Brief Communication

EEG as an easy diagnostic tool in differentiation of Alzheimer and non-Alzheimer dementia

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Dementia is a common progressive disease, and Alzheimer type dementia (AD) is the most frequently diagnosed dementia among dementia subgroups. Other types of dementia can be classified as non-Alzheimer dementia (NAD) including Lewy bodies, fronto-temporal, Pick's, Creutzfeldt-Jacob, vascular, genetic, metabolic, toxic, constitutional, and idiopathic types.[1] The Clinical Dementia Rating (CDR) scale is used to characterize the level of cognitive and functional performance in patients at risk or suspected of having AD or another dementing disorder.[2] Objective, rater-independent, cost-effective, quantitative methods that can be used in place of, or with, CDR are needed as CDR is: i) time-consuming involving interview with at least 2 people, ii) subjective due to potential unreliable data gathered from the patient or informant, iii) inapplicable in several situations such as aphasia, deafness or loss of hearing, and finally iv) results are rater-dependent. Conventional visual analyses of the EEG in AD patients have demonstrated a diffuse slowing of the brain rhythms. However, quantitative EEG (QEEG) analysis may be a useful adjunct to interpretation of the routine EEG.[3] Clinical use of QEEG techniques by practitioners, who are not physicians, highly skilled and properly trained in clinical EEG interpretation, or without reviewing the original record, may give misleading results. Despite these difficulties, computer analysis should be the method of preference since it is more observer-independent. The EEG software and systems have not yet been sufficiently investigated for simple diagnosing and differentiation of AD and other dementia types. In this study, we aimed to investigate whether there is a difference in EEG recordings in patients with AD, NAD, and healthy subjects; if a difference is present, which variable can be used to discriminate these groups and whether there is a relation between EEG findings and severity of clinical dementia, with the use of simple digital EEG recording.

Eight AD, and 16 NAD patients, and 16 healthy volunteers were included in the study, which took place in 2005. All AD and NAD patients were selected among the dementia patients who are in follow up at the neurology outpatient clinic of the Research Hospital of Duzce University, Duzce, Turkey. Informed consent was obtained from all participants or their caregivers or close relatives, according to the Code of Ethics of the World Medical Association (Declaration of Helsinki) and standards established by the Institutional Review Boards. The AD patients were diagnosed according to the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) diagnostic criteria and DSM-IV criteria. The CDR scale was used to determine dementia severities, as it has broad valuation ability, and contains the Mini Mental Test. The categories of the CDR scale from normal to severe were: normal, CDR=0; very mild, CDR=0.5; mild, CDR=1; moderate CDR=2; and severe, CDR=3. Volunteer control subjects were chosen between patients' companions at the hospital. The following criteria for the control group was established: age and gender matched, and no disturbances of memory or other cognitive functions, and no deficits in the neurological examination. Exclusion criteria for all groups were those receiving neuroleptic, antidepressant, or sedative drugs, and having systemic or other disorders such as cerebrovascular diseases, diabetes, arterial hypertension, coronary disease, hypercholesterolemia (above 250 mg%), epilepsy, migraine, or psychiatric disorders. The EEG data were collected by a digital system (PowerLab/8sp, ADInstruments, Sydney, Australia), which included Chart 5.v3 software for recording through an isolated bio-amplifier (BIOamp, ADInstruments, Sydney, Australia). Precisely the same acquisition parameters and procedures were employed on all individuals included in the study. The pair of electrodes was located according to the International 10-20 system on the scalp at F3-F7, T3-P3, and O1-O2 points for left frontal, left temporo-parietal and occipital regions. We selected these pairs as previous studies showed that left hemisphere is are affected more in dementia. The EEG data were recorded in resting state subjects with eyes-closed. Subjects were kept awake as much as possible during the recording. In all subjects, EEG recordings were performed for 10 minutes in the late morning. Bio-amplifier sensitivity was set to 200 μV/cm with a high pass value of 1 Hz; low pass value of 50 Hz, and sampling rate of 200 Hz. All recordings were stored on a computer and analyzed offline. All artifacts were eliminated prior to subsequent analyses. Mean frequencies of EEG activities were measured by the data analysis tool of the Chart software. Mean frequencies for each subjects' EEG records were calculated and classified as alpha, theta, and delta rhythms according to their frequencies; delta (1-3Hz), theta (4-7Hz), alpha (8-

