# **Original Article**

# Modification of attentional bias and reduced craving from combined mindfulness+tDCS therapy in methamphetamine addiction: A randomized, sham-controlled, single-blinded clinical trial

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### Abstract

Although clinical findings support the significant effects of mindfulness and Transcranial Direct Current Stimulation (tDCS) on various disorders, especially Substance Use Disorder (SUD), their combined effect on methamphetamine addiction has not been investigated yet. This study examined the combined effect of mindfulness+tDCS therapy on Attentional Bias (AB) towards drug-related stimuli and craving in adolescents with methamphetamine addiction. The present research method is experimental. A total of 60 adolescents, with methamphetamine addiction were randomly assigned to the research groups, 20 people in each group aged between 18 and 21 (mindfulness group:12 sessions, two sessions per week), combined mindfulness + tDCS group (12 sessions mindfulness and +12 sessions tDCS), and sham group (12 sessions). The dorsolateral prefrontal cortex (DLPFC) was stimulated by DCS device with an intensity of 1.5 mA for 12 sessions of 20 minutes, and for psychological intervention the 12 sessions of 50 minutes mindfulness-based substance abuse treatment (MBSAT) was employed (2 sessions per week). AB and craving were measured before the intervention, after the 12 sessions and at one-month follow-up. Repeated measures analysis was used to analyze the data. The results showed that the combined mindfulness+tDCS therapy group was more effective in the modification of AB towards drug-related stimuli in 200 ms and 500 ms and craving. The results supported the increased effectiveness of tDCS combined with mindfulness in the modification of AB towards drug-related stimuli and craving in adolescents with methamphetamine addiction.

# Introduction

Substance use disorder (SUD) is one of the most common causes of death throughout the world (Facing Addiction in America, 2016). Drug dependence is a chronic and recurrent brain disorder incurring high costs for patients and society (Jansen et al., 2013). Adolescents with psychiatric disorders are mainly vulnerable to addictive disorders such as smoking and drug use (Mohammadi et al., 2019). Among all substances of abuse, methamphetamine is the second most commonly used illicit drug worldwide after cannabis (Paulus & Stewart, 2020). To date, no pharmacotherapies have been approved for methamphetamine use disorder. Thus, nonpharmacological interventions have emerged as alternative options (AshaRani et al., 2020).

Recent studies have tested cognitive goals to treat SUD (Robinson et al., 2017). Attentional bias (AB) has been

the focus of many researchers examining the cognitive processes of addiction (Marhe et al., 2013). AB is a phenomenon through which attention is directed to personal valuable stimuli, such as drug cues, although people try to ignore those (Fadardi & Cox, 2008). One of the most important factors that play an important role in strengthening, maintaining and relapsing various types of maladaptive (such as drug abuse) and adaptive behaviors is AB (Christiansen et al., 2015). Studies have indicated the increased AB of drug addicts under treatment and smokers who have quit, and this increase is a predictor of subsequent relapses (Robinson, & Berridge, 2008).

According to the incentive-sensitization model, having an attentional bias for methamphetamine-related cues (images) is positively correlated with an individual's past methamphetamine use behaviors (Huang et al., 2020). Therapies that target the impairment of executive functions or automatic processing changes in people with

#### **Keywords**

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tDCS
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Substance use
disorder
Adolescents

Received: 2023/01/01 Accepted: 2023/07/17 Available Online: 2023/09/05 SUD are promising (Sofuoglu et al., 2013).

The use of mindfulness approach on adolescents has been growing rapidly in recent decade and its effectiveness has been proven (Quach et al., 2016; Alizadehgoradel et al., 2019). Mindfulness has been proven efficient as a psychological intervention for both adolescents (Himelstein et al., 2012) and drug users (Bowen et al., 2011). In addition, recent studies have shown that tDCS of the frontal cortex can enhance the effects of mindfulness training and other psychological intervention by improving mood (Nikolin et al., 2019), prevention for smoking cessation (Khayyer et al., 2019) and enhance effects of cognitive bias modification (den Uyl et al., 2017). According to recent studies, the combination of mindfulness with tDCS may be more effective in reducing SUD symptoms than either alone because of a synergistic effect (Witkiewitz et al., 2019).

