

The Effect of Transcranial Direct Current Stimulation (tDCS) on Cognitive Flexibility in Children with Specific Learning Disorders

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Abstract

Children with specific learning disabilities exhibit lower cognitive flexibility compared to typically developing children. The purpose of the present study was to investigate the effect of Transcranial Direct Current Stimulation (TDCS) on Cognitive Flexibility of children with learning disabilities in Tehran. A semi-experimental design with pre-test, post-test, and control group study was conducted. The study population consisted of all students with Specific Learning Disorders in Tehran during the academic year 2022-2023. A total of 30 students, aged from 7 to 12, were selected as the sample group using the purposeful sampling method. We randomly divided the participants into two control and experimental groups ($n = 15$ each). The research tool was the Wisconsin Card Sorting Test. The experimental group underwent a stimulation protocol involving a weak direct current. The protocol consisted of 10 sessions, with the initial five sessions utilizing a low intensity of 1mA, followed by a slight increase to 1.5mA for the remaining five sessions. The anode electrode, measuring 5 x 5 cm, was inserted in the left dorsolateral prefrontal cortex (DLPFC) at the F3 location, while the cathode electrode, also measuring 5 x 5 cm, was placed on the right ventromedial prefrontal cortex (VMPFC) at the Fp2 location. Each session lasted for 20 minutes. Data were analyzed using one-way analysis of multivariate covariance analysis (MANCOVA) and independent t-tests. The results showed that TDCS has been effective in Cognitive Flexibility.

Introduction

According to the DSM-5, Specific Learning Disorder (SLD) is identified as neurodevelopmental disorders by difficulties in academic abilities, including reading, writing, or mathematics for a minimum duration of 6 months. These skills are fundamental for further academic learning and development (American Psychiatric Association, 2013; Petretto, & Masala, 2017). Students with Specific Learning Disorder (SLD) may also face an increased risk of experiencing executive function difficulties (EdF) (Livanis, Mertturk, Benvenuto, & Mulligan, 2014; Khan, & Lal, 2023). Executive functions (EF) encompass three distinct yet interrelated "core" dimensions: inhibitory control, working memory (WM), and cognitive flexibility (Friedman, & Miyake, 2017). These core dimensions of executive functioning work together synergistically to support higher-order cognitive processes like planning, self-regulation, attentional control, and goal-directed behavior (Livanis et al., 2014). Deficits in important executive functions, including cognitive flexibility, play a significant role in learning disabilities among students with specific learning disorders (Kieffer, & Christodoulou, 2020).

Cognitive flexibility refers to the human ability to adapt cognitive processing strategies, responses, and representations in response to new or unexpected conditions in the environment (Legare, Dale, Kim, & Deák, 2018). It involves being able to mentally shift between tasks or quickly switch courses when necessary, demonstrating adaptability in one's thinking and behavior (Diamond, 2013; Koch, Poljac, Müller, & Kiesel, 2018). Children with specific learning disorders can benefit from developing thinking skills that enable them to adapt and think innovatively in response to their surroundings (Sweid, 2013). Cognitive flexibility assists students in generating automatic responses to new problems and situations. It enables them to effectively handle academic tasks (Nugiel, Mitchell, Demeter, Garza, Cirino, Hernandez, & Church, 2023). Research has shown that flexible thinking, including the ability to shift between different strategies and approaches, is vital for the development of mathematics proficiency (Cragg & Gilmore, 2014; Stad, Van Heijningen, Wiedl, & Resing, 2018). Furthermore, there is a direct correlation between cognitive flexibility and early word reading, as well as reading fluency and comprehension. (Colé, Duncan, & Blaye, 2014; Cartwright, Marshall, Huemer, & Payne, 2019).

In the last two decades, there has been a significant increase in the utilization of transcranial direct current stimulation (tDCS) on human subjects. This method has been widely used to alter cognitive brain processes (Polanía, Nitsche, & Ruff, 2018), as well as alleviate symptoms in clinical populations affected by plasticity-related symptoms or deficits (Fregni, El-Hagrassy, Pacheco-Barrios, Carvalho, Leite, Simis, & Brunoni, 2021). Neuroanatomically, studies using tDCS in humans have shown that the dorsolateral prefrontal cortex (dlPFC) plays a significant role in modulating cognitive flexibility. Specifically, research has indicated that anodal tDCS applied to the dlPFC can enhance performance on tasks involving cognitive flexibility (Borwick, Lal, Lim, Stagg, & Aquili, 2020), while cathodal stimulation may hinder it (Gómez-Ariza, Martín, & Morales, 2017).

The left dorsolateral prefrontal cortex (DLPFC) has been the most frequently targeted brain region using anodal stimulation in various studies due to its documented role in executive functions (Salehinejad et al., 2020; Salehinejad et al., 2022). The DLPFC is a critical region involved in working memory, attention, decision-making, and other higher cognitive processes (Papazova et al., 2018; Miler, Meron, Baldwin, & Garner, 2018; Salatino et al., 2022). DLPFC is commonly activated bilaterally during task-switching involving both emotional and non-emotional material (Piguet et al., 2013). However, there seems to be a hemispheric difference in DLPFC activation patterns, with the left hemisphere being more involved in non-emotional tasks (Wendelken et al., 2012) while the right hemisphere is more active during tasks requiring effective switching between different cognitive processes or emotional states (Krug, & Carter, 2012). Additionally, the DLPFC has been implicated in preventing interference from irrelevant or distracting information, inhibiting unwanted responses, planning complex behaviors or actions, and maintaining information in working memory (Brunoni, & Vanderhasselt, 2014).