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13Hz). Group differences in gender and brain rhythms were assessed by Likelihood ratio chi-square test. Age and CDR were assessed using one-way ANOVA and Mann-Whitney U test. Repeated measures ANOVA followed by Bonferroni test were used to compare the EEG frequency both between groups and between brain regions. Pearson's and Spearman rank correlation analysis were performed to detect the relation between EEG frequency and CDR. The level of significance was set at $p \leq 0.05$. In all statistical calculations, SPSS for Windows (release 11.0.5) was used.

The male-female distributions in the AD, NAD, and control groups were 3-5, 9-7, and 7-9. Mean±SD values of age were 72.0±10.38 for AD, 73.2±8.41 for NAD, and 70.0±4.57 for the control group. The age and gender distributions of the groups were similar. The CDR scores of groups were 1.25±0.85 for AD, 0.69±0.44 for NAD, and 0 for the control group. The mean score of the AD group was significantly higher than the NAD group (p=0.05). The differences between the 3 groups, and between the 3 regions were evaluated according to mean EEG frequencies. Mean EEG frequencies (Hz) in the frontal region were 5.9±2.53Hz for AD, 8.9±2.54Hz for NAD, and 10.2±2.69Hz for the control groups. In the temporo-parietal region, these values were 8.3±2.55Hz for AD, 10.4±2.10Hz for NAD, and 9.1±3.04Hz for the control group. The occipital mean EEG frequencies were 8.6±2.83Hz for AD, 9.6±2.39Hz for NAD, and 9.2±1.9Hz for the control groups. In the frontal region, the mean frequency of the AD group was found significantly lower than other groups (p=0.026 for NAD, and p=0.001 for control). The difference between the NAD and control groups was not statistically significant in this region. The mean frequencies of temporo-parietal and occipital regions showed no difference between groups. When we compared the regions for mean frequency in each group separately, the mean frequency of the frontal region was significantly lower than the temporo-parietal (p=0.045) and occipital (p=0.05) regions in the AD group. However, the mean frequency of the temporo-parietal and occipital regions was not different in this group. In addition, frequencies of regions in the control and NAD groups were not statistically different. Interaction between groups and regions was found statistically significant according to mean frequencies (p=0.024). After mean frequency of EEG data of each subject were classified as brain rhythms, the distribution of rhythms in all regions and groups was recorded as shown in **Table 1**. Theta was the most frequently observed rhythm in the frontal region of AD patients compared to other groups (p=0.035). There was no significant difference between groups in other regions (**Table 1**). Any possible correlations between CDR scores and frequencies in all groups and regions were also investigated, but there was no significant correlation (**Figure 1**).

The present study shows that the mean frequency of EEG activity recorded from the frontal region in AD patients was significantly lower than NAD patients and healthy control subjects. This finding can be used to discriminate AD from NAD. However, no correlation could be found between the differences in EEG frequencies and CDR. In a study of Adler and his colleagues,[4] the determination of especially left temporal alpha accordance in quantitative EEG analysis indicated that EEG could be a useful and assisting method in the diagnosis of AD. The EEG rhythms differ in AD patients compared to normal controls and/or vascular dementia subjects. The AD patients were characterized by higher delta (0-3Hz), higher theta (4-7Hz), lower posterior

Table 1 - Count and percentage of different rhythms recorded in each group and region.

