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Investigating the Relationship between Theta/Beta Ratio and Intensity of Disease in Children with ADHD

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ABSTRACT

Purpose: Electroencephalography based biomarkers including the measurement of the brain's theta/beta waves in the vertex(Cz) region can be useful to achieve diagnostic and therapeutic objectives in Attention/Deficit-Hyperactivity Disorder (ADHD). EEG biomarkers have been under extensive use in ADHD researchs, even though they have not been clinically confirmed so far. This study attempted to examine the relationship between theta/beta ratio and the disease intensity in ADHD children as well as the sensitivity and theta/beta ratio characteristic to detect ADHD and healthy children. The accuracy of this ratio would help differentiate diseased children from the healthy ones in terms of ADHD.

Materials and Methods: This study is a case-control test, in which the statistical population consisted of 59 healthy children and 61 children with ADHD who had been chosen through simple random sampling. All patients were examined in terms of disease intensity using parental Conner's questionnaire. The theta/beta ratio in Cz and Fz points was tested and recorded individually each once during waking hours with open eyes with no mental task, and another time during a specific mental task by neurofeedback.

Results: Theta/beta without test was larger in the Fz region in the cases than in the controls ($p<0.001$). There was a medium relationship between theta/beta ($p<0.001$) in Fz region and Conner's score. Theta/beta without test in Fz(sensitivity=62%; specificity=71%) and in Cz (sensitivity=51%; specificity=73%) would differentiate two groups only at a medium level.

Conclusion: It seems that further research should be conducted using more precise tools like QEEG with a larger sample volume and more limited age group.

1. Introduction

Attention Deficit/Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder, in which the children's ability in concentration and impulse control is clearly less than the natural level, such that it causes impaired academic and social function for the affected child[1].

This disorder is the most common disorder of childhood period. The prevalence of the disease differs given the population out of which the sample is taken, diagnostic criteria, and the

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diagnostic tools are used. Studies have reported the prevalence as around 4%[2] and 6%[3]. Another meta-analysis has reported this value as 5.3% around the world[4]. DSM-IV has also estimated ADHD prevalence as 3-5% among public children in school ages. This suggests that ADHD is one of the most common psychiatric conditions during school ages[5]. Currently, ADHD has widely been accepted as a heterogeneous disorder resulting from impaired function of central nervous system (CNS). There is some evidence suggesting different impairments in neurological function, which develop similar behavioral profiles[6].

Studies indicate that the main cause of ADHD is genetic (75%). The clinical symptoms of this disease are a result of an interaction between the neuroanatomical and neurochemical systems. Most ADHD children have no structural developmental disorder in their CNS[7].

This disease usually manifests itself with disorders such as learning, anxiety and mood disorders. The main symptoms including inattentiveness, impulsivity, and hyperactivity can be inferred by accurately examining the child's primary evolutionary pattern especially in conditions requiring attention and concentration. Hyperactivity may be severe in some situations like school, or sometimes it may be mild in one-person interview[7].

ADHD diagnosis needs the presence of hyperactivity/impulsivity or attention deficit symptoms in at least two different situations[7]. The Quantitative Electroencephalography (QEEG) data can be useful in predicting the response to treatment with stimulants and in the selection of neurofeedback protocols[8]. Biomarkers based on EEG including the measurement of the brain's theta/beta waves ratio in vertex(Cz) region can be helpful as a noninvasive method to achieve diagnostic and therapeutic objectives[9]. These biomarkers add a new dimension to the current diagnostic criteria, and for this reason EEG biomarkers have been widely used in ADHD research, though they have not been confirmed so far[10].

EEG studies indicate that in ADHD children, the theta-wave activity increases[6, 11, 12], which is primarily in the frontal zone[13, 14]. Also, elevated delta in posterior regions[15, 16], and diminished alpha and beta[16] in posterior regions are evident[6, 13, 14].

Furthermore, in ADHD children, during the alteration of a task given to the patient, an abnormal pattern in EEG activity is observed[17].

Nevertheless, Clark *et al.*[6] revealed that 15% of ADHD children have significantly higher levels of beta activity in the EEG.

Most results reported on ADHD are related to increased range of theta-to-beta ratio, which has been measured during resting in frontocentral regions [18-22].

