Comparison of Electrophysiological Indices of Children With Attention Deficit Hyperactivity Disorder (ADHD) Comorbid With and Without Reading Disorder (ADHD & RD)

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Research

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Abstract

Background

Attention Deficit Hyperactivity Disorder (ADHD) is a neuropsychiatric disorder. Most children and adolescents with ADHD have at least some developmental or mental disorders identified from the early years of elementary school. The most common of these are educational and learning problems in these children, which are probably due to the attention deficits of these children. Therefore, it is expected that the cortical activity pattern of ADHD children is different from ADHD comorbid with learning disabilities, which we have examined in this study.

Methods

This study evaluated the pattern of cortical activity in children 6 to 12 years old with ADHD comorbid with and without the reading disorder (ADHD & RD) using 21-channel electroencephalography. Multivariate analysis of variance with repeated measures in a $2 \times 3 \times 7$ design and T-test was used for statistical analysis.

Results

The results show that in ADHD children, the activity of different bands increases compared to ADHD comorbid with RD children. In the ADHD group compared to the ADHD comorbid with RD group, the theta/beta ratio in all three regions, especially the anterior region, is higher than the theta/alpha activity in those areas, and this group has significantly higher activity in all three brain regions, especially the anterior region, compared to ADHD comorbid with RD patients.

Conclusions

Functional changes in the left parietal cortex, which is part of the frontoparietal attention network and involved in phonological processing, reading, and calculation, are evident in children with ADHD comorbid with and without the reading disorder (ADHD & RD). However, ADHD without reading disorder shows more activation of the frontoparietal network than ADHD comorbid with reading disorder, and therefore it can be said that ADHD without reading disorder exerts more cognitive control. Therefore, it is likely to be possible to prevent educational problems in these children by using neurofeedback or prescribing drugs that increase the activity of the areas involved in attention.

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is a common, early-onset neurodevelopmental disorder, with an estimated prevalence of 5–6%, often persisting into adulthood [1,2]. The majority of children and adolescents with ADHD have at least one comorbid developmental or mental health disorder that the most common of these are learning disorders and academic problems, including low scores on standard reading and math tests, and dropout [3-6]. One of the most common symptoms of this disorder is attention problems that affect phonological processing and cause academic and learning difficulties in these children [3,7]. In fact, approximately 18-45% of children with ADHD have a reading disorder (RD) [8]. Also, some neuroimaging studies indicate a defect in right hemispheric frontostriatal and frontoparietal attention networks in ADHD [9]. Therefore, ADHD and reading disorder are often associated because the importance of attention has been documented since the early stages of schooling (between 5 and 7 years old), and the ability to directly control attention influences the efficiency in information processing and improves learning [10].

Dyslexia or reading disorder is characterized by impairments in a specific phonological process called word decoding [11] that hypoactivation in the primary neural network for decoding includes the posterior superior temporal gyrus and inferior parietal lobe are frequently reported in RD in neuroimaging studies [12].

Neuroimaging studies show different activation of frontal, parietal, occipital, and cerebellar regions while reading in the RD, ADHD comorbid with RD, and control groups, have confirmed that children with RD and those with ADHD comorbid with RD have distinct differences alterations in neural circuits related to reading deficits. In these studies, the control group showed increased functional connectivity between reading-related networks and cognitive-control networks. These studies also reveal dominant activation in the right hemisphere and significant activation of the frontal lobe in children with reading disorders compared to the control group and increased functional connectivity between networks related to their reading deficit; mainly between networks related to lower-level visual processing (including the fusiform gyrus) and those associated with executive function and language processing (semantic) [13]. In addition, children with ADHD comorbid with RD show decreased activity of the right angular gyrus, and bilateral frontal, parietal, and occipital cortex and increased activity in the right supramarginal gyrus, and they show poor functional connectivity between neural circuits related to attention, visual processing, and neural networks related to executive functions, mainly due to their attention deficit [14] that predict poorer phonological ability in ADHD comorbid with and without RD.

