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Original Research Article

Neurodynamics of Temporal Lobe Epilepsy in Fronto-Central region of Cerebral Cortex

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Abstract: Temporal lobe Epileptic (TLE) seizures are preceded by changes in signal properties detectable by scalp EEG but our ability to understand brain dynamics associated with epilepsy remains limited. EEG-based epilepsy diagnosis and seizure detection is still in its early experimental stages. The problem is further amplified for the design and development of automated algorithms, which requires a quantitative parametric representation of the qualitative or visual aspect of the markers. The study was performed in Department of Physiology, SMS Medical College in collaboration with Department of Neurology and Medicine. Using EEG data from 16 controls and 16 temporal lobe epilepsy (TLE) patients, in this study we characterize how the dynamics of the healthy brain differ from the dynamically balanced state of the brain of epilepsy patients treated with anti-epileptic drugs in the context of resting state during eye close session. Such differences can be observed by using absolute spectral band power from BESS ((Brain Electro Scan Software) of the Axxonet System and network measures by applied unpaired student t -test. During eye close, fronto- central theta (p 0.0004), beta (p 0.00005) and gamma (p 0.0179), bands absolute spectral power found significant difference in temporal lobe epileptic patients during interictal period of epilepsy when compared with healthy controls. In conclusion we found that low frequency band mainly theta and high frequency band beta were more pronounced in fronto central region of brain in temporal lobe epileptic patients. Though frontal region is requisit to short-term memory so the patients of TLE may be suffer from memory dysfunction in future. Various linear and nonlinear analytical methods would be helpful in extracting information from EEG signals in diagnosing specific neuronal correlates for TLE.
Keywords: Absolute spectral power analysis, Dynamics of brain, EEG analysis, Neurodynamics**,** Temporal lobe epilepsy.

INTRODUCTION

The entity of epilepsy is found under many names in Ancient Greek texts namely, Seliniasmos, Sacred Disease, Herculean Disease (as it inflicted the Semi God, Hercules) or Demonism. The Greeks considered the disease to be sacred due to its esoteric and cryptic etiopathogenesis. The word “Epilepsy” has its composite origin from Anglo-French and Latin language. “Epilepsy” originates from Greek word ‘epilambanein’, which means to seize, posses, or afflict [1].

Epilepsy is a neurological disorder with a prevalence of about 1 – 2% [2]. It is a neurological condition that is characterized by sudden paroxysmal, recurrent and transient seizures (neuronal avalanche), the pathophysiology of which is exemplified by a synchronization of electrical activity with abnormal

bursts of electrical discharges of distributed cortical neuronal networks in space – phase of the respective neurophysiologically coupled neuronal pools by International League Against Epilepsy [3].The cause of epilepsy is usually idiopathic, though etiopathogenesis of epilepsy in some cases has been linked to genetic abnormalities [4], developmental anomalies [5], febrile convulsions [6], brain infections and craniofacial trauma [7], hypoxia [8], ischaemia [9] or tumors [10].

