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The Effectiveness of Transcranial Direct Current Stimulation on Improving Cognitive Functions and Cognitive Emotion Regulation Strategies in Cannabis Users: A Randomized Sham-Controlled Trial

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Original Article

Abstract

Introduction: The present study aimed to investigate the effectiveness of transcranial direct current stimulation (tDCS) in improving cognitive functions and cognitive emotion regulation strategies among cannabis users. Given the cognitive and emotional impairments associated with cannabis use, and the role of these deficits in the persistence of use and the challenges of cessation, evaluating the efficacy of non-invasive brain stimulation interventions in addressing these impairments is of considerable clinical and scientific importance.

Materials and Methods: A randomized sham-controlled trial design was employed in this study. During the withdrawal phase, 30 male cannabis users were randomly assigned to either the experimental or sham group. Participants in the intervention group received 10 daily sessions of anodal stimulation over the left dorsolateral prefrontal cortex (DLPFC) and cathodal stimulation over the right DLPFC. In contrast, the sham group received only sham stimulation. Cognitive functions and cognitive emotion regulation strategies were assessed in both groups before and after the intervention.

Results: The findings indicated that tDCS significantly improved cognitive flexibility, attention, and working memory in the experimental group. In addition, the use of adaptive cognitive emotion regulation strategies increased, while maladaptive strategies decreased following the intervention.

Conclusion: The findings of the present study indicate that transcranial direct current stimulation (tDCS), by modulating dorsolateral prefrontal cortex (DLPFC) activity, not only improves cognitive functions but also enhances adaptive cognitive emotion regulation strategies in cannabis users. Therefore, tDCS may serve as an effective adjunctive intervention to support cannabis cessation and improve treatment adherence.

Keywords: Transcranial direct current stimulation; Dorsolateral prefrontal cortex; Cannabis; Cognitive functions; Cognitive emotion regulation

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Introduction

Cannabis use in the United States has increased substantially in recent years, driven by factors such as the legalization of recreational cannabis in 24 states and the COVID-19 pandemic (1, 2). Currently, more than half of American adults report lifetime cannabis use, and over 55 million individuals—approximately 15% of the population—are identified as current users (3). In 2022, daily cannabis use surpassed daily alcohol consumption (4). This trend is expected to persist and may be further intensified by the commercialization of cannabis, like alcohol and tobacco. Although cannabis is frequently used for self-medication purposes, including mood regulation, sleep disturbances, and pain management, evidence supporting its therapeutic efficacy remains limited (5).

The rising prevalence of cannabis use is associated with considerable health risks; however, systematic monitoring of its misuse-related harms has historically received insufficient attention (6). Recently, increasing and concerning evidence has highlighted the potential for both acute and persistent cognitive effects of cannabis use, particularly impairments in working memory among young adults, as well as an elevated risk of psychosis-spectrum disorders (7). These risks are especially concerning in individuals using cannabis for medical symptom management, as such use may paradoxically exacerbate cognitive deficits and mental health problems rather than alleviate them.

In addition, heavy cannabis use places approximately 30% of users at risk of developing cannabis use disorder (CUD) (8). Compulsive use, characterized by withdrawal symptoms and functional impairment, significantly disrupts daily functioning (9, 10). Although evidence supports the efficacy of interventions such as cognitive-behavioral therapy, motivational enhancement therapy, and contingency management in CUD treatment (11), access to these interventions remains limited for many individuals, particularly those facing geographical, transportation, or healthcare accessibility barriers (12).

Targeting the neural circuits underlying addiction has emerged as a promising therapeutic approach for substance use disorders. Within this framework, the dorsolateral prefrontal cortex (DLPFC) is considered a central hub in the three-stage model of addiction (13, 14). In this model, addiction cycles are maintained by negative affective states such as distress, which reinforce compulsive drug-taking behaviors and hinder recovery processes (15, 16). The DLPFC plays a critical role in executive control and emotion regulation and has therefore become a primary target for neuromodulation techniques, including transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS) (17). These non-invasive brain stimulation techniques modulate cortical excitability and help restore dysregulated prefrontal–limbic circuits, thereby facilitating abstinence and recovery (18). Among these approaches, tDCS offers additional advantages, including safety, low cost, non-invasiveness, and feasibility for home-based application (19).

However, the therapeutic efficacy of tDCS depends on cumulative dosing delivered through repeated sessions. Evidence suggests that protocols involving 10 or more stimulation sessions yield greater and more sustained clinical and cognitive benefits compared to single-session or low-dose interventions in addiction-related outcomes (20). Nevertheless, logistical constraints in clinical trials often limit participants' ability to complete the full treatment dose, resulting in subtherapeutic exposure. In this context, structured home-based repeated stimulation protocols may provide a safe and feasible strategy to ensure adequate dosing while maintaining treatment accessibility for individuals unable to attend in-person sessions (21).

