ORIGINAL ARTICLE

Index of Theta/Alpha Ratio of the Quantitative Electroencephalogram in Alzheimer's Disease: A Case-Control Study

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Abstract- Alzheimer's disease (AD) is a devastating neurodegenerative disorder in human beings associated with cognitive, behavioral and motor impairments. The main symptom of AD is dementia, which causes difficulties in carrying out daily practices. Brain waves are altered in people with AD. Relative indices of brain waves can be beneficial in the diagnosis of AD. In this case-control study, 50 patients with AD and 50 matched healthy individuals were enrolled in case and control groups respectively. With recording and analyzing of brain waves with the utilization of quantitative electroencephalogram (QEEG), index of theta/alpha ratio was assessed in both groups. The index of theta/alpha ratio was significantly higher in patients with AD in comparison to healthy individuals (P<0.05). Index of theta/alpha ratio obtained by QEEG provides a non-invasive diagnostic marker of AD, which may be helpful in identification of non-advanced disease in susceptible individuals.

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Introduction

Dementia is the most common cause of the decline in the mental ability to perform cognitive and behavioral functions in elderly. Alzheimer’s disease (AD) is the most common known cause of dementia. AD has involved more than 35 million individuals worldwide since its first description in 1906 (1). The disease ensues in behavioral problems (e.g., depression, anxiety, speech or physical conflict and sleep problems) and cognitive dysfunction (e.g., decline in memory especially recent memory, speech deficit and disability to solve daily problems) (2).

The partially revealed pathophysiology of AD demonstrates that it is basically linked to the brain. Therefore, the study of all the processes related to the brain is the high yield in the diagnostic evaluation of AD. One of the most important aspects of brain functions is its electrical activity that can be studied by recording brain waves using electroencephalogram (EEG). Although studies were done in recent years about brain electrophysiology were limited to morphologic changes of brain waves in different diseases, nowadays quantification of brain electrical activity is also possible with new improvements in the neuroscience field.

EEG analysis has been shown to be an alternative method in diagnosing of AD (3). Thus, recently, utilizing quantitative EEG (QEEG) in assessing multiple electrical functions of the brain has been helpful in AD diagnosis. Recent investigations have focused on amplitudes of brain waves called relative powers. It is feasible to determine a relative power for each brain wave in any brain region. Studies have shown that indexes of brain electrical function in elderly people demonstrate a decrease in relative power of alpha wave especially in occipital, temporal and parietal lobes (4-6). Oscillations in the relative power of brain waves in AD patients show increase in relative power of delta and theta waves and decrease in relative power of alpha wave in posterior regions of the brain (7). These changes in the electrical function of the brain have been associated with alterations in its blood circulation and metabolism (8). Among different brain waves, the alpha wave has been known to have more association with learning processes, attention and short memory (6).

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Theta to beta index has been shown to be a strong diagnostic index in diagnosing of attention deficit hyperactivity disorder (ADHD). This index can differentiate between multiple subtypes of ADHD too (9).

It seems that finding an index which defines different conditions of brain waves can be important in the diagnostic approach to patients with AD. Decrease in the relative power of the alpha wave and increase in relative power of theta wave which both explained in previous studies, guide us to calculate theta to the alpha ratio as an important diagnostic index in AD patients.

Materials and Methods

Case and control groups

Upon local ethical committee approval, 50 individuals with AD from northwest of Iran were included in our study according to ICD-10 criteria. After getting written consent, demographic data including age, gender, family history of AD and educational level were obtained. There was no other neurologic disease in this group of patients. For the control group, 50 normal individuals with the same sex and age were enrolled in the study and their demographic data were collected as well.

Brain waves recording

In both groups, EEG was obtained utilizing Nihon-Kohden model EEG system in closed-eyes and opened-eyes conditions for 10 minutes in each person. Information obtained by EEG was transferred to quantitative form using Mitsar software (Mitsar Co. Ltd., St. Petersburg, Russia) and FFT algorithm. The relative power of alpha and theta waves and theta to alpha ratio was obtained in two groups.

Statistical analysis

To perform statistical analysis, *SPSS 17* software was used, and descriptive data such as frequency, percentage, average and standard deviation were calculated. A *t*-test was used to compare two groups in regard to the relative power of alpha and theta waves and theta to alpha index. *P* equal or less than 0.05 was counted as statistically significant.

Results

Mean age in AD group was 73.4±6.2 with the minimum of 60 and maximum age of 83. Mean age in control group was 67.6±6, which was not significantly different from the AD group ($P>0.05$). General demographic data are mentioned in table 1.

Brainwaves obtained by electrodes in mid-head such as Fz, Cz, Pz, and Oz, were not considered. Waves gathered by Fp1 and Fp2 electrodes which record artifacts as a consequence of eyebrows and eye movements, were eliminated too. Potentials of alpha and theta waves were measured separately for electrodes and recorded. Then theta to alpha ratio was calculated for each electrode.