The midline sagittal plane of the skull, (FpZ, Fz, Cz, Oz) is present mostly for reference/measurement points. It was confirmed that P3b was reliably identified at all the midline electrode sites in the 360–600 ms post-stimulus interval, the P3b peak amplitude was measured at Fz, Cz and Pz, whereas peak latency was only measured at Cz electrode site. Up to now, only a single EEG channel is typically used to calculate feedback information in EEG NF training. For theta/beta training in ADHD, the most often electrode Cz and Fz is considered[13, 15].

As currently there is no objective diagnostic test for ADHD, and the reports published out of studies are related to theta/beta ratio measurements, which are heterogeneous and incongruent, and also since no study has considered both of the confounding factors of age and gender together[23, 24], it seems that the relationship between the disease intensity and theta/beta has not been extensively investigated[25]. Various studies have examined the behavioral and neurological results in theta/beta through neurofeedback, even though limited results are available about the mechanism of action of theta/beta in neurofeedback[26]. Assuming that the size of relationship between theta/beta ratio and the disease intensity degree is large according to Kohen's criterion, this study attempted to determine the relationship between theta/beta ratio and the disease intensity in ADHD children as well as the sensitivity and theta/beta ratio characteristic to identify children with ADHD and healthy children as well as the accuracy of this ratio to differentiate diseased children with healthy ones in terms of ADHD.

The results obtained from this study will help to either confirm or reject incongruences of the previous studies. The results can also be used to confirm the neurofeedback diagnostic test in diagnosing patients and determining the disease intensity.

2. Materials and Methods

This study is a treatment-control test, in which the study population consisted of healthy and ADHD five-to-ten-year-old children visiting pediatric and adolescent psychiatric clinic at Zareh Hospital, Sari, Iran. The patients who received ADHD diagnosis by a pediatric psychiatry subspecialist were evaluated by K-SADS interview for a complete assessment.

Kiddie-Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present & Life Time (K-SADS-PL) interview is a diagnostic semi-structured interview, designed to assess the recent and previous episodes of psychopathology in children and teenagers between 6 and 18 years of age. In this interview, the required information is taken from parents, children, and other information sources, and eventually scoring is done based on the clinician's judgment. Most children get a score of 0-2: "0" represents insufficient information; "1" means an absence of symptom, and "2" signifies the presence of symptoms. The reliability and validity of this instrument have been reported to be acceptable in Iran. In research conducted in Iran, it was found that this instrument has good-to-excellent concurrent validity in diagnosing major disorders. Further, its retesting validity in ADHD and ODD diagnoses has been reported as excellent[27, 28].

The exclusion criteria included:

1. Child's lack of cooperation in neurofeedback

2. Existence or history of any psychiatric disorder causing ADHD and passive-aggressive disorder, as confirmed by pediatric and adolescent psychiatry subspecialist (mental retardation, learning disorders, depression, anxiety, etc.)

3. Studying at exceptional schools or a history of a serious problem in academic measurement performed at the very beginning of entrance to school by training and education authorities

4. History of consuming or current use of psychiatric drugs (antidepressants, antipsychotics, stimulants, etc.)

5. Use of any drug in the assessment day (including stimulants, anti-cold drugs, antipyretics, etc.)

6. History of neurological diseases including epilepsy with confirmation of a neurologist or consumption of antiepileptic drugs (even a history of fever and convulsion)

7. Parents' or children's refusal to participate in the study

The sample volume considered 60 children in each group.

Out of the children visiting Psychiatric Clinic at Zareh Hospital, Sari in 2015, 61 children who had received ADHD diagnosis were selected through a convenient sampling. The control group were chosen out of the same age range randomly from typical schools around the hospital. For a preliminary screening of the control group, SDQ was used. Finally, 59 children were included in the study as the control group after the preliminary screening and diagnostic interview and the confirmation of pediatric and adolescent psychiatry subspecialist stating the absence of any psychiatric disorder.

2.1. Strengths and Difficulties Questionnaire (SDQ)

It is a brief behavioral screening questionnaire for 3-16-year-old individuals with 25 items, which is filled by parents or teachers. This questionnaire was developed by Goodman *et al.* (1997) according to ICD-10 to assess 3-16-year-old children. This questionnaire has been normalized in Iran by Tehranidoost *et al.*[29, 30].