In tDCS, a weak constant direct current is delivered to the scalp via at least two electrodes (saline-soaked or dry). Key parameters include current intensity (typically 0.5–2 mA), stimulation duration (up to 40 minutes per session), number of sessions, and electrode size, placement, and montage configuration. Low-intensity current modulates neuronal membrane potentials and cortical excitability in targeted brain regions. Under the anodal electrode, membrane depolarization increases cortical excitability, whereas under the cathodal electrode, membrane hyperpolarization decreases excitability (22, 23). Evidence indicates that tDCS has been widely investigated not only for chronic pain, major depressive disorder, and Parkinson's disease, but also for substance use disorders, including alcohol, tobacco, methamphetamine, and cannabis (24).

Individuals with substance use disorders commonly exhibit cognitive impairments, including deficits in memory, attention, executive functions, and language, which significantly affect daily functioning and quality of life (25). Chronic substance use, associated with both physical and psychological dependence, alters brain structure and function and contributes to progressive cognitive decline (26). Substances such as alcohol, opioids, cocaine, and cannabis have been shown to reduce prefrontal cortex activity, particularly within the dorsolateral prefrontal cortex (DLPFC), resulting in impairments in memory, attention, and executive control (27). Cognitive

dysfunction not only complicates abstinence and recovery but also increases the risk of relapse (28).

Although pharmacological (29) and psychotherapeutic interventions have demonstrated efficacy in addressing cognitive dysfunction in substance use disorders, relapse rates remain high (40-60%), and medication-related adverse effects further limit their clinical utility (30). Moreover, the long-term effectiveness and generalizability of psychotherapeutic approaches such as cognitive-behavioral therapy and motivational interviewing remain uncertain, as these interventions are resource-intensive and depend heavily on patient engagement and access to trained clinicians (31).

Evidence indicates that individuals with substance use disorders often exhibit high relapse rates during the abstinence phase, largely because of insufficient motivation to seek treatment and maintain treatment adherence (32). One of the key cognitive correlates and determinants of substance use and treatment-seeking behavior is cognitive emotion regulation (33). Although transcranial direct current stimulation (tDCS) has demonstrated therapeutic benefits across various forms of substance use disorders, most previous studies have primarily focused on craving reduction and cognitive dysfunction (34). Researchers have suggested that one of the major components of behavioral self-regulation impaired by substance use disorders is emotion regulation (35). Within the context of substance use disorders, effective emotion regulation reduces craving, whereas reliance on maladaptive emotion regulation strategies predicts poorer treatment outcomes (36). Cognitive emotion regulation, which encompasses cognitive processes involved in regulating emotional processing, facilitates adaptive coping responses in high-risk situations (37). Conversely, maladaptive emotion regulation contributes to a cycle of dysregulation by impairing cognitive functioning, thereby increasing vulnerability to craving and relapse. In substance use disorders, cognition and emotion are closely interconnected through prefrontal–limbic neural circuits (31).

Overall, interest in the application of transcranial direct current stimulation (tDCS) for the treatment of substance use disorders has increased considerably in recent years (25). Although a substantial body of research has examined the effects of tDCS on cognitive dysfunction and craving in individuals with substance use disorders, its effects on motivation for change, treatment readiness, cognitive–emotional control, and emotion regulation remain largely unexplored. Therefore, the present study investigated the effects of excitatory and inhibitory modulation of the dorsolateral prefrontal cortex (DLPFC) using tDCS on cognitive functions and cognitive emotion regulation strategies in individuals diagnosed with cannabis use disorder. Accordingly, this study is among the few that have evaluated the efficacy of a 10-session tDCS protocol in this population. It is expected to provide important implications for addiction medicine regarding the therapeutic potential of extended-course tDCS interventions.

Materials and Methods

This study employed a randomized sham-controlled design. It was conducted as a single-masked experimental trial in which the investigators were aware of the study protocol, whereas the participants were blinded to their treatment allocation. Participants were recruited from among outpatients with cannabis use disorder attending the Iran Psychiatric Hospital, a tertiary psychiatric teaching hospital in District 21 of Tehran, Iran. Eligible individuals had been diagnosed with cannabis use disorder by a board-certified psychiatrist and were in the early abstinence phase following cannabis cessation. After providing written informed consent, eligible participants were invited to participate in the study.

