DETECTION OF ALZHEIMER'S DISEASE USING OPTIMIZED EEG DATA ACQUISITION AND SIGNAL PROCESSING TECHNIQUES

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Abstract - Alzheimer's disease is a growing health problem in the elderly population. Efficient detection of Alzheimer's disease is still a challenge. Previous studies have shown that EEG can be used for the detection of Alzheimer's disease. However, this has been done using expensive EEG systems. This study is aimed at building a low cost EEG based Alzheimer's disease detection system. This study proposes a low cost EEG based wireless headset system, EMOTIV EPOC, for the detection of Alzheimer's disease. The slowness of EEG in alpha and beta bands were measured using spectral analysis methods. EEG signals of AD patients showed a significant increase (at $p<0.05$) in relative power of low frequency bands than those of control subjects. Most significant change was observed in Delta band (2-4 Hz) of AD patients for all 14 channels recorded. Reduced complexity of EEG signals was calculated using Approximate Entropy (ApEn) method to detect Alzheimer's disease. It was observed that AD patients have significantly lower ApEn values than control subjects at electrodes F8, P7, P8 and T8 ($p<0.05$).

I. INTRODUCTION

Alzheimer's disease (AD) is one of the most common neurological disorders and a growing health problem among the elderly population which causes problems with memory, thinking, and behavior [1]. Research suggests that different proteins are involved in the process of Alzheimer's disease, but the exact sequence of events is still not understood. With the progression of the disease, many more nerve cells are affected that lead to different symptoms of AD.

Currently, the early diagnoses of AD involves clinical assessment by the medical expert. Positive signs can then lead to asking the patients to undergo brain scans and blood screening [2]. The accumulated result could then be observed for potential existence of AD. Automated and accurate detection of AD from the elder control group is an important and challenging task. Different approaches have been used in the literature for the detection of AD such as positron-emission tomography (PET) [1], [3] single-photon emission tomography (SPECT) [4], magnetic resonance imaging (MRI) [5], [6], [7] and electroencephalogram (EEG) [8], [9], [10]. The use of EEG for the detection of AD has a clear advantage over the other methods as it can provide a low cost and non-invasive way of detecting AD. Previous studies on AD detection using the EEG have found that the power of alpha and beta decreases while the power of theta and delta increases in AD patients compared with elder control group subjects [8]. In EEG bands, the power change starts at very early stages of AD but is not easy to detect and requires efficient signal processing techniques. Different signal processing techniques have been used in the literature for artifact removal, feature extraction and classification. In this paper, an AD detection scheme using an economical portable EEG system is proposed. It is hypothesized that by using a cost effective EEG data acquisition system (Emotiv EPOC® headset) and optimized signal processing techniques, AD can be efficiently diagnosed at its early stages. This not only potentially reduces the financial burden of diagnostic procedure but also reduces the prognoses time. The proposed technique can also benefit researchers working in this area to rely on an economical EEG hardware system instead of using expensive data acquisition systems.

II. MATERIALS AND METHODS

A. Subjects

6 Patients (3 males, 3 females, Average age 60 years, SD = 4.5 years) with apparent symptoms of Alzheimer's disease were studied. Patients were referred from outpatient memory clinic of Railway Hospital Rawalpindi (Pakistan). All patients were subjected to multidisciplinary clinical test performed by clinicians and were evaluated on diagnostic staging scales mini–mental state examination (MMSE). All patients were diagnosed with MMSE value of less than 25. The control group consisted of 6 healthy elderly subjects (3 males, 3 females, Average age = 60 years, SD = 4.5 years). Healthy and cognitively normal control subjects without past or present neurological disorders volunteered for the study, and gave their consent in the study in writing. The study was allowed by Ethics committee of Riphah International University (Pakistan) and New Zealand College of Chiropractic (NZCC), Auckland (New Zealand).

