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Research Paper

The Effect of Different Transcranial Direct Current Stimulation (tDCS) Protocols on Drug Craving and Cognitive Functions in Methamphetamine Addicts

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ABSTRACT

Introduction: Drug craving is a major problem in addiction treatment. Neuroimaging research has revealed various areas for drug craving, among which two key areas are the Dorsolateral Prefrontal Cortex (DLPFC) and the cerebellum. The DLPFC is involved in different cognitive tasks, such as inhibitory control over seductive options that promise an immediate reward. The cerebellum is related to cognition and memory and activated by drug-related cues. Therefore, we decided to study the effect of Transcranial Direct Current Stimulation (tDCS) on six different protocols in reducing drug craving and increasing cognitive functions in methamphetamine addicts.

Methods: The present study is quasi-experimental, with a pre-test-post-test design and a control group. Based on a simple sampling method, 15 male methamphetamine addicts were recruited from two rehabilitation centers in Tehran City, Iran. The participants were aged 18-65 years with a minimum of 12-month history of methamphetamine dependence. The Visual Analog Scale (VAS), the go/no-go task and the n-back task were administered before and after a single session of tDCS. The tDCS was applied on six protocols: 1) the right DLPFC anodal and the left DLPFC cathodal stimulation, 2) the right DLPFC cathodal and the left DLPFC anodal stimulation, 3) the right DLPFC anodal and the right arm cathodal stimulation, 4) the left DLPFC anodal and the left arm cathodal stimulation, 5) the right cerebellar hemisphere (O2) anodal and the left cerebellar hemisphere (O1) cathodal stimulation, and 6) the right cerebellar hemisphere (O2) cathodal and the left cerebellar hemisphere (O1) anodal stimulation. The data were analyzed by covariance method using SPSS software v. 22.

Results: Study results indicated that while single-session tDCS effects on craving were not significant, it increased cognitive inhibition, especially in protocol 2: the right DLPFC cathodal and the left DLPFC anodal stimulation.

Conclusion: Single-session tDCS affects craving insignificantly, but it can increase cognitive inhibition significantly. These findings support the results of previous studies on the effects of brain stimulation on reducing drug craving in other drug-type settings.

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Highlights

- One session of Transcranial Direct Current Stimulation (tDCS) intervention is ineffective for reducing addiction craving in methamphetamine addicts.

- DCS intervention significantly increases cognitive inhibition.

- The best results with tDCS intervention in addiction recovery are use of the right DLPFC cathodal stimulation and left DLPFC anodal stimulation protocol.

Plain Language Summary

One of the primary concerns in treating addiction is to choose an effective intervention for reducing craving. tDCS is a non-invasive and safe way of reducing craving, which can be used in different ways to decrease addiction craving and treat addiction. While his study founds that one session of tDCS protocols is not effective in reducing the methamphetamine craving, They are effective for increasing cognitive inhibition, which is essential in addiction recovery and saying no to cravings. This effect on the cognitive inhibition ability has important implications for those seeking new and non-invasive addiction recoveries, especially in methamphetamine addiction.

1. Introduction

Drug craving is a major problem in addiction treatment (Skinner, & Aubin, 2010), and greater drug craving is associated with an increased risk of relapse to drug use (Sinha, Garcia, Paliwal, Kreek, & Rounsaville, 2006).

Different definitions of drug craving have complicated matters further because it can be conceptualized and addressed as the history of a stable tendency toward drug addiction as well as the experience of an intense or compelling desire (Rosenberg, H. 2009).

Recent neuroimaging research has revealed that the dorsolateral prefrontal cortex (DLPFC), among other brain areas, is crucially involved in drug craving (Hartwell, et al. 2011). The DLPFC is involved in reward, motivation, and decision-making, and its circuits provide the substrate for integrating relevant cognitive and motivational information and the inhibitory control over seductive options that promise immediate reward (Goldstein, Volkow, 2002; Bechara, 2005).