A total of 30 participants who met the inclusion criteria were enrolled and assigned identification numbers from 1 to 30. Participants were then randomly allocated to either the tDCS intervention group or the sham group using concealed simple randomization. Allocation was performed by drawing participant identification numbers from sealed envelopes; the first participant selected was assigned to the tDCS group, the second to the sham group, and so on until all participants had been assigned.

The mean (SD) age of participants was 29.31 (3.61) years in the tDCS group and 30.45 (3.78) years in the sham group, with ages ranging from 23 to 35 years in both groups. Inclusion criteria were: (1) cannabis use for at least 12 months; (2) a diagnosis of cannabis use disorder confirmed by a board-certified psychiatrist; (3) no concurrent use of other illicit substances; and (4) provision of written informed consent. Exclusion criteria included withdrawal from the tDCS sessions or unwillingness to complete the study assessments at the pre-intervention, post-intervention, or follow-up evaluations. No participants were excluded during the screening process.

The required sample size was determined using Cohen's sample size table for a mixed factorial design. Assuming a significance level of 0.05, an effect size of 0.25, and a statistical power of 0.80, a total sample of 30 participants was considered sufficient for the study (29).

Demographic characteristics of male participants in the active tDCS and sham groups are presented in Table 1.

Table 1. Demographic Characteristics of the Participants

Variable	Sham	tDCS
Sample size	15	15
Age, mean (SD)	30.45 (3.65)	29.31 (3.61)
Marital status		
Single	6	5
Married	5	5
Divorced	4	5
Education		
Below diploma level	6	5
Above diploma level	9	10

SD: Standard deviation; tDCS: transcranial direct current stimulation

Measures and Instruments

Wisconsin Card Sorting Test (WCST): The Wisconsin Card Sorting Test (WCST) is a widely used neuropsychological instrument for assessing cognitive flexibility and executive functioning (38). It is extensively applied in both experimental and clinical settings to evaluate prefrontal cortex dysfunction (39, 40). In the present study, the 64-card computerized version of the WCST was administered.

The test consists of 64 response cards that vary across three stimulus dimensions: color, shape, and number. Participants are required to infer the correct sorting principle based on examiner feedback ("correct" or "incorrect"), while the underlying rule (color, shape, or number) is not disclosed. After 10 consecutive correct responses, the sorting rule is changed without informing the participant. The task continues until all four categories are completed or all cards are exhausted (41). In the present study, consistent with prior research, a maximum of 35 trials per rule was allowed.

Outcome measures included perseverative errors (reflecting deficits in cognitive set-shifting and concept formation) and non-perseverative errors (reflecting inefficiency in maintaining task rules) (41). Test–retest reliability over a two-week interval has been reported as 0.71 (42).

Stroop Color–Word Test: The Stroop Color–Word Test (1935) was used to assess selective attention and inhibitory control (43). The task included 48 congruent and 48 incongruent stimuli. Participants were instructed to inhibit automatic reading responses and identify the ink color of each stimulus.

In Iranian adaptations, congruent, incongruent, and neutral conditions are typically distinguished, and the task has been widely validated in experimental research (44). Reported test–retest reliability is 0.71 (45), with values exceeding 0.80 in other Iranian studies (46).

Wechsler Working Memory Test: Working memory was assessed using subtests of the Wechsler Adult Intelligence Scale (WAIS), including Digit Span, Letter–Number Sequencing, and related indices (47, 48). In this study, a computerized version of the Wechsler Working Memory Software was used to evaluate both verbal and visuospatial working memory (49).

Test–retest reliability for the computerized version has been reported to range from 0.82 to 0.85 (44, 45).

Selective and Divided Attention Test: Selective and divided attention were assessed using a computerized test developed by the Sina Institute for Cognitive Science. According to prior validation studies, test–retest reliability coefficients were 0.86 for selective attention and 0.93 for divided attention (49). Convergent validity has been supported through significant correlations with Stroop interference performance (50).

Cognitive Emotion Regulation Questionnaire (CERQ–Short Form): The original version of the Cognitive Emotion Regulation Questionnaire (CERQ) (51) consists of 36 items assessing nine cognitive emotion regulation strategies: self-blame, other-blame, catastrophizing, rumination, acceptance, positive reappraisal, putting into perspective, positive refocusing, and refocus on planning. Responses are rated on a 5-point Likert scale ranging from 1 (never) to 5 (always).

