

Abstract

Objective: Drug addiction is one of the most important health issues because of the difficulty of achieving sustainable treatment and high rates of relapse despite the need for detoxification and medical and psychological interventions. The aim of this study was to investigate the effect of transcranial direct current stimulation (tDCS) on the degree of substance use craving and cognitive self-control in substance abusers. **Method:** This research was indeed a pilot study with randomized assignment in experimental and control groups with pre-test and post-test. The number of 40 opiate dependent patients presenting to methadone treatment centers was selected by random sampling. After responding to questionnaires of craving and cognitive self-control, they were randomly divided into experimental (n=20) and control (n=20) groups. The measurement tools used in this study were Franklin's Craving Questionnaire (2002) and Grasmick's Cognitive Self-Control Inventory. Therapeutic sessions of tDCS included 20 minutes of F3 anodic stimulation and F4 cathodic stimulation with a flow rate of 2 mA. **Results:** The results of multivariate covariance showed that the mean scores of groups in the degree of craving and cognitive self-control were different in the post-test phase. **Conclusion:** It is hereby concluded that tDCS can reduce depression and increase cognitive self-control in substance abusers. Therefore, therapists can use this treatment as an addiction treatment method.

Keywords: transcranial direct current stimulation, drug use craving, cognitive self-control

The Effect of Transcranial Direct Current Stimulation (tDCS) on Drug Use Craving and Cognitive Self-Control in Substance Abusers

Khosravian, B., Solimani, E.

Khosravian, B.

Ph.D Student, Urmia University, Urmia, Iran

Solimani, E.

Assistant Professor, Urmia University, Urmia, Iran, E-mail : E.soleimani@urmia.ac.ir



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Introduction

Addiction is a chronic and progressive condition characterized by features such as compulsive behaviors, uncontrollable craving, drug seeking behavior, and continuous substance consumption along with detrimental social, psychological, physical, familial, and economic consequences (Dawe, Gullo, & Loxton, 2004). According to the definition of addiction proposed by the World Health Organization in 1996, the term "addiction" is defined as "any substance that enters the living body and causes a change or modification in the existing property and activity of the living organism". The Diagnostic of Statistical Manual of Mental Disorder (5th Ed.) refers to the presence of one of the cognitive, behavioral, and physiological symptoms as the important feature of substance abuse disorder that makes people continue drug use despite the significant problems associated with drug abuse. In addition, this diagnostic manual also suggests that substance abuse brings about some metabolic changes in brain circuits (especially in people with severe disorders), which may also remain after detoxification (Diagnostic and Statistical Manual of Mental Disorders, 2013).

One of the most controversial topics that we face with regard to the treatment of addictive disorders is craving, temptation, or eagerness of consumption. Tiffany, & Drobes (1991) defined craving as a term that covers a wide range of phenomena, including the expectation of reinforcing effects and a strong tendency to drug use. Hormes, & Rozin (2010) defined craving as "one's highly strong sense and urgent demand for something in such a way that it is impossible to concentrate on anything else than the subject matter". Various studies have shown that drug use craving is recognized as a central phenomenon and the main cause of continued abuse, as well as addiction relapse after therapeutic courses. Studies have also shown that the long-term use of drugs is associated with high levels of neuro-psychiatric deficiencies and there is ample evidence that there is an increased risk of cognitive impairment as a result of substance use even after addiction abstinence (Eckardt, Chen, Lin, & Yang, 2005).

One of the cognitive variables associated with substance use is cognitive self-control where a wealth of pertaining evidence has shown that individual differences in cognitive self-control can play a role in the therapeutic outcomes of substance-related disorders. Self-control is an intrapersonal conflict between logic and desire, cognition and motivation, and planning and inner action whose result is the domination of the first part of each of these pairs on the latter (Gilbert, 2005). The reinforcement of the self-control belief system increases the individual's readiness to avoid smoking craving. As a result, success in reducing the smoking rate is strengthened by the belief in self-control (Shapiro, Astin, Bishop, & Cordova, 2005). Hence, individuals with low self-control are prone to turn to drug use and get trapped in subsequent problems (Gilbert & Irons, 2005).