Because all of these functions are based on brain function, one of the tools to study the cortical functions of the brain is electroencephalography (EEG) [15]. To quantify the pattern of cortical activity and its excitation, various engineering methods such as Fast Fourier transform (FFT) are used, called Quantitative electroencephalography (QEEG).

A meta-analysis study of QEEG in ADHD compared to the control group showed dysfunction in the frontal, parietal, and temporal lobes. EEG pattern in these children also showed increased delta, theta, and beta bands in frontal areas [16], an increase in the intra-hemispheric coherence of the delta and theta bands in the left hemisphere, decreasing relative power of alpha and beta, and an increase in the absolute power of alpha1 in the frontal regions. An increase in the absolute power of delta and theta in the front-central area, a decrease in the absolute power of high-frequency waves (especially the beta band) in the frontal and central regions, and decreased beta in the posterior regions was also shown.

Theta and beta bands and theta/beta and theta/alpha ratios are parameters of QEEG that are commonly studied in electrophysiological studies of ADHD [17]. These are reliable criteria for distinguishing ADHD children from healthy children or between ADHD subtypes, in which, an increase in these ratios was observed in the right frontal lobe and an increase in theta/beta ratio in the parietal-central areas. These alterations indicate a decrease in right hemisphere function, especially the right frontal lobe [18-20].

In contrast, when examining the brain regions related to language processing, about 87% of children with reading disorders showed increased beta in the cingulate cortex, frontal pole, anterior temporal and left parietal lobes, increased the absolute and relative power of delta and theta in the frontal and temporal bilaterally, and the left parietal, and increasing the theta/alpha ratio. Also, decreased absolute power of alpha2 and alpha3 in the left occipital, temporal and parietal lobes, reduced absolute power of alpha and beta bands in the right frontal and occipital lobes (due to impaired attention and memory retrieval), and decreased theta in the right parietal and the cingulate cortex observed in these children [21-23].

Also, It has been reported an increased relative power of the theta, the increased absolute power of the delta band in the left posterior regions, increased the relative power of delta band in the right posterior regions, decreased absolute power of the alpha band in the left posterior regions, and reduced relative power of the alpha band in the left hemisphere in children with ADHD comorbid with RD compared to children with ADHD [24,25].

According to the above, there is a significant difference between the electrophysiological indices in children with ADHD comorbid with and without RD. However, there has been no research to compare electrophysiological indices in these groups so far that the current study examines this issue.

Method

Participants

The statistical population of the present study was children 6 to 12 years old with attention deficit hyperactivity disorder (ADHD) comorbid with and without the Reading disorder (ADHD & RD) referred to specialized centers of psychiatric in Tabriz, Iran in 2020.

ADHD subjects met the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria for ADHD. These children were screened using Conners Questionnaire (Teacher and Parent Version), Test Dyslexia and Reading (NEMA), and diagnostic interviews and were grouped into two groups of children with ADHD with and without RD.

From the above statistical population, a sample of 30 children with ADHD ($M_{age} = 8.63$ years, $SD = 1.21$) and 30 children with ADHD comorbid with RD ($M_{age} = 9.18$ years, $SD = 1.83$) were selected by the causal-comparative method on the following including and excluding criteria. Inclusion criteria include: having a diagnosis of ADHD based on a clinical interview by a child and adolescent psychiatrist and based on diagnostic criteria DSM-5, age range 6 to 12 years, first visit by a specialist for diagnosis, having an average level of intelligence. Exclusion criteria included: the presence of other comorbid psychiatric disorders, history of brain injury, trauma, epilepsy, mental retardation, autism, and inability to collaborate in the study.

After selecting these groups based on including and excluding criteria, the necessary explanations were provided on how to test, research steps, and assuring the respondents that the information in the questionnaire is confidential. If satisfied, they completed the informed consent form of the research. This study is approved by the Research and Technology Department of Azerbaijan Shahid Madani University – Tabriz, Iran.