All patients were evaluated in terms of disease intensity based on parental Conner's questionnaire.

2.2. The Revised Conner's Parent Rating Scale (CPRS-R)

Conner's *et al.* have standardized this questionnaire in 1998. It is a 26-part questionnaire, which is filled by parents. The following indices are extracted from this scale: oppositional problems, hyperactivity-impulsivity problems, attention deficit problems and hyperactivity index. Rating of this questionnaire is performed at four levels (0= Never, 1= Only a little, 2= Somehow much, 3= Very much). The minimum score obtained from this questionnaire in every subscale is 35, while the maximum score is 90. According to the degree of importance of ADHD diagnosis, this questionnaire has been used as one of the inclusion criteria and to assess the intensity of symptoms. The validity of the original version and Persian translation of this questionnaire has been shown in the literature[31, 32].

Conner's *et al.* (1999) reported the reliability of this scale as 0.90. The validity of this questionnaire has been reported to be 0.85 by the Institute of cognitive sciences[17, 33].

The questionnaire of the subjects' information was also completed for all patients.

The questionnaire of the subjects' information included questions about age, gender, the level of education, and the method of treatment. To record the brain theta/beta ratio, the subjects were requested to avoid consuming stimulant drugs during the measurement day, in case they consumed. Neurofeedback was performed by the Procomp2 device as well as thought technology software. It was performed for all subjects within a specific and the same time interval during the day by a trained psychologist in cooperation with a medical student. Theta/beta ratio was measured and recorded in Fz and Cz points separately each once during the waking hours with open eyes without a mental task and another time during a specific mental task. In spite of the short duration of the measurement and recording by neurofeedback (2 minutes and 10 seconds), due to the probability of hyperactivity of the participants and problems in recording, it was not possible to repeat the measurement and recording process. The mothers were also trained for important points including the sufficient sleep of the child during the night before measurement, not consuming stimulants like Ritalin, anti-cold medications, caffeine containing foods, etc. in order to prevent any disruption in the accuracy of the job. Recording brain waves were performed on all children in the control group again in the same sites and with the same method, after completing the subjects. Information about the questionnaire.

2.3. Features of EEG Acquisition System

Signals on scalp are very small - microvolt range (1/1,000,000 Volts). Presents some challenges for acquisition. Acquisition involves – Amplification – Filtering – Digitizing (sampling) – Storage. Results in one time series per channel (64 in our lab). Typically adopt an accepted placement scheme for applying electrodes to the scalp. The international 1020 placement system is the most widely adopted. It uses a set of measurements relative to landmarks on the head. Name reflects the fact that electrodes are placed at intervals that are 10% or 20% of the distance between landmarks. Requires distance from front to back of head and distance from left to right. Front to back defined as distance from nasion to inion. Nasion - intersection of the frontal bone and two nasal bones inion - the most prominent projection of the occipital bone at the posterior inferior (lower rear) part of the skull. Electrode placement begins at 10% from these landmarks. Electrodes are placed at 20% intervals. Allows for 19 recording electrodes. Electrode names reflect location. – Even number right/ odd left; z = midline – C = central; F = frontal; P = parietal; T = temporal; O = occipital – Larger numbers are farther from the midline Approx. Size: 2.2 x 2.8 x 7.5" (75x55x19mm), Approx. Weight: 40 g w/o Batteries, EEG Resolution: ≤0.1 μV RMS (Channel A), Sample Rates: 256 samples/second (Channel A, B) 32 samples/second (Channel C, D), Battery Life: 10 Hours (minimum) (1 Alkaline AA cell)[34].

