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Evaluating the Effect of Applying Cathodal tDCS to the Left Dorsolateral Prefrontal Cortex on Visual Working Memory

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ABSTRACT

Objective: Contemporary research has studied non-invasive brain stimulation modalities regarding their impact on various cognitive functions, particularly in the areas of learning and memory. Studies are being pursued to delve into the manipulation of these cognitive facets through this methodology. The aim of the current study was to examine the effects of application of cathodal transcranial direct current stimulation (tDCS) to the left dorsolateral prefrontal cortex (DLPFC), on visual working memory.

Materials and Methods: The study consisted of two separate groups, an active and a sham group, in which a total of 42 university students participated. Two mA cathodal direct current was applied to the left dorsolateral prefrontal cortex. To measure visual working memory, the study applied a visual 1-back task consisting of Chinese letters before and after tDCS and compared the obtained data.

Results: The study observed significant differences between the active and sham groups, with the active group having an increased number of omissions, a decreased number of correct responses, and prolonged response times.

Conclusion: The findings of the study revealed the suppressive effect of cathodal tDCS on visual working memory. Studies in the literature revealed various results regarding the contributions of left and right DLPFC on working memory. The findings of this study showed that right DLPFC also has an effect on visual working memory.

Keywords: Working memory, tDCS, *n*-back task

INTRODUCTION

Memory-related studies began in the 18th century and have continued to the present day. The scholarly work titled "The Magical Number Seven, Plus or Minus Two," authored by Miller, could be assumed to have exerted a profound influence on the conceptualization of short-term memory. Miller's study emphasized individuals to be able to typically hold an average of seven numbers in their short-term memory and underscored this capacity to be able to vary with individual differences (1).

Within the realm of contemporary psychological discourse, the multicomponent model as propounded by Baddeley and Hitch in 1974 has garnered widespread acceptance. This theoretical framework encompasses three fundamental constituents: the phonological loop, the visuospatial sketchpad, and the central executive (2).

This study focused on the temporary retention of visual information in the visuospatial sketchbook (3).

To date, experimental research has provided evidence that both the right and left dorsolateral prefrontal cortex (DLPFC) are involved in numerous cognitive functions,

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including but not limited to learning, memory, and the study and processing of cognitive structures (4). This finding has played a significant role in accepting the notion that the DLPFC forms the core of working memory (5).

Transcranial direct current stimulation (tDCS) aims to stimulate brain tissue by placing anode and cathode electrodes on the scalp. When applying tDCS, anodal stimulation induces depolarization of the membrane potential in the targeted cerebral area, thus bringing it closer to the threshold (6). In contrast, cathodal stimulation induces hyperpolarization in the stimulated area (7).

Contemporary research provides examples where tDCS has been applied to manipulate cognitive performance. Nitsche et al. observed inhibition in the motor cortex following application of cathodal tDCS for 5-7 minutes. The same effect was reported to have been repeated in a new stimulation applied after an hour post-stimulation (8).

Another study on the left DLPFC gave participants forward and backward counting tasks after applying cathodal tDCS. That study presented participants with a 5-min 2-forward task followed by a 5-min 3-back task. The study revealed a significant difference between the active and sham groups, with the active group showing improved performance on the forward counting task, unlike the sham group. However, no significant difference was found in the execution of the backward counting task (9).

Another study on healthy adults divided 12 participants into two separate groups, one group receiving a 2 mA anodal tDCS and the other a sham stimulation. During and after the tDCS stimulation, participants were presented with 3-back tasks and Sternberg tasks. As a result of the study, the reaction time of the active group was shown to be decreased compared to the sham group (10).

