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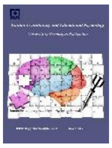

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The Effectiveness Transcranial Direct Current Stimulation on Depression and Working Memory in Children with Attention-Deficit/Hyperactivity Disorder (ADHD)

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Abstract: Children diagnosed with Attention Deficit/Hyperactivity Disorder (ADHD) face a range of behavioral and emotional challenges. This study aimed to explore the effectiveness of transcranial direct current stimulation (tDCS) in mitigating depression and improving working memory among children with ADHD. This research followed a semi-experimental design, incorporating pre-test, post-test, and follow-up phases, along with a control group for comparison. The study's target population encompassed children between the ages of 6 and 12 who were diagnosed with ADHD and seeking treatment at the Nirvana Neuropsychological Clinic of Shiraz (Iran). The study involved 30 children who were selected through random selection and assigned to two distinct groups: the experimental group, which underwent transcranial direct current stimulation, and the control group, which did not receive any form of intervention. At the outset and conclusion of the therapy sessions, as well as during the follow-up period, both groups completed tasks involving Geometric Shapes and Digit Span (DS). Data were subjected to analysis using analysis of covariance. The results underscored a noteworthy decrease in depression levels and a notable enhancement in working memory among participants in the experimental group as compared to those in the control group (P<0.001). These research findings furnish compelling evidence that transcranial direct current stimulation (tDCS) can be considered an efficacious intervention for ameliorating mood disorders such as depression and bolstering executive functions, including working memory, in children with ADHD.

Keywords: Transcranial Direct Current Stimulation (tDCS), Attention Deficit/Hyperactivity Disorder (ADHD), Depression, Working Memory

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is distinguished by the inability to regulate motor behaviors, deficits in attention, learning disabilities, aggressive tendencies, academic difficulties, agitation, and restlessness of movement (1). According to the Diagnostic and Statistical Manual of Mental Disorders, the diagnosis is established by verifying the presence of multiple symptoms pertaining to inattention or hyperactivity-impulsivity, or both, and it is categorized into three subtypes: predominantly inattentive, predominantly hyperactive-impulsive, and combined presentation (2). Children afflicted by this disorder frequently struggle to sustain their attention on routine activities; they often exhibit carelessness in the completion of their homework, regularly fail to finalize their assignments, and display persistent restlessness (3). Attention Deficit Disorder is typically diagnosed for the first time during elementary school, specifically when adaptation to the academic environment is compromised (4). Furthermore, it has been evidenced that the incidence of various educational,

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occupational, and social challenges among these children is markedly elevated in comparison to the general population (5). It is associated with the fact that, in certain contexts, individuals suffering from this disorder may be erroneously diagnosed with anxiety and depression (6). According to research findings, the prevalence of mental disorders and conditions such as social isolation, anxiety, psychological distress, and depressive symptoms in individuals with Attention Deficit/Hyperactivity Disorder is greater than in their peers (4). The coexistence of depression and attention deficit hyperactivity disorder is exceedingly prevalent, to the extent that a significant majority of individuals with this disorder also experience depressive symptoms (7). Furthermore, it has been demonstrated that in patients with Attention Deficit/Hyperactivity Disorder, depressive symptoms and their associated complications, such as lack of motivation, feelings of hopelessness, and mental fatigue, may correlate with a deterioration in the prognosis of this disorder and, additionally, through the analysis of the patient's performance, may heighten the likelihood of academic, occupational, and professional failures (8).

According to the results of various studies, the principal concern for individuals afflicted with attention deficit/hyperactivity disorder lies in deficiencies in neurological capabilities, particularly deficits in executive functions and working memory (7). Working memory constitutes a cognitive framework for the temporary retention of information (both visual and auditory) for the purpose of facilitating the organization, arrangement, planning, and learning of activities (8). From a neurological perspective, executive functions, and particularly working memory, are interconnected with an extensive network of functions associated with the frontal cortex, forming the foundation for a substantial portion of cognitive and emotional processes, including behavioral, emotional, and social self-regulation (9). This exists notwithstanding the fact that findings from various studies suggest that individuals with attention deficit/hyperactivity disorder exhibit deficiencies in working memory (10), while the results of other studies indicate that the underlying behavioral, emotional, and social challenges faced by children with attention deficit disorder/hyperactivity are fundamentally linked to weaknesses in working memory (8). Indeed, the inadequacies experienced by children with attention deficit/hyperactivity disorder in both individual and interpersonal tasks are related to this matter; these tasks necessitate the utilization of working memory and associated functions, including activity continuity, attention maintenance, planning, organization, problem-solving, and appropriate information processing (11). Moreover, findings from diverse studies suggest that individuals suffering from this dysfunction experience deficits in the functioning of the frontal cortex, an area of the brain associated with these cognitive activities (12). In light of this, and given the presence of a fundamental cognitive impairment in children with attention deficit/hyperactivity disorder, which serves as the origin of numerous behavioral, emotional,

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and psychological challenges encountered by them (13), it is imperative to pursue effective intervention strategies aimed at enhancing memory performance in this population.