2.4. Statistical Analysis

To determine whether the data have been distributed normally or not, the Shapiro-Wilk test was used. The basic descriptive characteristics of the two groups (patient and control) were tabulated as mean (SD), median (Interquartile Range (IQR), or as a number (percentage). A comparison of the two groups in terms of comparative data was analyzed by chi-square or Fisher-exact test. To compare the EEG data obtained from the neurofeedback in the patient and control groups, the raw scores of age and the child's ranking were used as ANCOVA. The impact size was evaluated using eta squared (eta^2), and according to guidelines (Cohen, 1988), they were categorized into medium, small (<0.06), large (>0.14), and (0.06-0.14) groups. To associate the EEG data with behavior, a partial correlation (by controlling the age and child rank) was employed. Receiving Operational Characteristic (ROC) curve (as a statistical validation tool to determine the relationship between a continuous variable and a binary result), was utilized to determine the accuracy of EEG neurofeedback parameters to separate ADHD children and the members of the control group. The accuracy of neurofeedback parameters was measured by the area under curve (AUC) of ROC. An area of 1 represents a complete test, while 0.5 denotes a worthless test. Using a guideline, guess is considered for the classification of accuracy of a diagnostic test as follows: 90-100%= excellent, 80-90%= good, 70-80%= fair, 60-70%= poor, and 50-60%= failure. All data were analyzed by SPSS 22. The significance level was considered 0.05.

3. Results

A total of 120 children (61 patients and 59 children in the control group) were included in the study. The basic demographic data as well as the clinical characteristics are provided in Table 1. As can be seen in the Table, no significant difference was observed between the two groups in most basic characteristics. The child rank was higher in the patients' group than in the control group (p=0.03).

Table 1. Basic demographic and clinical characteristics in patients and control group members

		Group		P value
		Case (n=61)	Control (n=59)	
Age, year, mean (SD)		8.33 (1.52)	8.25 (1.53)	0.79
Sex, F/M ratio		12/49	12/47	0.92
Education, n (%)	kindergarten	3 (4.9)	2 (3.4)	0.57
	Pre school	4 (6.6)	7 (11.9)	
	School	54 (88.5)	50 (84.7)	
Child number, median (IQR)		2 (1-2)	2 (1-2)	0.23
Child rank, median (IQR)		1 (1-2)	1 (1-2)	0.03
Diagnosis age, mean (SD)		4.72 (1.64)	---------	--------
Drug use, n (%)		28 (45.9)	---------	--------

*IQR: Inter Quartile Range

**SD: Standard Deviation

The CPRS-R score was examined among the group members. The mean (SD) of the scores was 75.51 (19.22), and only two subjects had a score below 34 (min=35, max=90). EEG recorded results by neurofeedback for both patient and control groups are provided in Table 2. As shown in the Table, beta, theta, and theta/beta without test were higher in Fz region in the patients' group than in the control group (p<0.001). Beta and theta with the test in Fz region were higher in the patients' group (p<0.05). Beta with test in Cz was higher in the patients' group, when compared to the control group (p<0.05).

The relationship between CPRS-R score and neurofeedback parameters is provided in Table 3. As shown in the Table, there is a medium relationship between theta/beta (r=0.48; p<0.001) in Fz region and Conner's score.

Theta without mental task (eta^2=0.05; p=0.02), beta without mental task (eta^2=0.04; p=0.04), theta/beta without mental task (eta^2=0.06; p=0.01) in Fz region, theta without mental task

(eta^2=0.09; p= 0.001), beta without mental task (eta^2=0.04; p=0.03), theta/beta without mental task (eta^2=0.05; p=0.02) in Cz region, and theta with mental task (eta^2=0.03; p=0.05), beta with mental task (eta^2=0.08; p=0.02) in Cz region separate the patients' and control groups.

Other EEG parameters recorded with neurofeedback do not differentiate between the patient and control groups (p>0.05). ROC curve in Figure 1 indicates the relationship between the sensitivity and theta/beta characteristic in Fz and Cz. The diagonal curve reveals null hypothesis (0-hypothesis). As can be observed, theta/beta without test in Fz (AUC=0.62; 95%CI: 0.52-0.72; p=0.02; sensitivity=62%; specificity=71%) and in Cz (AUC=0.61; 95%CI: 0.51-0.72; p=0.03; sensitivity=51%; specificity=73%) separates the two groups only by a medium level.