Tools

Conners Questionnaire

The short form of Conners questionnaire (teacher and parent versions) was used to screen for Attention-Deficit / Hyperactivity Disorder symptoms. The teacher version of this questionnaire consists of 28 items, and the parent version consists of 27 items. This questionnaire includes 4 subscales (coping behavior, attention deficit, hyperactivity, and compound type), rated from 0 to 3, and the alpha coefficients of these subscales are reported 0.87, 0.89, 0.87, 0.91, respectively [25]. The cut-off scores for the Attention Deficit, Hyperactivity Disorder, and the Combined Scale are 7, 8, and 13, respectively, and a score equal to or higher than the cut-off scores indicates the presence of these symptoms in the participant.

Shahim et al. (2008) investigated the validity and reliability of this questionnaire in Iran. In this study, Cronbach's alpha coefficients for the total score were 0.86, and were 0.88 for behavioral problems, 0.89 for inattention-dreaming, 0.74 for hyperactivity, 0.81 for anxiety-shyness, and 0.80 for passivity, respectively, and correlation coefficients for these subscales were 0.86, 0.74, 0.85, 0.52 and 0.29, respectively. Also, a retest method was used to evaluate the reliability of the scale, whose coefficients for the total score were 0.76, and for the subscales ranged from 0.68 (passivity) to 0.82 (inattention - daydreaming) [26].

Test Dyslexia and Reading (NEMA)

This test was standardized in Iran by Kormi Nouri and Moradi (2005) for monolingual (Persian) and bilingual students (Tabriz and Sanandaj), girls, and boys from the primary school. The alpha coefficient of the total test was 0.82. This test set contains ten sub-tests. The overall Cronbach's alpha for the word reading tests with high-frequency words, words with medium frequency, low-frequency words, word string, the test of rhyme, calling pictures 1, 2, text comprehension, words understanding, elimination of sounds, and pseudo-word, reading fake-words were 0.97, 0.98, 0.98, 0.95, 0.89, 0.67, 0.68, 0.48, 0.71, 0.95 and 0.97, respectively [27].

Electroencephalography (EEG)

Cortical electrical activities of patients were recorded by 21 channels EEG with a Mitsar amplifier with a sampling rate of 500 Hz with eyes opened. The electrodes were placed in different head parts according to the standard protocol 10-20 using an electrocap. The recording range was between 0.3 and 40 Hz. For quantitative analysis, the recorded waves were converted to numbers using complex Fast Fourier transform mathematical processes, and the numbers were converted to images and graphs. Electrophysiological parameters of different bands for anterior (set of Fp and F electrodes), central (set of electrodes T and C), and posterior regions (set of electrodes P and O) in two hemispheres calculated by neuroguide software and according to age group and gender were converted to Z score. Based on the results, the frequency bands include the following: delta band (1 to 4 Hz), theta band (4 to 8 Hz), the alpha band (8 to 12 Hz): alpha 1: 8 to 10 Hz, and alpha 2: 10 to 12 Hz, the beta band (13 to 30 Hz): beta 1: 13 to 15 Hz, beta 2: 15 to 18 Hz, and beta 3: frequency 18 To 30 Hz.

Result

Multivariate analysis of variance with repeated measures was used in a 2 * 3 * 7 design for statistical analysis. In this study, 2 represent intergroup variables (group of children with ADHD and ADHD comorbid with RD), 3 Indicators of intra-group variations of brain regions (anterior, central, and posterior), and 7 represents the different bands of the brain's electrical activity (delta, theta, alpha1 and alpha 2, beta 1, beta2 and beta 3).

Descriptive statistics for the research variables are shown in the table 1. The results of Multivariate analysis of variance with repeated measures for relative power shows the significance main effect of the region ($df=1.486$, $f=98.659$, $p=0.001$), band ($df=3.070$, $f=42.012$, $p=0.001$), and

