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Synergistic efficacy of cognitive-behavioral therapy and transcranial direct current Stimulation targeting the dorsolateral prefrontal cortex on baseline craving and cue-induced craving in methamphetamine dependence

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Abstract

Introduction: Methamphetamine (crystal meth) is a highly addictive stimulant with devastating effects on the human mind and body. This study aimed to investigate the synergistic efficacy of combined Cognitive-Behavioral Therapy (CBT) and transcranial Direct Current Stimulation (tDCS) targeting the DorsoLateral PreFrontal Cortex (DLPFC) in reducing baseline and cue-induced craving among methamphetamine users.

Materials and Methods: The statistical population included all patients with clinical symptoms of methamphetamine use disorder who attended addiction treatment centers in Mashhad, Iran, between 2022-2024. Using convenience sampling, 40 clinically diagnosed methamphetamine users were selected and randomly assigned to four groups (CBT, tDCS, CBT+ tDCS, and control). Data were analyzed using descriptive statistics, independent t-test, ANOVA, and ANCOVA.

Results: Findings demonstrated that the interventions reduced both baseline and cue-induced craving in methamphetamine users. The most pronounced effects were observed in the group receiving both therapies simultaneously (CBT+ tDCS).

Conclusion: The results indicate combined cognitive-behavioral therapy and transcranial direct current stimulation reduces craving among methamphetamine users.

Keywords: Cognitive-behavioral therapy, Craving, Methamphetamine abuse, Transcranial direct current stimulation

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Introduction

Stimulant addiction, particularly to methamphetamine (crystal meth), is a significant global mental health challenge. This substance not only severely impacts the central nervous system but also leads to extensive cognitive, emotional, and behavioral consequences for users, complicating treatment (1). Methamphetamine dependence is associated with heightened craving, impaired cognitive functions, and symptoms of depression and anxiety—all of which are predictors of relapse in individuals with substance use disorders (SUD) (2). Traditional treatments, including pharmacotherapy and conventional psychotherapy, have shown limited success in alleviating these symptoms and preventing relapse (3). Thus, exploring innovative, non-invasive, and combined therapeutic approaches is imperative. One well-established method for treating substance dependence is Cognitive-Behavioral Therapy (CBT), which helps patients modify maladaptive thought patterns and enhance coping skills (4). Research indicates that CBT plays a critical role in reducing craving and improving emotional regulation, though its standalone effects remain modest and require reinforcement (5). In recent years, transcranial direct current stimulation (tDCS) has emerged as a non-invasive intervention to modulate cortical neuron activity. Studies suggest that stimulating the dorsolateral prefrontal cortex (DLPFC) can reduce both baseline and cue-induced craving in substance-dependent individuals (6). Given that CBT and tDCS each have limited but complementary effects, combining these methods may offer a more effective therapeutic strategy (7). Some studies report synergistic effects, enhancing treatment efficacy (8). Craving—a key driver of continued use and relapse—manifests in two forms: baseline craving (a persistent internal urge to use) and cue-induced craving (triggered by environmental stimuli like paraphernalia or contexts) (9,10). Craving is a primary predictor of relapse in methamphetamine users, necessitating interventions that substantially mitigate it (11). Various treatments for methamphetamine dependence have been explored, with CBT and tDCS being among the most prominent (12). CBT targets dysfunctional thought patterns, identifies craving triggers, and teaches coping skills to manage impulsive behaviors (13). Conversely, tDCS, as a non-invasive brain stimulation technique, modulates neuronal activity in prefrontal regions, enhancing cognitive inhibition and impulse control (14).

Evidence suggests that combining these methods may yield synergistic effects. For instance, tDCS-induced enhancement of cognitive control, when paired with CBT behavioral strategies, could lead to greater reductions in craving and relapse (15).

A critical mechanism underlying this synergy is the improvement of cognitive flexibility and attentional bias toward drug-related cues (16). While CBT helps individuals recognize and manage triggers, tDCS strengthens neural circuits supporting self-control (17).