The ventromedial prefrontal cortex (VMPFC) appears to be most engaged in situations of increased impulsivity, playing a key role in integrating reward and emotion. It may be less engaged when higher cognitive control is required, possibly due to the recruitment of the DLPFC (Manuel, Murray & Piguet, 2019). According to a neuropsychological study, the VMPFC plays an important role in both experiential and observational learning (Kumaran, Warren & Tranel, 2015). Research on cathodal tDCS targeting the VMPFC has shown mixed results. Some studies have reported negative effects on mood and decision-making, while others have reported positive effects such as reduced anxiety or improved cognitive flexibility (Schroeder, & Plewnia, 2017). Cathodal stimulation of the VMPFC has been studied as a potential intervention for changing decision-making behavior (Vicent et al., 2019). According to Li et al. (2020) research, cathodal stimulation of the VMPFC resulted in a significant increase in conformity tendency and decrease in response time when participants' initial decision differed from the majority opinion (Li, Wang, Ye, & Luo, 2020).

The notable distinction between our research plan and previous studies lies in the placement of the cathode electrode. Our stimulation protocol is most closely aligned with Borwick et al.'s (2020) study, where the cathode is positioned on the contralateral supraorbital ridge (Borwick, Lal, Lim, Stagg, & Aquili, 2020). However, in other studies similar to the present research, where the anode was positioned over the left dlPFC centred on F3, the cathode has been connected to various locations such as the left superior trapezius muscle, the right shoulder, the wrist, or right dlPFC (Ruf, Fallgatter, & Plewnia, 2017; Clarke, Van Bockstaele, Marinovic, Howell, Boyes, & Notebaert, 2020; Qiu, Kong, Li, Yang, Huang, Huang, & Kong, 2021). Another innovative aspect of this design is the method used to increase the voltage of direct current electrical stimulation to the brain. In previous research, a voltage of 2 milliamperes has been commonly used for adults, while for children, lower voltages of 1.5 or 1.0 milliamperes are employed (Schertz, Karni-Visel, Genizi, Manishevitch, Lam, Akawi, & Bikson, 2022; Salehinejad, Vosough, & Nejati, 2022). However, in this particular research, a cautious approach was taken in order to acclimate children to the potential side effects of brain stimulation, such as heartburn, headache, itchy head,

dizziness, sleepiness, and nausea. To mitigate any discomfort, a voltage of 1 milliampere was initially utilized. After undergoing five sessions at this voltage, it was then increased to 1.5 milliamperes to assess its impact on cognitive flexibility. This step-wise approach aimed to ensure the safety and well-being of the children participating in the study.

The impact of applying anodal tDCS over the left DLPFC and cathodal tDCS over the right VMPFC has not been extensively studied in specific learning disorders, despite evidence suggesting that this approach may be beneficial. The left DLPFC and right VMPFC, appear to be involved in multiple aspects of decision-making processes, including cognitive control, emotion regulation, and reward processing (Nejati, Mirikaram, & Rad, 2023). The results of a study that investigated the role of DLPFC and VMPFC in cognitive bias associated with generalized anxiety disorder (GAD) suggest that both DLPFC and VMPFC are involved in cognitive bias, but with partially different roles. Specifically, anodal stimulation over the right VMPFC and left DLPFC reduced attention bias, which supports the connection of these areas for attention bias (Heeren et al., 2017; Nejati, Khalaji, Goodarzi, & Nitsche, 2021). In a separate study examining the impact of dorsolateral and ventromedial prefrontal cortex on emotion regulation in females with major depressive disorder (MDD), it was found that anodal left DLPFC/cathodal right VMPFC stimulation led to an improvement in working memory performance (Nejati, Majidinezhad, & Nitsche, 2022). Moreover, in both individuals with and without ADHD, the combination of anodal stimulation of the left DLPFC and cathodal stimulation of the right VMPFC resulted in enhanced performance on attention tasks and a reduction in mind wandering (Nejati, Majidinezhad, Yavari, & Nitsche, 2023). Previous studies have demonstrated that applying anodal stimulation to the left DLPFC can enhance neural excitability and improve cognitive function in individuals with diverse neuropsychiatric disorders, including ADHD (Sotnikova et al., 2017; Soff et al., 2017).

Aims and Hypotheses

Although there is limited evidence from noninvasive brain stimulation studies regarding the imbalanced function between these regions in specific learning disorder (SLD) pathophysiology, our current study aimed to examine whether a combination of anodal left DLPFC and cathodal right VMPFC stimulation could improve cognitive flexibility in individuals with SLD. Therefore, we hypothesized that transcranial direct current stimulation (tDCS) Or combination of anodal left DLPFC and cathodal right VMPFC stimulation has an effect on cognitive flexibility in children with specific learning disabilities.

Methods

Design

We conducted a randomized, one-blinded study with two experiment and control group. Participants were randomly assigned to either the control or the experimental group.

Participants

thirtychildren aged from 7 to 12 diagnosed with SLD (16 males, mean age = 8.69/ 14 females, mean age = 9.3) were recruited from one private clinics across Karaj, Iran. Diagnosis of all children was conducted by a clinical psychologist and based on their academic records. They don't have any current or past history of epilepsy, seizures, or head injury. All patients' parents were fully informed about the experimental procedures and potential risks before giving their consent.

Measures

Demographics

We used a demographic questionnaire to gather participants' personal information, including age, gender, study major, prior study of special education-related courses, previous contact experiences with people with ASD, and prior experiences with contemplative practices.

