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EEG Pattern in Alzheimer's Disease at Resting Condition

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ABSTRACT
The aim of present Electroencephalography (EEG) study was to investigate the role of absolute power to discriminate Alzheimer's disease patient and normal elderly subjects. EEG was recorded at rest in age-sex matched 30 normal elderly subjects and 20 amnesic Alzheimer's disease patients (55-75 years) for Mini Mental State Examination. The EEG bands so evaluated were delta (0.2-3.9 Hz), theta (4.0-7.9 Hz), alpha (8.1- 12.9 Hz), beta (13.0 -30.0 Hz) and gamma (30.1-80 Hz). A significant decrease MMSE score was observed in patients when compared to controls (p=0.000). Amnesic Alzheimer's patients showed significant (p=0.001) increased delta absolute power in fronto-central and parieto-occipital region of the brain. Theta bands tended to increased (p=0.000) absolute power in parieto-occipital region in Amnesic Alzheimer's patients. Significant decreased (p=0.000) alpha, beta and gamma absolute power were observed in both fronto-central and parieto-occipital region of the brain in Amnesic Alzheimer's patients. These results suggest that absolute power can discriminate Amnesic Alzheimer's patients from normal elderly subjects.
Keywords*: Amnesic Alzheimer's patients, Electroencephalography (EEG), Mini Mental State Examination.*

INTRODUCTION

The German Physician, Alois Alzheimer (in 1906) was the first to profile and define the clinical entity of Alzheimer's disease as a form of dementia way. Clinically diagnosed Alzheimer's disease, alone or in combination with other illness, accounts for up to 90% of reported dementia cases in the west [1]. Incidence rate of Alzheimer' disease was 9.19 (9.03-9.35) per 1000 person-years, reported from southern India [2].The pathophysiology of Alzheimer's disease has been hypothesized and documented to be dysfunction of synaptic mechanisms with loss of functional neuronal pools. The features of Alzheimer disease are progressive deficits in memory and other aspects of cognition. Due to the deficits, patients with Alzheimer disease are unable to perform their daily course, leading to total dependence on their caregivers[3]. The DSM-IV-TR (American Psychiatric Association 2000) has laid down criteria for diagnosis of Alzheimer's disease which include impairment in memory, orientation, language, visual processing, executive function and praxis.

The Mini Mental State Examination (MMSE) [4] is used as a questionnaire - based tool that is employed to evaluate the cognitive profile of a subject/patient in clinical practice and helps in the determination of severity of dementia. Neuritic plaques and neurofibrillary tangles are the most important and characteristic pathognomic features in patients of Alzheimer's disease. Neuritic plaques are extracellular and microscopic, consisting of abnormal proteinaceous material known as amyloid beta that shows cross β – sheet structure [3]. Oligomers of amyloid beta (Aβ) cause synaptic loss by inducing metabolic and morphologic changes in pyramidal neurons of the hippocampus and neo-cortex that lead to cognitive decline in symptom complex of Alzheimer's disease [5]. Early onset of familial Alzheimer's disease prior to age 55 years, occurs in <5% cases, who follow an inheritance pattern with mutations in the amyloid precursor protein gene (APP) on chromosome 21q [6], in the presenilin 1 gene (PSEN 1) on chromosome 14q, and the presenilin 2 gene (PSEN 2, a homolog of PSEN 1) located on chromosome 1q [7]. These mutations cause excess production of Aβ [8, 9]. In Alzheimer's disease neurochemical abnormalities have been observed with respect to changing concentration of various neurotransmitters found in central nervous system. Acetylcholine is a neurotransmitter that has been implicated in cognitive neurophysiology and severity of the diseases has been observed to be correlated with the loss of cerebral cortical markers for acetylcholine metabolism [10].