Recent studies have proposed the dorsolateral prefrontal cortex (DLPFC) activation therapies as a new therapeutic approach to addiction treatment (McClernon et al., 2015) and shown greater interest in the use of non-invasive brain stimulation techniques in the treatment of addiction (Coles et al., 2018; Alizadehgoradel et al., 2020). A popular method of brain stimulation is transcranial direct current stimulation (tDCS), which involves spreading a weak electrical current to modulate neural activity in the target area (Lee et al., 2019). Researchers have studied children and adolescents with psychotic disorders through tDCS. These recent studies show the safety and therapeutic potential of this method in this age group (Lee et al., 2017). With this evidence, it is assumed that the direct electrical stimulation of the DLPFC involved in cognitive control modulates the anterior cingulate cortex in drug users' brains, thereby causing changes in the processing of drug-related stimuli (Conti, & Nakamura-Palacios, 2014). New findings show that a promising method for attentional bias modification (ABM) is to stimulate the left DLPFC through non-invasive methods (Heeren et al., 2015).

Although most studies have used tDCS as an effective alternative treatment, recent studies have shown that it can enhance the effects of other treatments. (Brunoni et al., 2012). In addition, studies have shown that tDCS becomes more effective when combined with other psychological interventions (Andrews et al., 2011; Ditye et al., 2012; Koganemaru et al., 2015; Nejati et al., 2017). A new therapeutic approach called PIN-CODES was introduced by Nejati et al. (2017), which combines psychological interventions witht DCS. This study showed the effectiveness of the combined use of tDCS and psychotherapy in treating MD. The psychological intervention used in this study is the Mindfulness-Based Substance Abuse Treatment (MBSAT) specifically designed by Himelstein and Saul (2015) for adolescents with SUD.

The present study evaluated the effect of mindfulness, and combined tDCS+mindfulness therapy on improving the AB and craving of adolescents with methamphetamine addiction. Using a three- arms parallel design, we compared the impact of receiving 1) 12 sessions of active tDCS combined with mindfulness, 2) 12 sessions of mindfulness, and 3) 12 sessions of sham tDCS on AB and craving. It was assumed that tDCS+mindfulness will improve AB and craving more effectively than mindfulness alone or sham. It is also expected that tDCS+mindfulness will have more longterm effects in comparison with other interventions. This was the first study conducted to improve the AB and craving of adolescents with methamphetamine addiction.

#### Method

#### **Participants**

Sixty adolescent boys aged 18 to 21 diagnosed with methamphetamine use disorder according to the DSM-5 criteria entered the study (Mean age= 19.47, SD= 1.14). Adolescents were recruited from the Azadi Rehabilitation Center for Addiction in Ardabil. Iran. The inclusion criteria were: (1) Methamphetamine use disorder diagnosis based on a clinical interview by an experienced psychiatrist according to the DSM-5 criteria (2) age between 18 and 21 years, (3) no use of any drug except nicotine, as confirmed by a negative urinalysis, and (4) no use of psychoactive drugs during the study. Exclusion criteria for other Axis I disorders such as schizophrenia, bipolar disorder, and any axis II (personality and developmental) disorders and having no previous history of neuro-psychological diseases, brain injury, head trauma, brain surgery, epilepsy, seizures, or metal brain implants. Before participation, we had all their consent and we told them that they were free to withdraw from the study at any time. In this study, the ethical principles contained in the latest edition of the Declaration of Helsinki have been observed and it has been approved by the Ethics Committee of Shahid Beheshti University of Tehran with ID (IR.SBU.ICBS.97/1036).

Among the 60 participants, twelve withdrew before completing the study. Thus, a total number of 48 participants completed the study.

Demographic information of the participants is shown in Table 1 and flowchart of study inclusion in Fig. 1.