Cognitive Assessment

In this study, cognitive flexibility was evaluated using the Wisconsin Card Sorting Task (WCST), which is widely recognized as the most commonly employed neurocognitive assessment tool for evaluating cognitive flexibility. (Miles, Howlett, Berryman, Nedeljkovic, Moseley, & Phillipou, 2021).

Wisconsin Card Sorting Test (WCST): It is a complex task that necessitates the engagement of multiple executive functions, such as attention, memory, implicit learning, and cognitive flexibility (Wu, Brockmeyer, Hartmann, Skunde, Herzog, & Friederich, 2014). The WCST was first introduced by Grant and Berg in 1948 and is widely used in cognitive psychology research. This task requires participants to sort cards according to different criteria or rules that can change over time, requiring them to flexibly adapt their behavior based on new information (Kopp, Lange, & Steinke, 2021). Four variables derived from WCST were used to assess participant performance. These variables include perseverative error, clusters, total time (measured in seconds), and total score. Deficits in cognitive flexibility, which is recognized as one of the core executive functions, are widely believed to be manifested by an increased number of perseverative errors observed during WCST (Lange, Brückner, Knebel, Seer, & Kopp, 2018). We used its computer version, which takes about 10 minutes.

Procedure

The experiment took place in a quiet psychology laboratory and supervised by a research assistant. All the questions and doubts of the participants about the educational and research program were answered and the informed consent of the parents was obtained for their children to attend the meetings. Cognitive flexibility was assessed by utilizing the Wisconsin Card Sorting Test (WCST). To mitigate the potential influence of fatigue on the child's pain tolerance, a pre-test was conducted one day prior to the initial stimulation session. Similarly, a post-test was administered one day after completing all ten stimulation sessions to minimize any impact from side effects induced by the stimulation on the child's performance.

The tDCS device in use was "Neurostim2" with a rechargeable battery (8 hours of continuous operation with both channels). This device was manufactured and invented by the research and development team of Medinateb company for the first time in Iran and was launched on the market in 2015. A direct electrical current was applied to participants using sponge electrodes that were soaked in saline solution. For children with smaller head circumferences, 25 cm² (5 x 5) electrodes were selected. Each participant underwent a total of 10 sessions of electrical stimulation and received anodal DLPFC/cathodal VMPFC for 20 minutes in each session with a ramp up and down time of 30 seconds. The study involved a total of ten stimulation sessions, with a one-day break between the initial five sessions and the subsequent five sessions. The current intensity during the first five sessions was set at 1mA, which was then increased to 1.5mA for the remaining five sessions. The rationale behind employing this particular protocol was to acclimate children to potential side effects, such as head burn, headache, head itching, dizziness, drowsiness, and nausea. An anodal electrode was placed over left DLPFC (F3)

and a cathodal electrode was positioned over right VMPFC (Fp2). The distance between these electrodes was at least 6 cm to minimize the likelihood of current shunting through the scalp. In the study design, the control group did not receive any stimulation or treatment, while participants in the experimental group received only transcranial direct current stimulation (tDCS) and no other form of intervention.

Data Analysis

The hypothesis of this research is “Does the use of transcranial direct current stimulation (tDCS) improve cognitive flexibility skills in children with specific learning disorders?”. To examine this research question, the researchers employed the method of repeated multivariate measurement analysis of variance. In this approach, the between-group variable was the group, with levels of experimental and control. Meanwhile, the within-group variable was the stage variable, which encompassed levels of pre-test, post-test, and follow-up. To accomplish this objective, the researchers first examined the descriptive statistics of the variables pertaining to this hypothesis. Subsequently, they assessed the key assumptions of the repeated multivariate measurement variance analysis method. This involved verifying the normality of the variables and assessing the independence of the pre-test variables and the group variable.

Results

Table 1 presents the mean, standard deviation, Kolmogorov-Smirnov statistic, and the corresponding significance level. These measures were utilized to assess the normality of the distribution of the dependent variable scores for the cognitive flexibility skill dimensions (perseverative error and clusters) in both the experimental and control groups. Additionally, the analysis was conducted across three stages: pre-test, post-test, and follow-up. It is important to highlight that the tDCS (transcranial direct current stimulation) technique was specifically administered to the experimental group throughout the study.

Table (1) mean, standard deviation, Kolmogorov-Smirnov statistic and its significance level for cognitive flexibility skill dimensions of two groups (experimental and control) and in three stages of pre-test, post-test and follow-up

Cognitive flexibility skill dimensions	group	Statistical index	Time		
			pre-test up	post-test	follow-up
Perseverative Error	Experimental	Mean	10/87	6/87	6/80
		Standard deviation	2/031	1/407	1/265
		Kolmogorov-Smirnov	0/207	0/198	0/203
		Significance level	0/083	0/119	0/097
	Control	Mean	11/20	11/33	10/13
		Standard deviation	1/265	1/543	1/125
		Kolmogorov-Smirnov	0/163	0/186	0/214
		Significance level	0/200*	0/175	0/063
Clusters	Experimental	Mean	3/60	5/67	6/00
		Standard deviation	0/910	0/976	1/069
		Kolmogorov-Smirnov	0/270	0/234	0/167
		Significance level	0/054	0/057	0/200*
	Control	Mean	3/60	3/60	3/93
		Standard deviation	0/986	1/183	0/961
		Kolmogorov-Smirnov	0/195	0/168	0/200
		Significance level	0/128	0/200*	0/110

*: This value represents the minimum threshold of statistical significance.