A meta-analysis of brain imaging research on *n*-back tasks suggested the right DLPFC to be a region associated with both information manipulation (updating) and retention (11). The right DLPFC has been recognized to play a specific role in attentional control, which is closely related to selective attention and maintenance of task-related information (12). Meanwhile, this region has also been shown to be important for inhibition control, such as the suppression of inappropriate responses (12, 13). Cathodal tDCS over the right DLPFC has been shown to be able to improve recognition memory performance by suppressing interference in the task, with cathodal tDCS on the right DLPFC also reported to significantly increase nonverbal recognition memory performance (14). Therefore, both anodal and cathodal tDCS of the right DLPFC may have the potential to improve working memory. A study examining the effect of tDCS applied to the right DLPFC on different components of working memory showed cathodal tDCS to facilitate the maintenance of working memory and anodal tDCS to have a suppressive effect (15). The literature contains studies showing the right DLPFC to be associated with non-verbal processes in working memory and the left DLPFC to be associated with verbal working memory (16-19). Recent studies have shown both types of stimulation applied to the right DLPFC to have a positive effect on visual working capacity (12-14). The aim of this current study was to examine the effects of application of cathodal tDCS to the left DLPFC on visual working memory, regarding the visual 1-back task.

MATERIALS AND METHODS

The study involved the participation of 42 healthy university students between the ages of 18-30 who are right-handed and unfamiliar with Chinese characters. Two separate groups took part in the study: an active group and a sham group, with the participants being randomly assigned to the groups.

After the participants signed the informed consent form, they were informed about the tasks and procedures to be performed for about 5 minutes. The participants were then given a 1-minute trial test regarding a visual 1-back task. After the trial, participants performed a visual 1-back task lasting approximately 5 minutes. After completing the visual 1-back task, the participants were immediately applied 20 minutes of cathodal tDCS. After the tDCS, the other form of the visual 1-back task was administered. The whole experiment lasted approximately 1 hour, including the insertion and removal of the electrodes. All participants in this study gave signed informed consent before being included in the study. This

Figure 1. Chinese letters used in the pretest.

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Figure 2. Chinese letters used in the posttest.

study was found ethically and scientifically appropriate by Istinye University, Clinical Research Ethics Committee, through decision no. 4/2023.K-14, thus obtained ethical approval.

Visual 1-Back Task

The study gave participants a task consisting of 28 different Chinese characters to assess their visual working memory performance. The task is called the *n*-back task, in which the participants were asked to press the number 1 or number 2 key on the keyboard according to the characters displayed on the screen. The *n* value expresses the number of times the stimulus on the screen will be the same as the previous stimulus, with $n = 1$ in this study. Accordingly, the participants were asked to memorize the Chinese character shown on the screen. They were asked to press the number 1 key if the next stimulus was the same as what had been shown on the previous screen, or to press the number 2 key if it was different.

Although the participants became familiar with the characters during the pre-tDCS test (Figure 1), a different stimulus set was used in the post-tDCS (Figure 2). Stimuli consisting of Chinese characters were presented for 300 ms in the middle of a 24 cm x 42 cm screen using the program E-Prime 3.0 (Figure 3).

Responses during the test were given using a QWERTY Turkish keyboard, with the number 1 and number 2 keys on the right side of the keyboard being designated as the target and standard keys, respectively. During the administration, a total of 50 stimuli were presented to each participant, with 35% of these stimuli being identified as targets. Of the characters, 17 were categorized as "target" characters while 33 were categorized as "standard" characters. The stimuli were presented on the screen for 300 msc at 1500 msec intervals. When participants failed to press a key in time, the response was defined as an "omission" error. A response involving an incorrectly pressed key is defined as a "commission" error (Figure 4).