Other psychological interventions, such as the matrix model and mindfulness, combined with tDCS, have also shown promise in reducing craving (18). This supports the hypothesis that CBT + tDCS may outperform either method alone in addressing baseline and cue-induced craving in methamphetamine dependence (19).

Such combined approaches may not only reduce craving but also improve executive functions, cognitive inhibition, and emotion regulation (20). The present study investigates the synergistic efficacy of CBT and tDCS in craving among methamphetamine users.

Materials and Methods

The statistical population consisted of the dependents on methamphetamine (crystal meth) who attended addiction treatment centers in Mashhad, Iran, between 2022-2024. We selected the cases using a convenience method.

The study sample included 40 patients exhibiting clinical symptoms of methamphetamine use disorder (crystal meth), selected through convenience sampling and randomly assigned to three experimental groups and one control group. Inclusion criteria included having the substance use disorder diagnosis according to DSM-5, aged 18-45, having at least a six-month history of regular substance use, willingness to participate, and not receiving other pharmacological or psychotherapeutic treatments. Exclusion criteria included having history of severe psychiatric disorders such as schizophrenia or bipolar disorder, having neurological diseases or brain damage, taking medications that affect cognitive function and mood, and not cooperating in treatment sessions. After coordinating with eligible patients, 10 individuals were randomly assigned to the first experimental group (CBT), 10 to the second experimental group (tDCS), 10 to the third experimental group (CBT + tDCS), and 10 to the control group. The control group was placed on a waiting list and received no intervention.

Research instruments

A) tDCS Side Effects Questionnaire: This questionnaire assesses the common side effects of tDCS (21).

B) Amphetamine Craving Scale (ACS): Developed by Ogai et al. (2007), this scale was used to evaluate craving levels in methamphetamine-dependent individuals. The questionnaire consists of 35 items assessing five subscales: anxiety and intention to use (8 items), emotional disturbances (8 items), compulsion to use (4 items), positive expectations and loss of control (6 items), and lack of negative expectations from substance use (4 items). Additionally, it includes a lie detector scale (5 items) to measure the individual's insight into their substance abuse problem (22).

C) Picture-Induced Craving Test (PICT): This test was designed to assess the intensity of cue-induced craving by using visual stimuli that trigger or induce craving in crystal meth addicts. It evaluates the impact of environmental cues on craving. In this test, participants were shown 10 images, including meth paraphernalia, the substance itself, people using the substance, and two neutral images. They were then asked to rate their craving intensity on a Visual Analog Scale (VAS) ranging from 0 to 100. This method is one of the most validated tools for assessing craving induced by external cues (23). In a study by Ekhtiari et al., the Cronbach’s alpha for the questionnaire was reported as 0.693 (24).

Treatment protocol

- CBT: 10 weekly 60-minute sessions, based on short-term CBT for addiction, focusing on cognitive restructuring, coping skills, and emotion regulation. Sessions covered addiction education, impulse control, cognitive restructuring, problem-solving, self-efficacy enhancement, relapse prevention, and future planning to reinforce cognitive-behavioral changes.
- tDCS: Administered in 10 weekly sessions (20 minutes each) using the neuroConn DC-Stimulator. The anode was placed over the left DLPFC (F3) and the cathode over the right DLPFC (F4), with a 2 mA current. Participants received one tDCS session per week. During stimulation, they performed cognitive exercises, deep breathing, and meditation to enhance efficacy. Post-session, the current was gradually reduced, electrodes were removed, and the skin was cleaned with saline solution.
- Control Group: Received sham tDCS (30 seconds of initial current followed by discontinuation to mimic real stimulation without active effects). Data were analyzed using SPSS version 26. First, descriptive statistics (mean and standard deviation) were calculated. Next, the Kolmogorov-Smirnov test was used to assess data normality.

To compare group means, one-way analysis of covariance (ANCOVA) was applied to control for intervention effects and examine changes in dependent variables. Levene’s test was used to check homogeneity of variance, and repeated measures analysis was conducted to evaluate the stability of intervention effects over time.

Results

Table 1 presents the demographic characteristics of the participants. Table 2 presents the descriptive statistics of the variables. The results indicated a decrease in mean values for all variables during post-test measurements compared to pre-test in all groups.