Table 1. General demographic data in Alzheimer's disease and control groups

	AD	Control
Number	50	50
Age (mean±standard deviation)	73.4 ± 6.2	67.6 ± 6
Gender (male/ female)	27/23	30/20
Educational level (years)	6.56	8
History of AD (months)	22.54 ± 16.16	0

To assess any difference between two groups in regard to the relative power of alpha wave in O1 (left occipital) and O2 (right occipital) regions, we used independent t-test. The descriptive data are mentioned in table 2. Our study showed that there is a significant difference in relative power of alpha wave between 2 groups ($P<0.05$). Descriptive data in regard to the relative power of theta wave in O1 and O2 are mentioned in table 3. Using t-test, there was also a significant difference between two groups in regard to the relative power of theta wave ($P<0.05$).

By assessment of theta to the alpha ratio in AD and control groups (Table 4), it is evident that there is the statistically significant difference between these two groups in O1 and O2 regions of the brain ($P<0.05$).

Table 2. Descriptive data of alpha wave relative power in left and right occipital lobes in Alzheimer's disease and control groups

	Groups	Number	Mean	Standard deviation
1	**AD**	50	4.49	11.18
	Control	50	9.29	14.34
2	**AD**	50	6.9	13.59
	Control	50	10.51	16.65

Table 3. Descriptive data of theta wave relative power in left and right occipital lobes in Alzheimer's disease and control groups

	Groups	Number	Mean	Standard deviation
1	AD	50	12.19	3.54
	Control	50	4.21	7.31
2	AD	50	13.97	5.42
	Control	50	5.55	5.67

Table 4. Descriptive data of theta to alpha ratio in left and right occipital lobes in Alzheimer's disease and control groups

	Groups	Number	Mean
1	AD	50	2.71
	Control	50	0.45
2	AD	50	2.02
	Control	50	0.53

Discussion

Experimental evidence shows that amplitudes of the delta, beta and alpha waves of EEG are reliable indicators of cognitive and mental functions in human. Assessment of the alterations in these waves can be representative of multiple structural and mental disorders. Utilizing quantitative methods can augment the sensitivity of EEG in depicting such disorders (10).

Many previous studies have reported abnormalities in EEG of patients with AD such as decrease in rhythms and changes in frequencies of bands, usually presented with increase in the activity of theta and delta waves, and decrease in the activity of alpha and beta waves (11). These abnormalities are also bound to the severity of the disease.

EEG has been an advantageous tool to diagnose dementia in last three decades, but a simple relationship between the decrease in activity of EEG and cognitive malfunction has not been described yet (12). EEG findings in patients with AD suggest the dominance of delta and theta waves and decrease in alpha waves in the background (5). These findings are the same as our study.

Sandmann *et al.*, have described a direct relationship between some types of cognitive malfunction and activity of low-frequency theta waves that is confirmed by our study indicating that these waves are produced with increased activity in patients with AD (13).

In another hand, the activity of alpha and beta waves is decreased in patients with AD in comparison to healthy individuals. Pucci *et al.*, suggested alpha rhythm as a diagnostic indicator of AD, so that 6.0-8.0 Hertz decrease in alpha frequency is present even in patients with mild AD (14).

This increased activity of low-frequency waves in comparison to high-frequency waves has also been shown in other types of dementia. Martin-Loeches *et al.*, has reported an expanded distribution of slow brain rhythm in vascular dementia (15).

Multiple investigations have demonstrated the correlation between slow waves of EEG and progression of AD (7,16). These studies have also indicated a reduction in alpha to theta ratio in patients with AD in comparison to healthy individuals.

The method explained in our study is a non-invasive ancillary tool for diagnosing AD. Our results show that dominance of alpha waves are more than theta waves in posterior regions of healthy individuals, but this finding is vice versa in patients with AD. This finding supports the cholinergic theory of pathologic and physiologic aspects in AD. Alterations in cholinergic system of elderly and patients with AD are an accepted topic (17). This theory proposes a significant decrease in the presynaptic cholinergic material in cortical synapses of patients with AD (18) and explains a correlation between decreased cholinergic activity and cognitive dysfunction in normal elderly people and patients with

AD (19). The majority of studies done in EEG of AD patients are indicative of significant reduction in the coherence of alpha band which is associated with increased genetic susceptibility of ApoE and derangements in the transfer of cholinergic neurotransmitter (20).

In functional point, increase in relative power of theta waves is an indicator of inner hippocampus activity and decrease in alpha activity is in correlation with cortico-thalamo-cortical function (21). It has been specified that thalamus is the main source of alpha activity in resting patients (22). The decrease in alpha rhythm and increase in theta band activity can occur in an extensive collection of neurologic and mental disorders such as Alzheimer dementia (23). Multiple noninvasive methods and techniques have been developed in recent decades for premium diagnosing of AD. In recent years, applying FFT algorithm with the ability to present numerical data has placed quantitative EEG as one of the most important tools in this aspect.

Converting brain sine waves to quantitative forms helps in comparing of different individuals' EEGs and produces brain maps, which makes diagnose of diseases feasible. In the presence of multiple indices like absolute power and coherence of brain waves, the probability of assessment of brain functions is more scientific. As previous literature and our study show, the waves with lower frequency like theta are more active in patients with dementia. Also, alpha waves are weaker in this group of patients in comparison to healthy individuals.

In conclusion, it seems that assessment of theta to alpha ratio can be utilized to differentiate the brain function between healthy and dementia patients. Evaluating this index will probably help us to diagnose non-advanced AD and prevent this type from progression to a more advanced disease.

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