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Effectiveness of Transcranial Direct Current Stimulation on Cognitive Function: A Pilot Study

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Abstract

Background: Cognitive impairment, which is one of the debilitating consequences of traumatic brain injury (TBI), leads to long-term adverse outcomes that disrupt an individual's participation in daily activities. This study aimed to investigate the effects of combining occupational therapy with transcranial direct current stimulation (tDCS)—a non-invasive and safe electrical method for targeting specific areas of the brain—on the cognitive function of individuals with TBI.

Methods: This semi-experimental study utilized convenience sampling, resulting in the inclusion of 24 patients with moderate to severe TBI. We then randomly assigned them to one of two groups: an experimental group (n = 12) or a control group (n = 12). Both groups underwent 10 sessions of daily occupational therapy, but the experimental group also received 20 minutes of tDCS during their occupational therapy sessions.

Cognitive functions, such as working memory, divided attention, problem solving, and planning, were assessed using computer-based versions of the Wisconsin Card Sorting Test (WCST), Tower of London, N-back, and Stroop tests at the baseline and the day after the intervention's conclusion. To implement the data analysis phase, we used SPSS Version 27. Depending on the normality of data distribution, either independent samples t-tests or Mann–Whitney U tests were used to compare the outcomes between the experimental and control groups.

Results: After the 10-session intervention, executive functions improved in both groups ($P < 0.05$). When comparing the groups, the experimental group demonstrated significant improvements in working memory ($P = 0.002$), planning ($P = 0.002$), and problem-solving ($P = 0.001$); however, no significant difference was observed in selective attention ($P = 0.310$).

Conclusion: The findings suggest that employing tDCS techniques plays a pivotal role in enhancing specific executive functions, such as working memory, problem-solving, and planning, in patients with traumatic brain injuries. tDCS can be considered a complementary treatment option in the rehabilitation of TBI patients.

According to the findings, the use of tDCS can improve executive functions, including working memory, problem-solving, and planning, in TBI patients. As a complementary treatment, tDCS can be utilized in the rehabilitation of TBI patients.

Keywords: Traumatic Brain Injury, Transcranial Direct Current Stimulation, Cognition

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Introduction

Traumatic brain injury (TBI) is a prevalent condition resulting from a head impact, rapid deceleration or acceleration, or skull fractures that penetrate the brain (1, 2). These factors can result in internal bleeding, tissue disruption, focal and diffuse injuries, hypoxia, and interrupted axonal connections (3). It is estimated that 50 million people

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↑What is "already known" in this topic:
Traumatic brain injury (TBI) causes cognitive impairments, especially in executive functions. Transcranial direct current stimulation (tDCS) is a noninvasive method known to improve cognition when combined with therapies, but optimal parameters are not well defined.

→What this article adds:
This pilot study shows that tDCS using a current intensity of 2 mA with a current density of 0.057 mA/cm² with the anode over the left dorsolateral prefrontal cortex and the cathode at the right supraorbital (combined with occupational therapy) enhances executive functions (working memory, planning, problem-solving) in TBI patients.

worldwide experience a TBI each year (4).

Even moderate traumatic brain injuries can cause cognitive impairments and dementia (5, 6). The main cognitive impairments in individuals with TBI are related to high-level cognitive functions such as attention, memory, communication, and executive function (7). Executive function disorder is among the most prevalent symptoms of TBI (8). It typically encompasses cognitive processes like shifting (i.e., transitioning between different tasks), inhibition (stopping oneself from making an unsuitable response), and updating (refreshing working memory content). These processes are widely acknowledged as fundamental components of executive function (7).

Current interventions for traumatic brain injury aimed at enhancing cognitive functions include pharmacotherapy and cognitive rehabilitation. Pharmacotherapy has modest and often unpredictable effects on cognition (9). Although research on cognitive rehabilitation remains limited, it has shown some effectiveness in improving cognitive and functional outcomes for post-acute traumatic brain injury patients (9, 10). These limitations have driven researchers to explore alternative therapeutic options. Transcranial direct current stimulation (tDCS) is a cutting-edge neuromodulation technique that delivers a weak direct electric current (approximately 1 to 2 mA) through electrodes placed on the scalp (11). Studies have shown that tDCS can enhance performance in diverse patient populations when used alongside treatment, making it a valuable addition to therapeutic regimens (9).