 Table 1. Demographic data

	MBSAT	MBSAT+tDCS	Sham	p-value*
Sample size ( <i>n</i> )	15	17	16	
Age – Mean (SD)	19.46 (1.12)	19.52 (1.23)	19.43 (1.15)	0.995
Sex – Male (female)	15 (0)	17 (0)	16 (0)	
Marital Status – Single (married)	11 (4)	12 (5)	13 (3)	0.861
Length of methamphetamine use- mean (SD)	3.13 (1.06)	2.88 (0.99)	2.87 (0.89)	0.812

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Age of onset of substance use – mean	(SD)	15.26 (2.15)	15.88 (1.61)	15.00 (2.12)	0.541
Substance use by family members- Ye	es (No)	6 (9)	11 (6)	9 (7)	0.556
Education	under the diploma	9	8	11	0.633
	diploma	6	9	5	0.055
	All men with substance disorders in addiction c:	abuse			
	( <i>n</i> =602)				
	,××				
	Assessed 138 Adolescents	(18-21			
	age) with Substance U	Jse	0200000		1
			Did not meet	inclusion	
	·	'	criteria ( $n = 3$ ) Refused to p	38); articipate	1
	v		(n = 23):	articipate	1
	70 Adolescents with	1	Other reason	( <i>n</i> = 7)	l.
	Methamphetamine Use Di	sorders			1
					-
	<u>-</u>	'			
	to participate $(n - 6)$	nsent			
	to participate $(n = 0)$				
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Allocated to sham tDCS	Allocated to MBSAT	Allocate	ed to MBSAT+		
( <i>n</i> = 20)	( <i>n</i> = 20)	tDCS	(n = 20)		
· · · · · · · · · · · · · · · · · · ·			·	'	
Completed the dot probe task	Completed the dot probe	Completed	the dot probe task		
as pre-test ( $n = 20$ )	task as pre-test $(n = 20)$	as pre-test (	n = 20)		
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Discontinued sham tDCS	Discontinued MBSAT	Discontinue	MBSAT+tDC		
(n=2)	(n=2)	Discontinue	(n = 1)		
it	1	.;	1		
Completed the dot probe task as post-test $(n - 18)$	task as post-test $(n - 18)$	Completed	the dot probe task $(n - 19)$	Σ I I	
			(II = 1))	_1	
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Lost to follow-up ( <i>n</i> =2)	Lost to follow-up ( <i>n</i> =3)	Lost to fe	ollow-up ( <i>n</i> =2)		
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Completed the dot probe task	Completed the dot probe	Completed	the dot probe task	ς Ι	
as follow-up $(n = 16)$	task as follow-up ( $n = 15$ )	as follow-u	p (n = 17)		

Figure. 1. Flowchart of study inclusion

# Instrument

### Dot-Probe Task:

To assess AB, we used a modified version of the original dot-probe task developed by MacLeod et al. (1986) in which drug-related images were used instead of words. The participants were placed at a distance of 50 cm from the computer. The task consisted of 42 trials. Each trial began with a fixation cross (+), which appeared in the center of the computer screen to focus

the participant's attention and disappears after 500 ms. Then, a pair of stimuli (one drug-related image and one neutral image) was displayed horizontally, one on the right side and the other on the left side of the screen (randomly). The two images remained on the screen for either 200 ms or 500 ms depending on the stimulus presentation duration condition. Immediately following the image disappearance, a probe (\*) randomly appeared in the location previously occupied by one of them. Participants were told to indicate whether the probe was on the left or on the right side by pressing one of the two arrow keys (left or right) on the computer keyboard as quickly and accurately as possible upon seeing the sign (\*). On drug-congruent trial, the probe appeared in the location of the drug-related stimulus, whereas on drug-incongruent trial, the probe appeared in the location of the neutral stimulus. The participants' response times were measured. Two stimulus presentation duration conditions were used in this task, a duration of 200 ms and a duration of 500 ms, and 20 pairs of stimuli were used in the two conditions. (See figure 2).



#### Desires for Drug Questionnaire (DDQ):

This craving questionnaire contains 14 items, the original version of which is designed to measure the craving for heroin (Franken, Hendriks, & van den Brink, 2002). In this study, we used a version adapted for methamphetamine addiction. Its measurement scale is distance. Evaluation of the factorial structure of this questionnaire has shown that it has good convergent validity, internal consistency and retest reliability. On the other hand, Cronbach's alpha of this questionnaire was reported as 0.85, which indicates an acceptable score (Franken et al., 2002). The validity and reliability of this scale has been confirmed on Iranian samples (Poor-seyed Mosaie et al., 2013).