B. Experimental Procedure

EEG-recordings were performed for 2 minutes in two conditions, "Eyes open" (EO), and "Eyes closed"

(EC). The EEG signal was registered by using the following protocol. An initial 30 seconds recording was made with EC condition, followed by another 30 seconds recording in EO conditions, followed by another 30 seconds in EC condition and finally 30 seconds in EO condition. Subjects were given an auditory signal to transition between the two states EO and EC. Subjects were briefed about the protocol prior to the start of data acquisition. They were also instructed to stay as still and relaxed as possible during the 2 minutes of EEG-recording.

C. Data Acquisition

Data was acquired using Emotiv (Emotiv EPOC®, San Francisco, USA) Headset with 14 channels and 2 references. Fig. 1 shows the Raw EEG signal of both the AD subjects and the control for 10 seconds. Channel names based on the international 10-20 electrode location system are: AF3, F7, F3, FC5, T7, P7, O1, O2, P8, T8, FC6, F4, F8, AF4, with Common Mode Sense/Driven Right Leg (CMS/DRL) references in the P3/P4 locations. Data Acquisition parameters were: Sampling Frequency = 128 Hz, Resolution 14 Bits (1LSB = 0.51μV), Bandwidth = 0.2 to 43 Hz (5th order Sinc Filter, 50 Hz Notch).

Each EEG signal was judged by visual inspection to be free from movement artifacts and noise. After removing mean offset and using a Bandpass filter (0.5 to 40 Hz, 10% Sinc, FIR), all channels were visually inspected for artifacts. The EEG Signal was segmented into 5 seconds (640 bits) epochs. The number of artifact-free epoch per channel per condition was 6.

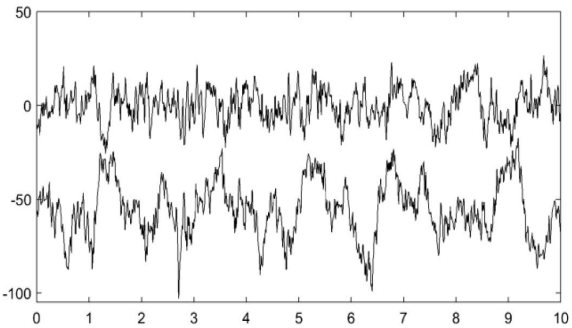

Figure 1. A ten seconds EEG signal acquired using Emotiv of Closed Eye for both the Alzheimer Disease (AD) (top) and Control Subjects (bottom).

D. Data Analysis

In the last years, several groups have studied different data analysis and signal processing techniques to investigate the potential of EEG signals in diagnosis of Alzheimer's disease. Different groups have reported that AD has (at least) two major effects on EEG signals, depending upon the severity of the AD condition: slowness of EEG signal, and enhanced complexity in EEG signal. Jeong J. et.al [14] have written an in-depth review on the topic. However these effects tends to change from one AD patient to another, and it is difficult to diagnose AD from just studying a single effect [11]. This paper studies these two effects on EEG signals of clinically diagnosed AD patients and normal subjects of same age group.

1) Slowing of EEG Signal: Alzheimer's disease and MCI effects different frequency bands of an EEG signals in a certain way. This effect is most associated with increase of power in low frequency bands (Delta 0.5Hz to 4 Hz), and (Theta 2 Hz to 4 Hz), and a decrease of power in high frequency bands (Alpha and Beta 4Hz to 8Hz) [12],[13],[14] Average power of following frequency bands were calculated: delta: 0.5–4 Hz, theta: 4–8 Hz, alpha1: 8–11 Hz, alpha2: 11–14 Hz, beta1: 14–25 Hz, beta 2:25–35 Hz. Calculations of relative band spectra of the above mentioned bands were performed using Matlab® 2015 Software. The total power over each of the frequencies in a band is summed and a normalized power of each of the band is calculated by the total power. This resulted in relative power of each band of interest.

