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Original Research Article

Diagnosis of Alzheimer's Disease on the Basis of Mini – Mental State Examination and EEG Coherence at Rest

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Abstract

The aim of present study was to investigate the role of Mini Mental State Examination (MMSE) and EEG coherence to discriminate Alzheimer's disease patient and normal elderly subjects. Electroencephalography (EEG) was recorded at rest in age-sex matched 30 normal elderly subjects and 20 amnesic Alzheimer's disease patients (55-75 years). 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 decreased coherence in frontal (F3-F4) lobes in alpha-1(8-9.9 Hz), alpha-2 (10-12.9 Hz) and beta (13-30 Hz) bands (p=0.000) at rest as compared to healthy, age and sex matched control subjects. These results suggest that EEG coherence can discriminate Amnesic Alzheimer's patients from normal elderly subjects.

Keywords: Amnesic Alzheimer's patients, Electroencephalography (EEG), Mini Mental State Examination, Coherence.

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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].

Promising markers of functional neural connectivity derive from the measurement of the functional coupling of resting state eyes closed EEG rhythms between pairs of electrodes. Linear components of such coupling, functional co-ordination, and mutual information exchange can be evaluated by the analysis of spectral coherence [6, 7]. Spectral coherence is a normalized value that quantifies the temporal synchronization of two EEG time series between pairs of electrodes in the frequency domain and can be derived by Fast Fourier Transform (FFT) [8, 9]. EEG coherence is a useful measure to evaluate the functionality of cortical connections and for obtaining information

regarding synchronization of the regional cortical activity. 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.

In this context the present study was undertaken to explore MMSE score and EEG coherence 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, extrapyramidal 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 [10].

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	12.75	28.23	0.000
	SD	3.537	1.194	

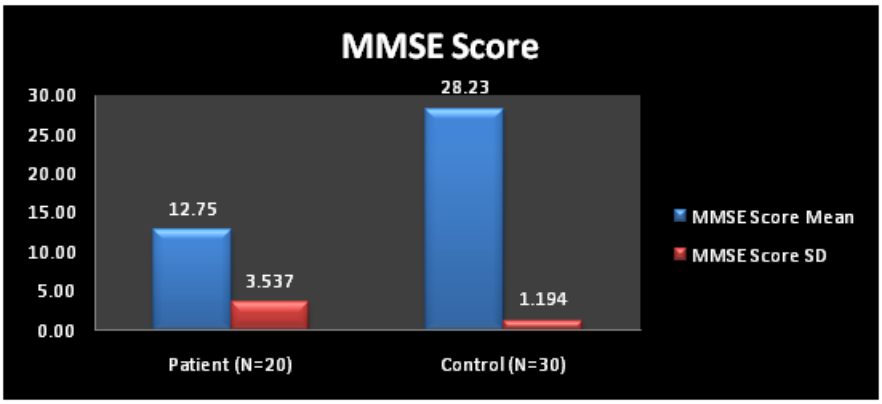

Figure 1: MMSE score of patients and controls

Table 2: Coherence Mean (SD) value in F3-F4 channels during eye close session

EEG Bands	Control	Patient	p value
	Mean (SD)	Mean (SD)	
Delta	0.450 (0.276)	0.361 (0.282)	0.275
Theta	0.563 (0.255)	0.466 (0.220)	0.169
Alpha-1	0.533 (0.304)	0.303 (0.286)	0.010*
Alpha-2	0.504 (0.267)	0.363 (0.292)	0.084
Beta	0.516 (0.252)	0.386 (0.258)	0.082

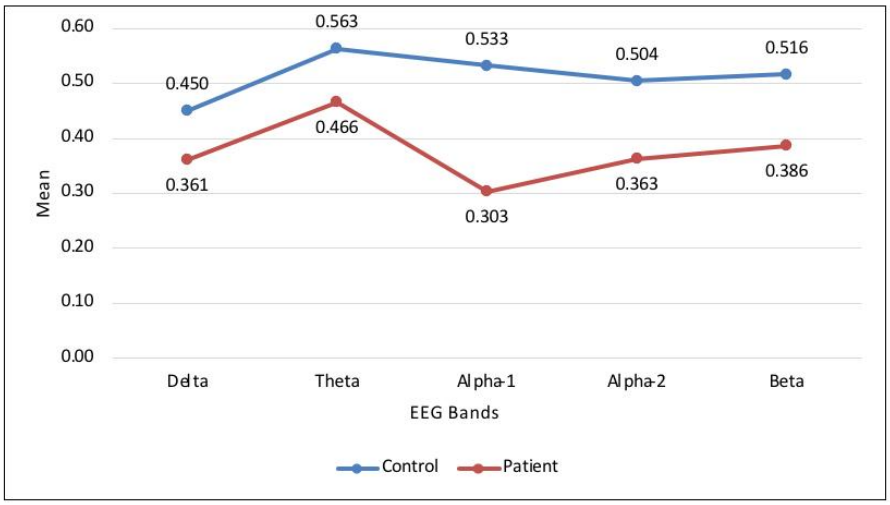

Figure 2: Coherence Mean value in F3-F4 channels during eye close session

In the present study we reported decrease MMSE score in patients when compared to controls (p=0.000) (Table 1 and figure 1). A significant difference of coherence analysis was observed in alpha-1 (p=0.010) band zone of EEG at F3-F4 EEG lead pairs during eye close session (Table 2 and figure 2) in Alzheimer's disease patients as compared to controls.

Discussion

In the present study a significant decreased MMSE score (p=0.000) was observed in patients suffering from AD as compared to age and sex matched healthy controls (Table 1 and figure 1). This finding supported by Stam et al,(2003) who observed that low MMSE scores in AD patients also exhibit low beta band synchrony. They concluded that loss of beta band synchrony occurs early in mild AD patients and correlates with cognitive impairment [11].

High spectral coherence and linear correlation are shown by the functionally coordinated two cortical areas. Reduced linear functional coupling and information transfer among cortical areas are reflected as decrease of coherence. Spectral coherence may reflect the integrity of cortical neural pathways [12]. Loss of functional connectivity has been demonstrated in patients with AD, in particular over the frontal and anterior-temporal regions [13].

In the present study a significant decreased coherence value was observed at F3-F4 lead pairs of the EEG in alpha-1 band zone (p=0.01), where

as the coherence value decreased non significantly at F3-F4 lead pairs of the EEG in delta, theta, alpha-2 and beta bands zone in patient with AD as compared to controls ($p>0.05$) during eye close session (Table 2 and figure 2). In previous studies, Locatelli et al (1998) found significant decreased alpha coherence in AD patients and a significant increased delta coherence in some patients between frontal and posterior regions [12]. The pathophysiological changes such as the alpha coherence decrease could be related to the lack of influence of subcortical cholinergic structures on cortical electrical activity. Functional coupling of resting state, eyes closed cortical EEG rhythms can differentiate the normal subject, MCI, and AD subjects. A prominent decrease of coherence at alpha rhythms was observed in AD compared to normal subjects [12,14,15,16,17,18,19,20,21,22,23] .

Conclusion

The present study concluded that decreased MMSE score and EEG coherence in frontal lobe can differentiate the patients with Alzheimer's disease from the normal healthy control group. Reduced coherence represents the loss of functional coupling and neural network communication between the lobes of the cortex, possibly resulting from atrophy of lobes. 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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