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EEG patterns in temporal lobe epileptic patients during working memory task

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Abstract

Various studies of memory-impaired patients with medial temporal lobe (MTL) damage led to the view that the hippocampus and related MTL structures are in immediate memory and working memory are independent of these structures. This traditional idea has recently been revisited. The study was performed in Department of Physiology, SMS Medical College in collaboration with Department of Neurology and Medicine. EEG data from 16 controls and 16 diagnosed temporal lobe epilepsy (TLE) patients were included characterize how 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 working memory task. 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 and a working memory task could be run to access the score of memory in temporal region. Significant value < 0.05 are considered. Temporal alpha (p 0.0225) and beta (p 0.009) bands absolute spectral power was significant found in patients of temporal lobe epileptic patients when compare with healthy controls. We do not found any significant difference between TLE patients and healthy controls during working memory task score. Medial Temporal lobe is related to working memory. Pathophysiology of temporal lobe in temporal lobe epilepsy causes memory impairment. The most parsimonious and consistent interpretation of are the data are supported that working memory are independent of the MTL, though EEG findngs shown increased alpha and beta activity in temporal region.

Keywords: EEG power spectrum, Epilepsy, Working Memory, Temporal lobe epilepsy

Introduction

Epilepsy is characterized by recurrence of seizures at evenly or oddly placed intervals. The epileptic seizures are episodes which can vary from brief and nearly undetectable episodes to long periods of vigorous self – evident shaking [1].

Epilepsy is a chronic disorder of the brain that affects 2% people worldwide. It is characterized by recurrent seizures, which are brief episodes of involuntary movements that may involve a part of the brain (*Partial*) or the entire cerebral hemosphere

(*Generalized*), and are sometimes accompanied by loss of consciousness [2].
Epilepsy was redefined conceptually in 2005, as a disorder of brain characterized by an enduring predisposition to generate seizures [3]. The International League Against Epilepsy [4] accepted the practical definition for special circumstances that do not meet the two unprovoked seizures criteria in task force. "The task force proposed that epilepsy be considered to be a disease of the brain defined by any of the following conditions: (1) At least two unprovoked (or reflex) seizures occurring >24 h apart; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; (3) diagnosis of an epilepsy syndrome."
Gottfried et al in 1805 documented the fact that Atreya way back in the sixth century B.C. (CharakaSamhita) had attributed the phenomenon of *epilepsy* arising due to dysfunctional operative mechanisms of the brain. In CharakaSamhita Sutra (6^{th} century B.C.), Atreya had defined epilepsy as [5], "Paroxysmal loss of consciousness due to disturbance of memory and understanding of mind attented with convulsive seizure".
In epileptic patients who are refractory to standard treatment of antiepileptics and/or surgery may respond to neurostimulation or ketogenicdietary changes that are of another accepted modality of management of epilepsy influencing the disease profile and course of epilepsies [6]. It has been observed that ketogenic diet has a beneficial effect on reducing the intensity and frequency of epileptic seizures in some patients [7].
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 [4]. Seizures which originate from temporal lobe are usually not managed of symptoms completely by the presently available anti – epileptic drugs [8] and surgical resection still remains a viable alternate treatment option for focal epilepsy. In TLE, the seizures usually originate from the mesial – basal temporal lobe including hippocampus, amygdala and parahippocampalgyrus [9]. The hippocampal complex is responsible for genesis and evolution of memory [10] and subsequently dysfunctions in memory along the axes of genesis, evolution, and consolidation and retrieval complaints are commonly observed in such type of epilepsy. The designate memory dysfunctions are dependent on laterality of the epileptic focus
[11], in which verbal episodic memory deficit (less consistently) occur in left temporal lobe epilepsy, and right TLE affects non-verbal memory [12]. The temporal lobe epilepsy has been classified by ILAE [13] as mesial temporal lobe epilepsy (mTLE) and lateral temporal lobe epilepsy, the features of which have been designated as:

1) Mesial Temporal Lobe Epilepsy (mTLE): It arises from the medial part of temporal lobe like hippocampus, parahippocampousgyrus and amagdala.
2) Lateral Temporal Lobe Epilepsy (LTLE): It is rarest type of epilepsy which arises in the neocortex at the outer surface of the temporal lobe [14].

Memory dysfunction is the primary feature that is particularly related to temporal lobe epilepsy (TLE), in which memory related brain structures including hippocampus are directly influenced by seizure activity [12]. Some studies have shown that verbal memory deficit has been primarily observed in patients with left TLE and patients diagnosed as suffering from right TLE have nonverbal type of memory dysfunction [15] or visual memory impairment [16].
Neuronal structures/substrates responsible for declarative memories are situated in mesial temporal lobe (MTL) that is composed of neocortical structures of

hippocampal formation (CA fields, dentate gyrus and subiculum) and amygdala [17] and subcortical parts which include perirhinal, entorhinal and parahippocampal cortices. Destruction, inactivation or surgical removal of MTL due to accidents, injury or stroke results in severe anterograde amnesia, which is manifested by profound forgetfulness [18]. The loss of parts of MTL causes temporally graded retrograde amnesia and such types of memory loss could range up to 15 years in time in humans as reported by [18, 19].