Another important area for drug craving is the cerebellum. This part is related to cognition, learning, and memory, and research has shown that drug-related cues activate the cerebellum (Moreno-Rius, & Miquel, 2017).

Transcranial Direct Current Stimulation (tDCS) as a novel method has attracted the attention of researchers. Many studies have focused on the effects of tDCS on DLPFC and reported a decline in drug craving following the application of tDCS (Boggio, et al., 2008; Fregni, Orsati, et al., 2008; Boggio et al., 2009).

Methamphetamine (crystal meth) abuse is a prevalent addiction without any established pharmacological treatments (Farhadian, Akbarfahimi, Abharian, Hosseini, & Shokri 2017), (Schottenfeld et al., 2018) tolerability, and potential efficacy of atomoxetine for treating ATS use disorder. Methods: Participants with opioid and ATS dependence (n=69, and applied methods are potentially helpful to reduce methamphetamine craving (Shahbabaie et al., 2014)we aimed to test whether tDCS of DLPFC could also alter self-reported craving in abstinent meth users while being exposed to meth cues. In this double-blinded, crossover, sham-controlled study, thirty two right-handed abstinent male meth users were recruited. We applied 20 min 'anodal' tDCS (2 mA. A serious challenge facing individuals with methamphetamine use disorder is executive dysfunction (Farhadian et al., 2017). Hence, the present study examined the effect of six tDCS protocols applied to the DLPFC and cerebellar areas on reducing drug craving and enhancing executive functions, such as cognitive inhibition and working memory.

2. Materials and Methods

Study participants

Quasi-experimental research with a pre-test-post-test design was conducted on 15 male individuals with meth-

amphetamine use disorder. They were recruited from two rehabilitation centers of Ekbatan Neshat Salamat and Aramesh and received tDCS. The participants signed a written consent form and then enrolled in the study. The participants were aged 18-65 years (Mean=37.06 years) with a minimum 12-month history of methamphetamine dependence. The participants reported methamphetamine abuse at least three times a week over six months. During the treatment process, the participants received no opioid or stimulant medication except for cigarettes. Those with a maximum of two weeks of abstinence were excluded from the study due to ethical considerations, as well as the participants with other neurological disorders, such as epilepsy or those receiving medications that affected the central nervous system.

Study instruments

In this study, the following instruments were used. The tDCS was an ActivaTek system for stimulating the skin/scalp (the USA).

Visual Analog Scale (VAS)

A Visual Analog Scale (VAS) is a commonly used technique to assess the level of craving based on a 0 to 10 scale and includes two sides: one side with numbers which indicates the craving, and the other side without numbers. The participants show their drug craving levels on the plain side, and the examiner records the numbers from the back side of this tool. Each participant is asked to show the level of his drug craving on the scale, which indicates the temptation and desire to use the drug (Rosenberg, H. 2009).

Go/No-Go task

The go/no-go task measures inhibitory control, which allegedly plays a major role in daily life. This quality requires the capacity to choose the appropriate behavior and control, inhibit, and suppress negative and disturbing behaviors, which is called response inhibition (Barkley, 1997).

N-Back task

The n-back task is considered a highly effective and widely used method to measure working memory since it includes recording and manipulating cognitive information (Chen, Mitra,& Schlaghecken,2008).

Study procedures

All participants received 6 protocols for one session with a 72-hour washout period randomly in a crossover method. The participants underwent the current intensity of 2 mA for 20 minutes in each session using the tDCS system via two anode and cathode electrodes in the form of the following protocols:

1. The first protocol was the right DLPFC anodal stimulation and the left DLPFC cathodal stimulation.

2. The second protocol was the right DLPFC cathodal stimulation and the left DLPFC anodal stimulation.

3. The third protocol was the right DLPFC anodal stimulation and the right arm cathodal stimulation.

4. The fourth protocol was the left DLPFC anodal stimulation and the left arm cathodal stimulation.

5. The fifth protocol was the right cerebellar hemisphere (O2) anodal stimulation and the left cerebellar hemisphere (O1) cathodal stimulation.