The pharmacological management of this condition encompasses stimulants targeting the central nervous system (11). Nevertheless, reliance solely on pharmacotherapy seldom fulfills the comprehensive treatment requirements of children afflicted with this disorder; thus, it is imperative to integrate it with psychological therapies. In this context, empirical evidence suggests that the amalgamation of pharmacological, psychological, and neurocognitive treatments markedly enhances the efficacy of interventions for attention deficit/hyperactivity disorder (12). It appears that transcranial direct current stimulation, which entails the direct electrical stimulation of the brain through the cranial surface, may serve as a potent modality for ameliorating depressive symptoms and enhancing working memory in children diagnosed with attention deficit/hyperactivity disorder. This neurotherapeutic technique administers a direct and mild electric current to cortical regions, thereby facilitating or inhibiting spontaneous neuronal activity (14). Over the past decade, transcranial direct current stimulation has been extensively evaluated and researched, representing a non-invasive, cost-effective, and safe alternative approach to modulating cerebral cortex excitability through alterations in the resting potential of cortical neurons (15). This mild and direct current stimulates the underlying neurons via the connection of two electrodes with opposing poles, typically consisting of an anode and a cathode, positioned at disparate locations on the cranial surface (16). Stimulation via the cathode diminishes neuronal excitability, while stimulation via the anode induces an elevation in neuronal excitability (17). Indeed, the modulation of neuronal excitability and the alteration of the membrane potential of surface neurons toward depolarization or hyperpolarization result in the firing of a greater or lesser number of cerebral cells (18). The outcomes of various investigations indicate that transcranial direct current stimulation can be beneficial in the treatment of an array of disorders, including anxiety and depression, by enhancing executive functions, active memory, and attentional capacities (15-19). Given the imperative to develop effective and innovative therapeutic strategies for working with children experiencing attention deficit/hyperactivity disorder to address their cognitive and emotional impairments, the current study examines the impact of transcranial direct current stimulation on depressive symptoms and active attention in this population.

Material and Methods

The current research was a semi-experimental type of pre-test-post-test with a follow-up phase and with a control group. The statistical population of this study included all children aged 6 to 12 with attention deficit/hyperactivity disorder who referred to the Nirvana Counseling and Psychological Clinic in Shiraz in the first six months of 2018 to May 2019, among which 30 people who They had full consent for cooperation and other conditions of entry into the study, were selected and randomly assigned to two experimental and control groups. Direct electrical stimulation of the brain was performed for the experimental group and the control group did not receive any intervention. At the beginning and end of the treatment sessions, as well as for the follow-up period, people from both groups completed the Andre Ray test and the children's depression questionnaire. The criteria for entering the research include the following: having attention deficit hyperactivity disorder, willingness to participate in the research, living with parents, no history of other mental disorders and epilepsy and convulsions, being right-handed. Exclusion criteria were: having any disability such as deafness, blindness, mental retardation, movement coordination disorders according to the case file, simultaneous participation in similar intervention programs and absence of more than two sessions in the intervention program.

Research tools

Test figure complex: This test was invented by Andre Ray in 1942 in order to measure the type of perceptual activity of visual memory of those who refer to psychology and psychiatric clinics (20). This test consists of two cards B and A, each card is selected and executed separately according to the situation. Card A consists of 18 perceptual components and is used for people 4 years and older. The effective performance of this card is for people from 7 years old and it is practically more useful for teenagers and adults. Card B consists of 11 geometric components, complements card A and is made for children under 8 years old. The fullness and difficulty of card A is a problem for many children, and for this reason, it is recommended that card B be used for them. Also, this card is used for adults with severe mental retardation. After selecting each card, the test is performed twice; In the first turn, the card (A or B) is placed in front of the subject in the correct direction and he is suggested to draw its counterpart on an unlined white paper. In the second turn, while the card is removed from the subject and three minutes have passed, he is asked to carefully draw the previously observed image. Judging about the subject is done according to the comparison of his performance in each stage of drawing. Usually, the first stage of drawing is taken into account of the subject's ability to develop drawing and perceptual construction, and the second stage, according to the quantity and quality of the drawing of the first stage, will show the working level of his visual memory. In a study in Iran that was conducted in order to normalize the Andre Ray visual memory test, in order to check its criterion validity, the correlation between the scores of the second stage of the Andre Ray test and the scores of the third stage of the Kim Karad visual memory test was calculated. , and the retest method has been used to estimate the reliability. Criterion validity coefficient equal to 0.5 and reliability coefficient 0.62 were obtained, and both coefficients were reported to be statistically significant at the 0.01 level. The test-retest method was used to calculate the reliability coefficient and its reliability coefficient was 0.62, which indicates the validity and reliability of the test (21).

