



Effectiveness of Transcranial Direct Current Stimulation in Behavioral and Cognitive Aspects of Executive Function in Children with Autism Spectrum Disorder

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Abstract

Background: Despite their high effectiveness, rehabilitation therapies can reduce the number of families with children with autism spectrum disorder (ASD) visiting clinics due to the number of treatment sessions and the long duration of treatment. The use of technological methods, such as transcranial direct current stimulation (tDCS) as one of the therapeutic interventions to improve cognitive function in rehabilitation clinics, can help reduce the duration of treatment for these children.

Objectives: The present study was carried out to examine the effectiveness of tDCS in behavioral and cognitive aspects of executive functions in children with ASD.

Methods: A pretest and posttest design with follow-up were used in this study. The subjects were children with high-functioning ASD aged 8 - 11 years who were selected by the convenience sampling method from occupational therapy clinics in Tehran, Iran. A total of 20 eligible candidates were included in the study according to inclusion and exclusion criteria. The subjects were randomly divided into two groups (10 subjects in each group). The intervention group received tDCS during 12 sessions of 20 minutes in the dorsolateral prefrontal cortex area, with an electrode size of 35 cm² for 3 weeks (four sessions per week). The control group received common cognitive interventions used in occupational therapy clinics in 12 sessions of 60 minutes (one hour) for 6 weeks (two sessions per week). Follow-up was performed one month after the end of the interventions. The research instruments included the Behavior Rating Inventory of Executive Function and computer-based tests, such as the Tower of London, Wisconsin Card Sorting Test, and Stroop test.

Results: The results demonstrated that tDCS, similar to cognitive rehabilitation, could affect the cognitive functions of the brain, such as executive functions, and several basic cognitive processes, such as inhibitory control, cognitive flexibility, and mental planning.

Conclusions: The findings recommended using tDCS as a new intervention method to improve the cognitive function of individuals with ASD. This is due to the lasting effect of the results of this intervention as a technological instrument with faster results than other clinical interventions.

Keywords: Autism Spectrum Disorder, Executive Function, TDCS, Transcranial Direct Current Stimulation

1. Background

Autism spectrum disorder (ASD) is one of the most common neurodevelopmental disorders in children. It is characterized by a lack of social communication and restricted and repetitive behaviors and interests, according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (1). According to the United States Centers for Disease Control and Prevention, the prevalence of the disorder in children in 2012 was

1.5% (1 in 68 live births); however, since 2016, the prevalence of the disorder has increased and has currently reached 1.7% (1 in 59 live births) (2). Among the cognitive deficits of ASD children, which also lead to behavioral problems, the deficit in executive function can be mentioned (3). This cognitive ability consists of several special functions, namely decision-making, problem-solving, planning, organization, cognitive flexibility, self-monitoring, constructing strategies, setting goals, and sequencing complex tasks (4).

Brain imaging studies show some structural defects in the brains of individuals with ASD (5). Regarding the anatomical structure of the brain, executive functions depend on the function of the frontal and prefrontal lobes (6). Neuropathological studies also confirm the involvement of the frontal lobe in children with ASD (7). Due to the unknown etiology of ASD and attributing various factors as effective factors in the development of this disorder, no definitive treatment has been offered for it; nevertheless, various interventions have been suggested to improve the cognitive problems of ASD children that are not unanimous (8). Therapeutic interventions in the field of ASD include medication and behavioral therapies; behavioral therapy is introduced as the first line of treatment, and medication therapy is used along with other treatments to help with the child's functions and activities of daily living. Pharmacological interventions in ASD are mainly offered for the management of mood disorders associated with this disease, and despite having beneficial therapeutic effects, they are not without side effects (9). Therefore, most families prefer to use nonpharmaceutical and rehabilitation services to solve their children's problems.

According to the disruptions in the structure and function of the brain in autistic children that lead to cognitive dysfunction, one of the types of neurorehabilitation methods that have been considered in recent years is transcranial direct current stimulation (tDCS) (i.e., a kind of method to stimulate the brain) which is used in cognitive rehabilitation (8). This is one of the noninvasive methods for the electrical stimulation of the brain that is tolerable for an individual and has no special risks or complications (10, 11). In this technique, a low-intensity electric current (usually less than 3 mA) enters the brain through electrodes placed on the scalp. The electric current flows through the skin, subcutaneous tissue, skull, and cerebrospinal fluid to the gray matter of the brain. The electrical current of 1 mA for 7 to 13 minutes can have excitatory or inhibitory effects on motor cortex excitability (12, 13).