Brain region and rhythm	Group, n (%)		
	AD (n=8)	NAD (n=16)	Control (n=16)
Frontal			
Delta (1-3Hz)	1 (12.5%)*†	0 (0.0%)	0 (0.0%)
Theta (4-7Hz)	5 (62.5%)*†	4 (25.0%)	3 (18.7%)
Alpha (8-13Hz)	2 (25.0%)*†	12 (75.0%)	13 (81.3%)
Temporo-parietal			
Theta (4-7Hz)	4 (50.0%)	2 (12.5%)	4 (25.0%)
Alpha (8-13Hz)	4 (50.0%)	14 (87.5%)	12 (75.0%)
Occipital			
Theta (4-7Hz)	4 (50.0%)	3 (18.7%)	2 (12.5%)
Alpha (8-13Hz)	4 (50.0%)	13 (81.3%)	14 (87.5%)

*$p \leq 0.05$, statistically significant compared to NAD, †$p \leq 0.05$, statistically significant compared to control, AD - Alzheimer type dementia, NAD - non-Alzheimer type dementia

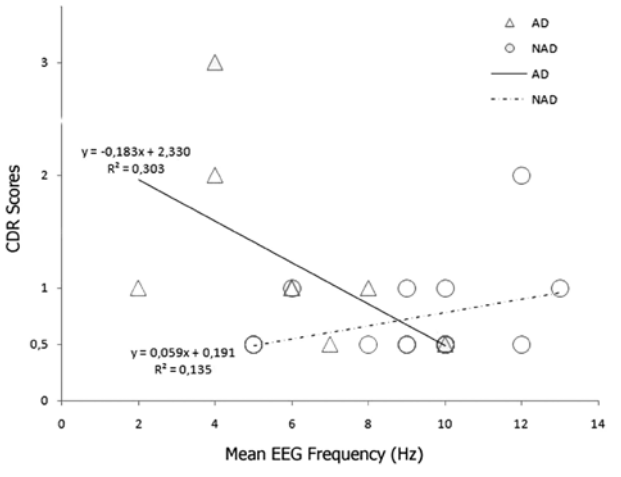

Figure 1 - Shows the linear relationship between frontal mean EEG frequency and CDR scores in demented patients. AD - Alzheimer type dementia, NAD - non-Alzheimer type dementia, CDR - Clinic Dementia Rating score.

alpha (8-12Hz), slowing in alpha peak frequency and lower beta (14-30Hz) and gamma (around 40Hz).[5] Our findings support previous data showing slowing of EEG in AD. When compared with normal elderly individuals, a general slowing was observed in the EEG rhythms of AD patients. This mostly occurred as an increase in the delta and theta activities and a decrease in the alpha activities. As a reason of this slowing, the effect of partial cholinergic deformation in the cortical intelligence was considered. The changes in alpha rhythm are a more sensitive marker than changes in slow wave for neocortical dysfunction. Although it might be seen in early periods of AD cases, it is known that a decrease in alpha activities has significant meaning in the diagnosis and separation of NAD cases. Our study provided further evidence that EEG may be a useful tool to distinguish AD, NAD patients, and healthy subjects. In Alzheimer disease, the degree of EEG change is related to severity of disease. However, regarding dementia severity in separation of 2 diseases at similar stages, it is known that EEG changes on its own do not have adequate determinative power. Since most of the patients had mild to moderate dementia in this research, it was not possible to distinguish advanced AD and advanced NAD patients by EEG. We showed that there is no significant correlation between EEG findings and dementia severity. This situation, which is one of the potential limitations of this study, may be a result of small sample size. A prospective study design with a larger sample size would provide additional information concerning EEG and dementia severity.

In conclusion, EEG is a useful tool for diagnosing and differing dementia. Visual EEG analysis, as a less precise tool failed to show any differences in demented patients. Computer analysis should be the method of preference as it is more observer-independent. Since complex and expensive digital EEG recording and analyzing systems need highly skilled, trained persons, most practitioners and physicians have avoided using EEG in diagnosing and differing dementia. We determined mean frequency differences by a simple, single-channel EEG method, and these changes appeared more pronounced in AD than NAD patients. Our analysis method again showed that EEG is relatively cheap, usable by all practitioners and physicians, available everywhere and only mildly uncomfortable for the patient, but it seems does not have the power to determine dementia severity, at least with this method.

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