Table 1 Descriptive statistics of variables by study groups

Standard deviation	mean	group	variable	Standard deviation	mean	group	variable	Standard deviation	mean	group	variable
.49045	.5416	Group1	Delta posterior	.68565	.2429	Group1	Delta central	.78064	.0671	Group1	Delta Anterior
.63302	.8051	Group2		.61460	.6132	Group2		.52900	.6991	Group2	
.66977	.6714	Group1	Theta posterior	.71946	.3515	Group1	Theta central	.75415	.3321	Group1	Thete anterior
.81043	.7037	Group2		.73663	.3581	Group2		.56206	.0581	Group2	
.77115	-.8318	Group1	Alpha 1 posterior	.84913	-.3932	Group1	Alpha1 central	1.00525	-.2091	Group1	Alpha 1 anterior
.83062	-1.1430	Group2		.72978	-.7778	Group2		.78917	-.8110	Group2	
.78734	-.2813	Group1	Alpha 2 posterior	.88818	-.0526	Group1	Alpha2 central	.74507	-.0023	Group1	Alpha 2 anterior
.68968	-.5583	Group2		.68312	-.3951	Group2		.57879	-.4789	Group2	
.89165	.5455	Group1	Beta 1 posterior	.89906	.2686	Group1	Beta 1 central	.89801	.2542	Group1	Beta 1 anterior
.97734	.4325	Group2		.90625	.1581	Group2		.91683	-.0175	Group2	
.79225	.5392	Group1	Beta 2 posterior	.79426	.1419	Group1	Beta 2 central	.83978	.1067	Group1	Beta 2 anterior
.95407	.3166	Group2		.79662	.0496	Group2		.78569	-.0975	Group2	
.69570	.5372	Group1	Beta 3 posterior	.65049	.1400	Group1	Beta 3 central	.56674	-.0788	Group1	Beta 3 anterior
.69429	.4254	Group2		.56352	.0965	Group2		.68020	-.1705	Group2	
1.16440	-.7903	Group1	Theta / Alpha posterior	.97119	-.2786	Group1	Theta / Alpha central	.92730	-.0888	Group1	Theta / Alpha anterior
.86824	-1.0787	Group2		.67787	-.5998	Group2		.71978	-.3871	Group2	
6.93298	.3796	Group1	Theta / beta posterior	3.79329	.2445	Group1	Theta / beta central	1.86004	.1855	Group1	Theta / Anterior beta
.76327	-1.0453	Group2		.67753	-.6803	Group2		.70170	-.3375	Group2	

Group1: ADHD

Group2: ADHD comorbid with RD

interactive effect of region * band ($df=5.014$, $f=41.570$, $p=0.001$), region * group ($df=1.486$, $f=5.531$, $p=0.05$), band * group ($df=3.070$, $f=4.487$, $p=0.01$) and region * band * group ($df=5.014$, $f=3.747$, $p=0.01$). In other words, the results show that the two groups of ADHD and ADHD comorbid with RD patients differ in brain activity in the three brain regions (anterior, central, and posterior) and also among the seven activity bands (Delta, Theta, Alpha 1, Alpha 2, Beta 1, beta2 and beta 3). Comparison of means using the independent group t-test showed that ADHD patients had significantly higher activity in all three brain regions, especially the anterior region, compared to ADHD comorbid with RD patients. Also, the follow-up test results showed that ADHD patients showed increased activity of these bands compared to ADHD comorbid with RD group. So that the delta, theta, beta 1, beta 2, and beta3 bands activity in the posterior region is more than center and anterior. However, alpha1 and alpha2 bands activity in the anterior and center area is more than in the posterior region. Also, the results of Multivariate analysis of variance with repeated measures for power ratio show the significance main effect of the region ($df=1.048$, $f=5.890$, $p=0.05$) and the interactive effect of the region * group on the anterior ($df=118$, $f=5.671$, $p=0.05$) and central areas ($df=118$, $f=3.938$, $p=0.05$). But this effect is not significant in the posterior region ($df=118$, $f=3.225$, $p=NS$). Also, theta/alpha ratio was significant in two groups ($df=118$, $f=2.119$, $p=0.05$), but the effect of theta/beta ratio was not significant in both groups ($df=118$, $f=4.115$, $p=NS$). In other words, the results show that the two groups of ADHD and ADHD comorbid with RD patients differ in brain activity in the three brain regions (anterior, central, and posterior) and between theta/alpha and theta/beta ratios. Comparison of means using the independent group t-test showed that ADHD patients had significantly higher activity in all three brain regions, especially the anterior region, compared to ADHD comorbid with RD patients. The follow-up test results showed that the ADHD groups showed an increase in theta/alpha and theta/beta ratios compared to the ADHD comorbid with RD groups. So that the theta/beta ratio in all three regions, especially the anterior region, is higher than the theta/alpha activity in those areas.