According to cerebral imaging, Dorso Lateral Prefrontal Cortex (DLPFC) plays an important role in craving as well as mood and cognitive disorders (Da Silva et al., 2013). Similarly, according to these studies, some changes have been detected in brain prefrontal lobe, especially in DLPFC during addictive disorders. These cerebral changes, which are associated with drug use craving, are intensified by the strong desire for drug use and disrupted inhibition control (Jansen et al., 2013).

One of the treatment methods used to regulate the DLPFC activity and, as a result, to reduce craving and cognitive disorders, is transcranial direct current stimulation (tDCS). A simple tool is used in this method, which passes a continuous and mild electric current from the head by means of the large electrodes placed on the head. The effectiveness of this method is contingent on the direction of the electric current. Anodal stimulation increases the brain activity and arousal, and cathodic stimulation, on the contrary, reduces this activity (Nitsche et al., 2003). This technique is regarded some sort of top-down processing (Moos, Vossel, Weidner, Sparing, & Fink, 2012; Wright, & Krekelberg, 2014).

The logic of using tDCS as a treatment for addiction and drug craving is that the DLPFC, which plays an important role in the top-down mechanisms of inhibition control and reward mechanisms, malfunctions in these disorders (Goldstein, & Volkow, 2002). In this regard, research findings on patients addicted to alcohol, cocaine, crack or cigarette have shown positive effects of tDCS on quality of life (Klauss, Penido Pinheiro, Merlo, de Almeida, Fregni, & Nitsche, 2014; Batista, Klauss, Fregni, Nitsche, & Nakamura-Palacios, 2015) or on drug use craving (Boggio et al., 2008; Fecteau et al., 2007; Batista et al., 2015).

Fregni, Liguori, & Fecteau (2008) investigated the influence of tDCS on the reduction of induced craving by symptoms in cigarette smokers and showed that the stimulation of the right or left prefrontal cortex by tDCS results in the decrease of craving. Trojak et al. (2016) showed that tDCS can reduce the degree of alcohol consumption in alcoholic patients. Klauss et al. (2014) indicted a lower rate of relapse during six months in patients with alcohol drinking disorder treated by tDCS. In the same way, Wietschorke, Lippold, Jacob, Polak, & Herrmann (2007) showed that frequent tDCSs can lead to long-term behavioral changes, including reduced drug use craving and reduced drug abuse. In this regard, Wietschorke, Lippold, Jacob, Polak, & Herrmann (2016) showed that tDCS on the prefrontal cortex caused a significant decrease in craving for alcohol drinking. Previous studies have observed the beneficial effects of tDCS on attention and executive functions (Fecteau et al., 2007; Gladwin, den Uyl, Fregni, & Wiers, 2012), and showed that this stimulation requires high top-down cognitive control (MacDonald, ACohen, Stenger, & Carter, 2000).

In the same vein, Matochink et al. (2003) argue that the consumption of drugs, such as cocaine affects those brain structures that play a major role in

behavioral control. In this regard, it has been proven that the repeated use of cocaine brings about metabolic and structural abnormalities in areas, such as prefrontal lobes, which play a significant role in executive control. It has also been revealed that persistent drug users show several psychosocial neurological defects in evaluation tests of executive functions (Garvana & Hester, 2004). Garvana & Hester (2004) argue that the reduced ability in impulse control in cocaine addicts is associated with the reduced activity of anterior cingulate cortex and frontal lobe, i.e. two areas that are thought to play a very important role in cognitive control. In this regard, another study showed that smoking, alcohol consumption, marijuana use, and consumption of other drugs have a negative relationship with self-control (Sussman, Dent, & Leu, 2003). Chauchard, Levin, Copersino, Heishman, & Gorelick (2013) also concluded that self-knowledge, self-control, health concerns, interpersonal relationships, and social acceptance are likely to have a pivotal role in individuals' abstinence after quitting drug use.