Previous studies have identified tDCS as a safe and effective method to enhance cognitive functions in patients with TBI (12). When examining motor and cognitive improvements in TBI patients, both clinical and empirical evidence favor the use of tDCS. However, further research is necessary to determine the optimal parameters for tDCS (such as electrode placement, current density, stimulation duration, and timing intervals) and to explore the interactions between tDCS and other concurrent treatments for various disorders (13).

Optimal electrode placement and stimulation duration for improving cognitive outcomes have not yet been established. The researchers recommended further studies to explore adjustments in tDCS parameters, such as the number of sessions and electrode placement. Previous studies applied 1 mA current for 15 minutes over 15 sessions, comparing excitation or inhibition on the dorsolateral prefrontal cortex (DLPFC) with the anode over the left DLPFC and the cathode at the right supraorbital (14, 15). This study was conducted to evaluate the efficiency of tDCS, using a current intensity of 2 mA with a current density of 0.057 mA/cm^2 for 20 minutes. The anode electrode was positioned over the left DLPFC, and the cathode electrode was placed over the right DLPFC, combined with routine occupational therapy, to improve executive functions in individuals with TBI. Also, the feasibility of the study protocol, intervention acceptability, and the most appropriate outcome measures were examined.

Methods

Participants

In this semi-experimental study, a single-blinded sham-controlled clinical trial, 24 individuals with a history of TBI were enrolled. Participants were conveniently selected from Pasteur Hospital of Bam. Participants eligible for inclusion were aged between 18 and 40 years, presented with predominant right hemiparesis, scored between 10 and 24 on the Mini-Mental State Examination (MMSE), had no history of epilepsy or other neurological or neuropsychiatric disorders, and had no metal implants in their bodies. Individuals who underwent additional therapeutic interventions or missed more than 2 sessions were excluded from the study.

Intervention

Eligible participants were randomly allocated to either the experimental group or the control group using a random-number table. Both groups received 20-minute routine occupational therapy sessions 3 times per week. Routine occupational therapy interventions for patients with TBI commonly involve strength training, motor relearning, neurodevelopmental treatment, task-specific motor training, and functional ambulation exercises (16-18). These interventions are tailored to each individual based on their baseline abilities and are implemented in a progressive, individualized method. Accordingly, in our study, routine occupational therapy included stretching and strengthening exercises for the upper and lower limbs, range of motion activities, balance training, and functional task practice. The experimental group received tDCS at an intensity of 2 mA and a density of 0.057 mA/cm^2 for 20 minutes, with the anode electrode placed on the left DLPFC and the cathode electrode on the right DLPFC. The Activa Dose (USA) apparatus was used for electrical stimulation. Sham treatment sessions matched the duration and electrode placement, but the device was set to sham mode, stopping the current after 25 seconds without the participants' awareness (19).

Participants were evaluated using the Persian versions and computer forms of the Stroop, Wisconsin Card Sorting Test (WCST), Tower of London, and N-back tests to assess selective attention, problem-solving, planning, and working memory, respectively. The interventions for both groups were conducted by an occupational therapist with 4 years of experience in the rehabilitation of patients with neurological disorders. Baseline and post-treatment evaluations were performed by another experienced occupational therapist who was blinded to group assignments. Participants were assessed before the treatments and 24 hours after the last treatment session.

Outcome Measures

Stroop test

The Stroop Test was used to assess selective attention. Participants were instructed to quickly identify the color of the designated shape in a set using the corresponding key on the keyboard (20). In the second stage, participants were shown 48 consonant color words and 48 consonant color words in colors red, blue, yellow, and green. Consonant words had colors that matched their meaning in Persian,

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while incongruent words had colors that differed from their meaning in Persian. A total of 96 consonant and incongruent color words were presented randomly and sequentially. The participants' task was to identify only the apparent color, disregarding the words' meaning. The measured indicators were accuracy (number of correct responses) and speed (average reaction time in milliseconds to correct responses) (21).The Stroop is considered valid and reliable based on the research of Oetelo and Graf (22).

Tower of London

The Tower of London (TOL) test is designed to evaluate strategic planning and problem-solving, which are key components of executive function (21). Evidence suggests that the TOL may be particularly sensitive to detecting frontal lobe dysfunction (23). During the test, participants must move colored pieces to form a specified pattern with the fewest possible moves. If the participant completes a stage or fails to solve the problem after 3 attempts, the next issue is presented. The test measures variables such as delay time, trial time, total trial time (combined delay and trial times), errors, and the overall score (21).