In the study by Hosseinabadi and Shokri (52), which aimed to develop and evaluate the psychometric properties of the Persian short form of the CERQ among Iranian university students, the original 36-item version was initially administered. Following the recommendations of Garnefski and Kraaij (53) and based on the "Cronbach's alpha if item deleted" criterion, 18 items were retained to construct the short form. In that study, Cronbach's alpha coefficients for the short-form subscales of self-blame, acceptance, rumination, positive refocusing, refocus on planning, positive reappraisal, putting into perspective, catastrophizing, and other-blame were 0.55, 0.64, 0.62, 0.71, 0.73, 0.75, 0.67, 0.63, and 0.74, respectively.

tDCS Device: Transcranial Direct Current Stimulation (tDCS): tDCS was administered using the NEUROSTIM2 device (Medina Teb Co., Iran), which provides two independently controlled stimulation channels capable of delivering both transcranial direct current stimulation (tDCS) and

transcranial alternating current stimulation (tACS). The stimulation intensity was adjustable from 0.1 to 2.0 mA, and the device also included a built-in sham stimulation mode. Circular sponge electrodes (2.5 cm in diameter), soaked in 0.9% saline solution, were positioned over the predetermined scalp locations. Saline-soaked sponge electrodes were used to improve electrical conductivity and minimize skin heating during stimulation. The electrodes were secured in place using an elastic headband. Electrical current was delivered transcranially via electrodes on the scalp, while the investigators fully controlled stimulation intensity and duration.

Procedure

Following written informed consent and a detailed explanation of the study objectives and procedures, participants were randomly assigned to either the active tDCS or sham stimulation group. The intervention consisted of 10 stimulation sessions administered over 5 consecutive days, with two 20-minute sessions per day separated by a 20-minute rest interval. At baseline (pre-intervention), all participants completed the assessment battery, including computerized cognitive function tests and the Cognitive Emotion Regulation Questionnaire (CERQ).

For active stimulation, circular saline-soaked sponge electrodes were positioned according to the international 10–20 EEG system, with the anode placed over the left dorsolateral prefrontal cortex (F3) and the cathode over the right dorsolateral prefrontal cortex (F4). Stimulation was delivered at 2 mA in accordance with established tDCS protocols. Following each stimulation session, participants were asked to report any adverse effects using a standardized side-effect questionnaire.

Participants in the sham group underwent an identical electrode placement procedure. To maintain blinding, sham stimulation consisted of a 30-second ramp-up period followed by a 30-second ramp-down period, after which the current was automatically discontinued. At the same time, the electrodes remained in place for the remainder of the session. This sham protocol has been validated in previous studies as an effective method for maintaining participant blinding.

Immediately after completion of the tenth stimulation session (Day 5), all participants completed the post-intervention assessment battery. A follow-up assessment was conducted one month after the final stimulation session using the same outcome measures.

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Islamic Azad University (Approval No. IR.IAU.TNB.REC.1403.245), and the trial was prospectively registered with the Iranian Registry of Clinical Trials (IRCT No. IRCT20260628069988N1). Written informed consent was obtained from all participants prior to enrollment. Participants were assured of the confidentiality of their data and informed of their right to withdraw from the study at any time without penalty. Statistical analyses were performed on participants who completed all study assessments (complete-case analysis). Because of the single-masked design, all cognitive assessments were administered by the same investigator to ensure procedural consistency.

Results

Table 2 presents descriptive statistics, including means and standard deviations, for the study variables across the three groups and three measurement time points (pre-test, post-test, and follow-up).

In this section, to examine the effects of the between-subjects factor (group) and the within-subjects factor (time) on the collected measures of cognitive flexibility, attention, memory, and adaptive and maladaptive cognitive emotion regulation strategies, a simple mixed factorial ANOVA was employed. Prior to conducting this statistical analysis, several assumptions were tested and confirmed, including: Box's M test for the homogeneity of covariance matrices; Mauchly's test of sphericity to assess the equality of variances of the differences (i.e., homogeneity of covariances between pairs of within-subject levels); Levene's test for homogeneity of error variances; and the Kolmogorov–Smirnov test for normality of the distribution of scores across variables. In addition, Box's M test, conducted to examine the homogeneity of covariance matrices of the dependent variables across levels of the between-subjects factor (group), indicated that the covariance matrices were equal across groups.

The mixed-design analysis of variance (mixed ANOVA) revealed significant main effects of Time on categorization ($F(2, 56) = 13.91$, $p < .05$, $\eta p^2 = .63$), perseverative errors ($F(2, 56) = 10.46$, $p < .05$, $\eta p^2 = .27$), Stroop reaction time ($F(2, 56) = 33.27$, $p < .05$, $\eta p^2 = .54$), Stroop interference score ($F(2, 56) = 25.39$, $p < .05$, $\eta p^2 = .48$), selective attention ($F(2, 56) = 9.89$, $p < .05$, $\eta p^2 = .26$), divided attention ($F(2, 56) = 8.41$, $p < .05$, $\eta p^2 = .23$), visual memory ($F(2, 56) = 9.88$, $p < .05$, $\eta p^2 = .26$), auditory memory ($F(2, 56) = 16.53$, $p < .05$, $\eta p^2 = .37$), adaptive cognitive emotion regulation ($F(2, 56) = 37.13$, $p < .05$, $\eta p^2 = .57$), and maladaptive cognitive emotion regulation ($F(2, 56) = 48.71$, $p < .05$, $\eta p^2 = .64$).