As per the World Health Organization, epilepsy is a treatable entity, leaving aside epilepsy of genetic abnormalities. Seizures can be controlled with medication in about 70 % of patients suffering from epilepsy [11].Many studies from India have given a prevalence rate of epilepsy in India as 5.59-10 per 1000 [12-15]. An epileptic seizure is due to abnormal, excessive and synchronous neuronal discharge in the brain [16]. Epilepsy can be classified as: Generalized epilepsy also known as primary generalized epilepsy or idiopathic epilepsy is characterized by generalized seizures with no apparent cause [17]. These are Tonic-clonic, Tonic seizures, Clonic type, Myoclonic seizures, Absence seizures, Atonic seizures, Partial or Temporal Lobe Epilepsy is a type of focal or partial epilepsy that originates in the medial or lateral aspect of the temporal lobe of brain [17]. Seizures which originate from temporal lobe are usually not managed of symptoms completely by the presently available anti – epileptic drugs [18]. Partial or Temporal Lobe Epilepsy is a type of focal or partial epilepsy that originates in the medial or lateral aspect of the temporal lobe of brain and classified in three types of seizures: simple partial seizures, complex partial seizures and secondarily generalized tonic clonic seizures [17]. Seizures which originate from temporal lobe are usually not managed of symptoms completely by the presently available anti – epileptic drugs [18]. In TLE, the seizures usually originate from the mesial – basal temporal lobe including hippocampus, amygdala and parahippocampalgyrus [19]. The hippocampal complex is responsible for genesis and evolution of memory [20] and subsequently dysfunctions in memory along the axes of genesis, evolution, and consolidation and retrieval complaints are commonly observed in such type of epilepsy**.** A correlation exists between the pathologic changes in hippocampus and temporal lobe epilepsy reported by [21]. Sufian *et al* [22] have reported pathologic changes in temporal lobe that mainly comprise of hippocampal sclerosis (HS), while other pathologies namely, malformative lesions, tumors, old traumatic injuries and inflammatory lesions have also observed.

EEG pattern in temporal lobe epilepsy

The interictal EEG has the potential to act as signature to the underlying dysfunctional neural dynamics that could be pathognomic to patients of epilepsy. EEG abnormalities present in the form of Interictal Epileptiform Discharge (IEDs), Focal-Slowing or Periodic- lateralized epileptiform discharge (PLEDs) and frontal intermittent rhythmic delta activity (FIRDA). IEDs and PLEDs has been reported to be associated with epilepsy [23]. The EEG findings in TLE in the interictal phase could exhibit, unilateral or bilateral slowing of cerebral activity in the temporal lobe channels or unilateral or bilateral epileptiform spikes, sharp waves and /or slow waves. During seizure, ictal EEG activity may begin at a time of onset of aura before a fully evolved complex partial seizure reflected as neuronal avalanche on the EEG time – series [24, 25].

Non – Linear Dynamics of EEG

EEG is a signature of underlying neural dynamics in health and disease states. It is widely accepted that EEG analysis could be employed for early detection of varied dysfunctions of the human brain such as depression, epilepsy, autism and Alzheimer [26]. The human mind, the neurophysiological correlate of human brain, observes and obeys the principles of chaos with stochastic trajectory sub-serving a particular defined function [27].The present study has been undertaken to assess the underlying neural dynamics of the human mind patients of Temporal Lobe Epilepsy in basal rested state.

MATERIAL AND METHODS

The study was conducted in the Department of Physiology in collaboration with Department of Neurology and Medicine of SMS Medical College and attached Hospitals, Jaipur. The present study duely approved by the institutional Ethical committee and the subjects who participated in the study gave written informed conscent before participating in the study. The present study included 16 diagnosed temporal lobe epileptic patients, on the basis of Magnetic Resonance (MR) Protocol and Electroencephalography (EEG) findings, who were suffering from complex partial seizures, from the outdoor of Neurology department of SMS hospital, Jaipur and 16 age and sex matched healthy controls. The study included confirmed patients

of temporal lobe epilepsy that undergo temporal lobe MR Protocol of the brain and Electroencephalography.

Sample Size: The sample size required is 16 in each group at 95% confidence and 80% power to verify the expected minimum difference of 0.66 [± 0.64] [28] mean working memory task score of temporal lobe epileptic cases and age and sex matched healthy controls.

Inclusion Criteria adopted for the present study would be:

- Patients between 20 – 30 yrs.
- Patients with epilepsy satisfying the guidelines lay down by the International League Epilepsy Society.
- Patients in interictal period of epilepsy.

Exclusion Criteria for the study where in the subjects would not form part of the study:

- Patients with known contraindications to Temporal Lobe MR Protocol epilepsy.
- Any previously diagnosed non central nervous system disorders liable to cause seizures.
- Syncope and hypoglycemic attacks, pseudo- seizures or drug induced seizures.
- Patients presenting with head injury.
- Patients with malignancy, previous craniotomy or cervical spine surgery.
- Patients with Cardiopulmonary or cereberovascular disease.