The reduction of craving is currently the first important phenomenon in relapse; and the psychological symptoms and signs which play a major role in individuals' desire for substance and the return to its use are the treatment challenges. Also, cognitive functions, such as attention, control, and cognitive resilience that lead the person to drug-related stimuli can be used to identify the factors associated with drug uses' orientation. Thus, in the present study, we aimed to investigate the effect of transcranial direct current stimulation on craving and cognitive self-control among substance abusers. Therefore, the main question of the present study is formulated as follows: Does tDCS have an effect on craving and cognitive self-control in opiate abusers?

Method

Population, sample, and sampling method

Regarding the nature and objectives of the research, the present study is a quasi-experimental research with pre-test and post-test, in which an experimental group and a control group existed. The statistical population of the present study contains all male abusers in Miandoab city who presented to treatment and rehabilitation centers in 2017. In this way, 40 addicts under methadone treatment being volunteer to participate in the study and enjoyed the necessary entry criteria were selected via random sampling method. The candidates who did not have the necessary criteria for entering the research were excluded and the next volunteers were replaced. This process continued until saturation. After sample selection, 20 subjects were randomly assigned to both experimental and control groups. The experimental group received tDCS. The entry criteria of the study were complete informed consent from participants, age range of 20 to 40 years, drug dependence, the fixed amount of consumed drugs (methadone, buprenorphine, etc.) until the end of the plan, and having education above primary school. Exit criteria were history of treatment with tDCS for any

disorder, presence of acute and chronic psychological and physical disorders other than addiction, addiction to non-opioids, history of seizure or head injury, having metal or prosthesis or cranial implantation, and being left handed.

Instruments

1- Craving Questionnaire: This questionnaire, developed by Franken, Hendriks, & Van den Brink, consists of 14 items (2002). The questionnaire has been extracted from Alcohol Craving Questionnaire, which is used for heroin dependents. However, due to its capability to measure overall drug use, it was later used to measure the craving of other drugs, as well. It examines the current state of craving and has three sub-scales, namely desire and intention, negative reinforcement, and perceived control over substance use. The questionnaire is scored based on a 7-point Likert scale (strongly disagree to strongly agree). Franken et al. (2002) obtained the Cronbach's alpha reliability of this scale equal to 0.85 and reported the values of 0.77, 0.80, and 0.75 for the components of desire and intention, negative reinforcement, and perceived control, respectively. Mousayi, Mousavi, & Kafi (2012) reported the total Cronbach's alpha of 0.96 for opium users, 0.95 for crack users, 0.90 for methamphetamine users, 0.94 for heroin inhalers, 0.94 for heroin sniffers, and 0.98 for heroin injectors. In this study, Cronbach's alpha was obtained equal to 0.90 for this questionnaire.

2. Cognitive Self-Control Inventory: This scale is a 23-item instrument and has been developed by Grasmick et al. (1993) to assess individuals' cognitive self-control. The items are scored on a 5-point Likert scale from strongly disagree (1) to strongly agree (5) where the low score indicates high cognitive self-control and vice versa. According to previous research, the factor analysis led to the extraction of only one factor. Respondents' scores on this scale show good correlation with other self-control cognitive measures and its coefficient was obtained equal to 0.81. This questionnaire has been translated and used by Aliverdina (2009) in Persian and has been reported for acceptable content and formal content. Also, the internal consistency of the questionnaire was reported to be 90%. Cronbach's alpha coefficient of this scale was reported 0.86 in a study (Basharpour et al., 2013). In this study, Cronbach's alpha was obtained equal to 0.88.