Table 2. Descriptive Statistics of Study Variables Across Groups and Time Points

Variable	Subscale	Time Point	tDCS: Mean	tDCS: SD	Sham: Mean	Sham: SD
Cognitive Flexibility	Levels	Pre test	3.40	1.30	3.20	1.32
		Post test	5.73	1.09	3.40	1.40
		Follow-up	5.40	1.12	3.33	1.35
	Perseveration error	Pre test	4.27	1.83	4.40	1.64
		Post test	3.07	1.44	4.53	1.68
		Follow-up	2.88	1.13	4.50	1.73
Stroop	Reaction Time	Pre test	1127.20	114.69	1131.40	81.65
		Post test	1098.87	106.14	1122.80	80.02
		Follow-up	1099.53	106.05	1122.20	79.14
	Interference-score	Pre test	5.60	1.59	5.53	1.92
		Post test	3.80	1.52	5.33	1.88
		Follow-up	3.93	1.44	5.47	1.99
Attention	Selective attention	Pre test	126.01	9.30	126.07	8.85
		Post test	131.47	9.13	124.47	8.24
		Follow-up	132.73	9.53	123.80	7.24
	Divided Attention	Pre test	71.53	11.43	70.73	10.32
		Post test	77.53	10.13	70.07	10.56
		Follow-up	78.27	10.12	69.60	9.16
Working Memory	Visual	Pre test	4.47	1.13	4.40	1.19
		Post test	5.60	1.55	4.20	1.15
		Follow-up	5.27	1.33	4.40	1.24
	Auditory	Pre test	5.20	1.37	4.93	1.03
		Post test	6.20	1.57	4.87	1.46
		Follow-up	6.27	1.22	4.80	1.15
Emotion Regulation Strategies	Adaptive	Pre test	20.33	4.37	20.53	4.49
		Post test	23.07	1.15	20.67	4.39
		Follow-up	23.67	4.01	20.60	4.81
	Maladaptive	Pre test	21.07	4.35	20.73	4.01
		Post test	18.47	4.67	21.01	3.96
		Follow-up	17.80	4.55	21.13	3.74

Significant Time × Group interaction effects were also observed for categorization ($F(2, 56) = 34.91$, $p < .05$, $\eta p^2 = .55$), perseverative errors ($F(2, 56) = 15.67$, $p < .05$, $\eta p^2 = .36$), Stroop reaction time ($F(2, 56) = 8.94$, $p < .05$, $\eta p^2 = .24$), Stroop interference score ($F(2, 56) = 18.36$, $p < .05$, $\eta p^2 = .40$), selective attention ($F(2, 56) = 22.68$, $p < .05$, $\eta p^2 = .45$), divided attention ($F(2, 56) = 12.54$, $p < .05$, $\eta p^2 = .31$), visual memory ($F(2, 56) = 37.74$, $p < .05$, $\eta p^2 = .57$), auditory memory ($F(2, 56) = 29.75$, $p < .05$, $\eta p^2 = .52$), adaptive cognitive emotion regulation ($F(2, 56) = 33.08$, $p < .05$, $\eta p^2 = .54$), and maladaptive cognitive emotion regulation ($F(2, 56) = 77.89$, $p < .05$, $\eta p^2 = .74$).

Furthermore, significant main effects of Group were found for categorization ($F(1, 28) = 12.67$, $p < .05$, $\eta p^2 = .31$), perseverative errors ($F(1, 28) = 3.95$, $p < .05$, $\eta p^2 = .13$), Stroop reaction time ($F(1, 28) = 3.90$, $p < .05$, $\eta p^2 = .12$), Stroop interference score ($F(1, 28) = 4.09$, $p < .05$, $\eta p^2 = .13$), selective attention ($F(1, 28) = 3.89$, $p < .05$, $\eta p^2 = .12$), divided attention ($F(1, 28) = 5.05$, $p < .05$, $\eta p^2 = .15$), visual memory ($F(1, 28) = 3.90$, $p < .05$, $\eta p^2 = .12$), auditory memory ($F(1, 28) = 4.01$, $p < .05$, $\eta p^2 = .13$), adaptive cognitive emotion regulation ($F(1, 28) = 3.98$, $p < .05$, $\eta p^2 = .13$), and maladaptive cognitive emotion regulation ($F(1, 28) = 3.90$, $p < .05$, $\eta p^2 = .12$).

