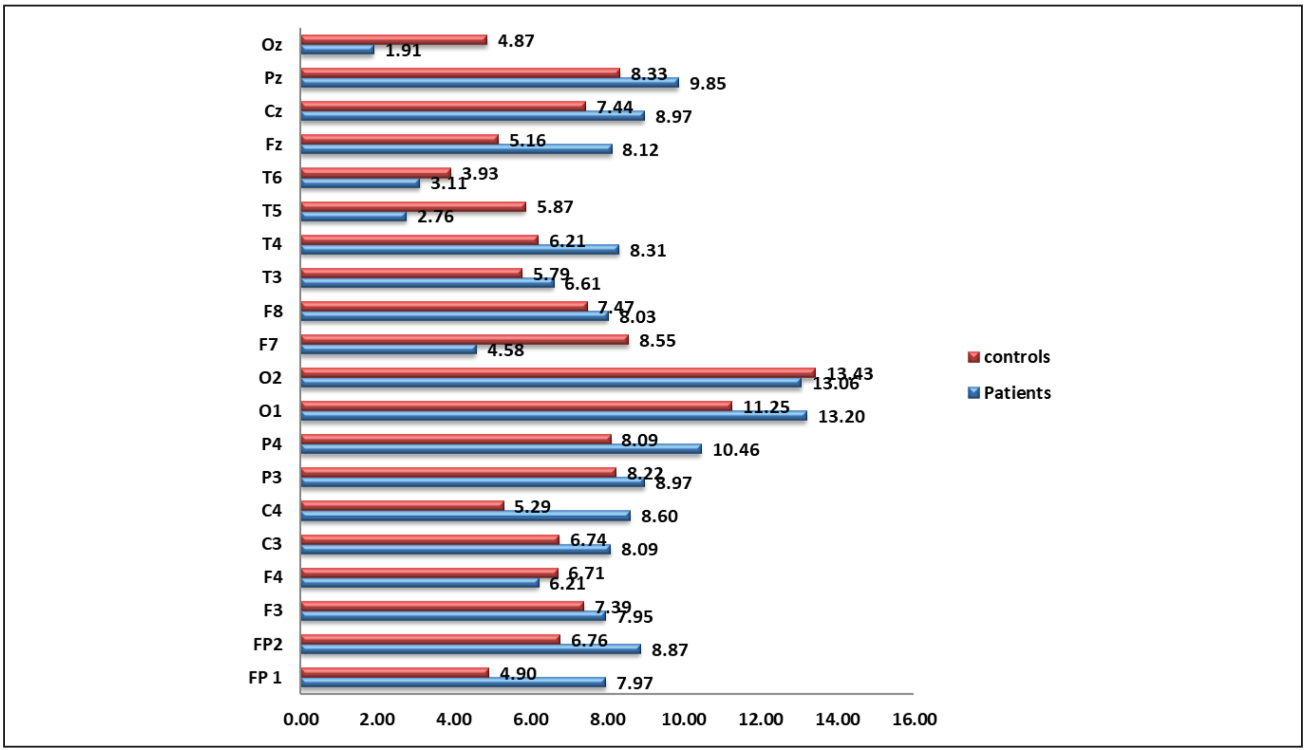

Figure 3: In alpha band of EEG the absolute power was significantly observed in FP1 (p= 0.012), C4 (p= 0.013), F7 (p= 0.017), T4 (p= 0.036), T5 (p= 0.0139), FZ (p= 0.036) and OZ (p= 0.006) channels of EEG in patients of temporal lobe epilepsy when compare with that of healthy control population (Table III; Figure 3)