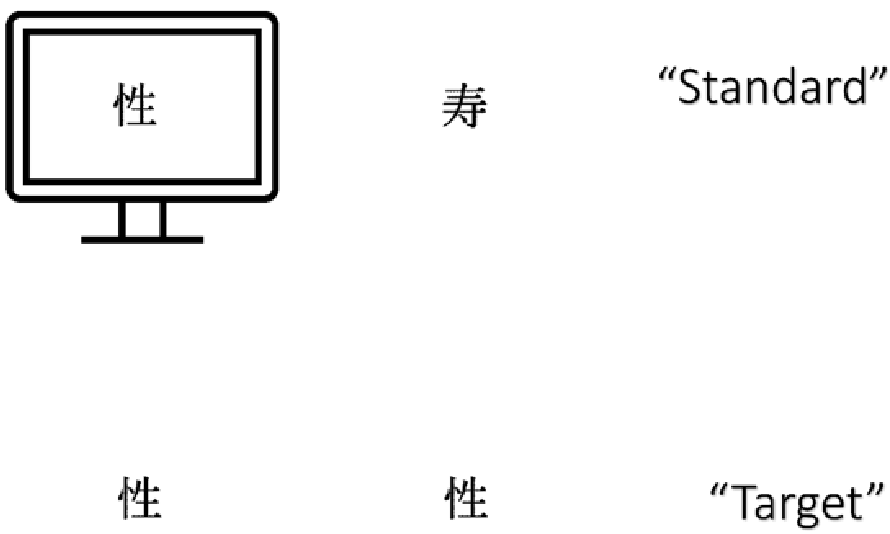

Figure 3. Task chart.

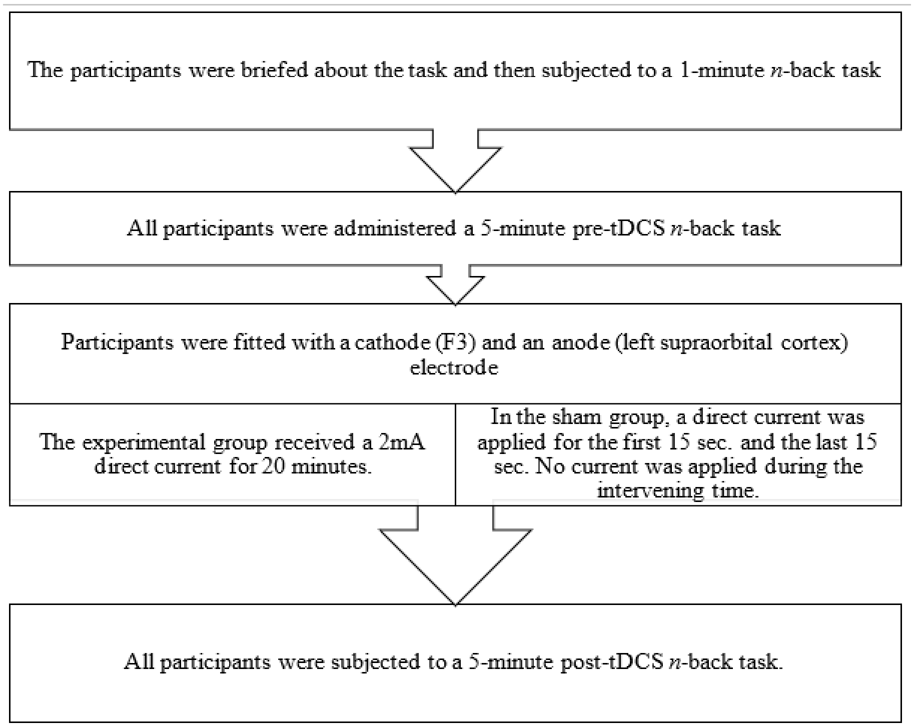

Figure 4. Experimental chart.

The study had the cathode electrode placed in the F3 region in accordance with the 10-20 EEG system and corresponding to the left DLPFC, with the anodal electrode placed on the left supraorbital cortex. The study uses electrodes measuring 5x7 cm^2 (Figure 5).

Application of tDCS

The active group received 2 mA of direct current for 20 minutes. The sham group received a current that was increased to 2 mA within the first 15 seconds, continued for 15 seconds upon reaching 2 mA, and then decreased to zero again within 15 seconds to create the sensation of having received the test current, with no current being applied for the rest of the time.

Figure 5. Placement of the cathode (blue) and anode (red) electrodes.

Statistical Analyses

The data obtained from the visual 1-back task were analyzed using IBM-SPSS 26 software. As the values obtained did not fit the Gaussian distribution, nonparametric statistical methods were used for further analysis. In addition, between-group comparisons were evaluated using Mann-Whitney U test and within-group comparisons were evaluated using Wilcoxon test. Significance limit was accepted as $p<0.05$.

RESULTS

A mini-mental test was administered to the 42 participants before the study. When analyzing the within-group values, the active group showed an average score of 28.9, while the sham group had an average score of 28.7 (p=0.309; Table 1).