Subsequently, Bonferroni post hoc tests were conducted to examine pairwise comparisons within the within-subjects factor (time).

The results indicated that all pairwise comparisons between pre-test and post-test, as well as pre-test and follow-up, were statistically significant across all cognitive performance measures and cognitive emotion regulation strategies. However, no statistically significant differences were found between post-test and follow-up scores (Table 3).

Discussion

This study aimed to determine the effectiveness of transcranial direct current stimulation (tDCS) in improving cognitive functions and cognitive emotion-regulation strategies among cannabis users. In other words, using a mixed factorial analysis of variance design, the effectiveness of tDCS stimulation was compared with sham stimulation over the dorsolateral prefrontal cortex (DLPFC) across domains such as cognitive functioning and adaptive/maladaptive cognitive emotion regulation strategies.

Table 3. Bonferroni Post Hoc Pairwise Comparisons of Mean Scores

Variable	Comparison	Mean Difference	Standard Error	Significance	Confidence Interval 95%	
					Lower bound	Upper bound
Levels of Cognitive Flexibility	Pre-test/Post-test	-1.27	0.13	0.001	-1.59	-0.94
	Pre-test/Follow-up	-1.07	0.15	0.001	-1.46	-0.68
	Post-test/Follow-up	0.20	0.14	0.49	-0.55	0.15
Perseveration Errors	Pre-test/Post-test	0.55	0.13	0.001	0.16	0.91
	Pre-test/Follow-up	0.63	0.16	0.001	0.16	1.11
	Post-test/Follow-up	-0.12	0.10	0.95	-0.36	0.16
(Stroop) Reaction Time	Pre-test/Post-test	-18.47	3.12	0.001	10.50	26.43
	Pre-test/Follow-up	-1.43	3.20	0.001	10.28	26.59
	Post-test/Follow-up	-0.03	0.65	0.99	-1.63	1.69
(Stroop) Interference-score	Pre-test/Post-test	1	0.13	0.001	0.66	1.34
	Pre-test/Follow-up	0.87	0.18	0.001	0.40	1.33
	Post-test/Follow-up	0.13	0.12	0.98	-0.21	0.48
Selective Attention	Pre-test/Post-test	-0.43	0.10	0.002	-0.69	-0.18
	Pre-test/Follow-up	-0.37	0.08	0.01	-0.57	-0.16
	Post-test/Follow-up	0.07	0.12	0.99	-0.39	0.26
Divided Attention	Pre-test/Post-test	-0.47	0.14	0.001	-0.83	-0.11
	Pre-test/Follow-up	-0.45	0.10	0.001	-0.73	-0.21
	Post-test/Follow-up	0.02	0.14	0.99	-0.37	0.37
Visual Working Memory	Pre-test/Post-test	-1.93	0.44	0.001	-3.04	-0.82
	Pre-test/Follow-up	-2.23	0.67	0.001	-3.94	-0.53
	Post-test/Follow-up	-0.30	0.50	0.99	-0.99	1.59
Auditory Working Memory	Pre-test/Post-test	-2.67	0.49	0.001	-3.91	-1.43
	Pre-test/Follow-up	-2.80	0.69	0.001	-4.55	-1.06
	Post-test/Follow-up	-1.13	0.44	0.99	-1.27	1.01
Adaptive Emotion Regulation	Pre-test/Post-test	-1.43	0.22	0.001	-1.99	-0.87
	Pre-test/Follow-up	-1.70	0.25	0.001	-2.35	-1.05
	Post-test/Follow-up	-0.27	0.15	0.25	0.11	0.65
Maladaptive Emotion Regulation	Pre-test/Post-test	1.17	0.18	0.001	0.71	1.62
	Pre-test/Follow-up	1.43	0.18	0.001	0.98	1.99
	Post-test/Follow-up	-0.27	0.19	0.20	-0.03	0.50

The results showed that, among cannabis users, the tDCS group differed significantly from the sham-stimulation group in terms of improvements in cognitive functions and adaptive emotion-regulation strategies, as well as reductions in maladaptive emotion-regulation strategies. Accordingly, the findings provided empirical support for the statistical significance of the effects of tDCS on cognitive functions and adaptive/maladaptive emotion-regulation strategies among cannabis users. In this regard, the results indicated that improvements across multiple indicators of cognitive functioning and adaptive cognitive emotion-regulation strategies persisted and remained stable at the follow-up assessment, approximately one month after the application of tDCS.