According to the results of this table, it can be observed that the average scores of cognitive flexibility dimensions, including “Perseverative Error” and “Clusters,” for the experimental group in the pre-test phase were 10/87 and 3/60, respectively. In the post-test phase, these scores were 6/87 and 5/67, and in the follow-up phase, they were 6/80 and 6/00, respectively. These values indicate that the dimension “Perseverative Error” decreased in the post-test phase compared to the pre-test, and this decrease was maintained in the follow-up phase. Additionally, the dimension “Clusters” increased in the post-test phase compared to the pre-test, and this increase was also maintained in the follow-up phase. It is worth noting that appropriate statistical tests have been used to assess the significance of these changes.

Moreover, based on the above table, it is observed that the normality of the distribution of all variables is accepted in all conditions. This is indicated by the fact that the Sig value (significance level) of the Kolmogorov-Smirnov statistic for all conditions is greater than 0/05.

Considering the assessment of the independent variable's effect on the levels of dependent variables (cognitive flexibility dimensions), multivariate analysis of variance for repeated measures will be used. Therefore, in addition to the normal distribution, the independence of the dependent variables in the pre-test stage from the group membership variable is another basic assumption of this method that is examined in this section. To evaluate this assumption, the levels of dependent variable (cognitive flexibility dimensions) in the pre-test phase were compared between the experimental and control groups. The M-Box index was calculated to be 4/748, which was not statistically significant at the 0/05 level (Sig = 0/223). This issue indicates that the observed covariance matrices of the dependent variables are statistically homogeneous in the groups.

To test the assumption of homogeneity of error variances of the "Perseverative Error" and "Clusters" variables in the pre-test phase between the control and experimental groups, the Levene's test was used. The results of this test are presented in Table (2).

Table (2) Results of Levene's Test to Examine the Homogeneity of Error Variances of "Perseverative Error " and "Clusters" Variables

variable	F-statistic	Degrees of Freedom (Numerator)	Degrees of Freedom (Denominator)	Sig
Perseverative Error	1/275	1	28	0/268
Clusters	0/204	1	28	0/655

Based on the observations from Table 2, it can be noted that the F-statistic values for the variables "Perseverative Error" and "Clusters" in the pre-test phase were 1/275 and 0/204, respectively. The corresponding Sig values are 0/268 and 0/655, respectively. Since the Sig values were greater than 0/05, therefore, at a significance level of 0.05, we accept the equality of error variances of "Perseverative Error" and "Clusters" variables between the control and experimental groups during the pre-test phase. Consequently, the assumption of homogeneity of error variances of the dependent variables in the pre-test stage between the control and experimental groups is supported. As a result, the MANOVA (Multivariate Analysis of Variance) is an appropriate method for comparing cognitive flexibility skill dimensions in the pre-test stage between the experimental and control groups.

Table (3) shows the results of multivariate tests in MANOVA. In other words, this table shows whether there is a statistically significant difference between the experimental and control groups in the linear combination of "cognitive flexibility skill" dimensions or not. There are various statistics to choose from, including Wilks' lambda, Hotelling's Trace, Roy's largest root, and Pillai's Trace. The most commonly reported statistic is Wilks' Lambda. However, if the data have problems such as small sample size, unequal values of n, and violation of assumptions, Pillai's Trace is considered more robust (Tabachnick & Fidell, 2007, p. 252). In situations where there are only two groups, the value of the F statistic is the same for all three methods. In the present research, Wilks' Lambda is reported.

Table)3(Multivariate Tests

Effect	Wilks' Lambda	F-statistic	Degrees of Freedom (Hypothesis)	Degrees of Freedom (Error)	Sig	Value of Partial Eta Squared
Y-Intercept	0/010	1351/409	2	27	0/000	0/990
Group	0/988	0/169	2	27	0/845	0/012

The above table indicates that the F values (sig = 0/845, F = 0/169, =0/012, Wilks' Lambda = 0/998) are not statistically significant at the 0/05 level. Based on this, it is concluded that the dimensions of cognitive flexibility skills in the pre-test phase do not significantly different between the experimental and control groups, and the assumption of independence of pre-test variables from group membership variable is established among the data of the current research.

Therefore, the necessary assumptions for using the repeated measures multivariate analysis of variance (MANOVA) are met. Consequently, this method can be employed for hypothesis testing. To examine the sphericity assumption or equality of error covariance matrices, the Mauchly's sphericity test was used. Table 4 presents the results of the test for equality of error covariance matrices in the dimensions of cognitive flexibility skills.

Table (4) Mauchly's Sphericity Test for Equality of Error Covariance Matrices in Cognitive Flexibility Skill Dimensions

Variable	Mauchly's W	Chi-Square	Degrees of Freedom	Sig	
Perseverative Error	0/901	2/800	2	0/247	0/995
Clusters	0/882	3/404	2	0/182	0/985

Based on Table 4, it is observed that the assumption of sphericity holds for the dimensions of "Perseverative Error" (Sig > 0/05 and =2/800) and "Clusters" (Sig > 0/05 and =3/404). Table 5 indicates the significance of the main effect of "Time" and the interactive effect of "Time*Group" for each dimension of cognitive flexibility skill.