Table 2. Electroencephalogram (EEG) neuro-feedback parameters (median (IQR)) are presented in patients and control group members

	Group		P value
	Case (n=61)	Control (n=59)	
Fz teta Without task	16.76	14.21	0.03
Fz beta Without task	7.25	6.7	0.03
Fz teta/beta Without task	2.21	1.89	0.02
Fz teta With task	18.03	15.45	<0.001
Fz beta With task	7.89	6.84	<0.001
Fz teta/beta With task	2.36	2.22	0.2
Cz teta Without task	16.20	12.95	0.009
Cz beta Without task	7.21	6.09	0.11
Cz teta/beta Without task	2.32	1.96	0.03
Cz teta With task	18.76	16.21	0.13
Cz beta With task	7.63	6.12	0.04
Cz teta/beta With task	2.42	2.4	0.86

Table 3. Correlations between Conners' Parent Rating Scale and EEG neuro-feedback parameters are presented in patients and control group members

	Fz teta_beta (without task)	Fz teta_beta (with task)	Cz teta_beta (without task)	Cz teta_beta (with task)	Conners
Conners	.124	.478**	-.056	.059	1.000
Fz teta_beta (without task)	1.000	.498**	.301*	.098	.124
Fz teta_beta (with task)	.498**	1.000	-.007	.104	.478**
Cz teta_beta (without task)	.301*	-.007	1.000	.688**	-.056
Cz teta_beta (with task)	.098	.104	.688**	1.000	.059

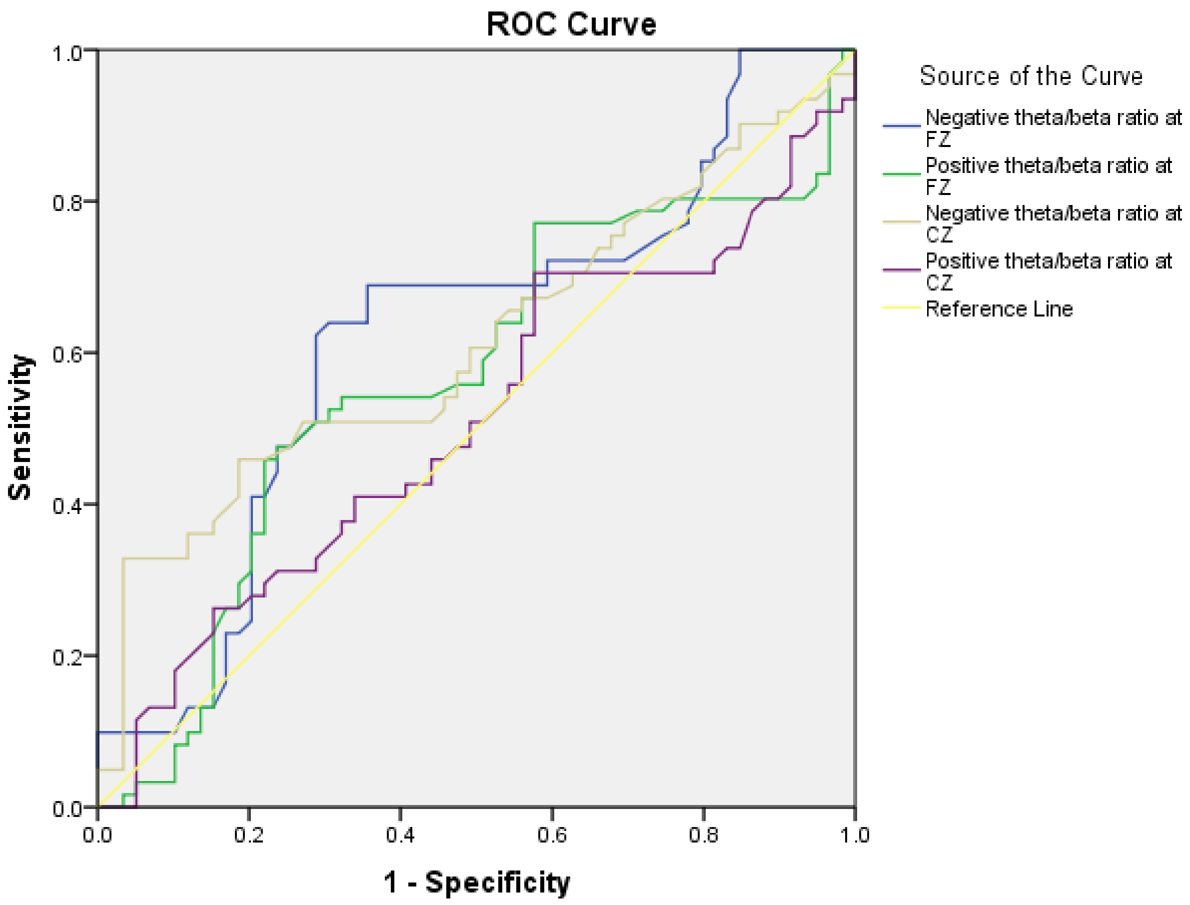

Figure 1. ROC curve showing the accuracy of with task and without task theta/beta ratios at FZ and CZ