#### tDCS protocol:

This tDCS was delivered by a stimulator (ActivaDose II Iontophoresis Delivery Unit, USA). Direct electrical currents of 1.5 mA intensity it was applied through a pair of 35 cm2 saline-soaked sponge electrodes (7 x 5 cm) for 15 minutes with a 15-second up ramp and a 15-second down ramp. Recent studies have used and confirmed the intensity and duration of the stimulus used in this study on children and adolescents (Nejati et al., 2017; Lee et al., 2019). Electrodes were placed over

the scalp according to the protocol of the international system 10-20 in order to fix the EEG electrode. The anode was positioned over F3 (to target the left DLPFC) and the cathode over F4 (to target the right DLPFC). Electrode position in this study is based on other studies in this field (Shahbabaie et al., 2018). For sham tDCS, the same electrode montage was used as for the active tDCS, but no current was delivered during the 20-min period. tDCS-related safety was assessed by screening for the presence of 6 potential tDCS-related side effects.

#### **Psychological intervention:**

Mindfulness-based substance abuse treatment (MBSAT) protocol was used as a psychological intervention (Himelstein and Saul, 2015). MBSAT is a group-based educational program for adolescents that combines a variety of strategies including mindfulness, selfawareness, and substance abuse treatment for substanceusing adolescents. It is also an evidence-based program that provides the educational framework during weekly sessions for professionals to take action. Each session includes clear instructions, examples, discussion points, drama scenarios to illustrate different types of resistance, and optional lectures. (Himelstein and Saul, 2015). In Table 2, you can see the content of the meetings in structured program. а

MDGAT	The context of each costion				
NIDSAT	The content of each session				
Session					
Cassian 1	Introduction to the Program: first session: 1) Informal greetings. 2) Introducing the program. 3) Group agreements. 4) Definition				
Session 1	or initiatiuness. 5) Meditation: initiatiuness of deep breating, 6) Group survey: 1 oung people's feating interests. 7) Homework				
	Mindfulness of Drugs and Their Health Effects: 1) Focused meditation (2) Informed entry (3) Drug classification activity (4) Lethal				
Session 2	medicinal compounds. 5) Meditation: mindfulness of deep breathing. 6) Homework and the end.				
	Reacting vs. Responding: 1) Role playing: mental strength vs. physical strength. 2) Debate: Reaction vs Response. 3) STIC (Stop,				
Session 3	Breathe, Imagine Future Consequences, Choose) Thinking. 4) STIC plays a role. 5) Meditation: mindfulness of self. 6) Informed				
	entry. 7) Homework and the end.				
Session 4	Mindfulness of Delusion: 1) Focused meditation. 2) Poetry: "The perfect top. 3) Informed entry. 4) Discussion: advantages and				
Session .	disadvantages of using materials. 5) Personal pros and cons of substance use. 6) Meditation: body scan. 7) Homework and the end.				
Session 5	<i>Emotional Awareness</i> : 1) Focused meditation: Bodyscan. 2) Emotional categories. 3) Emotional expression and gender norms. 4)				
	Stand if. 5) Deep disclosure. 6) Game: Concentration. 7) Homework and the end.				
Session 6 The Brain and Drugs: 1) Focused meditation led by youth. 2) Informed entry. 3) Presentation of brain I. 4) meditation Presenting the Brain II: Substance Use, Trauma, and the Mastermind. 6) Meditation: body scan. 7) Homework and the end.					
	eraving in utug use. 5) Non-moving scale of worksheet. The roots of eraving. () from work and the end. Mindfulase of Tripages () Found and instance of the provide a strategy of the strategy				
Session 8	influences 5) Antigers, 1) Focused mediation led by your. 2) minimum endy, 5) Minimum ess of stimut. 4) Three levels of influence 5) Mediation: attention to awareness 6) Homework and the end				
	The Family System and Derges: 1) Focused mediation led by youth 2) Thinking of my children 3) The effect of drug use on family				
Session 9	relationships. 4) Addiction and intergenerational trauma. 5) Meditation: Compassion for family members. 6) Informed entry, 7)				
Session 2	Homework and the end.				
Session	Mindfulness of the Peer System: 1) Role play with peer pressure. 2) Debate: friend's vs accomplices. 3) Informed review with				
10	notification. 4) Conscious communication 5) Role of peer pressure games developed by youth. 6) Meditation: Compassion for				
10	friends and accomplices. 7) Homework and the end.				
Session	Mindfulness of the External Environment: 1) Focus on youth leadership. 2) Informed entry. 3) Mindfulness of the external				
11	environment. 4) Conversion of penetration systems. 5) Meditation: Compassion meditation towards society. 6) Homework and the				
	end.				
Session	Closing Ceremony: 1) Meditation: The ultimate practice. 2) Informed entry. 3) focus group 4) group appreciations. 5) Pizza				
12	party/food party. 6) Certificate of completion. 7) Conclusion and closing ceremony.				
Himelstein and Saul (2015)					