Children's Depression Inventory: The depression questionnaire was designed by Smaker et al. (22), which is a 27-item self-report tool and is used to assess depression symptoms in children and adolescents. The depression questionnaire includes 5 subscales, which are: negative mood (items 1, 6, 8, 10, 11, 13), interpersonal problems (items 3, 15, 23, 24), sense of futility (items 5,12,26,27), lack of pleasure (items 4,16,17,18,19,20,21,22) and low self-esteem (items 2,7,9,14,25) . The items are scored based on the classification of 0 (absence of symptoms) to 2 (presence of specific symptoms). The overall score ranges from 0 to 54, and the higher the score, the greater the severity of depression. A score of 0 to 8 is a sign of a healthy person, a score of 9 to 19 is a sign of depression threshold, and a score of 20 and above is a sign of depression. The creators of this depression questionnaire showed that this instrument had a correlation of 0.57 with other questionnaires related to depression in childhood and adolescence, including the Reynolds Depression Scale for adolescents, which indicates its concurrent validity, and the internal consistency based on Cronbach's alpha was 0.86. They brought (22). A number of researches in Iran showed that the score of depressed children is significantly higher than non-depressed children in the control group, which indicates its differential validity (23).

Direct electrical stimulation of the brain intervention: the people in the experimental group were subjected to direct electrical stimulation of the brain for 30 minutes individually; The sessions of this intervention were conducted 3 days a week for a period of 4 weeks in the form of 12 30-minute sessions. For this purpose, the anode pole of the device was placed in the posterior lateral region of the left frontal cortex and the cathode was placed in the posterior lateral region of the right frontal cortex and secured in place by special elastic bands. Its current intensity was one milliampere. The respective sponges were kept moist with 9% distilled water during this period. During the work, possible symptoms of the child were checked in terms of dizziness, itching or burning, and if the child had any of these symptoms, the electrodes were checked. Usually, after two sessions, the subject gets used to this feeling, but in case of unwillingness, that child left the treatment process.

Results

Based on the demographic information of an experimental and a control group, each of which had 15 participants; The average age of the subjects in the experimental group was 11.89 and the control group was 11.24 years. 7 participants from the experimental group and 8 participants from the control group were girls. Descriptive statistics including the mean and standard deviation of the scores of the two groups of subjects in the studied variables are presented in Table 1.

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Table 1. Descriptive characteristics of research variables in two groups

Group	Pretest				Posttest			
	Control		Experimental		Control		Experimental	
Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Depression	25.76	6.21	25.12	6.28	22.24	5.86	19.24	5.41
Active memory	23.68	7.06	23.84	7.06	22.24	7.41	16.32	4.23

As can be seen in Table 1, the average scores of depression and working memory in the post-test compared to the pre-test have changed in the treatment group, but in the control group these values have not changed. In order to compare the difference between groups in depression and working memory, univariate analysis of covariance test was used. Before using this parametric test, its assumptions, namely the normality of the data, the homogeneity of the variance-covariance matrices, and the homogeneity of the regression slope were checked. For the data obtained from all variables, the results of the Kolmogorov-Smirnov test indicated that the data were normal ($P>0.05$). Levine's test was used to measure the equality of variance and error of the investigated variable. According to the results, since the significance level of the F statistic was greater than the alpha value, it can be said that the error variance of the groups was equal to each other and no difference was observed between them. Also, the non-significant interaction between the variance variable (pre-test) and the group was indicative of the assumption of homogeneity of the regression slope. Therefore, there was no obstacle to perform covariance analysis.

Table 2. The results of univariate analysis of covariance of depression and working memory

Variable	Effect	SS	DF	MS	F	P	Effect size
Depression	Group	2812.50	1	2812.50	253.50	0.001	0.72
Active memory	Group	5554.58	1	5554.58	261.87	0.001	0.77

The results of covariance analysis in Table 2 show that by controlling the pre-test scores, the effect of the group on the post-test scores of depression and working memory is significant (P 0.001). =). So that after the treatment of direct electrical stimulation of the brain, the scores of depression and working memory in the intervention group have improved significantly compared to the control group. The effect size of the group on depression and working memory variables is 72% and 77%, respectively, and therefore the effect of the group (intervention) has been able to explain 72% of the changes in depression and 77% of the changes in working memory.