EEG recording

In the present study, 21 channels scalp electroencephalography was done according to International 10-20 system with biauricular reference [29]. Electrode impedence was kept <5kΩ electrical activities, amplified with a band pass filter of 0.5-30.0 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 [30].

EEG was recorded from frontal (Fz/ Fp1/ Fp2, F3/F4, F7/F8), and Central (C3/C4/ Cz) region of brain for analysis of neurodynamics of 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 in the Neurophysiology Lab of Department of Physiology. The unpaired t-test was used for the mean comparison of all parameters between patients and control subjects and with intension we considered two-sided p values < 0.05 to be significant.

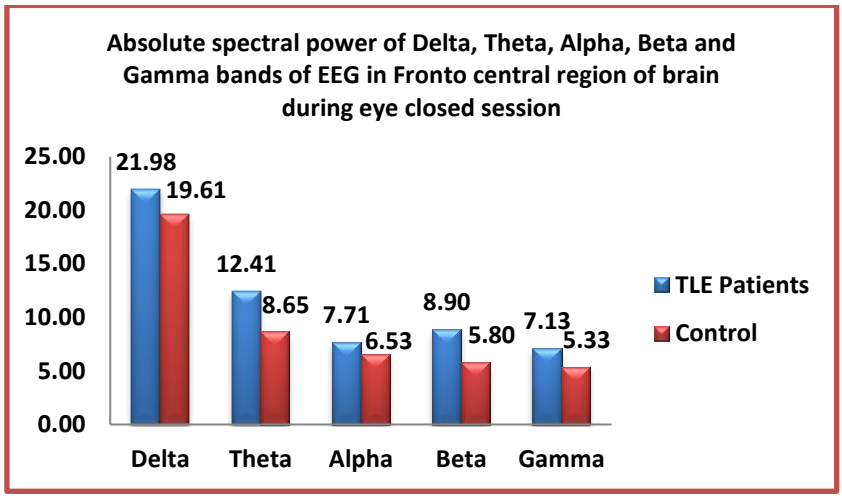
Observations and results

Table-1: Socio demographic variables

Demographic and clinical Variables		Patient (N=16)	Control (N=16)	p-value
Gender	Male	13	14	0.625
	Female	3	2	
Age	Mean	24.19	25.38	0.321
	SD	2.926	3.686	
Residence	Urban	10	12	0.441
	Rural	6	4	
Dietary Habits	Vegetarian	11	7	0.141
	Non- Vegetarian	5	9	

Table-2: Absolute spectral power in fronto- central region of brain during eye close session

EEG Bands	Patients Mean (SD)	Controls Mean (SD)	p- value
Delta	21.979(8.789)	19.608(18.537)	0.3572
Theta	12.406(5.226)	8.65(6.440)	0.0004
Alpha	7.709(3.522)	6.532(4.683)	0.1105
Beta	8.900(3.904)	5.800(3.800)	0.00001
Gamma	7.131(4.390)	5.329(4.102)	0.0179



Graph-1: Mean Absolute spectral power in delta, theta, alpha, beta and gamma bands of EEG in fronto-central region (F3, F4, C3, C4) of brain

RESULTS:

Table 1 is related to socio-demographic and clinical characteristics of 16 diagnosed temporal lobe epilepsy patients suffering from complex partial seizures and 16 healthy controls. The mean age of Temporal lobe epileptic patients and healthy controls was non-significant (p 0.321). The gender distribution between patients and controls was non-significant with probability as (p 0.625). In relation to residence and dietary habits was also found non-significant in the present study (p 0.441 and p 0.141 respectively) in both patients and healthy controls. Positive family history was not found in both the groups.

During eye close, fronto- central theta (p 0.0004), beta (p 0.00005) and gamma (p 0.0179), bands absolute spectral power found significant difference in temporal lobe epileptic patients during interictal period of epilepsy when compared with healthy controls (Table: 2).