A study by Gomez et al. showed that 20 sessions of noninvasive electrical stimulation on the dorsolateral prefrontal cortex (DLPFC) could improve the symptoms of children with ASD (14). In a review study, Demirtas-Tatlidede et al. reported that the noninvasive electrical stimulation of the brain could cause positive changes in the autistic behavior questionnaire in addition to changes in physiological function (15). The results of a study by Amatachaya et al. showed that transcranial electrical stimulation leads to improved cognitive function in children with ASD and a significant reduction in the Childhood Autism Rating Scale (8). Cognitive interventions used by occupational therapists in the field of social functions are often based on educational approaches that use rehabilitation

tasks to improve attention, memory, and perception functions. In recent years, the use of tDCS has been introduced as one of the new methods in studies to improve cognitive functions, and its most common use has been in individuals without disorders. Although the use of tDCS in rehabilitation clinics as an intervention method is expanding, there are still a limited number of studies that confirm its effectiveness in promoting cognitive functions.

2. Objectives

The present study aimed to investigate the effectiveness of using tDCS in promoting the executive functions of individuals with ASD.

3. Methods

A pretest and posttest design with follow-up were used in this study. The subjects were children with high-functioning ASD aged 8 - 11 years who were selected by the convenience sampling method from occupational therapy clinics in Tehran, Iran. Based on the changes in the results of a similar study [i.e., the study by Amatachaya et al. (8)] with the closest intervention method to the present study and considering the alpha and beta of 0.05 and 0.2, respectively, in the proper formula, the required sample size for each group was calculated as 8 individuals. Considering the probability of drop-out in each group, 10 individuals were considered. Accordingly, 20 eligible candidates were included in the study according to inclusion and exclusion criteria. The inclusion criteria were a diagnosis of ASD according to the DSM-5 by a child psychiatrist, not receiving transcranial electrical stimulation interventions during the previous year, and not receiving psychiatric medication interventions during the past 6 months. The exclusion criteria were the initiation of the medication regimen, occurrence of neurological problems during treatment, and absence in more than two treatment sessions.

The parents were explained that they were free to withdraw from the treatment at any stage of the treatment. After identifying the participants with the inclusion criteria and explaining to the parents how to do the work, informed consent was obtained. Then, the children entered the study. After completing the demographic information questionnaire, the Behavior Rating Inventory of Executive Function (BRIEF) was filled out by the parents, and the rater answered their possible questions about completing the questionnaire. At the end of the parent interview, the evaluator performed computer-based tests, including the Tower of London (ToL), Wisconsin Card Sorting Test (WCST), and Stroop tests for each child, taking 5 minutes of rest

between each test, respectively, and recorded the results. Based on the design of this study, the evaluations were performed before, after, and one month after the end of the interventions by a blind rater who was uninformed of the grouping.

After determining the subjects, they were randomized into intervention and control groups. The tDCS was performed for the intervention group during 12 sessions of 20 minutes in the DLPFC area, with an electrode size of 35 cm² for 3 weeks (four sessions per week). The control group received common cognitive interventions used in occupational therapy clinics in 12 sessions of 60 minutes (one hour) for 6 weeks (two sessions per week). The duration of each tDCS session (20 minutes) is one-third of the routine treatment (i.e., cognitive occupational therapy), and the number of weeks that individuals have to undergo tDCS (3 weeks) is one-half of the routine treatment, which saves the participants' time and money. On the other hand, tDCS does not require family follow-up at home; however, part of the common occupational therapy practices requires the family to do the same at home. Furthermore, it was decided that if positive effects were observed, the control group would use the tDCS method after the end of the study, all of which motivated the participants to participate in this study.

The following instruments are used in this study.

3.1. Demographic Questionnaire

For example information about age, gender, educational background, and the family's economic and cultural status.