*Negative theta/ beta: without task

**Positive theta/beta: with task

4. Discussion

This research aimed to determine the relationship between theta/beta ratio and intensity of disease in ADHD children and specify the power of theta/beta ratio to differentiate healthy children from ADHD counterparts. The results indicated that there is a medium relationship between theta/beta (r=0.48; p<0.001) in Fz region and Conner's score. Further, theta/beta without mental task (eta^2=0.06; p=0.02) in Fz region and theta/beta without task (eta^2=0.05, p=0.02) in Cz differentiate the control and patients' groups. In addition, a medium relationship was observed between theta/beta (r=0.48, p<0.001) in Fz region and Conner's score.

Moreover a number of research studies have found high levels of theta and/ or reduced levels of beta to be typical for patients with ADHD. Concluded that elevated relative theta power and reduced relative alpha and beta, together with elevated theta/alpha and theta/beta power ratios are most reliably associated with ADHD. They also emphasized the heterogeneity of ADHD and the fact that different EEG profiles may be found[5]. It has been shown that patients had an increase in absolute and relative theta, which was primarily found frontally. Another study however failed to find any EEG differences between ADHD and control subjects. So do children with ADHD had higher absolute and relative theta than controls. This pattern was clearer in the combined type of ADHD than in the inattentive type. Elevated theta persisted into adolescence and adulthood in patients with ADHD[6]. The theta/beta ratio was found to discriminate ADHD patients and normal controls with sensitivity of 86% to 90% and specificity from 94% to 98%. Also theta/beta ratio has much higher predictive power than rating scales do, for separating ADHD and clinical controls. The literature related to the theta/beta ratio and elevated theta as diagnostic tools in ADHD is inconclusive[16]. The theta/beta ratios of 209 subjects with ADHD were compared with those of a mixed clinical group with oppositional defiant disorder, mood disorder, or anxiety disorder without comorbid ADHD. An in- creased theta/beta ratio was found in 78% of ADHD subjects, and was not present in 97% of the other subjects. In a comparison of a group of 91 ADHD children with normal age-matched controls and children with conduct disorders; excessively slow wave activity was found only in the ADHD group[13].

Meta-analysis of EEG and ADHD including 9 studies (1498participants) reported significant effect sizes for theta and beta power, and theta/beta ratio (effect size=1.31, −0.51, 3.08, respectively). However, recently, it has been suggested that at least two different EEG subtypes in ADHD, a subgroup with true frontal slow EEG (i.e., enhanced theta activity)and a subgroup with slow alpha peak frequency, might lead to the finding of increased 'theta' power, and thus increased theta/beta ratio, in ADHD[35].

Vollebregt MA *et al.* investigated theta/beta index and Individual Alpha Peak Factor (IAPF) and its relationship with the behavioral function in ADHD children. Theta/beta and Theta values were significantly correlated with central symptoms of ADHD[36]. The results of this study emphasized that theta/beta and theta values are related to behavioral symptoms in ADHD children. In the present study, there is a medium relationship between theta/beta (r=0.48; p<0.001) in Fz region and Conner's score. However, in the study by Vollebregt MA *et al.*, the site of theta/beta measurement and whether it is with task or not have not been differentiated.

In a case-control study, Wiersema JR examined EEG activity before and after a mental task with the help of a computer software called 3n-back in ADHD children. Three-minute EEG with closed eyes in rest state regarding theta/beta or theta or other frequency bands before and after 3n-back in 21 ADHD children was compared with 22 normal children. No significant difference was observed neither prior to nor after the test (p>0.05). This suggests that theta/beta or theta cannot be considered universal for this disorder[37]. However, in our study, theta/beta without mental task in Fz region was higher in the patients' groups than in the control group (p<0.001). Also, theta/beta with mental task in Fz region had p=0.2.