Wisconsin Card Sorting Test

Researchers have found the Wisconsin Card Sorting Test (WCST) to be an effective tool for studying cognitive deficits following brain injuries (24). In this test, 4 sample cards are displayed at the top of the screen, each differing in shape (triangle, circle, star, and cross), number (ranging from 1 to 4), and color (green, blue, red, and yellow). A deck of 64 cards (4 colors * 4 shapes * 4 numbers = 64 cards) is situated at the bottom of the screen, with only the top card visible. Each card in the deck possesses unique characteristics based on the same 3 rules. The task is to place the top card from the deck onto one of the sample cards, following an inferred rule, and to discover the classification rule based on the feedback provided on the screen. Once the cards are correctly classified, the rule changes, and the subject must identify the new rule based on the feedback. The participant's score is determined by the number of 10 categories successfully classified. If the participant continues to classify cards based on the previous rule despite the change, a perseveration error occurs. Perseveration errors represent the repetition of a previously learned response despite the new rule (21).

N-back Test

The N-back test is widely regarded as one of the most suitable measures for assessing working memory as part of executive function (25). During the test, some visual stimuli are presented sequentially on the screen at intervals of 1800 milliseconds, and the subject must compare each stimulus with the previous one, pressing the corresponding key if they are identical. The results of this test are recorded as the number of correct and incorrect responses (25).

Data Analysis

The Kolmogorov-Smirnov test was used to check the assumption of normal distribution. An independent samples t-test was conducted to compare quantitative demographic variables, while chi-square tests were used for qualitative demographic variables. Paired t-tests were applied for within-group comparisons when data followed a normal distribution (N-back tests and Stroop test, the overall score of the Tower of London). The Wilcoxon signed-rank test was used for data that were not normally distributed.

Inter-group comparisons had $P \geq 0.05$ for the N-back test, the correct and incorrect subsets of the WCST, the time subset of the Tower of London test, and the interference time subset of the Stroop test. For these comparisons, independent t-tests were used. For other between-group comparisons where data did not follow a normal distribution, the Mann-Whitney U test was applied.

Results

The study initially included 29 patients with TBI. However, five participants were excluded from the study: 2 from the experimental group due to coronavirus disease 2019 (COVID-19) infection, and 3 from the control group—1 attributable to COVID-19 infection and 2 due to receiving other treatments during the study period. Ultimately, 24 participants (12 in each group) completed the study (Figure 1). No significant differences were observed between the groups in baseline variables. Participants in both groups had moderate to severe TBI, with Glasgow Coma Scale scores ranging from 5 to 13 (26), and experienced MMSE score of 14-24). The demographic characteristics of the participants in the 2 groups are shown in Table 1.

According to the paired samples test and the Wilcoxon test, significant changes were observed between the baseline and post-intervention in all subscales of the 4 tests in both groups, except for the speed subscale of the Stroop test ($P > 0.05$). Independent samples t-test and Mann-Whitney test results showed no significant differences between the groups in all subscales of the 4 tests at baseline ($P > 0.05$). However, significant differences were observed between the groups in all subscales of the N-back test, the total score subscale of the Tower of London test, and the total correct number and total incorrect number subscales of the WCST ($P < 0.05$). No significant difference was found between the groups in any subscale of the Stroop test, the trial time of the Tower of London test, and both the categories and preservative error subscales of the WCST ($P > 0.05$). In brief, both the control and experimental groups displayed significant improvements in nearly all subscales of the N-back, WCST, and Tower of London tests. Still, the experimental group showed greater improvement in all tests except for the Stroop test, where the result was not significant (Table 2).

The results suggest that combining routine occupational therapy with tDCS proved more effective in enhancing problem-solving, planning, and working memory than routine occupational therapy alone (Table 1).

Discussion

In this pilot study, we aimed to investigate the influence of applying tDCS to the left DLPFC on enhancing executive functions, including problem-solving, working