2) Complexity of EEG Signal: Among the many disorders induced by Alzheimer's disease is a neuro-degeneration which lowers the neural interaction and the neural dynamics be-come simpler, regular and less complex. Conjecturing that the complexity of the AD patient's EEG is lower than that of age-matched controls. Approximate Entropy (ApEn) of both patients and controls were estimated to distinguish data sets by a measure of regularity. ApEn is a non-linear statistically valid formula tool that will quantify the irregularity of time series and is attractive for dynamic analysis due to the salient features it bears [15]. ApEn is resistant to transient interference and can be used for short-length data. A lower value of ApEn indicates that the time series is more rhythmic; a higher value indicates more complexity or irregularity [16]. Two parameters are to be fixed to calculate ApEn, r and m. The parameter r is the similar tolerance or filter factor and m is the "embedding dimension" [17].

As suggested by Pincus et.al. [18], m=1 and r=0.2 standard deviation of the original data was used. The results of the approximate entropy were averaged and Student's t-test was used to evaluate the statistical differences between the 6 control subjects and 6 AD subjects.

III. RESULTS AND DISCUSSION

A.EEG Frequency Spectral Analysis

A significant difference between groups (Control vs. AD) was observed in the Delta Band for all 14 channels. Relative power was higher in AD group than that in control group for all channels, $F = 303$, $p<0.000001$, $SS=10.65$, $MSe=0.04$. Fig. 2 shows the relative power of delta band in AD patients as compared to Control subjects for all 14 channels. However only a marginal difference in delta band power was observed between two condition (Eyes Open vs. Eyes Close) $F= 1.78$ $p<0.182454$ $SS=0.06$

MSe=0.03.

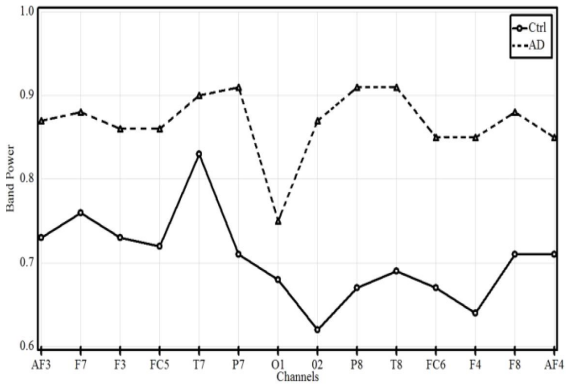

Figure 2. Normalized Delta band power of AD versus Control subjects in all 14 channels.

B. EEG Complexity

ApEn was estimated for all channels with m=1 and r=0.2 times the SD of the original data sequence for both EC and EO EEG data. Increasing ApEn value corresponds to intuitively increasing process complexity underlying in the brain. The ApEn values (Mean ± SD) for the AD patients and control subjects and the p-values of the student's t-test performed to examine the differences between both groups are shown in table I and II. These results indicate that the degree of complexity of EEGs corresponding to the control subjects is higher (higher ApEn values) than the one of EEGs from patients with AD. This confirms the fact that a diffuse slowing of the background activity may be found in the EEGs of patients with AD [19] and that the dynamic processes underlying the EEG recording are less complex for AD patients than for normal subjects.

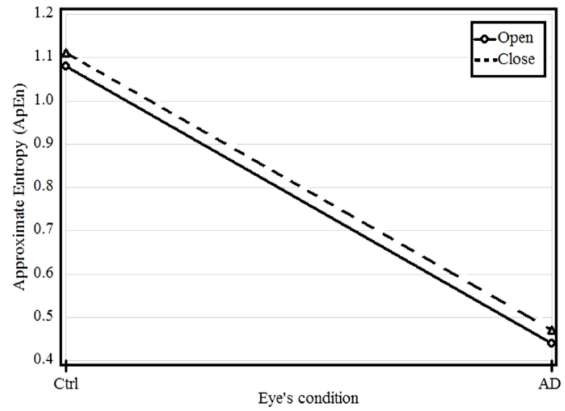

Figure 3. Averaged Approximate Entropy comparison between AD and Control for both Eyes Open and Eyes Close conditions.