Usage of neuropsychiatric EEG based assessment aid was confirmed by FDA in 2013 as the first instrument to assess ADHD. However, until 2014, no study examined the size of theta/beta1 (beta: 15-18Hz) and theta/beta2 (beta: 18-21Hz) separately, and no data have been released suggesting that EEG can differentiate between diagnostic ADHD subgroups.

In a cross-sectional study in 2014, Delgado-Mejía *et al.* investigated theta/beta value in 6 to 2 patients between eight and 17 years of age. The aim of that study was to measure theta/beta values in terms of QEEG in a sample of patients with completely proper ADHD diagnosis to compare neurophysiological patterns based on diagnostic subtopics. The patients were divided into two groups in terms of diagnostic subtopics. Elevation of theta/beta-1 and theta/beta-2 which had been recorded in Cz region was higher than the levels in C3 and C4 regions. Medium and significant differences were observed between the two subsets only at beta: 15-18Hz in the occipital region. Therefore, although NEBA evaluation may be helpful in the differentiation of ADHD in control samples and other neurodevelopmental disorders, this study showed that beta-1 and beta-2 should be assessed separately[38].

In a pilot and follow-up study, children referred for possible ADHD were diagnosed with these of clinical interviews and rating scales. They were also examined with QEEG. A sensitivity of 87%, a specificity of 94%, and an overall accuracy of 89% was reported for the theta/beta ratio. Accuracy was between 47% and 58% for the rating scale. No significant QEEG changes were induced by the administration of methylphenidate in the resting state. These data suggest that methylphenidate has greater electrophysiological influences on the cerebral topographical activities during the performance of attentional tasks, as compared to the resting state, in boys with ADHD[14]. The advantages of the QEEG method in comparison with these other brain imaging methods are that it allows attentional tasks to be performed simultaneously, as well as being safe and inexpensive. This technique quantifies the EEG recorded across the more than 19 regions included in the International 10/20 system, and has been shown to be a sensitive indicator of cortical electrophysiological dysfunction in neuropsychiatric disorders Studies using QEEG have previously attempted to investigate the cerebral functional changes in ADHD[35]. However the results of these previous studies were inconsistent. Callaway *et al*. reported that ADHD children showed decreased α wave and β wave activities in the parietal and occipital cortex compared to normal children, whereas Kuperman *et al.* reported a relative increase of β wave activities in ADHD children[15]. Some researchers reported an absolute increase of activities in all EEG bands, and suggested that there were two subtypes of ADHD: the first exhibiting a slowing-down of EEG activities in the frontal regions and the second showing increased EEG activities in the frontal regions[13].

In the present study, theta/beta in both Fz and Cz regions were measured both with mental tasks and without any mental task. The results suggested that theta/beta without the test in Fz region was higher in the patients' groups than in the control group ($p<0.001$). In this study, the age group of patients and control groups had an average age of 8 years, which is mostly in the age group defined for the prevalence of the disease (7-8 years)[7].

The present investigation is consistent with the studies which show grand-average ERPs at the Fz, Cz and Pz sites for rest (without task) trails. The rest amplitudes at Cz and Pz sites significantly decreased after the fatigue-inducing phase ($F(1,34) = 9.64$, $p < 0.01$, $\eta\ p2 = 0.22$; $F(1,34) = 4.63$, $p = 0.04$, $\eta\ p2 = 0.12$, respectively). The interactions between testing phase and condition were significant at the Cz and Pz sites ($F(1,34) = 8.95$, $p < 0.01$, $\eta\ p2 = 0.21$; $F(1,34) = 4.91$, $p = 0.03$, $\eta\ p2 = 0.13$, respectively). For the rest (without task) amplitudes, the main effect of testing phase was significant at the Cz site ($F(1,34) = 4.35$, $p = 0.05$, $\eta\ p2 = 0.11$).There were no other main effects or interactions found. It revealed that although rest amplitudes increased at the Cz site after the fatigue-inducing phase [13, 14, 16, 35].

In the studies by Dupuy FE *et al.*[39] EEG differences were examined among girls with ADHD, of attention deficit type and combined type. Only girls were included in the study and they did not report theta/beta results. In contrast, the present study included both girls and boys and in addition to beta and theta, theta/beta ratio were recorded in Fz and Cz regions in both states of presence of mental task and its absence.