Table 1. Comparison of mini-mental test values between groups

	Mini-Mental Test
Z	-1.016
p-value	0.309

Mann-Whitney U test

Table 2. Comparison between groups for the pre-tDCS visual 1-back task results

	Number of Omissions (mean ± *SD*)	Standard Stimulus		Target Stimulus		Commission	
		Number (mean ± *SD*)	Response Time (msec) (mean ± *SD*)	Number (mean ± *SD*)	Response Time (msec) (mean ± *SD*)	Number (mean ± *SD*)	Response Time (msec) (mean ± *SD*)
Pre-tDCS active group	8.47 ± 7.06	26.57 ± 5.96	193 ± 59.60	14.14 ± 2.72	190.57 ± 58.30	3.80 ± 3.01	170.38 ± 79.81
Pre-tDCS sham group	10.90 ± 8.76	22.09 ± 6.68	196.09 ± 63.94	14.04 ± 3.02	200.28 ± 62.70	5.14 ± 3.86	194.57 ± 86.76
Z	-0.733	-1.779	-0.277	-0.038	-0.667	-0.963	-2.233
p-value	0.464	0.075	0.782	0.969	0.505	0.336	0.217

Mann-Whitney U Test, SD: Standard deviation, TDCS: transcranial direct current stimulation

Comparison of Visual 1-Back Task Values Pre- and Post-tDCS

Visual 1-back Task Values Pre-tDCS

Before the tDCS application, no statistically significant difference was observed between the two groups in terms of the number of omissions (p=0.464), number of commissions (p= 0.336), number of standard stimuli (p=0.075), standard stimulus-response time (p=0.782), number of target stimuli (p=0.969), target stimulus-response time (p=0.505), and commission response times (p=0.217; Table 2).

Comparing the Active Group's Visual 1-Back Task Values

The within-group analyses revealed statistically significant differences to occur within the active group regarding the number of omissions (p=0.043), standard stimulus-response time (p<0.0001), number of target stimuli (p<0.0001), target stimulus-response time (p<0.0001), number of commissions (p=0.003), and commission response time (p<0.0001), but not regarding the number of standard stimuli (p=0.775; Table 3).

Comparing the Sham Group's Visual 1-Back Task Values

The data obtained from the sham group pre- and post-tDCS were examined and revealed statistical differences regarding standard stimulus-reaction time (p=0.007), number of target stimuli (p=0.004), target stimulus-reaction time (p<0.0001), and commission response time (p=0.046). However, no significant difference was found regarding the number of omissions (p=0.107), the number of standard stimuli (p=0.075), or the number of commissions (p=0.160; Table 4).

Table 3. Within-group comparison of the active group's pre- and post-tDCS visual *n*-back task results

	Number of Omissions (mean ± *SD*)	Standard Stimulus		Target Stimulus		Commission	
		Number (mean ± *SD*)	Response Time (msec) (mean ± *SD*)	Number (mean ± *SD*)	Response Time (msec) (mean ± *SD*)	Number (mean ± *SD*)	Response Time (msec) (mean ± *SD*)
Pre-tDCS group	8.47 ± 9.83	26.57 ± 5.96	193 ± 59.60	14.14 ± 2.72	190.57 ± 58.30	3.80 ± 3.01	170.38 ± 79.81
Post-tDCS group	11.19 ± 7.35	19 ± 7.04	247 ± 41.76	9.09 ± 2.40	238.90 ± 43.10	6.62 ± 3.57	245 ± 49.13
Z	-2.021[b]	-0.285[c]	-3.841[b]	-4.023[c]	-3.737[b]	-2.984[b]	-3.563[b]
p-value	**0.043**	0.775	**p<0.0001**	**p<0.0001**	**p<0.0001**	**0.003**	**p<0.0001**

Wilcoxon Signed Ranks Test, SD: Standard deviation; tDCS: Transcranial direct current stimulation; b: Based on negative ranks; c: Based on positive ranks.