# TABLE 2. Structure and guideline of each MBSAT session

#### Procedure

The study was a three-arm randomized, single blind, controlled trial. Participants (N=60) were randomly assigned to three groups: a group receiving 12 sessions of MBSAT (MBSAT, N=20), a group receiving 12 sessions of MBSAT combined with active tDCS (MBSAT+ tDCS, N=20) and a group receiving 12 sessions of sham tDCS (sham tDCS, N=20). Sessions (MBSAT, MBSAT+ tDCS or sham tDCS) during 6 consecutive weeks (two sessions per week) and the interval between sessions was 72 hours. MBSAT sessions lasted 45-50 min and tDCS sessions lasted 20 min. In the MBSAT+tDCS condition, tDCS was delivered right before the MBSAT session. A trained tDCS therapist administered tDCS sessions and two professional licensed psychotherapists managed MBSAT. All participants completed the dot-probe tasks to assess AB and the DDQ to assess craving three times (pre-test, post-test, follow-up). In the sham condition participants will be offered the opportunity to receive (active tDCS) at end of the study sessions. The present study was also registered in the Iranian Clinical Trials Registry. ID: IRCT20181013041327N1.

# Statistical analysis

To analyze the collected data, SPSS version 24 was used (IBM, SPSS, Inc., Chicago, IL). Using the Shapiro-Wilk and Levin tests, the normality of the data and the homogeneity of the variance were examined, and these assumptions were estimated. To measure the effectiveness of each treatment and their combined effects on the modification of attentional bias, mixed factorial analysis of variance (ANOVA) was used, with time (pre-test, post-test, follow-up) as the within-subject factor and group (MBSAT, MBSAT+active tDCS, sham tDCS) as the between-subject factor. Post hoc analysis was done using the Bonferroni correction. The correlation between changes in attentional bias performance and changes in craving was calculated via Pearson's correlation.

### Results

At baseline, all groups were similar in terms of age, sex, marital status, education, length of methamphetamine use, age of onset of substance use and the presence of substance use in the family members (all p < 0.05, see Table 1). Participants in the MBSAT+active tDCS and sham tDCS groups well-tolerated the stimulation. Moreover, the occurrence of side effects did not differ between stimulation conditions (all p < 0.05, See Table 3). Descriptive statistics results including means and standard deviations of attentional bias and craving are presented in Table 4 and Fig. 3.

tDCS session	Itching sensation	<b>Burning sensation</b>	Pain	Tingling	Fatigue	Trouble concentrating
tDCS + MBSAT	9	10	6	12	5	2
Sham tDCS	6	5	3	6	2	1
$\chi^2$ (active vs sham)	3.39	3.20	1.57	4.43	1.36	0.01
Р	0.75	0.78	0.95	0.61	0.85	1.00

Table 3. Reported tDCS side effects during stimulation

Table 4. Means and SDs attentional bias and craving before, after and 1 month following intervention

Task	Outcome measures	Time	Sham tDCS	MBSAT	tDCS+ MBSAT
			M (SD)	M (SD)	M (SD)
Dot-Probe	Attentional higg in	Pre-intervention	882.89 (190.39)	865.79 (212.47)	883.87 (181.47)
	Attentional bias in	Post-intervention	847.87 (116.34)	657.08 (92.57)	634.99 (119.16)
	presentation time of 500 (ins)	Follow-up	851.03 (152.74)	750.51 (173.39)	677.95 (135.78)
	Attentional bias in presentation time of 200 (ms)	Pre-intervention	667.88 (96.05)	678.48 (180.27)	679.19 (100.07)
		Post-intervention	719.12 (136.38)	553.63 (69.43)	512.02 (51.23)
		Follow-up	648.48 (114.28)	558.24 (97.92)	531.41 (66.94)
Craving		Pre-intervention	49.56 (6.89)	49.46 (5.51)	50.29 (13.99)
	DDQ	Post-intervention	47.25 (6.13)	36.53 (7.41)	31.47 (8.88)
		Follow-up	47.37 (5.73)	37.00 (7.98)	33.82 (10.06)





tDCS+ MBSAT

Figure. 3. Effects of interventions (MBSAT, tDCS+ MBSAT, Sham) on attentional bias and craving of participants in three-time points (pre-intervention, post-intervention, and follow-up)