EEG provides insight about neuronal functioning and seemingly represents the functioning of the human mind in real-time by representing the summated and synthesised electrical signals originating from various regions of the brain. Electrical brain activity has been described following a wave pattern consisting of different types of frequency bands, namely delta (0-4 Hz), theta (4-8 Hz), alpha (8-13Hz), beta (13-30 Hz) and gamma (30-50Hz) waves [11].In this context the present study was undertaken to explore neural dynamics as patterned through EEG rhythm and to appreciate an insight into the functioning of human mind in relation to cognitive decline.

MATERIALS AND METHODS

The study was conducted in the Department of Physiology in association with the Department of Neurology, S.M.S. Medical College, Jaipur and the Department of Neurosciences (Cognitive Function Section), Santokaba Durlabhji Memorial Hospital (SDMH), Jaipur. The study design was a hospital based observational case - control study. All experimental protocols had been approved by the Institutional Ethics Committee. Thirty healthy controls and twenty Amnesic Alzheimer's disease patients were enrolled in the present study. The Alzheimer's patients were recruited from the O.P.D. of Neurology, S.M.S. Medical College, Jaipur and the Department of Neurosciences (Cognitive Function Section), SDMH, Jaipur. All patients underwent history taking, physical and neurological examination, psychometric testing and neuroimaging procedures (magnetic resonance imaging, MRI with temporal lobe protocol of the brain) and laboratory testing to rule out other causes of cognitive impairment. The control group for study was composed of age and sex matched healthy subjects from the Institute.

The inclusion criteria adopted for the present study were: patients between 55 – 75 yrs., complaint by the patient, or report by a relative or the general practitioner of memory or other cognitive disturbances; patients rated and categorized with the standardized diagnostic and severity instrument of MMSE [4]. Patient with frontotemporal dementia, vascular dementia based on clinical and radiological grounds, extrapyr-amidal syndrome, psychiatric diseases, epilepsy, drug addiction, alcohol dependence, current or previous uncontrolled systemic diseases, traumatic brain injuries were excluded for the study.

EEG recordings

The EEG activity was recorded, continuously by using electrodes set in an elastic cap (Electro - Cap International,) and positioned according to

the 10–20 international system (Fp1, Fp2, Fz, F3, F4, F7, F8, Cz, C3, C4, T3, T4, T5, T6, Pz, P3, P4, Oz, O1, O2). Impedance was kept below 5 Ω and electrical activities, amplified with a band-pass filter of 0.5 - 30.0 Hz, were digitized at sampling rate 256 Hz. Recording of EEG was taken in a sound attenuated, dimly lit room. The patients were instructed to stay sit with closed eyes and relaxed and were awake during the procedure of basal and specialized manoeuvres EEG - test run. The EEG bands we use so evaluated were delta (0.2-3.9 Hz), theta (4.0-7.9 Hz), alpha (8.1- 12.9 Hz), beta (13.0 -30.0 Hz) and gamma (30.1-80 Hz). QEEG was done for all the patients and controls using BESS (brain electro scan software) of the Axxonet System (India). Artefact free epochs of 2 seconds each were chosen because after every of 2-3 seconds the changes both inclusive and exclusive in the amplitude were taking place more than 10% and their spectral content evaluated by means of Fast Fourier Transform analysis [12].

Statistical Analysis

The Microsoft excel 2007 was used for statistically analysis of data. The unpaired t-test was used for the mean comparison of all parameters between patients with Alzheimer's disease and control subjects. With intention to avoid type 2 errors, we considered two – sided p values < 0.05 to be significant.

RESULTS AND DISCUSSION

Table 1: Demographic and clinical data of the Alzheimer's disease and control population

Demographic and clinical Variables		Patient (N=20)	Control (N=30)	p value
Gender	Male	11	21	0.281
	Female	9	9	0.281
Age	Mean	69.10	66.63	0.124
	SD	6.146	3.986	
MMSE Score	Mean	28.23	12.75	0.000
	SD	34.136	30.406	

Table 2: Absolute Power of EEG band of delta, theta, alpha, beta and gamma during eye close session in fronto -central region of brain