6. The sixth protocol was the right cerebellar hemisphere (O2) cathodal stimulation and the left cerebellar hemisphere (O1) anodal stimulation.

The participants were asked to describe their temptation for methamphetamine in detail (e.g., date and time). Then, they were given a checklist to report any possible side effects. All participants did a self-report scale for measuring craving VAS, go/no-go task, and the n-back task before and after each tDCS intervention.

Data analysis

We used 1-way Analysis Of Covariance (ANCOVA) for data analysis to test the study's hypotheses according to the study's quasi-experimental design (pre-test and post-test) and the study's objectives. The pretest effect was considered as a covariate. The pretest measured the drug craving with VAS. The pretest effect obtained using ANCOVA was excluded as a precaution because it typically has no learning effect but possibly unmeasurable disturbing effects as a latent variable.

3. Results

Table 1 lists the ANCOVA results for the main hypothesis. The ANCOVA pre-assumptions, including the normal data distribution, variance homogeneity, and re-

Table 1. The significant tests of between-subjects effects of drug craving and cognitive inhibition of 15 male individuals with methamphetamine use disorder

Dependent Variables	Source	df	Sig.
Craving	Corrected model	6	0.001
	Pre-VAS	1	0.001
Cognitive inhibition	Corrected model	6	0.043
	Intercept	1	0.001
	Protocol	5	0.027
Elimination error	Intercept	1	0.003
Presentation error	Intercept	1	0.001
Average response time	Intercept	1	0.001

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Table 2. The significant pairwise comparisons of cognitive inhibition and presentation error of 15 male individuals with methamphetamine use disorder

Dependent Variables	(I) Protocol	(J) Protocol	Sig.
Cognitive inhibition	R.DLPFC.A/L.DLPFC.C	R.DLPFC.C/L.DLPFC.A	0.017
	R.DLPFC.A/L.DLPFC.C	R.DLPFC.A/R.Arm.C	0.044
	R.DLPFC.C/L.DLPFC.A	R.DLPFC.A/L.DLPFC.C	0.017
	R.DLPFC.C/L.DLPFC.A	L.DLPFC/L.Arm.C	0.008
	R.DLPFC.A/R.Arm.C	R.DLPFC.A/L.DLPFC.C	0.044
	R.DLPFC.A/R.Arm.C	L.DLPFC/L.Arm.C	0.024
	L.DLPFC/L.Arm.C	R.DLPFC.C/L.DLPFC.A	0.008
	L.DLPFC/L.Arm.C	R.DLPFC.A/R.Arm.C	0.024
	L.DLPFC/L.Arm.C	R.O2.A/L.O1.C	0.036
	L.DLPFC/L.Arm.C	R.O2.C/L.O1.A	0.033
	R.O2.A/L.O1.C	L.DLPFC/L.Arm.C	0.036
	R.O2.C/L.O1.A	L.DLPFC/L.Arm.C	0.033
Presentation error	R.DLPFC.A/L.DLPFC.C	R.DLPFC.C/L.DLPFC.A	0.021
	R.DLPFC.C/L.DLPFC.A	R.DLPFC.A/L.DLPFC.C	0.021
	R.DLPFC.C/L.DLPFC.A	L.DLPFC/L.Arm.C	0.011
	L.DLPFC/L.Arm.C	R.DLPFC.C/L.DLPFC.A	0.011

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L: left; R: right; A: anodal; C: cathodal; DLPFC: dorsolateral prefrontal cortex; O1: left cerebellar hemisphere; O2: right cerebellar hemisphere.

gression slope homogeneity, were all examined and then validated via statistical tests.