Discussion

ADHD and RD are often associated, and dyslexia is closely related to attention problems. Because the ability to control attention affects the efficiency of information processing and learning improvement [3,7]. Cortical studies in ADHD show attentional networks deficiency in the right hemisphere, and children with ADHD comorbid with RD show defects in the decoding neural network in the left hemisphere [22,24].

The results of electrophysiological indices analysis showed that in children with ADHD compared to children with ADHD comorbid RD, the activity of all three areas, especially the anterior areas, is more than the central and posterior areas. This is probably due to the increased beta1&2, involved in higher-order processing, in the anterior regions [28,29].

Other results of this study indicated an increase in slow waves and alpha activity in all areas, especially in the anterior areas in two groups. These findings are in line with other studies using Functional magnetic resonance imaging (fMRI) in these children at resting state that showed the increased amplitude of low-frequency fluctuation in the anterior cingulate cortex, left fusiform, right inferior temporal gyrus, sensorimotor areas and left supplementary motor cortex [30,31]. They also showed decreased functional connectivity in different areas of the brain, which altogether confirms brain hypoactivity and various cognitive defects in these children [30,31]. Furthermore, one of the main findings from a pioneering ADHD PET imaging study by [Zametkin et al \(1990\)](#) was that of global underactivity, with global cerebral glucose metabolism reported as 8.1% lower in ADHD patients than in healthy controls [32].

Increased delta activity indicates delayed brain maturation and decreased cortical arousal during information processing, especially in cognitive and attention tasks [33]. Therefore, increased delta activity in two groups indicates a delay in brain maturation, especially in attention systems [34]. Also, the theta/alpha ratio (TAR) is a biomarker for brain maturation, especially in central or posterior regions [35]. Increased TAR in the posterior regions in children with LD and in the frontocentral regions in ADHD has been seen, associated with hyperactivity, impulsivity, and inattention [36].

Attention deficits in these children can also be due to the dysfunction in different neurotransmitter systems because noradrenergic and dopaminergic neurotransmitters mediate executive functions. However, due to the degradation of dopamine and noradrenaline in the frontal lobe in ADHD, the increased theta may be due to decreased activity of the prefrontal cortex and the nigrostriatal system in the release of dopamine [37]. ADHD Positron emission tomography(PET) imaging study by [Zametkin et al. \(1990\)](#) also found that the ADHD group showed regional hypoactivity of attention and motor control areas including the dorsal anterior midcingulate cortex (daMCC), superior prefrontal cortex, and premotor cortex [32].

The theta/beta ratio (TBR), especially in fronto-central regions, is considered a biomarker for top-down control of attention and emotion [38]. Because, in addition to the frontal lobe, the parietal lobe is also critical in finding the target and attention to it. LD and ADHD children typically show an increased absolute theta power, decreased absolute beta power, and increased theta/beta power ratio in the right frontal lobe compared with the control group [22,39,40]; these results align with the present study's results. In addition to the dysfunction of the frontal and parietal lobes, recent studies indicate dysfunction of the temporal lobe in some ADHD children because the activity of the temporal increases to compensate for the decreased activity of the frontal and parietal lobes [41]. Interestingly, in a study which was done on children with ADHD by DTI, fronto-striatal and fronto-parietal circuitry abnormalities were also seen [42]

Also, the present study's results indicate a decreased absolute and relative alpha power in the posterior regions compared to the anterior and central regions in both groups, indicating that these children cannot attend to and process visual stimuli as efficiently as healthy children [43]. On the other hand, the alpha rhythm is also associated with various cognitive processes such as memory and arousal states, and an increased alpha band indicates low arousal in ADHD. The exciting paradox in ADHD is that while these children are hypoaroused (a factor that should increase alpha levels), they typically show a reduced alpha band compared to control subjects. This finding suggests that two factors impact the alpha band, the arousal factor that increases the alpha band, but another unknown factor reduces the alpha in these children [44].