Table (5) Significance of the main effect of Time and the interactive effect of Time*Group for each dimension of cognitive flexibility skill

Effect	Variable	Test	Sum of Squares	Degrees of Freedom	Mean of Squares	F	Sig	
Time	Perseverative Error	Sphericity Assumed	107/267	2	53/633	37/398	0/000	0/572
		Greenhouse-Geisser	107/267	1/821	58/917	37/398	0/000	0/572
	Clusters	Sphericity Assumed	30/467	2	15/233	31/778	0/000	0/532
		Greenhouse-Geisser	30/467	1/788	17/038	31/778	0/000	0/532
	Time*Group	Sphericity Assumed	68/422	2	34/211	23/855	0/000	0/460
		Greenhouse-Geisser	68/422	1/821	37/581	23/855	0/000	0/460
	Clusters	Sphericity Assumed	21/356	2	10/678	22/275	0/000	0/443
		Greenhouse-Geisser	21/356	1/788	11/943	22/275	0/000	0/443

Based on the results of the above table, the main effect of Time is significant for Perseverative Error ($F = 37/398$, $\text{Sig} < 0/01$, $= 0/572$) and Clusters ($F = 31/778$, $\text{Sig} < 0/01$, $= 0/532$) variables at a significance level of 0/01. Additionally, the Eta-squared values for the Perseverative Error and Clusters variables in the main effect of Time indicate that 57/2% and 53/2% of the variance of Perseverative Error and Clusters variables, respectively, is explained by the independent variable.

Furthermore, according to the results of Table 5, the interactive effect of »Time*Group« is significant for the Perseverative Error ($F = 23/855$, $\text{Sig} < 0/01$, $= 0/460$) and Clusters ($F = 22/275$, $\text{Sig} < 0/01$, $= 0/443$) variables at a significance level of 0/01. The Eta-squared values for the Perseverative Error and Clusters variables in the interactive effect of »Time*Group« suggest that 46% and 44/3% of the variance of Perseverative Error and Clusters variables, respectively, is explained by the independent variable.

Table 5 shows the significance of the main effect of »group« for each dimension of cognitive flexibility skill.

Table (5) The main effect of the group for each dimension of cognitive flexibility skill

Effect	Variable	Sum of Squares	Degrees of Freedom	Mean of Squares	F	Sig	
Group	Perseverative Error	165/378	1	165/378	45/837	0/000	0/621
	Clusters	42/711	1	42/711	19/858	0/000	0/415

Based on the results of this table, the main effect of the group is significant for the variables of Perseverative Error ($F = 45/837$, $\text{Sig} < 0/01$, $= 0/621$) and Clusters ($F = 19/858$, $\text{Sig} < 0.01$, $= 0/415$) at a significance level of 0/01.

These findings indicate that the utilization of tDCS has a different impact compared to the control group in each dimension of cognitive flexibility skill (Perseverative Error and Clusters). Figures (1) and (2) illustrate the interaction between time and group, differentiated by the dimensions of cognitive flexibility skill.

As Figure (1) illustrates, there is an interaction between group and time in the dimension of Perseverative Error ($F = 23/855$, $\text{Sig} < 0/01$, $\eta^2 = 0/460$). As the graph depicts, the experimental group shows significantly less Perseverative Error compared to the control group. In other words, the implementation of tDCS has significantly reduced the Perseverative Error in children with specific learning disorders.

As shown in Figure 2, there is an interaction between the group and time in the dimension of clusters ($F = 22/275$, $\text{Sig} < 0/01$, $\eta^2=0/443$). The graph illustrates that the “Clusters” score in the experimental group is higher than the control group. In other words, the implementation of tDCS significantly increases the “Clusters” score in children with specific learning disorders.

Thus, the hypothesis testing indicates that the application of tDCS has a meaningful impact on improving cognitive flexibility skill (Perseverative Error and Clusters) in children with specific learning disorders. Additionally, the interaction between the group (experimental and control) and time in the dimensions of cognitive flexibility skill, including Perseverative Error and Clusters, is significant. Ultimately, based on the examination of interaction graphs between the group and time in the dimensions of Perseverative Error and Clusters, it is concluded that compared to the control group, tDCS leads to a reduction in the amount of Perseverative Error and an increase in the number of clusters in children with specific learning disorders.

Now, we aim to answer the hypothesis of whether the effects of tDCS on improving cognitive flexibility skill (Perseverative Error and Clusters) in children with specific learning disorders persist over one month. To answer the above question, each of the two levels, ' Perseverative Error ' and 'Clusters' for the experimental group is analyzed using a one-way repeated measures ANOVA. The Mauchly's test of sphericity is employed to examine the sphericity assumption or equality of error covariance matrices. Table 6 presents the results of this test in the dimensions of cognitive flexibility skill.

Table (6) Mauchly's Test of Sphericity in the Equality Test of Error Covariance Matrices for Dimensions of Cognitive Flexibility skill in the Experimental Group

Variable	Mauchly's W	Chi-Square	Degrees of Freedom	Sig	
Perseverative Error	0/292	15/991	2	0/000	0/607
Clusters	0/277	13/286	2	0/000	0/911

As the above table indicates, the assumption of sphericity is not met for both variables, “Perseverative Error” and “Clusters” in the experimental group (tDCS) ($\text{Sig} < 0/01$). Therefore, the degrees of freedom were corrected using the Greenhouse-Geisser method. Table 7 displays the significance or insignificance of the unique effect of “tDCS implementation” on each level of dependent variables (Perseverative Error and Clusters)

Table (7) Unique Effect of Implementing TDSC on Each Level of Dependent Variable

Variable	Mauchly's W	Sum of Squares	Degrees of Freedom	Mean of Squares	F-Value	Sig	
Perseverative Error	Sphericity Assumed	162/711	2	81/356	42/219	0/000	0/751
		162/711	1/171	138/934	42/219	0/000	0/751
Clusters	Sphericity Assumed	50/711	2	25/356	89/240	0/000	0/864
		50/711	1/635	31/018	89/240	0/000	0/864
	Greenhouse-Geisser						

Based on the results of the above table, the F values related to individuals who underwent tDSC in both dimensions of Perseverative Error ($F=42/219$, $Sig < 0/01$, $\eta^2= 0/751$) and Clusters ($F = 89/240$, $Sig < 0/01$, $= 0/864$) are statistically significant at the 0/01 level. This indicates that at least one of the pairwise comparisons of means between pre-test, post-test, and follow-up is statistically significant. Subsequently, Table 8 presents pairwise comparisons between pre-test, post-test, and follow-up for the dimensions of cognitive flexibility skill for the experimental group (individuals who underwent tDSC).