According to Table 1, the pretest effect on craving was significant. When the pretest effect was eliminated, the tDCS effect was insignificant. Therefore, the first hypothesis of the study was rejected.

The effect of the pre-test (covariate) on cognitive inhibition was statistically insignificant, while the effect of tDCS was significant (Table 1). According to the results of the test, protocol 2 had the highest effect (right DLPFC cathodal stimulation and the left DLPFC anodal stimulation) (Table 2).

Neither the pretest nor the tDCS effect on the elimination error was statistically significant (Table 1).

The effect of the pretest on the presentation error was insignificant, whereas the tDCS error was significant (Table 1). The results of the test indicated that protocol 4 had the highest effect (Table 2).

Neither the pretest nor the tDCS effect on the average response time was significant (Table 1).

The test results can be summarized as follows: the tDCS effect on cognitive inhibition was significant, with the highest effect produced by protocol 2. Also, the tDCS effect on presentation error was significant, with the highest effect produced by protocol 4.

4. Discussion

The results of the present study are inconsistent with the research results obtained by Fregni, et al. (2008), Shariatirad, et al. (2016), and Da Silva, (2013), who reported the effectiveness of tDCS intervention in declining drug craving. Nevertheless, the results are consistent with those reported by Ehgartner (2012), who showed the ineffectiveness of tDCS therapeutic intervention, which can be attributed to the implementation of each protocol for only one session. So, it is recommended that participants attend more intervention sessions.

Also, the present study showed that tDCS intervention significantly enhanced the level of cognitive inhibition. This finding is consistent with the findings reported by Goldman, et al. (2011) and Wolkenstein, & Plewnia, (2013).

According to the findings, one session of six different protocols was ineffective in reducing drug craving. However, it increased cognitive inhabitation, which plays a vital role in addiction recovery.

Although more tDCS sessions are needed to reduce drug craving, even minimal use of tDCS may be helpful for the individuals to recover from addiction by increasing their cognitive inhabitation. Besides its effectiveness, tDCS is an easy-to-use, low-cost, and noninvasive technique. Therefore, in addition to recovery from addiction, it can be used as a complementary treatment for several other interventions such as psychotherapy and pharmacotherapy.

To achieve the best results with tDCS in addiction recovery, it is suggested to use the right DLPFC cathodal stimulation and left DLPFC anodal stimulation protocol.

The self-report tool for assessing craving was one of the limitations of this study because the participants might be reluctant to report their actual level of drug craving due to the fear of undergoing a longer treatment. Another limitation of our study was the sampling method. Our participants were individuals who actively sought treatment in rehabilitation centers under controlled conditions, which naturally reduced their cravings. Furthermore, the present study focused solely on male participants and consequently neglected the gender-related differences.

It is recommended to adopt an indirect objective assessment approach to obtain a more suitable measure of drug craving in future studies. Also, applying a random sampling method and testing on active male and female individuals with drug use disorder in both real and uncontrolled conditions is recommended.

5. Conclusion

Single session of different tDCS protocols Including anodal and cathodal stimulation of the right and left DLPFCs, and also different cerebellar cathodal and anodal tDCS protocols were not able to affect methamphetamine craving significantly; However, all mentioned protocols significantly increased cognitive inhibition, which is an important factor in management of craving and leads to the more ability to control methamphetamine craving and prevention of the lapses and relapse in methamphetamine addicted individuals.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed of the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information and were free to leave the study whenever they wished, and if desired, the research results would be available to them. A written consent has been obtained from the subjects. principles of the Helsinki Convention was also observed.

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Authors' contributions

Conceptualization, Supervision, Writing-review & editing: Peyman Hasani-Abharian; Conceptualization, Investigation, Writing-original draft, Data collection: Samira Rezvanian; Investigation, Writing - original draft, Data collection, and Investigation: Mohammad Amin Saraei; Data analysis and statistical methodology: Hossein Mohajeri.

Conflict of interest

The authors declared no conflict of interest.

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