EEG band	Control	Patient	p value
Delta	20.40(7.33)	24.07(9.16)	0.001
Theta	13.98(7.58)	9.29(5.03)	0.000
Alpha	9.13(5.82)	4.14(2.45)	0.000
Beta	11.34(7.19)	5.58(3.24)	0.000
Gamma	8.53(4.43)	3.75(3.36)	0.000
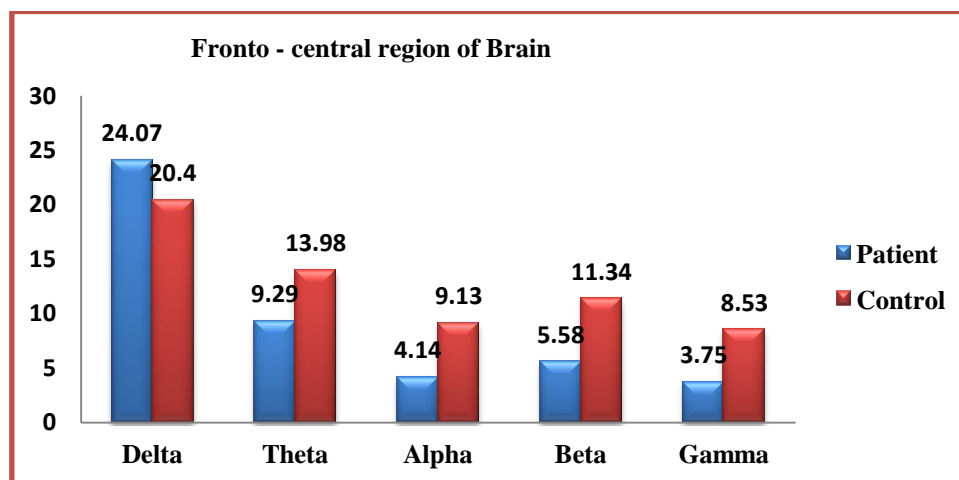
Graph 1: Absolute power of fronto - central region of brain during eye close session

Table 3: Absolute Power of EEG band of delta, theta, alpha, beta and gamma during eye close session in parieto-occipital region of brain

EEG band	Control	Patient	p value
Delta	21.12(8.36)	25.45(8.27)	0.001
Theta	14.43(6.07)	15.00(6.26)	0.522
Alpha	12.04(7.29)	4.44(2.47)	0.000
Beta	12.37(8.35	5.45(3.43)	0.000
Gamma	9.11(5.66)	3.60(3.58)	0.000
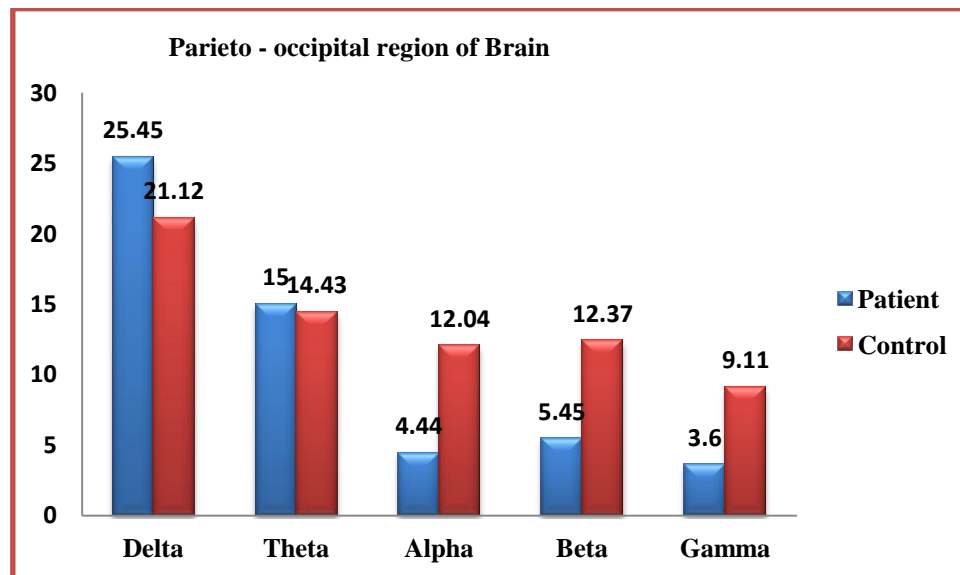
Graph 2: Absolute Power of parieto-occipital region during eye close session