Cannabis is the most commonly used illicit substance worldwide (6). Scientifically known as *Cannabis sativa*, it belongs to the Cannabaceae family and is commonly referred to as marijuana or hemp. In many regions of the world, cannabis has been used for centuries as a medicinal plant with a rich historical background (1, 2). Scientific studies have shown that cannabis may have beneficial effects, including inhibiting tumor growth and reducing nausea. In addition, it affects behavioral characteristics such as impulsivity, adaptability, and heat sensitivity. Cannabis may also modulate mood, appetite, and sexual activity. However, the presence of cannabinoid compounds, particularly delta-9-tetrahydrocannabinol (THC), produces rewarding effects associated with pleasurable experiences and may potentially lead to addiction. THC, the primary psychoactive compound in cannabis, interacts with specific receptors in the brain known as cannabinoid receptors. This interaction produces feelings of euphoria, relaxation, and temporary relief.

Nevertheless, THC may also have adverse effects on cognitive functions, including memory, learning, attention, concentration, and motor coordination (4). According to the 2018 World Drug Report, more than 269 million people worldwide had used various forms

of cannabis, including marijuana, hashish, cannabis resin, and cannabis oil. Cannabis is recognized as the most widely used illicit substance in the world (7). In 2017, the number of cannabis users was estimated at 238 million, compared with 183 million in 2015 (5). The main symptoms of cannabis withdrawal include anxiety, irritability, depressed mood, restlessness, sleep disturbances, gastrointestinal symptoms, and decreased appetite, most of which begin during the first week of withdrawal (8).

Transcranial direct current stimulation is a noninvasive neuromodulation technique that involves applying a weak direct current to cortical regions. This technique aims to facilitate or inhibit neural excitability in targeted areas (19). During the past decade, tDCS has emerged as a safe and relatively well-tolerated noninvasive technique for modulating cortical excitability. It provides a noninvasive and cost-effective approach with minimal adverse effects. The technique involves applying a direct electrical current to the brain, thereby altering the resting membrane potential of cortical neurons and subsequently changing cortical excitability (17). In this method, a weak electrical current of approximately 0.2–0.5 mA is used to stimulate targeted brain regions and achieve therapeutic effects (20). By attaching two electrodes—an anode and a cathode—to specific locations on the scalp, a weak direct electrical current is applied, thereby influencing the underlying neurons. Anodal stimulation generally increases cortical excitability, whereas cathodal stimulation generally decreases it (15, 16).

The important role of the DLPFC in cognitive functions, particularly executive functions such as working memory, goal-directed behavior, attention, memory, and inhibitory control, has attracted considerable research attention. Targeting this brain region may not only improve participants' cognitive functioning but may also contribute to the suppression of maladaptive behaviors (17). Consistent with the findings of the present study, studies by Zhang et al. (29, 30) have shown that electrical stimulation of the DLPFC has positive effects on working memory, information processing, attention and concentration, emotional processing, and problem-solving.

The findings in this area suggest that, when explaining the effectiveness of tDCS stimulation of the DLPFC, it should be acknowledged that tDCS modulates neuronal excitability and the membrane potential of superficial neurons by depolarizing or hyperpolarizing them. This modulation subsequently leads to increases or decreases in neuronal firing. Neuroimaging studies have also shown that the DLPFC plays a neural role not only in craving and substance misuse but also in mood and cognitive disorders (18). In addition, clinical observations have emphasized the role of the DLPFC in attentional control and in regulating processes associated with substance craving and decision-making (24). The results further suggest that neuromodulation of the DLPFC through tDCS may contribute to the reduction of addictive symptoms while modifying addictive behaviors. Accordingly, through increased activation of the DLPFC, tDCS may simultaneously enhance self-control and reduce craving by influencing dopamine activity and impaired executive functioning (21). Other studies have shown that tDCS stimulation affecting the DLPFC improves executive functioning and processing speed and thereby contributes to cognitive improvement in cannabis users. Studies have also indicated that the use of tDCS during abstinence may further reduce the adverse effects of cannabis withdrawal (23, 25).

The prefrontal cortex is a key cortical region involved in cognitive control (55). It plays a role in craving for cigarettes and alcohol, as well as in substance-use disorders involving opioids, cocaine, cannabis, and methamphetamine. Moreover, the prefrontal cortex influences cognitive emotion regulation and, when activated, may affect subcortical limbic regions involved in reward and punishment processing (36, 56, 57). In this context, transcranial direct current stimulation is a safe, accessible, and noninvasive brain-stimulation intervention that can be used to study and modify brain functions and to treat related disorders by altering activation of the frontal cortex (35).