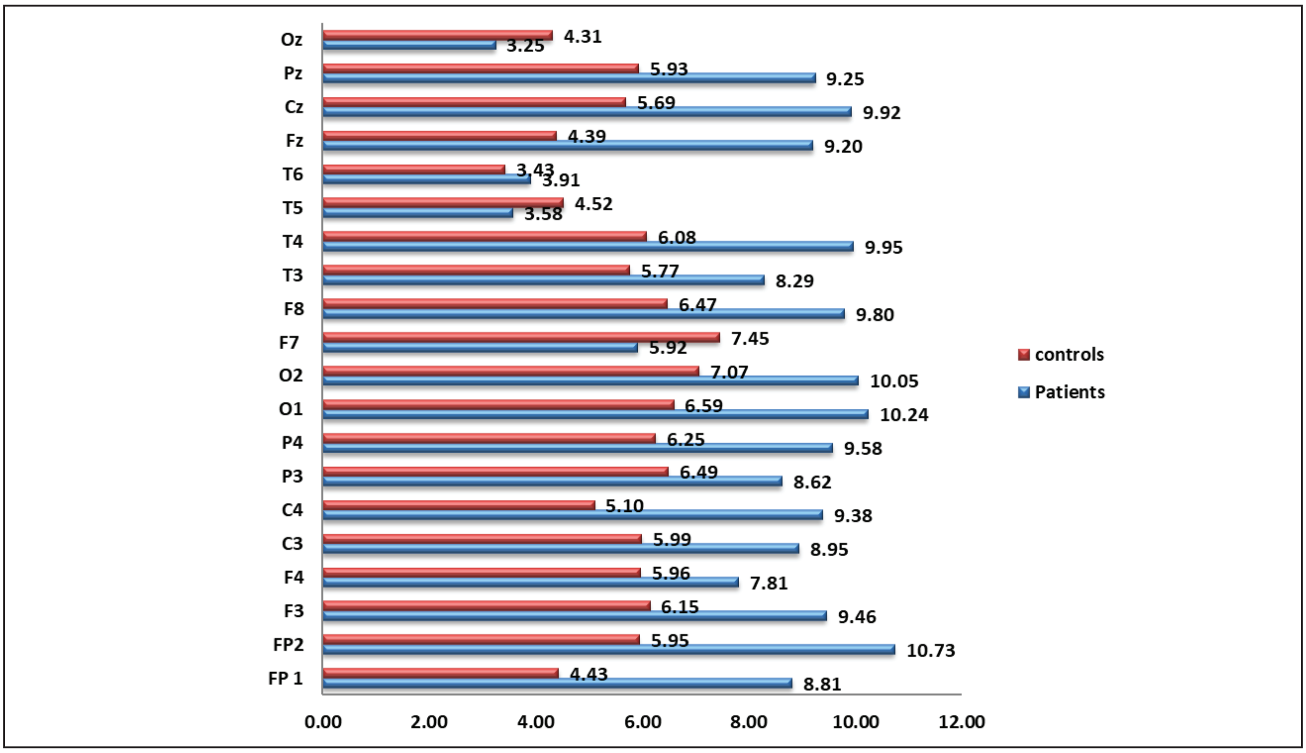

Figure 4: *The absolute power of EEG in different channels in beta band was significantly higher observed in FP1 (p= 0.0004), FP2 (p= 0.0003), F3 (p= 0.005), C3(p= 0.02), C4 (p= 0.001), P4 (p= 0.004), O1 (p= 0.0004), O2 (p= 0.01), F8 (p= 0.002), T3 (p= 0.034), T4 (p= 0.00007), FZ (p= 0.0003), CZ(p= 0.0002), PZ (p= 0.002) channels of EEG in patients of temporal lobe epilepsy when compare with that of healthy control population (Table IV; Figure 4)*