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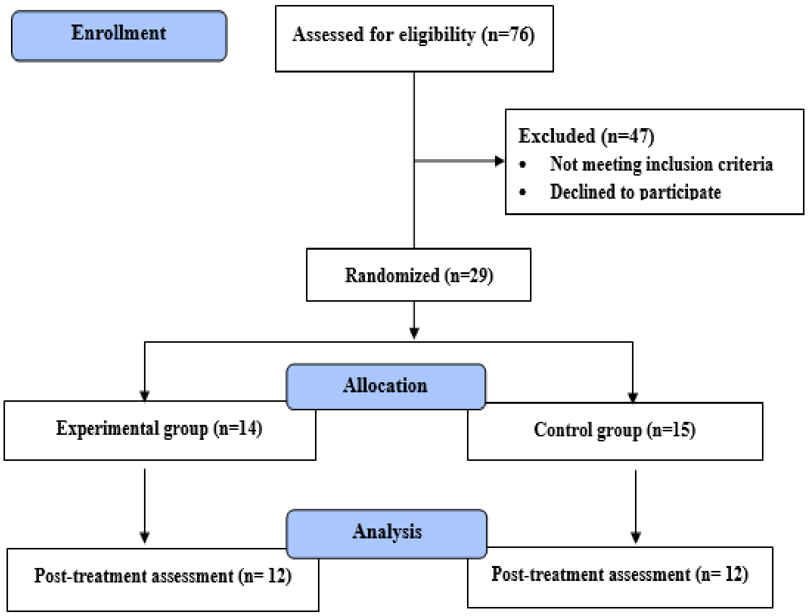

Figure 1. Flow diagram of the participants through the trial

Table 1. Demographic Characteristics of the Participants

Characteristic	Experimental group (n=12)	Control group (n=12)	*P* value
Sex (male/female)	8.4	9.3	0.831
Age(y)	29.67±6.28	28.25±5.97	0.070
Education (high school/university)	11.1	12.0	0.834
Mini-Mental State Examination (MMSE)	19.67±3.23	18.67±3.63	0.532
Glasgow Coma Scale (GCS)	8.75±2.56	9±2.79	0.512

memory, selective attention, and planning, in patients with moderate to severe TBI. The results indicated that tDCS significantly improved performance in working memory, planning, and problem-solving. Although the experimental group outperformed the control group in the selective attention test, this difference was not statistically significant. It is noteworthy that the safety of this stimulation method has been previously established, and no side effects were reported in this study.

Although the number of studies that hold resemblance to our scope of the study—appraising the efficiency of tDCS in individuals with TBI—is scant and often suffers from methodological issues (such as the void of blinding and randomization), the outcome of their study suggested amplifications in cognitive, neuropsychological, and neurophysiological performance (12, 13). Additionally, 1 study showed that the early administration of tDCS, particularly during the acute and subacute phases of severe traumatic brain injury, may contribute to improvements in both cognitive and motor functions (27).

There is also evidence suggesting that tDCS can enhance cognitive and executive functions. For example, a study by Telia et al. (2020) reported that combining tDCS with cognitive rehabilitation improved cognitive and executive functions, such as working memory, semantic reasoning, and information processing speed. Eilam-Stock et al. (2021) supported our findings (28). Chiang et al. (2021), in a case study assessing the effectiveness of tDCS on verbal skills and executive functions (working memory) in a TBI patient, observed significant improvements in executive functions and verbal skills, particularly immediately after the intervention (29).

It seems that tDCS, similar to other noninvasive brain stimulation techniques, promotes structural and functional neuroplasticity by enhancing synaptic connections and encouraging dendritic growth, which in turn accelerates clinical recovery. tDCS can target various brain networks, including motor and cognitive networks, thereby influencing motor and cognitive performance (13).

In the present study, the DLPFC regions were stimulated to influence participants' cognitive performance. The role of DLPFC is as crucial as other parts of the prefrontal lobe in various cognitive functions, including divided attention and working memory (30). These functions of the mind are pivotal to individuals' social and professional accommodation. Moreover, the importance of social, emotional, and physical health for cognitive health is discussed because stress, lack of sleep, loneliness, or lack of exercise each impairs executive function (31).

However, the study by Marcin Lesniak et al. (2014) did not find a significant effect of anodal tDCS on the left DLPFC combined with cognitive rehabilitation exercises (15). This discrepancy might be due to variations in current intensity, the duration of tDCS application, or differences

Table 2. Evaluation of WCST, N-back, Tower of London, and Stroop Test in Participants