Table (8) Pairwise Comparisons between Pre-test, Post-test, and Follow-up for Cognitive Flexibility skill Dimensions

Variable	Pre-test minus Post-test	Post-test minus Follow-up	Pre-test minus Follow-up
Perseverative Error	=4/000	=0/067	=4/067
	=0/647 SE	=0/228 SE	=0/547 SE
	=0/000 Sig	=0/995 Sig	=0/000 Sig
Clusters	=-2/067	=-0/333	=-2/400
	=0/182 SE	=0/159 SE	=0/235 SE
	=0/000 Sig	=0/166 Sig	=0/000 Sig

As observed in Table 8, in the dimension of “Perseverative Error” there is a significant difference between the mean scores of pre-test and post-test at the 0/01 level ($\Delta\bar{X}= 4$, $SE = 0/647$, $Sig < 0/01$). Additionally, in this dimension, there is a significant difference between the mean scores of follow-up and pre-test at the 0/01 level ($\Delta\bar{X}= 4/067$, $SE = 0/547$, $Sig < 0/01$). However, there is no significant difference between the mean scores of follow-up and post-test in this dimension ($\Delta\bar{X}= 0/067$, $SE = 0/228$, $Sig > 0/01$). Therefore, it can be concluded that the implementation of tDSC has significantly reduced the “Perseverative Error” and this improvement in mean scores remains even after one month. Thus, it can be inferred that the implementation of tDSC has a stable effect on improving the level of “Perseverative Error”.

In the dimension of “Clusters”, there is a significant difference between the mean scores of the pre-test and post-test at the 0/01 level ($\Delta\bar{X}= -2/067$, $SE = 0/182$, $Sig < 0/01$). Similarly, in this dimension, there is a significant difference between the mean scores of follow-up and pre-test at the 0.01 level ($\Delta\bar{X}= -2/400$, $SE = 0/235$, $Sig <$

0/01). However, there is no significant difference between the mean scores of follow-up and post-test in this dimension ($\Delta\bar{X} = -0/333$, $SE = 0/159$, $Sig > 0/01$). Therefore, it can be stated that the implementation of tDSC has significantly increased the number of "Clusters", and this improvement in mean scores remains even after one month. Thus, it can be inferred that the implementation of tDSC has a stable effect on improving the number of "Clusters."

Overall Conclusion: tDSC has an impact on cognitive flexibility skill (Perseverative Error and Clusters) in children with specific learning disorders, and its effects are sustained over the course of one month. Consequently, the answer to the second research question is affirmative.

Discussion

The present study investigated the effect of transcranial direct current stimulation (tDCS) on the cognitive flexibility of children with specific learning disorders. In this study, a combination of stimulation of the left anodal DLPFC and the right cathodal VMPFC was used to improve cognitive flexibility in people with specific learning disorders. According to previous research such as (Polanía, Nitsche, & Ruff, 2018), (Borwick, Lal, Lim, Stagg, & Aquili, 2020) transcranial direct current stimulation (tDCS) has a positive impact on cognitive processes, including cognitive flexibility skill. In general, the findings of the present study showed that tDCS is effective in improving the components of cognitive flexibility, including clusters, preservation error, and response time. In other words, the findings of the present study indicated that the combination of left anodal DLPFC and right cathodal VMPFC stimulation led to improvements in cognitive flexibility components, such as Clusters, perseverative error, and response time, in children with specific learning disorders compared to the control group.

By reviewing the existing research literature, studies such as Salehinejad & et al(2020); In a systematic review, Salehinejad & et al., (2022) have demonstrated the effectiveness of the left dorsolateral prefrontal cortex (DLPFC) stimulation in improving executive functions in individuals with autism spectrum disorder, attention deficit hyperactivity disorder and specific learning disorder. Similarly, studies conducted by Salatino et al., (2022); Miler, Meron, Baldwin, & Garner (2018) in a pilot study, have confirmed the positive impact of the left DLPFC stimulation on working memory, attention, decision-making and other higher cognitive processes in both normal individuals and those with various disorders. On the other hand, other previous research such as Schroeder, & Plewnia (2017) as well as Vicent et al., 2019 have investigated the effect of ventromedial prefrontal cortex (VMPFC) stimulation on enhancing mood, decision-making abilities, cognitive flexibility, and reducing anxiety. Additionally, Li, Wang, Ye, & Luo, (2020) have demonstrated the effectiveness of VMPFC stimulation in promoting adaptive tendencies and reducing response time in individuals.

The current research proposed a hypothesis that suggested the potential impact of tDCS on enhancing various components of cognitive flexibility, including preservation error, clusters, and response time, in the experimental group. However, upon reviewing the research literature, it was found that this hypothesis has not been previously examined specifically in a group of children with specific learning disorders. Simultaneous stimulation of DLPFC and VMPFC was performed in a group of people with generalized anxiety disorder (Nejati, Majidinezhad, & Nitsche, 2022), women with depression disorder (Nejati, Majidinezhad, & Nitsche, 2022), and the results of these studies show the effectiveness of stimulation. At the same time, DLPFC and VMPFC (Nejati, Majidinezhad, & Nitsche, 2022) have been shown to reduce cognitive biases and increase attention and decrease attention biases.