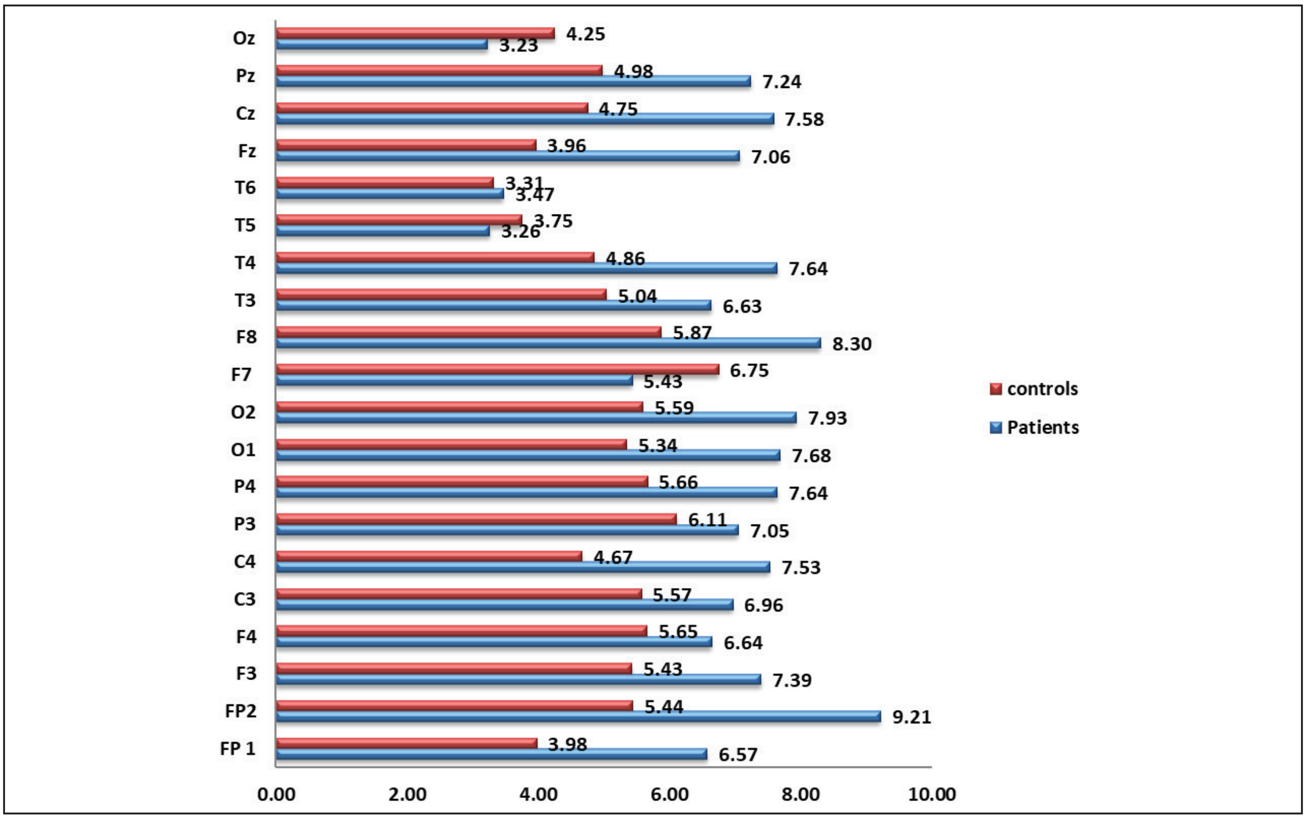

Figure 5: *The mean absolute power of gamma band was significant observed in FP1 (p= 0.0054), FP2 (p= 0.0109), C4 (p= 0.047), T4 (p= 0.034), FZ (p= 0.008) and CZ (p= 0.038) channels of EEG in patients of temporal lobe epilepsy when compare with that of healthy control population (Table V; Figure 5)*

Discussion

The significant difference was observed in TLE patients suffering from focal seizures. The results of power spectral analysis of different EEG waves (Delta, Theta, Alpha, Beta and Gamma) observed highly significant results mainly in low frequency wave mainly theta and high frequency wave beta during eye closed session.

Power Spectral Density (PSD) in low frequency EEG waves in focal epileptic patients (delta and theta) – According to our finding's delta wave was observed significant at frontal (FP1, FP2, F8, Fz), occipital (O2), central (Cz). No significant changes were observed at temporal regions of focal epileptic patients then controls. Theta wave of EEG was found more significant when compare to delta. Over 16 channels out of 20 were observed significant in focal epileptic patients in which topographically temporal regions was found maximum epileptic discharge (T3, T4, and T5). While other topographic regions like frontal (FP1, FP2, F3, F8, Fz), central (C4, Cz), parietal (P3, P4, Pz) and occipital (O1, O2, Oz) also showed significant results in TLE patients during interictal period then controls.