GeirOgrim, JuriKropotov, Knut Hestad conducted a case-control study (62 patients and 13 nine healthy individuals) to investigate whether theta/beta, theta, and beta values separately are associated with behavioral symptoms or not. The other objective was to see whether these criteria are different among children and adults with

ADHD and those in the control group. A major increase was observed in theta values in 25.8% of the patients, while it was observed only in one person in the control group (2.6%). In the patients' group, theta in Cz had a positive relationship with functional and attention deficit issues, while it had a negative relationship with hyperactivity. A significant growth was seen in theta among ADHD patients' subgroup, associated with attention deficit and executive problems. In this study, it was assumed that the accuracy of theta/beta, theta, and beta may be 80% for differentiating ADHD and healthy children, which was not obtained. Indeed, none of the three EEG scales differentiated patients from the control individuals significantly. The negligible errors in GO/NOGO differentiated between the patients' and control groups with an accuracy of 85% (theta made a differentiation of 63%, while theta/beta managed to differentiate the two groups by 58%). Although around 75% of patients with these criteria have not been identified, the sensitivity of these criteria are far lower than the value reported in the study by Synder *et al.* (2008), and was mostly similar to the results of Coolidge *et al.* (2007). Nevertheless, finding a considerable increase in the theta band may be considered a supportive evidence for ADHD diagnosis. Based on the data of this study, it can be predicted that these patients are identified behaviorally with attention deficit and executive problems, a pattern which is observed in ADHD-C as well as ADHD-I. The elevated theta as a marker of attention deficit and executive problems in ADHD children may be the most important finding of this study. It does not confirm the results of this research study suggesting that elevated theta/beta ratio can identify most cases of ADHD. However, it is mostly congruent with the studies indicating different EEG patterns in ADHD children. This diversity in the results may reflect different data collection methods and creation of artificial data. In this study, 30% of patient children had an IQ below 80. A large number of patients had also an IQ between 70 and 80, limiting generalizability of the results. In our study, the IQ of the children was not measured, and only patients with a history of being mentally challenged and based on a diagnosis of a podiatry psychiatrist were excluded from the study[25].

In the research by Tieme W. P. Janssen *et al.* to determine the relationship between brain theta/beta levels during a mental task training through neurofeedback to children with ADHD, the results suggested the lack of change in theta level and linear growth of beta level[26]. The sample volume in that research was considered 38, and no control group was taken into account.

4.1. Limitations

The group of ADHD children was compared only with healthy children, and thus no data were obtained as to whether theta, beta, or theta/beta can differentiate ADHD from other psychiatric and evolutionary diseases or not. The IQ of the patients was not measured with any instrument, and to exclude patients with mental retardation, only parental report, academic background, measurements done by training and education authorities and studying in typical schools and evaluation by a podiatry and adolescent psychiatry subspecialist were relied on. Beta band in individual beta 1 and beta 2 was not assessed. Out of the brain cortical regions, only Fz and Cz were examined. Finally, this study did not investigate executive problems neither at questionnaire level nor through computer software.

4.2. Strong Points

Both male and female children were included in the study. They were screened in terms of other psychiatric diseases and mental retardation. The most important interfering factors on brain waves including having a disease or consumption of medication and even the time of data registration were taken care of.

5. Conclusion

The diagnostic importance of theta and beta brain waves in ADHD has still remained unknown. Furthermore, whether training elevation of theta and beta activity in ADHD children is possible or not, or whether such training effects can influence underlying behavioral changes are still equivocal. Indeed, the theta/beta ratio in neurofeedback may be helpful in altering brain activity using major effective situations with the aim of promoting the level of neurocognitive function and behavior in ADHD children. Nevertheless, few studies have shown that real learning occurs during treatment with neurofeedback in ADHD children, where this is an element that is essential for effectiveness of the treatment. Neurofeedback can also affect a larger cortical area. Future studies may add more electrodes to measure EEG effects more extensively.

Future studies are encouraged to obtain electrophysiological training data and reports various training components in the treatments. This type of data can play a significant role in developing more effective neurofeedback interventions for ADHD through separating trainable components and enhancing our knowledge about the underlying mechanisms of neurofeedback.

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