The results of the present study further showed that, compared with the sham group, the tDCS group demonstrated improvements in adaptive emotion-regulation strategies and reductions in maladaptive cognitive emotion-regulation strategies. Therefore, it is necessary to discuss the underlying neurophysiological mechanisms through which the safe and noninvasive brain-stimulation intervention tDCS may affect emotion-regulation strategies in cannabis users (31).

One possible mechanism underlying the effects of prefrontal tDCS in cannabis users involves the role of the DLPFC in reducing negative emotions and increasing positive emotions, which may encourage treatment-seeking behavior. The DLPFC plays an important role in the cognitive control of emotional processing. The left DLPFC is associated primarily with positive emotions, whereas the right DLPFC is associated primarily with negative emotions. The left

DLPFC uses top-down processes to modulate emotion-processing regions, enabling individuals to manage their emotional responses and maintain equilibrium when confronted with emotional challenges (31). In contrast, inhibitory stimulation of the right DLPFC enhances attention to negative stimuli and reduces cognitive control.

Consistent with the available evidence, in substance-use disorders, altered prefrontal dopaminergic activation is associated with impaired decision-making and reward evaluation. In addition, the relationship between the neuroplastic effects of tDCS and dopaminergic modulation provides another explanatory pathway for understanding the effects of tDCS on emotion-regulation strategies in cannabis users (33). Furthermore, the effects of anodal DLPFC stimulation on the regulation of positive and negative emotions have been observed in substance-use disorders and other affective disorders. This finding, together with the contribution of the DLPFC to improved executive control in healthy and clinical populations—including individuals with substance-use disorders—may help explain, in a safe manner, the rationale for increasing individuals' motivation to seek treatment and improving their adaptive cognitive emotion-regulation strategies.

The findings in this section indicated that, following changes in participants' coping priorities and their greater tendency to use adaptive methods of dealing with stressful experiences, as well as their improved control over the adverse effects of cannabis withdrawal, tDCS stimulation was associated with noticeable changes in substance-use behavior and the activation of self-care motivation. In other words, by increasing adaptive emotion-regulation strategies and thereby reducing craving, targeting the DLPFC may be considered an effective intervention for motivating and encouraging users to seek and adhere to treatment (37).

Limitations

This study had several limitations. First, participants were selected exclusively from among male cannabis users; therefore, caution should be exercised when generalizing the findings to female cannabis users. Second, although cognitive outcomes and cognitive emotion-regulation strategies were assessed, physiological and behavioral indicators of the intervention's effectiveness were not examined. Third, participants were recruited from individuals undergoing withdrawal in an educational or treatment center; consequently, generalizing the findings to users who have not yet sought treatment is limited.

Fourth, the follow-up period was limited to one month, which prevented an assessment of the long-term persistence of the intervention effects. Fifth, the small sample size, single-center design, the possibility of practice effects on the cognitive tests, and the restriction of the sample to male cannabis users represent additional limitations. These limitations should be considered when interpreting and applying the findings of this study. Finally, in the Discussion section, the researchers attempted to emphasize, based on empirical evidence, the possible role of physiological mechanisms. Therefore, a realistic and highly cautious interpretation is necessary, particularly because the inferences regarding the physiological mechanisms remain hypothetical.

Recommendations

In light of the study limitations, future studies should examine the effectiveness of transcranial direct current stimulation in female cannabis users so that the generalizability of the findings to both sexes can be assessed. In addition, the use of physiological and behavioral indicators alongside cognitive and emotional assessments may provide more comprehensive evidence of this intervention's effectiveness.

Future research should also include cannabis users who have not yet sought treatment, allowing the role of this intervention in increasing motivation to seek treatment and adhere to treatment to be examined more accurately. Furthermore, studies with longer follow-up periods may provide more precise information about the durability of the therapeutic effects of transcranial direct current stimulation.

It is also recommended that future studies assess clinically important outcomes in addition to cognitive outcomes, such as craving, relapse rate, abstinence duration, and quality of life. Finally, future research should evaluate these clinical indicators alongside cognitive outcomes to provide a more comprehensive assessment of tDCS effects.

Conclusion

Overall, the findings of this study showed that repeated transcranial direct current stimulation (tDCS) of the dorsolateral prefrontal cortex during the cannabis-abstinence phase was associated with improved cognitive functioning and facilitated the use of adaptive cognitive emotion-regulation strategies. In addition to helping control the adverse effects of withdrawal, this intervention may increase individuals' motivation to seek treatment and adhere to it.

Therefore, upregulation and downregulation of DLPFC activity may not only improve cognitive functioning in cannabis users but may also play an

important role in increasing treatment-seeking motivation and treatment retention by facilitating the use of adaptive strategies when coping with withdrawal-related distress.

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Conflict of Interest

The authors did not have a conflict of interest.

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