The present study findings are in accordance with Quraan et al [17] who also documented similar observations high Power Spectral Density (PSD) in theta band zone in TLE patients. Tuunainen et al,[7] who have also reported an increased absolute power in the theta band zone (lower frequency band). finding that is not in accordance with the results of Quraan et al [17] who documented an increase in PSD only in the alpha band frequency in fronto-central region of brain. Adebimpe found significant differences in terms of both spectral power and cortical source densities between controls and patients.[18] Patients were characterized by significantly increased absolute spectral power in θ, α, $β_1$ and $β_2$ bands in the right centrotemporal areas over the spike zone and in the right temporo-parieto-occipital junction.[18]

PSD in high frequency EEG waves in focal epileptic patients (alpha, beta and gamma) –

A less significant results were observed in alpha and gamma waves when compare to beta waves. PSD was observed highly significant in beta waves of EEG at frontal (FP1, FP2, F3, F8, Fz), occipital (O1, O2, Oz) and temporal regions (T3, T4) when compare with alpha and gamma waves. Although PSD was observed highly significant in alpha waves at temporal regions (T3, T4) which suggests that focal discharge occur in TLE patients who are suffering from focal seizures during interictal period when compare to healthy controls.

Similar findings were also observed by Clemens et al [19] documented significant increase in epileptic discharge at different topographical regions of brain. Drake et al [20] were demonstrated that temporal lobe epileptic patients with abnormal interictal EEG had decreased ratio of PSD in the high frequency wave zone to low frequency wave zone across the EEG leads in fronto-central and parieto-occipital region of brain.

Our findings are similar to some studies that we observed significant results by using Power spectral analysis (PSD) of EEG waves between focal patients who are on anti-epileptic drugs then controls. Several studies [21-25] have reported enhanced θ power in children with epilepsy, with and without medication in comparison to controls. It has been shown that the increased theta power in some cerebral regions is more pronounced in epileptic patients taking anti-epileptic drugs during eye closed sessions of electroencephalography. [26-27]

This paper highlights the general information regarding the use of scalp EEG in TLE, EEG patterns resembling epileptiform discharges, and the interictal findings in mesial temporal lobe epilepsy. The utility of the automated seizure detection and computerized mathematical models increasing yield of non-invasive localization

In presurgical evaluation of patients with TLE, the identification of seizure focus is the most important prerequisite for surgery. [28, 29, 30]

Lateralized focal or regional polymorphic delta activity is frequently found in TLE and is highly associated with temporal spiking. Koutroumanidis et al. correlated the interictal temporal delta activity in TLE with the pathology and surgical outcome. They reported lateralized slow activity in 66% of 141 patients who had temporal lobe resection for intractable partial seizures. The delta activity correlated well with the side of the temporal spikes. It provided additional information in 15%, in whom EEG did not show lateralized interictal spikes. The authors concluded that in patients with TLE, whose MRI was either normal or suggestive of HS, interictal temporal slow activity had a lateralizing value similar to that of temporal spiking and was significantly associated with favourable surgical outcome.[31]

The present study was so designed to get an insight into neural dynamics during the interictal phase of temporal lobe epileptic patients that could act as a window into the disease diagnostic process of temporal lobe epilepsy.

Conclusion

Dynamical analysis of EEG recordings from patients with epilepsy has provided novel perspectives regarding epileptogenesis. The application of linear analysis for detection of interictal discharge of epileptogenesis allowed obtaining information on scale free properties and modularity, which improve our understanding on brain mechanisms at the systems levels and the dysfunction in neurological diseases. In this light, linear analysis seems to be a potentially sensitive instrumentation marker of temporal lobe epilepsy (TLE) and needs to be clinically validated through replication in more such numerous and independent patient cohorts.

Limitations

The sample was small though the linear analysis (absolute spectral power analysis of EEG waves) in the present study needs to further validation in the field for confirmation of the final outcome and the conclusion of the signature of the disease process that has been so underscored and highlighted in the present study.

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