Table 4. Within group gomparison of the sham group's pre- and post-tDCS visual *n*-back task results							
		Standart Stimulus		**Target Stimulus**		**Commission**	
	Number of Omissions (mean ± *SD*)	**Number (mean ± *SD*)**	**Response Time (msec) (mean ± *SD*)**	**Number (mean ± *SD*)**	**Response Time (msec) (mean ± *SD*)**	**Number (mean ± *SD*)**	**Response Time (msec) (mean ± *SD*)**
Pre-tDCS group	10.90 ± 8.76	22.90 ± 6.68	196.09 ± 63.94	14.94 ± 3.02	200.28 ± 62.70	5.14 ± 3.86	194.57 ± 86.76
Post-tDCS group	9.52 ± 9.83	24.52 ± 8.27	171.66 ± 62.58	15.19 ± 2.54	168.57 ± 68.37	3.76 ± 2.79	154.71 ± 68.54
Z	-1.612[b]	-1.778[c]	-2.677[b]	-2.914[c]	-3.529[b]	1.406[b]	-1.999[b]
p-value	0.107	0.075	**0.007**	**0.004**	**<0.0001**	0.160	**0.046**

Wilcoxon Signed Ranks Test; SD: Standard deviation; tDCS: Transcranial direct current stimulation; b: Based on negative ranks; c: Based on positive ranks.

Between Group Comparison of Difference in Data Regarding the Pre- and Post-tDCS Visual *N*-Back Results

When comparing the differences between the two groups' pre- and post-tDCS results, substantial variances were identified between the groups regarding number of omissions (p=0.013), standard stimulus-response time (p<0.0001), target stimulus count (p<0.0001), number of commissions (p<0.0001), and commission response time (p<0.0001). Meanwhile, no discernible statistical disparity was found regarding the standard stimulus quantification (p=0.181; Table 5).

When comparing the two groups' differences between the pre- and post-tDCS visual 1-back task results, statistical differences were found regarding the number of omissions (p=0.013), standard stimulus-response time (p<0.0001), number of target stimuli (p<0.0001), target stimulus-reaction time (p<0.0001), number of commissions (p<0.0001), and commission response time (p<0.0001) between the groups. However, no statistical difference was found regarding the number of standard stimuli (p=0.181; Table 5).

DISCUSSION

This study randomly assigned 42 healthy adult volunteers to the active and sham groups and performed the visual 1-back task to measure visual working memory performance pre- and post-tDCS application. In conclusion, when comparing the statistical values within and between groups, the study found the performance of the active group to be lower than that of the sham group.

Barbey et al. reported that left DLPFC damage caused impairment in verbal, auditory, and spatial tasks related to working memory (20). This study applied stimulation to the left DLPFC by considering studies in the literature that have emphasized the role the left DLPFC has in working memory (9, 21). Similar to the findings reported in the literature, the results from the current study observed impairment in working memory tasks in response to the suppression applied to the left DLPFC.

Table 5. Between group comparison of the two groups' pre- and post-tdcs visual *n*-back task data differences							
		Standart Stimulus		**Target Stimulus**		**Commission**	
	Difference In The Number of Omissions	**Difference In The Number of Standard Stimuli**	**Standard Stimulus-Response Time Difference (msec)**	**Difference in the number of target stimuli**	**Difference in Response Times (msec)**	**Difference in Number of Commission**	**Difference in Response Times (msec)**
Mean Data Difference	0.66	0.61	14.95	8.30	-1.95	0.66	24.19
Z	-2.485	-1.337	-4.780	-5.550	-5.108	-3.518	-3.837
p-value	**0.013**	0.181	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**	**<0.0001**

Mann-Whitney U test; SD: Standard deviation; tDCS: Transcranial direct current stimulation.

When examining the between-groups values for the pre-test, no statistically significant difference was found in the number of targets, omissions, commissions, and standard stimuli, as well as in their response times. This shows no significant difference to exist between the participants in both groups and that standardization had been strengthened (Table 2).

When comparing the pre- and post-test values in the active group, an increase was observed to occur in the number of omissions and commissions, a decrease in the number of correct target stimuli, and an increase in all reaction times (Table 3). In the sham group, an increase was found to occur in the number of correct target stimuli and a shortening in the target stimulus duration and commission reaction times (Table 5).