Graph 2 represents that theta band and beta band of EEG shown maximum significant absolute spectrum.

DISCUSSION

Spectral power from EEG signals is generally difficult to quantify at low and high frequencies due to ocular and muscle artefacts in these regions. Signals from ocular artefacts are orders of magnitude higher than neural signals and result in a sharp rise in spectral power at low frequencies like theta band (**p0.0004**) mainly but beta band (**p 0.000**)also represents a highly significant difference on patients of temporal lobe epilepsy when compare with healthy controls. It seems that in the neurodynamics of frontal and central region of brain in temporal lobe epileptic patients shows more spontaneously and high synschronization.

The Human Brain and the Human Mind are two separate entities that have baffled and mystified mankind since times immemorial. The Human Brain is the morphological or structural precept of the Central Nervous System and the Human Mind represents the working vignette of the structural moiety in real – time mental phase space characterized by a specific stochastic trajectory sub serving a precept specific to a mental function.

The EEG can be conceptualized as a series of numerical representation of numerical activity (voltages) over time. Such a series is called a “the EEG time series”. The standard methods for time series analysis (e.g. power analysis, linear orthogonal transforms, and parametric linear modeling) not only fail to detect the critical features of a time series generated by an autonomous (no external input) nonlinear system, but may falsely suggest that most of the series is random noise [31].

Dynamical analysis of EEG recordings from patients with epilepsy has provided novel perspectives regarding epileptogenesis. Some of the studies have provided evidence that epileptic seizures represent a nonlinear chaotic process [32]. Adebimpe et al [33] found significant differences in terms of both spectral power and cortical source densities were observed between controls and patients. Patients were characterized by significantly increased relative 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.

Present studyfound significant increases in absolute θ power in all brain regions especially in the epileptogenic zone in the centro-temporal region in comparison to healthy controls. Meanwhile, some study [34] found the θ power decreased in frontal and occipital regions in comparison to central region of epileptic patients. This observation is consistent with results from other studies conducted on Temporal Lobe Epileptic patients (TLE). Several studies [35- 37] have reported enhanced θ power in children with epilepsy with and without medication in comparison to controls [38]. However, it has been shown that the increased theta power in some cerebral regions is more pronounced in epileptic patients taking anti-epileptic drugs [39- 42].

Temporal lobe epilepsy is a condition characterized by recurrent seizures originating from the medial or lateral temporal lobe. Medial Temporal Lobe epilepsy (MTLE) arises in the hippocampus, parahippocampus gyrus and amygdale whereas lateral temporal lobe epilepsy (LTLE) arises in neocortex on the outer surface of the temporal lobe of the brain. About 40 % to 80% of people with TLE also perform repetitive, automatic movement (automatisms), such as lip smacking and rubbing the hands together [43].

The most common lesional abnormality identified in patients with TLE is the hippocampal sclerosis (HS) [44]. It is characterized by severe loss of the principal neurons associated with widening of the granule cell layer of the dentate gyrus, termed granule cell dispersion (GCD), which is observed in about 40%-50% of surgical temporal lobe specimens [45, 46].EEGs are widely being used to investigate different types of seizures, sleep disorders, neurodegenerative diseases, head injuries, tumors, and infections. It can confirm brain death in a comatose patient. Though EEG technology is considered relatively "primitive" and has limited spatial resolution compared to other techniques but still has benefits of being a non-invasive, safe, and low-cost method of neuroimaging, providing a valuable tool for neurodiagnostic [47]. Due to the small sample size (patients, n= 16 and controls, n = 16), however, we emphasize that the generalization of our findings remains to be established by future work.

CONCLUSION

Despite since many years our knowledge regarding brain dynamics is still limited. According to

present findings low frequency band theta had been observed more significant in fronto central region of brain in patients of Temporal lobe epilepsy. These findings encourage further investigation into the impact of neuro-dynamics of human mind on the resting state networks in temporal lobe epileptic patients.

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