In the present study an increased delta activity was observed during eye closed in fronto-central region (Table 2 and graph 1, p=0.001) and parieto-occipital region (Table 3 and graph 2, p=0.03) in Alzheimer's disease (AD) patient. Theta band absolute power tended to increased in parieto-occipital region during eyes closed in patient group (Table 3 and graph 2, p=0.522). Theta band absolute power decreased in fronto-central region (Table 2 and graph 1, p=0.000) Alpha, beta and gamma bands absolute power decreased in patient group in both fronto-central and parieto-occipital region (Table 2, 3 and graph 1, 2, p=0.000).

Moretti et al [13] found higher delta power in AD patients. Deursen et al [14] observed an increased power of low frequencies band (delta and theta) and decreased power of higher frequencies band (alpha and beta) in AD. Babiloni et al [15, 16] reported increased power of delta band and decreased power of alpha band in fronto-central region in Mild Cognitive Impairment (MCI) and AD subjects. When compared to normal elderly subjects, patients with Alzheimer's disease have shown a power increase of topographically widespread delta and theta rhythms and a power decrease of posterior alpha (8–13 Hz) and beta (13–30 Hz) rhythms [17,18]. Patients with Alzheimer's disease are characterized by a power increase of parieto-occipital theta and delta rhythms as well as by a power reduction of alpha and beta rhythms in parieto-occipital regions [19].

Compared to normal subjects, Alzheimer's disease (AD) patients are known to have 'slowing of the EEG,' namely through increase of the delta (0.5–4 Hz) and theta (4–8 Hz) power, along with decrease of the alpha power (8–13 Hz). 'Slowing' of the EEG rhythms may be sensitive and correlate to dementia severity and disease progression from the earliest stages [20, 21]. These findings are considered indirect evidence of the fundamental role of cholinergic system in modulating alpha rhythms, given the well-known selective deficit of acetylcholine occurring from

the earliest stages of AD. The alpha rhythm dominates the EEG power spectrum in resting normal subjects[22]. Scalp alpha rhythms result from sequences of inhibitory and excitatory post-synaptic potentials at the dendrites of cortical pyramidal neurons. These potentials depend mainly on the influence of near and distant cortical modules[23], as well as on the interactions of excitatory cortico-thalamo-cortical relay fibers and inhibitory thalamic reticular fibers[24]. An emerging feature of these integrated cortico-cortical and cortico-thalamo- cortical systems is that, in a resting condition, the higher the number of synchronously active neurons, the higher the amplitude of the alpha rhythm [25].

In the present study we reported decrease MMSE score in patients when compared to controls (p=0.000). Hsiao et al[26] found that MMSE scores were strongly correlated with the magnitudes of spectral power at the theta and alpha bands in posterior portion of default brain network.

The limitation of the present study is a reduced amount of data. To define the diagnostic role of the absolute power in the diagnosis of dementia, in the future, the present study data need to be interpreted with caution and they need to be replicated before a firm conclusion can be deduced.

CONCLUSION

The present study concluded the role of delta absolute power to differentiate the Alzhemier's disease patient from the control group in fronto-central and parieto-occipital region. Compared to normal subjects the AD patients' EEGs were characterized by a significant reduction of the alpha, beta and gamma power. These results put into question the classical inverse relationship between the frequency and power in normal EEG rhythms and emphasize the differential role of specific abnormalities in Alzheimer's disease patients. Future investigations are needed to validate the clinical usefulness of these findings in early differential diagnosis, disease staging, and therapy monitoring.

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