3.2. Behavior Rating Inventory of Executive Function

It is an inventory that evaluates the executive function deficits of individuals 5 - 18 years. It comprises two types of parent response and teacher response, which include the behavioral regulation index and metacognition index. The time to complete the form is within 15 - 20 minutes. The behavioral regulation index includes three subsets of emotional control, shift, and inhibit. The metacognition index includes five subsets of initiate, plan/organize, organization of materials, monitor, and working memory. Each item is answered and scored with three scales, including never (score 0), sometimes (score 1), and often (score 2) (16). The validity and reliability of the Persian version of this inventory showed a Cronbach's coefficient above 85%, and the correlation between scores was above 0.7 (16, 17), demonstrating that this inventory has good psychometric properties.

3.3. Wisconsin Card Sorting Computer-Based Test

In this test, there are four patterns of cards at the top of the page, different from each other in terms of number (from 1 to 4), color (green, blue, red, and yellow), and shape (triangle, star, cross, and circle). A 64-card deck at the bottom of the screen is located, with only the top card displayed. These cards have their own unique characteristics under the same three rules. In this test, the participant should place the top card of the deck into the group of one of the pattern cards according to the principle he/she has guessed (by pressing the number under the pattern card on the keyboard). In this way, the participant can discover the sorting rule by receiving the correct and incorrect feedback alarm. The participant's score is the number of 10 categories the participant has successfully sorted. If the participant persists in sorting based on the former rule, despite the change of the rule by the rater, he/she commits a perseveration error. Perseveration error is generally a repetition of a pre-learned response to the new law (18).

3.4. Tower of London Computer-Based Test

This test was presented by Shallice in 1984 in an article about special injuries in planning and organizing. In the present study, this test was used to measure planning ability. This test is designed to assess at least two sections of executive functions, namely strategic planning and problem-solving. During the test, by moving the colored beads (i.e., green, blue, and red) and placing them in the right place, the shape of the sample should be corrected with the least necessary movements. It is considered that only the upper beads are permitted to move, and there are 3, 2, and 1 beads in the long, middle, and short columns, respectively. The participant is then asked to complete the task. At this stage, the participant is allowed to do the task three times, and he/she should solve the example according to the instructions with the minimum necessary movements. After the successful completion of the task and after three times of failing, the next task question is given to the participant. The variables studied in this test include delay time, test time, total test time (i.e., the total delay time and test time), and the number of errors. Total scores are accurately calculated by computer.

3.5. Stroop Computer-Based Test

This test was designed to measure selective attention, inhibitory control, and cognitive flexibility. Ridley Stroop was the developer of the test in 1935. In the present study, the Stroop test was used to measure inhibitory control. This test consists of two steps; the first step is to name the color, and the participant is asked to indicate the color of the desired form in a range of colors with the maximum

speed that can be specified by the key associated with it on the keyboard (the colors of the circle in red, blue, yellow and green are displayed alternately on the monitor screen). The purpose of this step is to identify the colors and the placement of the buttons on the keyboard without any effect on the outcome. The principal part of the Stroop test is its second step. This stage is called uncoordinated effort or interference. At this stage, the participant is shown 48 matching color words and 48 inconsistent color words in blue, red, green, and yellow. Inconsistent words are words the colors of which are different from the meaning of the words in Persian. The participant's task is to determine only the appearance of the words, regardless of the meaning of the words. The presentation time of every stimulant on the screen is a pair of seconds, and the distance between the presentation of the two stimuli is 800 thousandths of a second. The second step of the test evaluates interference, cognitive flexibility, and inhibitory control. The indicators measured in this test are accuracy (i.e., the number of correct responses) and speed (i.e., the average reaction time of correct responses to the stimulus in thousandths of a second) (18). These tests have good validity and reliability in Iran, and in the present study, a computer-based version of the tests prepared by the Sina Behavioral-Cognitive Research Institute was used.

Statistical tests used in this study included descriptive tests of mean and standard deviation. The analytical test used in this study was a repeated measures analysis of variance, and SPSS software (version 21) was used to analyze the data. In the current study, the significance level was considered $P < 0.05$.

4. Results

A total of 20 children with high-functioning ASD were evaluated by a psychiatrist and included in the study, with a mean age of 128.2 months. No significant difference was observed between the two groups regarding age, gender, and diagnosis. Moreover, 100% of the subjects were male with ASD ($n = 20$). Table 1 shows the demographic information of the studied children. All the subjects were children with high-functioning ASD, which were divided into two intervention ($n = 10$) and control ($n = 10$) groups. The mean age values of the control and intervention groups were 123.8 and 132.6 years, respectively.