Procedure

For the conduct of the present study, the necessary permission was obtained from the relevant University of Medical Sciences and Welfare. Subsequently, the researcher presented to the addiction centers under the supervision of the relevant organizations for sample selection. Before the administration of the experiment, participants sat for the pre-test. Prior to answering the questionnaires, the respondents were provided with the necessary information about the research objectives, questionnaires, and how they were to respond to the questions. In the intervention phase, the tDCS device, namely Oasis pro with

tDCS made by MIELEO Company was used. Participants in the experimental group were treated with tDCS from the skull for 10 sessions (one session every other day). The anode electrode (stimulating) was placed on the dorsolateral left prefrontal cortex (F3) and the cathode electrode (inhibitor) on the dorsolateral left prefrontal cortex (F4). Then, two milliamperes of direct electric current was passed from cranium for 20 minutes. Also, since this research is of an interventional nature, the ethical standards and criteria of the American Psychological Association and the Iranian Psychological and Cognitive Organization, such as informed consent, respect for the principle of confidentiality, the priority of physical and psychological health, presentation of the results after the completion of the research, etc. were observed. After completing the intervention sessions, the research variables in the post-test were measured in both experimental and control groups. Data were then analyzed using multivariate analysis of covariance.

Results

The mean value of the experimental group's age was 32 years and that of the control group was 31 years; and the mean value of the consumption duration for the experimental group was 11 years and for the control group was 12 years. In addition, 11 participants in the experimental group and 12 ones in the control group were married. The descriptive statistics of the research variables are presented in Table 1.

Table 1: Descriptive statistics of the research variables for each group and test type

<i>Variable</i>	<i>Test type</i>	<i>Experimental group</i>		<i>Control group</i>	
		<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>
Desire and	Pretest	17.05	3.45	17.11	3.35
Intention	Posttest	14.82	2.29	17.05	3.03
Negative	Pretest	20.70	4.22	20.55	4.14
Reinforcement	Posttest	17.47	2.52	20.44	3.89
Perceived	Pretest	20.52	4.37	20.44	4.25
Control	Posttest	17.64	3.40	20.38	4.29
Total craving	Pretest	58.17	11.80	58.11	11.47
	Posttest	49.94	7.60	57.33	10.41
Cognitive self-	Pretest	65.23	12.60	71.66	14.76
control	Posttest	71.05	14.89	71.05	14.85

Multivariate covariance analysis should be used to evaluate the effectiveness of the intervention. Before running this analysis, the assumption of normal distribution of the data was measured via Shapiro Wilkes test. The results indicated that the distribution was normal. Also, to test the equality of error variances was assessed via Levene's test and the results are presented in Table 2.

Table 2: Results of Levene's test for examining the equality of error variances in the research variables

<i>Variable</i>	<i>F</i>	<i>DF</i>	<i>Sig.</i>
Desire and Intention	1.33	33	0.25
Negative Reinforcement	0.79	33	0.38
Perceived Control	3.64	33	0.06
Total craving	0.000	33	0.98
Cognitive self-control	0.91	33	0.07

As it has been shown in Table 2, the assumption of the equality of error variances has been observed in all variables ($P > 0.05$). Therefore, multivariate covariance analysis was soundly run and the results showed that there is a significant difference between the two groups the combination of variables. In other words, the intervention was effective (Effect size = 0.736, $p < 0.001$, $F = 12.820$, Wilks' lambda = 0.264). Univariate Analysis of Co-variance was used to examine patterns of difference, as shown in table 3.

Table 3: Univriate covariance of analysis examining the effectiveness of intervention in the research variables

<i>Variable</i>	<i>Sum of squares</i>	<i>Df</i>	<i>Mean Square</i>	<i>F</i>	<i>Sig.</i>	<i>Effect size</i>
Desire and Intention	38.23	1	38.23	26.01	0.0005	0.491
Negative Reinforcement	82.74	1	82.74	41.93	0.0005	0.608
Perceived Control	61.97	1	61.97	19.24	0.0005	0.416
Total craving	256.18	1	256.18	33.07	0.0005	0.551
Cognitive self-control	248.05	1	248.05	19.70	0.0005	0.422

As it has been shown in Table 3, there was a significant difference between the two experimental and control groups in the components of desire and intention, negative reinforcement, perceived control, and total craving ($P < 0.001$). In other words, tDCS has significantly reduced craving in the post-test group. There is also a significant difference between the two groups in cognitive self-control variable ($P < 0.001$) and tDCS could increase cognitive self-control in the experimental group during the post-test phase.