Variable		Evaluation time	tDCS group (n=12) Mean ± SD	Control group (n=12) Mean ± SD	*P* value	Effect size
Wisconsin Card Sorting Test	Total number correct	Pre-treatment	33.58±7.633	32.33±5.365	0.001	1.508
		Post-treatment	46.25±4.070	29±5.444		
	Total number incorrect	Pre-treatment	27.04±6.484	27.67±5.365	0.001	-1.508
		Post-treatment	17.38±5.984	21±5.444		
	Perseverative errors	Pre-treatment	5.04±1.517	5±1.537	0.022	-1.006
		Post-treatment	2.38±1.465	3.50±1.508		
	Number of categories completed	Pre-treatment	2.17±1.049	2.25±1.138	0.043	…..
		Post-treatment	4.04±1.233	3.50±1		
N-back test	Time	Pre-treatment	804.92±115.374	757.92±97.375	0.002	-1.430
		Post-treatment	566±84.520	690.58±89.705		
	Result	Pre-treatment	18±3.191	16.25±3.415	0.002	1.476
		Post-treatment	25.17±2.887	20±4.023		
Tower of London test	Trial time	Pre-treatment	806.33±402.708	836.83±510.122	0.931	…..
		Post-treatment	645.25±300.254	730.08±403.226		
	Total Score	Pre-treatment	24.08±3.777	22.58±2.275	0.002	1.417
		Post-treatment	29.08±2.151	25.92±2.314		
Stroop test	accuracy	Pre-treatment	21.83±7.673	20.33±7.203	0.310	…...
		Posttreatment	14.92±5.452	17.50±5.568		
	Speed	Pretreatment	111.08±38.635	95.08±35.577	0.144	0.618
		Posttreatment	104.42±47.799	77.67±35.600		

SD: Standard deviation
The effect size for the cases where the results were not statistically significant has not been reported.

in the severity of injuries between their study and the present one (15). Similarly, Rushby et al. (2020) did not find evidence supporting the effect of tDCS on working memory improvement in TBI patients, attributing the lack of significance to electrode placement on the brain (14).

The study by Kong Kang et al. (2012) showed that placing tDCS electrodes on the L-DLPFC reduced patients' response time after stimulation compared to their initial reaction. However, these differences were not significant at 3 or 24 hours post-stimulation (32). Similarly, Ulam et al. (2015) found that 10 sessions of anodal tDCS (AtDCS) could effectively modulate cortical excitability in TBI patients (33). Sacco et al (2016) also showed that tDCS combined with cognitive exercises was effective in rehabilitating attention in TBI patients and confirmed the efficacy of combined therapy in improving attention in these patients (19).

The trial time and the total score in the Tower of London test indicated that tDCS combined with routine occupational therapy had a greater effect on improving planning performance compared to occupational therapy alone. We hypothesized that tDCS induces changes in the brain's neural network, thereby enhancing planning performance. This rationale aligns with previous studies suggesting that AtDCS may facilitate brain plasticity in subacute and chronic stages (34, 35). Also, the literature suggests that tDCS plays an efficient role in improving planning performance (36) and problem-solving performance (37) in healthy individuals.

One limitation of this study is the lack of a follow-up phase to assess the durability of the results. Future studies should include a follow-up phase to evaluate the longevity of the intervention's effects. Moreover, this study focused on individuals aged 18 to 40 years. Given that age negatively impacts the degree of disability in TBI patients, with those aged >40 years experiencing more severe impairments despite less acute injuries than younger groups (16-26 years old) (38), the findings of this intervention may not be generalizable to individuals over 40 years. Since this was a pilot study with a low number of dropouts at the post-intervention assessment (2 in 1 group and 3 in the other group), the intention-to-treat analysis was not conducted.

This study aimed not only to appraise the acceptability of the intervention and viability of the study protocol, but also to identify the most appropriate outcome measure. Our findings suggest that tDCS at an intensity of 2 mA and a density of 0.057 mA/cm² for 20 minutes, with the anode over the left DLPFC and the cathode over the right DLPFC, appears to be a safe and potentially beneficial approach for TBI patients. However, further research is necessary to confirm these results. Furthermore, future studies are encouraged to examine both the short-term and long-term effects of these interventions on functional outcomes and patients' quality of life. Moreover, future studies are advised to compare the impact of tDCS combined with cognitive rehabilitation to the effects of tDCS alone.

Conclusion

According to the findings of this study, co-employing tDCS with daily occupational therapy can significantly enhance various aspects of cognitive function. However, further studies are required to confirm these results.

Authors' Contributions

All authors contributed equally to the conception and design of the study, data collection and analysis, interpretation of the results, and drafting of the manuscript. Each author approved the final version of the manuscript for submission.

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Ethical Considerations

The study received approval from the Ethics Committee of Shahid Beheshti University of Medical Sciences (IR.SBMU.RETECH.REC.1399.1089), and all participants provided written informed consent to participate in the study.

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Conflict of Interests

The authors declare that they have no competing interests.

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