TDCS causes brain cells to fire more or less by changing the excitability of neurons and shifting the membrane potential of surface neurons in the direction of depolarization or hyperpolarization. Stimulating the brain from the skull using direct electric current in order to change the excitability of the cortex in the desired areas increases executive functions. While the focus of direct electrical stimulation of the brain from the skull of tDCS is somewhat limited, but its functional effects appear directly in the limited area under the electrodes (Arkan & Yaryari, 2014).

The majority of studies examining the cumulative effects of tDCS on cognitive functions in various populations have reported significant positive outcomes. These findings can be further clarified by citing previous studies and research in the field. For instance, Fregni, El-Hagrassy, Pacheco-Barrios, Carvalho, Leite, Simis, & Brunoni, 2021 highlighted the importance of the left dorsolateral prefrontal cortex (DLPFC) in executive functions, such as cognitive flexibility. Additionally, Fregni et al., 2020 demonstrated that DLPFC stimulation strengthens brain regions associated with cognitive flexibility. Furthermore, studies conducted by (Salehinejad et al., 2020; Salehinejad et al., 2022) showed the effectiveness of DLPFC stimulation in enhancing executive functions. Papazova et al., 2018; Miller, Meron, Baldwin, & Garner, 2018; Salatino et al., 2022 provided evidence suggesting the involvement of DLPFC in higher cognitive processes, and the use of tDCS was found to enhance these processes in that specific area. It is important to note that DLPFC activation patterns exhibit hemispheric differences, with the left hemisphere being more engaged in non-emotional tasks. Consequently, the left DLPFC plays a crucial role in the manifestation of cognitive processes, including executive functions.

According to the research of Brunoni, & Vanderhasselt, 2014, the stimulation of the DLPFC has been found to be involved in preventing the interference of irrelevant or distracting information, as well as inhibiting unwanted responses. The results of the current research, which demonstrate the effectiveness of tDCS on various components of cognitive flexibility such as preservation error, clusters, and response time, support the argument that tDCS stimulates the DLPFC region. Specifically, the stimulation of the DLPFC helps the child answer more questions in the Wisconsin test, reduces unwanted responses, and decreases response time. Furthermore, research by Li, Wang, Ye, & Luo, 2020 argued that cathodic stimulation of the VMPFC leads to a significant increase in the tendency to adapt and a decrease in response time. This aligns with the findings of the current research, which also reported a decrease in reaction time for answering questions. Additionally, Manuel, Murray & Piguet, 2019 concluded that stimulation of both the DLPFC and VMPFC results in higher cognitive control. During the Wisconsin test, errors can occur while answering the questions. To reduce the occurrence of such errors, the child must receive instructions on how to answer the questions after completing several steps. The activation of the VMPFC is associated with impulsive behavior, while simultaneous stimulation of the DLPFC reduces impulsive behaviors and enhances cognitive control. According to research conducted by Kumaran, Warren & Tranel, 2015, it has been found that in addition to stimulating the DLPFC, the activation of the VMPFC facilitates experimental and observational learning. In other words, it can be concluded that during the Wisconsin test, the child achieves the accurate response by going through several steps, engaging in trial and error, and comprehending the instructions. The simultaneous stimulation of both the DLPFC and VMPFC regions expedites this process.

In general, children with specific learning disorders exhibit lower performance in executive functions, such as cognitive flexibility, compared to typically developing children. Cognitive flexibility is associated with brain regions such as the prefrontal cortex (PFC), basal ganglia, anterior cingulate cortex (ACC), and posterior parietal cortex (PPC). Additionally, Uddin, 2021 suggested that cognitive flexibility follows a developmental trajectory characterized by an inverted U-shaped pattern, peaking during the second and third decades of life and declining in late adulthood, starting from early childhood through adolescence and into adulthood.

Limitations and Future Research Directions

In terms of limitations, it should be noted that due to time constraints, a follow-up on the sustained improvement of cognitive flexibility throughout the year was not conducted in the present research. Therefore, considering these limitations, it is recommended for future studies to include a one-year follow-up period to determine whether the improvement in cognitive flexibility among children with specific learning disorders persists over time.

Furthermore, it is important to note that the Wisconsin test was utilized in this research. However, for future studies, an alternative approach could involve employing the brief executive functions test (specifically the cognitive flexibility section) from both the teachers' and the parents' forms. This approach would allow for more confident observations regarding the therapeutic effects of tDCS in enhancing cognitive flexibility, as it would consider the viewpoints of teachers and parents within the school and home environments, respectively. Additionally, given that children spend significant time in both settings, investigating parents' and teachers' perceptions of cognitive flexibility improvement through the use of a brief executive functions test after tDCS may provide valuable insights for future research. Additionally, it is worth considering that the current research focused on cognitive flexibility as the dependent variable within the scope of executive functions. However, future studies may benefit from exploring the effectiveness of tDCS on other executive functions as well.

Conclusions

In summary, the outcomes of this study provide support for the effectiveness of Transcranial Direct Current Stimulation (tDCS) sessions in improving various components of cognitive flexibility skill, such as preservation error, clusters, and response time, in children diagnosed with specific learning disorders. These findings suggest that tDCS shows potential for enhancing cognitive flexibility skills in this specific population.

Declarations

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Availability of data and materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

We have consent to publish the article

Financial resources

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Competing interests

No potential conflict of interest was reported by the authors.