Table 5. Results of mixed-model ANOVAs for the effects of group (Sham, MBSAT, tDCS+ MBSAT) and time (pre-intervention, post-intervention, follow-up) on attentional bias and craving

Task	Outcome Measures	Source	df	f	Р	eta2	Pairwise comparisons (Bonferroni)
Dot-Probe Attentional bia with presentation time of 500 (ms Attentional bia with presentation time of 200 (ms	Attentional bias	Time	2,90	18.78	0.001	0.29	tDCS+MBSAT > Sham
	with presentation	Group	2,45	2.34	0.044	0.12	(p < 0.006); MBSAT > Sham
	time of 500 (ms)	Time*group	4,90	3.34	0.013	0.12	(p < 0.041)
	Attentional bias	Time	2,90	18.18	0.001	0.28	tDCS +MBSAT > Sham
	with presentation	Group	2,45	5.29	0.009	0.19	(p < 0.002); MBSAT > Sham
	time of 200 (ms)	Time*group	4,90	7.88	0.001	0.25	(p < 0.025)
Craving	DDQ	Time	2,90	89.40	0.001	0.66	tDCS +MBSAT > Sham
		Group	2,45	17.44	0.001	0.43	(p < 0.001); MBSAT > Sham
		Time*group	4.90	16.15	0.001	0.41	(p < 0.014)

Effects on attentional bias: To analyze the effectiveness of each intervention (i.e., MBSAT, active tDCS+ MBSAT, sham tDCS) in improving the attentional bias, two mixed factorial ANOVAs were used, one for presentation duration 500ms and one for 200ms. Results showed a significant interaction effect of group\*time on both presentation time 200 ms ( $F(_{4,90}) = 7.88$ , p < 0.001,  $\eta p 2 = 0.25$ ) and 500 ms ( $F(_{4,90}) = 3.34$ , p < 0.013,  $\eta p 2 = 0.12$ ). A significant main effect of group and time was found for both 500 ms and 200 ms (see Table 5). Between-group comparisons of attentional bias outcome measures at pre-intervention showed no significant difference. But significant between-group differences were observed at post-intervention and at follow-up between MBSAT and sham tDCS groups and between active tDCS+MBSAT group and sham tDCS group.

*Effects on craving:* Mauchly's test was used to evaluate the sphericity of the data before performing the repeated measures ANOVA. In case that the assumption of

sphericity was violated, the degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity.

The ANOVA revealed a significant group\*time interaction on craving (F(4,90) = 16.15, p < 0.001,  $\eta p2= 0.41$ ). The main effects of time and group were also significant (Table 5). The Bonferroni-corrected post hoc t-tests showed that craving after the intervention and at follow-up were significantly lower compared to the pre-intervention measurement in the active tDCS+MBSAT group and MBSAT group but not in the sham tDCS Corrected. No significant between-group differences of craving in the pre-intervention measurement, but significant between group differences in the post-intervention and follow-up measurements.

**Table 6.** Correlation between craving reduction rate after the intervention with the rates of change from pre-to-post intervention in Attentional bias of MBSAT and tDCS + MBSAT group.

	Group		Attentional bias in presentation time of 500 (ms)	Attentional bias in presentation time of 200 (ms)
Craving Pre- Post Change rate	MBSAT	Pearson coeffitient	0.425	0.476
		p-value (2-taild)	0.114	0.073
	tDCS + MBSAT	Pearson coeffitient	0.596*	0.487*
		p-value (2-taild)	0.012	0.047

Note: Significant results are highlighted in **bold** at 0.01 level (\*\*) and 0.05 level (\*)

We lastly calculated Pearson's correlations to see if changes in craving scores were correlated with changes in attentional bias. A significant correlation between craving reduction and the improvement of the attentional bias on both presentation time including 500 ms (p < 0.012) and 200 ms (p < 0.047) in the active tDCS+MBSAT group not in the MBSAT group (Table 6).