Table 1. Descriptive statistics related to demographic characteristics

Variable	Category	Frequency	Percentage (%)
Age (Year)	20-30	12	30.0
	30-40	9	22.5
	40-50	19	47.5
Gender	Male	23	57.5
	Female	17	42.5
Marital status	Single	19	47.5
	Married	21	52.5
Education	Middle school	5	12.5
	High school diploma	15	37.5
	Associate degree	11	27.5
	Bachelor’s degree	9	22.5

Table 2. The descriptive statistics of baseline craving and cue-induced craving

Variable	CBT	tDCS	CBT ± tDCS	Control
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Baseline craving				
Pre-test	174.80 ± 1.15	159.90 ± 1.87	168.80 ± 1.89	165.60 ± 1.04
Post-test	108.00 ± 15.07	78.10 ± 14.82	78.00 ± 27.32	158.40 ± 13.35
Cue-induced craving				
Pre-test	145.50 ± 5.60	149.00 ± 14.25	166.00 ± 20.62	149.00 ± 14.25
Post-test	128.80 ± 7.84	112.40 ± 5.42	126.80 ± 6.94	149.00 ± 14.25

The results of Levene's F test to assess the homogeneity of variances of research variables across groups are reported. Given this non-significant finding, it can be concluded that the variances of baseline craving and cue-induced craving are equal across groups (baseline craving: 0.21, cue-induced craving: 0.50). Table 3 presents the results of one-way ANCOVA for group differences in baseline craving.

Table 3. Results of one-way ANCOVA for group differences in baseline craving

Source	Sum of squares	df	Mean square	F	P	Effect size (η^2)
Pre-test	22.054	1	22.054	0.063	0.804	0.002
Group	42995.295	3	14331.765	40.685	0.000	0.777
			Error	12329.246	35.00	352.264

The ANCOVA results indicated that group membership had a significant effect on the craving (F= 40.685, *P*< 0.001, η^2= 0.777), demonstrating a strong treatment effect on reducing craving. Conversely, the pre-test effect was not significant (F= 0.063, *P*= 0.804, η^2= 0.002), suggesting that initial between-group differences at pre-test were negligible and the main effects resulted from the intervention. The large effect size (η^2= 0.777) indicates that most observed variance can be attributed to experimental group membership and treatment, demonstrating the substantial efficacy of combined CBT and tDCS in reducing craving.

The mean baseline craving score was -50.882 for CBT group, -80.026 for tDCS group, and -80.577 for CBT + tDCS, while the control group mean was zero (*P*< 0.001) (Table 4). Table 5 presents the results of one-way ANCOVA for group differences in cue-induced craving.

Table 4. Estimated marginal means by group

Group	B coefficient	Std. Error	t	P	Effect size (η^2)
CBT	-50.882	8.612	-5.909	0.000	0.499
tDCS	-80.026	8.465	-9.454	0.000	0.719
CBT + tDCS	-80.577	8.424	-9.566	0.000	0.723
Control	0a	-	-	-	-

Table 5. Results of one-way ANCOVA for group differences in cue-induced craving

Source	Sum of squares	df	Mean square	F	P	Effect size (η^2)
Pre-test	423.582	1	423.582	5.582	0.024	0.138
Group	7032.048	3	2344.016	30.889	0.000	0.726
			Error	2656.018	35	75.886

According to Table 5, the F-statistic for treatment adherence in the pre-test (5.582) was significant at the 0.02 level, indicating statistically significant differences between groups in cue-induced craving. The effect size of 0.138 suggests this difference is substantial and clinically significant in the population. To determine which group showed the highest adjusted mean scores for cue-induced craving in the post-test (after controlling for pre-test scores), the adjusted means are reported in Table 6.

Table 6. Estimated marginal means by group

Group	B coefficient	Std. Error	t	P	Effect size (η^2)
CBT	-19.383	3.911	-4.956	0.000	0.412
tDCS	-36.600	3.896	-9.395	0.000	0.716
CBT + tDCS	-26.170	4.243	-6.168	0.000	0.521
Control	0a	-	-	-	-

According to Table 6, the mean cue-induced craving scores were -19.383 for CBT group, -36.600 for tDCS group, and -26.170 for CBT + tDCS group, while the control group mean was zero. These differences were statistically significant (*P*< 0.001). Therefore, the experimental groups showed significantly different levels of cue-induced craving. Tdcs group demonstrated the highest beta coefficient among all groups.