There is much evidence to suggest the MTL is independent of WM function [20, 21], proposing that damage to the MTL impairs WM performance only when the task depends more on long-term memory processes [22]. In contrast, several imaging studies have found hippocampal activation in WM tasks during encoding [23, 24]maintenance [25] and retrieval [26].

The present research has been designed to explore and assess the neural underpinnings of the esoteric phenomenon of *memory* in particular reference to the disease process of epileptic seizures originating from temporal lobe in order to gain insight into the singularity of *memory*. *Memory* forms the quintessence of the working human mind in real – time, the neural correlates of which could be evinced through non – invasive and invasive techniques and/or investigative tools. Electroencephalography (EEG) happens to be one such non – invasive investigative tool that gives an insight into the neural underpinnings of the human mind with a high degree of temporal resolution. In this backdrop, the present study was undertaken for a better understanding and appreciation of the neuro-physiological actuality and nonpareil of *memory* with particular referential system of patients with temporal lobe epilepsy.

Materials 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] [27], 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 [28]. 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 [29].

EEG was recorded fromTemporal region (T3, T4, T5, T6)of brain for analysis of neurodynamics of brain during working memory task with EEG.

Data Aquisition

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 working memory task. 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.

Working Memory Task

The neuropsychological test used in the present studyL B Memory Test.

LB-Memory Test is based on the computerised administration of standardised sequentially-ordered, auditory, verbal, free recall tasks. The method we propose describes organizational processes underlying memory search and retrieval. Specifically, it adopts a decomposition technique to evaluate distinct contributions of list structure and context on different components of recall.

This Memory task involved (named as: List A, List B, and List C) the sequential acquisition and immediate recall of 3 word lists. List A consists of 18 semantically unrelated items; whereas Lists B and C present 18 semantically-related items, equally distributed across 3 different mutually-exclusive taxonomic categories, 6 items for each category. During experimental testing, List B semantic structure is kept latent to subjects; differently, prompts are given to make the structure of List C explicit to subjects before acquisition.

The method provides measures of recall accuracy (Correct recalls and Intrusions), organization (Serial Position Analysis and Clustering Indexes), and time latency to response (by single item and by list total recall time).

The automatic scoring system provides the profile of results for each subject. Test administration takes 4-5 minutes. Its use of a computer as an expert system maximizes standardization and ease of administration, data collection, and analysis.

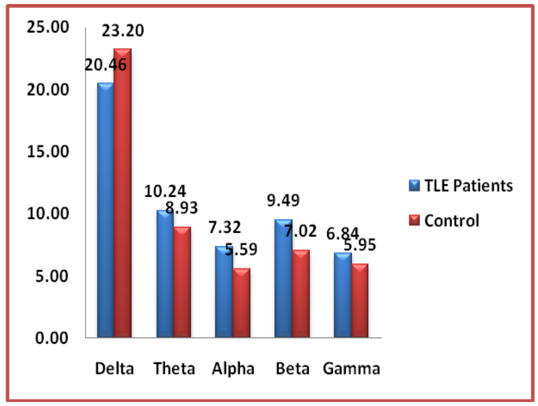
Statistical Analysis

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.

Results

Table 1 shown socio-demographic and clinical characteristic 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.

Table 2 During working memory task session of EEG, temporal alpha (p 0.0225) and beta (p 0.009) bands absolute spectral power was significant found in patients of temporal lobe epileptic patients when compare with healthy controls as shown in graph 1.



Graph 1: Represents absolute spectral power of delta, theta, alpha, beta and gamma bands of EEG in Temporal region of brain during working memory task.

Table 1: Socio demographic variables.

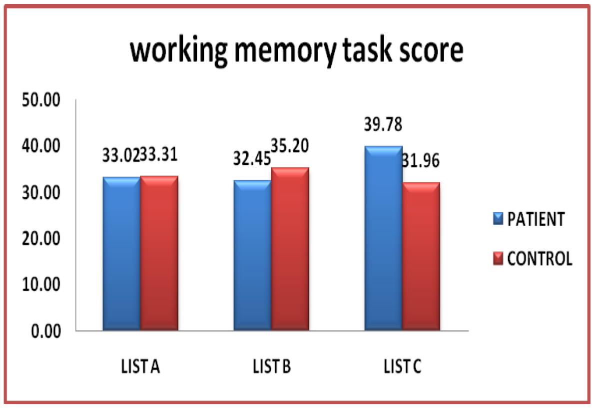
Demographic and clinical Variables		**Patient (N=16)**	**Control (N=16)**	**p-value**
Gender	Male	13	14	0.625
	Female	3	2	
Age	Mean	24.19	25.38	0.321
	SD	2.926	3.686	
Residence	Urban	10	12	0.441
	Rural	6	4	
Dietary Habits	Vegetarian	11	7	0.141
	Non- Vegetarian	5	9	

Table 2: Absolute Spectral Power of delta, theta, alpha, beta and gamma bands in temporal- region (T3, T4, T5, T6)during working memory task session.