4.1. Effect of Interventions on the Behavioral Aspect of Executive Functions (BRIEF)

Executive functions in this study were evaluated through the BRIEF. Table 2 shows the mean scores of the subjects in the two indicators of behavior and metacognition of this inventory before, after, and one month after

Table 1. Demographic Characteristics of Children with Autism Spectrum Disorder

Groups Type	Control Group	Intervention Group
Gender (male, female)	(10, 0)	(10, 0)
Mean age (y)	132.6	123.8
Group (n)	10	10

the end of the interventions. The results showed that both groups decreased in the scores of two indicators of behavior regulation and metacognition after the intervention, which indicated the effectiveness of the interventions; however, there was no significant difference between the mean of the intervention and the control groups after the intervention ($F = 1418.92$, $P > 0.05$). The aforementioned results were repeated and confirmed one month after the end of the interventions.

4.2. Effect of Interventions on Inhibitory Control (Stroop Test)

In measuring the inhibition function as one of the executive function processes evaluated by the Stroop computer-based test, the results showed that the mean inhibition scores increased in both groups, and the difference in increasing scores between the intervention and control groups was significant ($P < 0.05$). In the analytical statistics regarding the interactive effect of time on the group, the results showed a significant difference in the inhibition scores between the two groups ($F = 7109.60$, $P < 0.001$). This finding means that the scores of the inhibitory control process evaluation after the end of the intervention and one month after that indicated the improvement of the inhibitory control in the intervention group.

4.3. Effect of Interventions on Cognitive Flexibility (Wisconsin Card Sorting Test)

In measuring the cognitive flexibility function score as one of the executive function processes evaluated by the WCST, the results showed that the mean scores of cognitive flexibility increased in the two groups; nevertheless, there was no significant difference in cognitive flexibility scores between the intervention and control groups ($F = 2184.18$, $P > 0.05$). The evaluations confirmed the aforementioned results one month after the end of the intervention.

4.4. Effect of Interventions on Planning (Tower of London Assignment)

In measuring the planning function score as one of the executive function processes evaluated by the ToL test, the results showed that the planning score increased in both groups; however, there was no significant difference between the intervention and control groups ($F = 1019.79$, $P >$

Table 2. Descriptive Indicators of Variables Examined in the Behavior Rating Inventory of Executive Function Inventory^a

Intervention Groups	BRIEF	Time Assessments		
		Pretest	Posttest	Follow-up
Group 1 experiment	Metacognitive index	78.4 ± 6.32	71.5 ± 7.51	71.4 ± 7.79
Group 2 control	Behavioral regulation index	49 ± 5.56	45.2 ± 5.8	44.5 ± 5.35

Abbreviation: BRIEF, Behavior Rating Inventory of Executive Function.

^a Values are expressed as mean ± SD (standard deviation).

0.05). In the evaluations, the aforementioned results were confirmed one month after the end of the interventions. Table 3 shows the results of the three mentioned computer-based tests before, after, and one month after the end of the intervention.

5. Discussion

Due to the complex nature and extent of ASD symptoms, there are several approaches to treating them; nevertheless, there is no agreement on determining the best treatment intervention. Numerous effective therapeutic approaches in children with ASD, including cognitive rehabilitation, are offered by occupational therapists, and occupational therapy is one of the most effective therapies. The results of studies to date show that transcranial electrical stimulation is effective in brain processes, including executive functions. The results obtained in the present study showed that tDCS could have similar effects on both aspects of executive functions, namely daily behavioral aspects and basic cognitive processes, similar to cognitive rehabilitation interventions in occupational therapy.

The BRIEF examines executive functions, such as inhibitory control, cognitive flexibility, and mental planning, in real life and in the context of everyday life behaviors. In the behavioral aspects of cognitive processing evaluated by this inventory, the intervention and control groups did not differ significantly in the results, indicating that tDCS, similar to conventional occupational therapy interventions, led to improvement in behavioral components in children. As it turns out, cognitive functions are based on several cognitive processes in the brain, including cognitive functions. Some of these basic executive function processes include inhibitory control, cognitive flexibility, and planning, assessed by the Stroop, Wisconsin, and ToL computer-based tests, respectively. The results showed that tDCS could make positive changes in cognitive processing, similar to occupational therapy. Even in the case of inhibitory control in the tDCS intervention group, the increase in score was significantly higher than in the control group (i.e., common cognitive interventions). Because tDCS controls the facilitation and in-

hibitory mechanisms of the brain through electrical current, it might be that its effect on inhibitory control in the DLPFC region, which is the center of this processing, has been more significant than conventional cognitive occupational therapy interventions.