Discussion

This investigation was executed with the objective of examining the efficacy of direct electrical stimulation applied to the skull in relation to depression and working memory among children diagnosed

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with attention deficit/hyperactivity disorder. The findings indicated that direct electrical stimulation from the skull resulted in enhancements in both depression and working memory for children with attention deficit/hyperactivity disorder. These outcomes are consistent with the results of earlier studies concerning the therapeutic benefits of direct electrical stimulation from the skull, which have been shown to enhance executive functions, working memory, and attention, while also addressing various disorders, including anxiety and depression (15-19). Chan et al. (17) demonstrated in their investigation that direct electrical stimulation applied to the skull could effectively alleviate symptoms of depression and anxiety by fostering brain flexibility and facilitating the reorganization of neuronal structures within the brain. Galli et al. (18), in their comprehensive review, indicated that direct electrical stimulation from the skull, by promoting neuroplasticity, can significantly enhance and fortify neurons and synapses within the brain, thereby improving memory across diverse populations. In their research, Imburgio et al. (19) established that direct electrical stimulation from the skull may serve as an effective intervention for mental disorders such as obsessive-compulsive disorder and depression by altering and enhancing executive functions, including active memory, inhibition, and attention.

One hypothesis posits that the observed effects may be attributable to an elevation in the excitability of the cortical regions located in the left frontal and prefrontal areas, as anodic stimulation causes depolarization of the neurons, thereby inducing alterations in the resting state of the neurons and enhancing excitability in those regions. It is conceivable that the cortical networks responsible for response selection and related to the deployment of active memory in the frontal and prefrontal areas may be influenced by electrical stimulation of the brain; specifically, networks engaged in various cognitive tasks (14). Another proposition pertains to the involvement of dopamine in working memory processes. Indeed, a range of neurotransmitters, including dopamine, are integral to the functioning of working memory, and recent investigations suggest that direct electrical stimulation applied to the skull in the frontal and prefrontal regions leads to an increase in dopamine levels within these areas (15). Researchers focused on learning disorders also contend that electrical stimulation of the prefrontal cortex activates dopamine neurotransmission and augments its concentration in this region, which is correlated with cognitive flexibility and enhanced performance in individuals with learning disabilities (16). Consequently, the augmentation of surface excitability within the prefrontal cortex results in an increased release of dopamine, which in turn enhances the functioning of working memory. In essence, dopaminergic stimulation may be essential for sustaining the activity of the prefrontal cortex and the processes involved in working memory, while direct electrical stimulation from the skull, particularly through anodic means, yields stimulatory effects that are associated with heightened levels of glutamate, an amino acid implicated in working memory (17).

In the present investigation, the application of direct electrical stimulation from the cranial region, resulting from the enhancement of activity in the left prefrontal cortex, facilitated the enhancement of various cognitive functions, including working memory, in children diagnosed with attention deficit/hyperactivity disorder, which subsequently alleviated their depressive symptoms. Furthermore, empirical research substantiates that in individuals suffering from major depression, the aberrant functioning of the prefrontal cortex, which is associated with executive functions, correlates with symptoms of depression (17). This observation underscores the significance of this brain region in the physical pathology of major depression. Conversely, it has been determined that the capacity for cognitive flexibility enables the simultaneous contemplation of contradictory representations of an object or event when confronted with novel stimuli and environmental conditions (18). Consequently, it appears that this may diminish the capabilities of these patients, a notion proposed in the theory of mind as one of the etiological hypotheses concerning cognitive distortions; this elucidates that clinicians can enhance the positive mental states of patients by mitigating cognitive distortions and thereby alleviate behavioral symptoms of depression, ultimately contributing to their treatment (19).

Conclusion

In summary, it can be posited that the extant research evidence indicates that brain electrical stimulation may serve as a viable and cost-effective intervention for the enhancement of active memory and the treatment of major depressive disorder through the facilitation of cortical modifications within the brain, even subsequent to the cessation of stimulation. Consequently, it is imperative to consider this form of intervention as a safe methodology for cognitive rehabilitation and the prevention of disorders within psychiatric and counseling establishments, in conjunction with the application of psychotherapy for patients, and potentially for healthy individuals as well. Among the limitations of the present research are the constraints of the available sample, the restriction of the sample to children attending a clinic in Shiraz, and the limited sample size. Therefore, it is recommended that future investigations be conducted utilizing random sampling, encompassing a broader demographic of children and a larger sample size.

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