EEG Bands	**TLE Patients**	**Controls**	**p value**
Delta	20.455(8.26)	23.197(12.40)	0.1437
Theta	10.238(7.005)	8.92(4.35)	0.2058
Alpha	7.321(5.246)	5.587(2.923)	**0.0225***
Beta	9.493(6.674)	7.024(3.52)	**0.01***
Gamma	6.843(4.14)	5.954(3.361)	0.1849

Table 3: Working Memory Task Score in patients of temporal lobe epilepsy patients and healthy controls.

Working Memory Task Score					
Lists	**Control(16)**		**Patient(16)**		**p value**
	Mean	**SD**	**Mean**	**SD**	
List A	33.31	12.085	33.02	18.491	0.958
List B	35.20	12.372	32.45	15.910	0.589
List C	31.96	11.334	39.78	9.536	0.326



Graph 2: Working memory task score represents Mean (SD) between patients of temporal lobe epilepsy and healthy controls.

Table 3 In present study working (verbal) memory task was done during EEG. In this task temporal lobe epileptic patients memory score was compared with healthy controls. In our findings we do not found any significant difference between TLE patients and healthy controls

In the present study we perform verbal memory task during continuous EEG session in 16 complex partial epileptic patients and 16 healthy controls. In the task, there are 3 list each having 18 words. List A contain words which are unfamiliar, list B contain words in which two words are similar, and in list C there are three similar words in them. We compare the results by using student's t- test among patient and controls and we found no any significant difference between them as shown in Table 3 and graphical representation is shown in graph 2.

Discussion

In present study during working memory task run with continuous EEG, the alpha and beta band discharge was more significant in temporal region of brain. Its seems that as temporal lobe mainly medial temporal lobe is related to memory retrieval, memory, encoding and memory consolidation, so as the high frequency bands shows more discharge synchronously.

Alpha wave has been thought to indicate both a relaxed and awareness stage without any attention or concentration. It is reduced or eliminated by opening the eyes, by having unfamiliar sounds, anxiety, or mental attention [30]. But in present study in due to mental attention it was found significant in our findings. Beta band dominating over frontal and central region. It has been observed to appear during active thinking, active attention, and focus on the outside world and is usually the waking EEG rhythm of brain associated with normal waking consciousness. In panic state a high level beta wave may be observed [30], so as per our findings Beta band found significant.

Memory is a super ordinate concept referring to different mnemonic systems [31]. In the memory processing the medial temporal lobe and medial diencephalon (hippocampus and mammilary bodies), have been implicated [32]. The importance of signal input from hippocampus to mammilary body was proposed and confirmed by Papez (1937) in a model concerning emotion [33].

A well organized signal transmission between medial temporal lobe, diencephalic structures and neocortex is involved in the generation of the declarative memory. The parts of medial temporal lobe involved in this process are hippocampus, entorhinal cortex, parahippocampal cortex and the perirhinal cortex. These structures have widespread and reciprocal connections with cortical association areas which are crucial for the rapid acquisition of new information and for forming conjunctions between different stimuli and thus establishing declarative memory. It has been suggested that the capacity for later retrieval is achieved because the hippocampal system has bound together the relevant cortical sites that together represent memory for a whole event. Hippocampal system bounds the associated cortical areas together for the later retrieval of memory. These medial temporal lobe structures are often involved in partial epilepsy focal disorders affecting the declarative memory [34].

Hippocampal damage also highlighted the regional brain damage in limbic structures in medial temporal lobe epilepsy (MTLE) particularly which are related to hippocampus [35]. MTLE is a disease that affect not only the hippocampus but also involve a network of interrelated structures such as the entorhinal and perirhinal cortices [36], thalamus [37, 38], anterior cingulated [39] and cortical association areas [40].

Despres et al [41]assessed 30 patients with unilateral TLE (17 right TLE and 13 left TLE) on memory task and they found postoperative memory improvement in patients with temporal lobe epilepsy. Saling [42] concluded that perirhinal cortex is a key mode in a more extensive network mediating protosemantic associative memory and impairment in fundamental memory system is a proximal neurocognitive marker of medial temporal epileptogenesis.

Working memory (WM) refers to the temporary storage and manipulation of information, and is vital for daily life functioning [43]. Temporal Lobe Epilepsy (TLE) with unilateral hippocampal sclerosis (HS) is associated with significant impairment of the formation and storage of long-term memories [44]. In contrast, WM has traditionally been considered to be unaffected by medial temporal lobe (MTL) damage [45].

Disruption of WM in TLE may be a result of critical MTL involvement in WM processes [46], or it may be secondary to propagation of epileptic activity from the epileptogenic zone to eloquent cortex responsible for WM function [47]. This suggests that the classical functional–anatomical distinctions between long-term memory and WM need to be revised [48], and that the cognitive impact of TLE extends beyond episodic memory systems. 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. 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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