Statistical differences between groups at the different electrodes were evaluated with Student's t-test. Fig. 3 shows that there is a significant difference between the ApEn values for both the subjects at channel T8. It can be seen that AD patients had lower ApEn values, with significant differences between both groups ($p<0.05$) at electrodes F8, P7, P8 and T8. These results suggest that EEG activity of AD patients is more regular than in a normal brain.

Table I - THE AVERAGE APEN VALUES (MEAN ± SD) OF THE EEGS OF THE AD AND CONTROL SUBJECTS FOR ALL CHANNELS IN CLOSED EYES CONDITION. SIGNIFICANT CHANNELS ARE MARKED WITH AN ASTERISK.

State	Eyes Close				
Electrode	AD's ApEn		Control ApEn		p Value
AF3	0.61 ± 0.37		1.01 ± 0.37		0.081
F7	0.62	± 0.46	1.01	± 0.45	0.168
F3	0.50	± 0.26	0.98	± 0.45	0.095
FC5	0.72	± 0.44	1.06	± 0.51	0.236
T7	0.55	± 0.38	0.90	± 0.40	0.090
P7	0.52	± 0.35	1.14	± 0.52	0.041
O1	0.67	± 0.45	1.04	± 0.45	0.088
O2	0.50	± 0.27	1.12 ± 0.541		0.066
P8*	0.47	± 0.26	1.14	± 0.45	0.032
T8*	0.46	± 0.26	1.11	± 0.45	0.021
FC6	0.56	± 0.38	1.08	± 0.41	0.084
F4	0.62	± 0.33	1.06	± 0.47	0.143
F8*	0.55	± 0.25	1.11	± 0.56	0.028
AF4	0.63 ± 0.34		1.05 ± 0.45		0.092

Table II - THE AVERAGE APEN VALUES (MEAN ± SD) OF THE EEGS OF THE AD AND CONTROL SUBJECTS FOR ALL CHANNELS IN OPEN EYES CONDITION. SIGNIFICANT CHANNELS ARE MARKED WITH AN ASTERISK.

State	Eyes Open				
Electrode	AD's ApEn		Control ApEn		p Value
AF3	0.66 ± 0.53		0.98	± 0.44	0.250
F7	0.63	± 0.49	1.03	± 0.46	0.160
F3	0.56	± 0.36	0.96	± 0.40	0.169
FC5	0.72	± 0.52	1.05± 0.57		0.296
T7	0.56	± 0.43	0.82	± 0.43	0.184
P7	0.51	± 0.35	1.08	± 0.55	0.053
O1	0.64	± 0.46	1.00	± 0.48	0.113
O2	0.46	± 0.30	1.08	± 0.56	0.072
P8*	0.45	± 0.28	1.05	± 0.44	0.048
T8*	0.44	± 0.28	1.08	± 0.47	0.027
FC6	0.62	± 0.39	1.08	± 0.44	0.136
F4	0.63	± 0.35	1.04	± 0.50	0.194
F8*	0.55	± 0.24	1.07	± 0.40	0.046
AF4	0.68 ± 0.47		1.02	± 0.41	0.210

CONCLUSION

In this pilot study the EEG spectral analysis and background activity of 6 control and 6 patients with AD were analyzed. It was observed that AD patients have significant increase in the power at Delta band and lower ApEn values than control subjects at electrodes F8, P7, P8 and T8 ($p<0.05$). Inferring that

brain affected by AD shows a more regular and less complex electrophysiological behavior. It is concluded that EEG signals of the AD subjects show both the slowing and complexity changes. Possible future lines of research include using other non-linear analysis techniques with large patient population with more significant results useful to help physicians in the diagnosis of the Alzheimer's disease.

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