Code of ethics

This project was found to be accordance to the ethical principles and the national norms and standards for conducting Medical Research in Iran. Approval ID: IR.SBU.REC.1402.038 Approval Date: 07-02-2023

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Figures

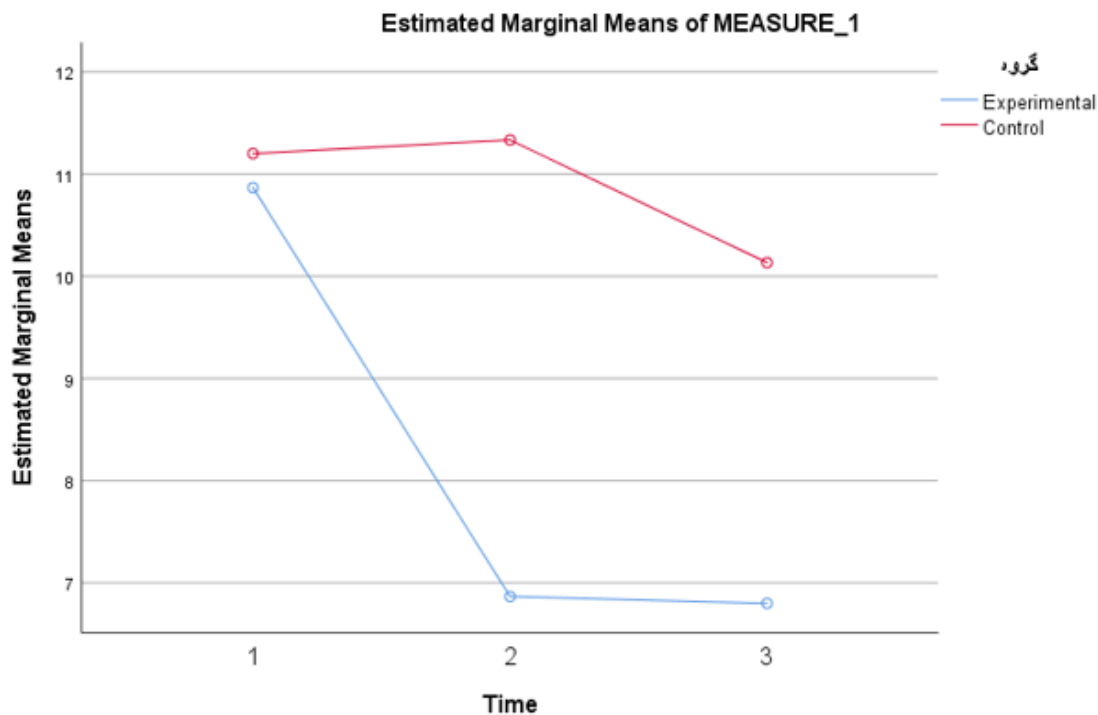


Figure 1

the interactive effect of »time*group« in the dimension of Perseverative Error

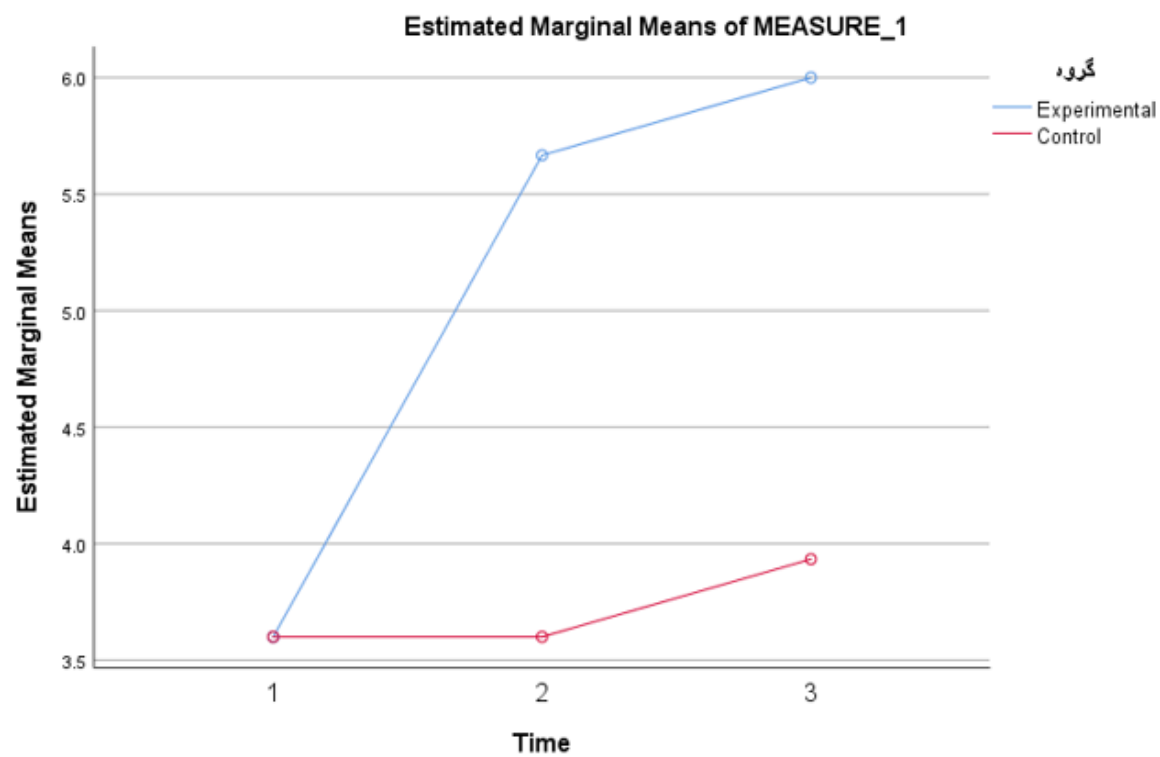


Figure 2

the interactive effect of »time*group«in the dimension of clusters