Neuroimaging studies suggest that word recognition skills in reading are associated with the functional integration of the two systems in the left posterior regions: a dorsal circuit (temporo-parietal) and a ventral circuit (occipito-temporal). The posterior system appears to be functionally disrupted in developmental dyslexia. Because the temporal and parietal regions involved in language and calculation have lower performance in LD, ADHD comorbid with and without RD [21,45]. Using PET and fMRI, studies performed by [Eraldo Paulesu et al. \(2014\)](#) showed a decreased activity in the left superior and middle temporal gyri, inferior frontal gyrus bilaterally, right inferior parietal lobule, and right precentral gyrus, during the phonological manipulation in children with RD compared to control [46]. Hence, high delta and theta activities in the frontal, temporal and parietal areas in this study are correlated with weakness of reading and phonological awareness, reduced accuracy and processing speed in these children [24,47,48]. For this reason, these children cannot process all the incoming information adequately and fail in different tasks that require multiple cognitive processes, such as learning, reading, writing, and mathematics [49].

During decoding, increased activity in the right supramarginal gyrus was also seen, supporting the connections between the executive control network and the language network in the left hemisphere. Thus, the increased activity in the right supramarginal gyrus in ADHD comorbid with RD suggests that attention may affect phonological processing [14]. Hence, the results indicate the role of attention as a link

between executive function and reading skills [50]. It is interesting that Makris et al. (2008), showed abnormalities of the cingulum bundle and superior longitudinal fascicle II—connection pathways that subserve attention and executive functions— in ADHD [51].

Attention also helps to detect the word early in the left hemisphere by activating the right inferior parietal lobe [14]; However, ADHD without reading disorder shows the increased activity of the superior parietal and frontal lobes compared to the control group, and therefore it can be said that ADHD without reading disorder applies more cognitive control [52].

Limitations

One of the limitations of the present study was the lack of drug control and its dose in these children because drugs used by these children, such as Ritalin and Risperidone, can affect electrophysiological activities. However, research on the effects of drugs on QEEG components is contradictory. Another limitation was the lack of a classification of children based on the duration of the disease. Also, in this study, two abnormal groups were compared.

Conclusions

The main problem in ADHD is the delay in brain maturation, especially in the attention systems [36], which causes reading and learning disabilities in these children. Because attention affects phonological skills [3,7], the prevalence of these defects is high in ADHD [8]. So there is a correlation between attention problems and reading problems.

Functional changes in the left parietal cortex, which is part of the frontoparietal attention network and involved in phonological processing, reading, and calculation, are evident in children with ADHD comorbid with and without the reading disorder (ADHD & RD) [50,53]. However, ADHD without reading disorder shows more activation of the frontoparietal network than ADHD comorbid with reading disorder, and therefore it can be said that ADHD without reading disorder exerts more cognitive control [54].

Therefore, part of their attention and educational problems can be mitigated by providing appropriate treatment strategies such as neuro-therapy [16,52, 55,56].

Abbreviations

ADHD: Attention Deficit Hyperactivity Disorder; RD: reading disorder; EEG: Electroencephalography; QEEG: Quantitative electroencephalography; DSM: Diagnostic and Statistical Manual of Mental Disorders; FFT: Fast Fourier transform; Functional magnetic resonance imaging (fMRI); Positron emission tomography(PET); dorsal anterior midcingulate cortex (daMCC); TBR: theta/beta ratio; TAR: theta/alpha ratio.

Declarations

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Authors'contributions

Gholamreza Chalabianloo and Zahra Keshtgar designed the project, and prepared the manuscript. Gholamreza Noorazar and Ahmad Poormohammad revised the manuscript. All authors approved the final version.

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Availability of data and materials

All data generated or analyzed during this study are included in this article.

Ethics approval and consent to participate

Subjects gave informed, written consent, and the Research and Technology Department of Azerbaijan Shahid Madani University – Tabriz, Iran approved this study. Written informed consent was obtained from the parents of all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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