#### Discussion

The current study a randomized, clinical trial aimed to examine the effects of combination MBSAT+tDCS on attentional bias and craving in adolescents with methamphetamine addiction. Our study showed that combination therapy significantly reduced attentional bias compared to MBSAT and sham stimulation groups and that these effects were associated with significantly reduced craving. These findings are in line with recent studies, which have shown that tDCS treatment is more effective when used as an add-on therapy (Nejati et al., 2017; Andrews et al., 2011; Brunoni et al., 2014; Koganemaru et al., 2015).

This study supported the combination of MBSAT+tDCS as a new and effective therapeutic approach to improving the AB towards stimuli associated with drug use and craving in adolescents with methamphetamine addiction. To the best of our knowledge, this is the first attempt to combine psychotherapy with tDCS to improve attentional bias and craving in a randomized trial. In the present study, the greater effectiveness of tDCS when combined with other psychological interventions is supported by the greater effectiveness of the combined effects of MBSAT+tDCS. This finding is in line with other studies that confirm the incremental effect of tDCS when combined with other methods (e.g., Bajbouj et al., 2018; Park et al., 2014; Alizadehgoradel, 2021; Alizadehgoradel et al., 2021). The combination of MBSAT+tDCS can better determine the mechanism of the effectiveness of the mindfulness. Previous studies show that in the clinical subjects (Heeren et al., 2017; Shahbabaie et al., 2018) attentional biases are redused by tDCS. Since these attentional biases are also targeted by mindfulness (Garland et al., 2018), the greater reduction of craving in the MBSAT+tDCS group may be related to the direct involvement of reducing attentional bias.

The effectiveness of the separate use of each of these two therapeutic protocols accounts for the findings of the present study. Brain regions associated with AB towards addiction include prefrontal cortexes such as anterior cingulate cortex (Luijten et al., 2012), lateral prefrontal cortex (Vollstädt-Klein et al., 2012), and insular cortex (Luijten et al., 2011), and subcortical structures such as nucleus accumbens (Nestor et al., 2011) and nucleus amygdalæ (Vollstädt-Klein et al., 2012). The new approaches to addiction treatment emphasize the neural modulation of the DLPFC region. Studies have shown that stimulation of this region leads to a decrease in the craving of people with SUD (da Silva et al., 2013). Shah Babaei et al. (2018) found that stimulation of the left DLPFC region leads to a reduction of AB towards drug-related cues when compared to sham stimulation and it can be said that tDCS as a non-invasive brain stimulation technique is a promising method for the treatment of drug addiction (Ekhtiari et al., 2019). Studies have shown that mindfulness is more closely linked to attention regulation (Chiesa et al., 2011). Many studies have shown how mindfulness exercises can alter the underlying mechanisms of addictive behaviors, craving, Mindfulness exercises can raise and relapse. metacognitive awareness of automatic processes associated with drug craving and seeking and use (Garland et al., 2014). Mindfulness exercises can also keep attention away from drug-related cues and eliminate AB towards these cues (Garland et al., 2014). The main limitation of the present study was the lack of a tool to measure brain changes after the intervention, which suggests that future studies use brain imaging techniques to better describe brain changes. Despite promising implications, some limitations of this study should be considered. First, although drug consumption (and therefore relapse) were controlled throughout the experiment and follow-up measurements bv performing urine tests, we were not able to obtain such measures beyond the one month after intervention, which would be important to make assumptions about the long-term clinical efficacy of the intervention. Nevertheless, the significant correlation between craving reduction and AB holds promise and encourages future studies that primarily target treatment-related parameters.

### Conclusion

With regard to the above-mentioned points and the neural modulation of the addiction-related regions (especially the prefrontal cortex) by each of the protocols used in this study, the incremental effect of MBSAT+tDCS can be accounted for since the addition of tDCS to a psychological intervention increases its effectiveness as an add-on treatment.

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#### **Disclosure Statement**

Author declare that they have no conflicts of interest.

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