Discussion

Methamphetamine (crystal meth) addiction represents one of the most complex challenges in mental health, leading to severe physical dependence (25). Conventional treatments, including pharmacotherapy and traditional psychotherapy, have shown limited efficacy in reducing craving and improving cognitive-emotional functioning in these patients (26).

This underscores the need for innovative, multimodal interventions that can effectively target various dimensions of substance use disorders (27).

The findings of this study demonstrated that the combined treatment approach was more effective than either treatment method alone. These results are consistent with previous studies that have confirmed the efficacy of CBT and tDCS individually in reducing craving and improving cognitive inhibition (5,28). One potential mechanism for craving reduction involves the enhancement of cognitive inhibition and reduction of impulsivity through tDCS stimulation of the dorsolateral prefrontal cortex. Evidence indicates that tDCS can increase neuronal activity in this region, thereby improving the ability to manage cravings and prevent impulsive behaviors (14). On the other hand, CBT, as a psychological intervention, reduces relapse probability by modifying maladaptive cognitions and teaching coping strategies (29). The combination of these two methods may yield greater efficacy than individual interventions through synergistic effects, a finding that has been confirmed in previous studies (19).

Compared to similar research, the current study produced results consistent with previous findings regarding tDCS effects on craving, while also demonstrating that simultaneous use of CBT and tDCS was more effective than either approach alone. For example, a study examining only tDCS effects found that this method could improve executive function and reduce craving, but its efficacy was not as strong as when combined with behavioral interventions (30). Additionally, these findings align with recent research on combining tDCS with other psychological treatments such as the matrix model and mindfulness (10,12). Another noteworthy finding was the particularly strong effect of the combined intervention on reducing cue-induced craving. This type of craving, which emerges in response to environmental drug cues, is typically more resistant to treatment. However, in the current study, the combined intervention achieved significant reductions in this variable. These results are consistent with studies showing that interventions based on modifying cognitive patterns and enhancing cognitive flexibility can reduce cue-induced craving (16). In this regard, research investigating the role of neuroplasticity in addiction treatment has shown that combining electrical brain stimulation with cognitive-behavioral therapy can produce more durable and profound changes in brain structure and function (18). However, the present research also has limitations. One of the significant challenges is the lack of long-term follow-up to examine the sustainability of therapeutic effects. Although the results indicated that the combined intervention was effective, it is unclear how long these effects will remain sustainable. Some studies have suggested that conducting long-term follow-ups can provide valuable information about the durability of these changes (31). Furthermore, the sample size of this study was relatively limited, and conducting research with larger samples and more diverse groups can contribute to greater generalizability of the results.

Conclusion

The findings showed that the combination of cognitive-behavioral therapy and tDCS is an effective approach for reducing craving for base and induced craving in methamphetamine abusers. This intervention can serve as a novel and non-invasive therapeutic option, contributing to the improvement of quality of life and facilitating treatment pathway. Considering the limitations of traditional treatments, utilizing such combined methods can offer more effective strategies for treating substance dependency.

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Conflict of Interest

This research has no conflict of interest.

Funding

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Ethical Considerations

To comply with medical ethics and protect patients' rights, the general framework, objectives, procedure, potential side effects of the device, participants' right to withdraw at any time, and other legal considerations were explained. This article is extracted from a Ph.D. dissertation in psychology from Islamic Azad University, Bojnourd Branch.

Code of Ethics

IRCT20230318057753N1
IR.IAU.BOJNOURD.REC.1401.024 from the Ethics Committee in Research of Islamic Azad University, Bojnourd Branch

Authors' Contributions

Morteza Modarres Gharavi conducted the writing and editing of the article, Mahdi Helmlzadeh performed the research and the data analysis, and Mehdi Ghasemi Motlagh interpreted the data.

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