The current study is in line with a study by Amatachaya et al. in 2014, who conducted the first randomized clinical trial using tDCS and showed that tDCS improves cognitive function in children with ASD (8). Additionally, the results obtained in this study are in line with the results of a study by Martin et al., who showed that tDCS could accelerate the acquisition of skills in working memory tasks as one of the processes and components of executive functions (19). In the present study, to confirm the effect of tDCS on executive functions in children with ASD, the results of using tDCS on executive function components were compared to the results of common occupational therapy interventions whose effectiveness has been accepted in previous studies (20).

Moreover, Farokhzadi et al. demonstrated that transcranial alternating current stimulation (tACS) was more effective and more durable than Ritalin in the areas of visual attention (e.g., visual vigilance, visual focus, and sustained attention visual) and response control visual and auditory prudence, which is consistent with the results of the present study on the cognitive effects of transcranial stimulation methods (21). It is worth noting that the results of this study are consistent with the results of a study by Loftus et al. They demonstrated that if tACS is applied to the left DLPFC alone, it can increase the function of this region and alleviate inhibitory control difficulties (22).

5.1. Conclusions

Due to the effectiveness of using tDCS as a new intervention method in improving the cognitive function of individuals with ASD, it is recommended to apply tDCS as a technological instrument with faster results than other clinical interventions. One of the questions in using brain stimulation methods is whether they, such as conventional cognitive interventions, have a lasting effect. The present study showed that with a 1-month follow-up, all the results

Table 3. Descriptive Indicators of Variables Examined in Computer-Based Tests ^a

Intervention Groups and Computerized Cognitive Task	Time Assessments		
	Pretest	Posttest	Follow-up
Group 1 experiment			
Stroop	82.5 ± 6.2	87.8 ± 7.56	86.6 ± 5.04
ToL	23.1 ± 4.88	26.1 ± 5.6	27.3 ± 4.66
WCST	35.7 ± 11.59	41.3 ± 4.27	41 ± 3.71
Group 2 control			
Stroop	84.9 ± 7.68	87.1 ± 12.62	87.6 ± 10.72
ToL	21.5 ± 4.32	22.5 ± 3.34	23.2 ± 3.67
WCST	38.3 ± 8.4	41.7 ± 3.19	42.5 ± 3.56

Abbreviations: ToL, tower of London; WCST, Wisconsin card sorting.

^a Values are expressed as mean ± SD (standard deviation).

obtained from tDCS were preserved as the results of occupational therapy interventions. This indicates that the results obtained using brain stimulation interventions, such as tDCS, are also sustainable; however, it is suggested to perform further studies with a longer follow-up period to achieve a definitive result in this case. Among the limitations of the present research project was the unfamiliarity of parents with this treatment method and their concern about brain stimulation, which the explanations about the noninvasive treatment helped to some extent. Additionally, the number of patients participating in this study was small. Therefore, it can be recommended to perform this study on a larger number of children with ASD. In addition, it is suggested to study the effectiveness of tDCS, along with other cognitive methods.

Footnotes

Authors' Contribution: M.A. and S.S. conceived and designed the evaluation and drafted the manuscript. S.K.E. participated in designing the evaluation, performed parts of the statistical analysis, and helped draft the manuscript. M.A.A. reevaluated the clinical data, performed the statistical analysis, and revised the manuscript. M.A.A. collected the clinical data, interpreted them, and revised the manuscript. M.A. reanalyzed the clinical and statistical data and revised the manuscript. All the authors read and approved the final manuscript.

Conflict of Interests: Mehdi Alizadeh Zarei, the corresponding author of this manuscript, is an associate editor, and Samaneh Karamali Esmaili, the second author of the current manuscript, is a reviewer of Iranian Journal of Psychiatry and Behavioral Sciences.

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Informed Consent: After identifying the participants with the inclusion criteria and explaining to the parents how to do the work, informed consent was obtained.

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