An increase in the number of omissions and commissions was observed in the active group's post-tDCS task. Also, the active group's post-tDCS commission response times were prolonged. In contrast, no significant differences were seen in the sham group's target numbers or omission numbers. In addition, a slight decrease was found in the number of commissions and commission response times for the sham group (Table 4). Reviewing other studies in the literature, results similar to those in the current study were observed when applying cathodal tDCS to the left DLPFC (8). Javadi and Walsh's (22) study on 32 participants observed similar negative effects when applying cathodal tDCS on verbal working memory as were observed in the current study regarding visual working memory.

A meta-analysis of 61 studies by Dedoncker et al. has reported anodal tDCS stimulation to improve performance regarding *n*-back tasks (i.e., 1-back, 2-back, and 3-back tasks) with response times being significantly reduced (23). However, no significant differences were found in the sham groups in the studies Dedoncker et al. have reviewed (23). In contrast, the current study suggests that improvements had been observed in the sham group possibly due to the shorter interval before starting the tasks pre- and post-tDCS compared to other studies. This supports the idea that performance can be increased by increasing the number of trials in cognitive assessments.

Moreover, when considering that both groups had gained experience after the first test, the fact that no improvement had occurred in the number of commissions and response times in the active group, with an increase in that group even occurring regarding the number of commissions and a significant prolongation in response times, shows the effect that applying cathodal tDCS to the left DLPFC has on visual working memory.

The lack of improvement in the active tDCS group relative to the sham tDCS group regarding the standard stimuli post-tDCS task (Table 3) confirms the suggestion of improved performance depending on the number of trials in the cognitive assessments (21, 23). In addition to these studies, examples are also found in the literature to have tried to modulate working memory with regard to visual and verbal dimensions (20-24). These examples mostly used *n*-back tasks created with complex or geometric shapes. Contrary to these examples, the current study created a visual 1-back task consisting of 28 different Chinese characters. Fregni et al. study, which applied cathodal tDCS to the left DLPFC, performed a similar 1-back task with Latin letters; their application did not create a significant difference with regard to working memory (25). However, the current study observed a very significant effect from the cathodal tDCS; the difference between the current study's results compared to those from Fregni et al.'s study are thought to be due to the current study's use of a visual 1-back task, which is difficult to verbalize, instead of a verbalizable *n*-back task, as Latin letters can be quickly verbalized (25).

This study has attempted to reveal the concrete effects the tDCS has on visual working memory and found a remarkable difference between the sham and active groups. This supports the studies examined in Dedoncker et al.'s (23) meta-analysis.

Unlike Fregni et al., the current study presented Chinese characters as stimuli, because the participants would have difficulty in verbalizing these, thus eliminating the stimuli being translated into verbal memory (25). This is thought to have contributed to a clearer demonstration of the effect tDCS has on visual working memory. The difference observed regarding the results of Fregni et al.'s (25) reveals the need for further studies using tDCS to better understand the differences. The inability to translate the presented visual stimuli into verbal memory and the clear effects of tDCS on visual working memory are considered the distinguishing features of the current study.

This study's findings are consistent with those in the literature, suggesting that the left DLPFC is critical for preserving verbal and spatial information in working memory. This study has been conducted with cathodal tDCS and *n*-back tasks and is thought to be able to contribute to the literature on the concrete results tDCS has shown on working memory, and therefore also on cognitive performance tasks. In this way, the current study is thought to be able to help future studies on tDCS.

Ethics Committee Approval: This study is approved by Istinye University, Clinical Research Ethics Committee (No: 4/2023.K-14).

Informed Consent: The participants signed the informed consent form, they were informed about the tasks and procedures to be performed for about 5 minutes

Peer-review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- Y.E.O., G.E.; Data Acquisition- Y.E.O., G.E.; Data Analysis/Interpretation- Y.E.O., G.E.; Drafting Manuscript- Y.E.O., G.E.; Critical Revision of Manuscript- Y.E.O., G.E.; Final Approval and Accountability- Y.E.O., G.E.

Conflict of Interest: The authors declare that they have no competing interests.

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