Discussion and Conclusion

The aim of this study was to investigate the effect of tDCS on drug use craving and cognitive self-control in substance abusers. The findings of this study showed that tDCS has a significant effect on reducing the craving and its components in substance abuse patients. These results are consistent with the research findings reported by Boggio et al. (2008), Fecteau et al. (2007), Batista et al. (2015), and Wagner et al. (2007). In order to explain these findings, it can be argued that although the action mechanism of this method is not well understood, evidence of possible changes caused by Repetitive Transcranial Magnetic Stimulation is attributed to the effect on

neurotransmitters and neuroplasticity of neural cells (Ziemann, 2004). Repetitive Transcranial Magnetic Stimulation has been introduced as a tool for the study and treatment of addictive disorders due to its effect on cortical irritability and dopaminergic neurotransmitters. Repetitive high frequency TMS (rTMS) has been proved effective in the change of dopaminergic neurotransmitters; and the effectiveness of rewarding and its reinforcing effect on underlying structures have been also proved in previous studies (Camprodon, Martinez.Regia, Alonso, Shih & Pascual-Leone, 2007). In order to account for these results, one can also refer to the reinforcement sensitivity theory, known as the nerve adaptation model, that views drug use craving due to the interconnection of neural circuit, neural substrate, and brain reward systems. Long-term changes in cortical irritability under the influence of rTMS on dopamine neurotransmitters can be an explanation for these results, and these are the underlying mechanisms of craving due to the high sensitivity of the dopamine neurotransmitter that lead to the increased reinforcing prominence of drugs. Amigdala, nucleus accumbens, some parts of dorsolateral prefrontal cortex in the memory, reward, and basal nodes are involved in the craving phenomenon. In particular, dorsolateral prefrontal cortex is an area that plays some part in rewards, motivation, and decision-making, and is a location for integrating motivational and cognitive information and creating preventive behaviors (Goldestein, & Volkow, 2002). In fact, stimulation in the dorsolateral prefrontal cortex can cause dopamine depletion in the subcortical lobe of caudate nucleus (Fitzgerald, Daskalakis, Hoy, & Farzan, 2008) and, then, it leads to the direct stimulation of target areas. Therefore, the effect of the stimulation also extends to the other hemisphere, and subcortical activity is stimulated in the neural network connected to the stimulation parts (Camprodon et al., 2007). In this regard, various studies (Franken, & Muris, 2006; O'Connor, Stewart, & Watt, 2009) show that rTMS in the right and left prefrontal cortex leads to the decreased behavioral activation system in substance abusers. Therefore, the decreased activity of the behavioral activation system can be used as a mediator for decreasing craving through rTMS in this area.

A wealth of research in this area on animals has shown that anodic stimulation increases neuronal firing and cathodic stimulation results in contrary outcomes. Therefore, it is assumed that the increase in the activity of both the right and left prefrontal lobes leads to a decrease in craving (Fregni et al., 2008). The dorsolateral prefrontal cortex is one of the most important lobes of the prefrontal cortex and is responsible for recognizing and identifying actions, assessing the future outcomes of current behavior, and predicting outcomes and social control. Therefore, a possible mechanism that can make the stimulation of this area lead to a decrease in drug craving is that this stimulation increases social control or increases the ability of participants to suppress their tendencies. Also, according to studies conducted in this area, it can be argued that the increasing or decreasing stimulation of the left or right prefrontal lobe can disrupt the

balance of activity in the two hemispheres and, therefore, the stimulation of left and right dorsolateral prefrontal cortex can reduce craving for drug use.

Also, the results of this study showed that tDCS has a significant effect on cognitive self-control of substance abusers. These results are consistent with the studies conducted by Sussman et al. (2003), Chauchard et al. (2013), and MacDonald et al. (2000). People with low self-control have difficulty predicting long-term negative outcomes. In this way, they review their addictive behavioral consequences to a lesser extent. On the contrary, people with high self-control are more likely to feel guilty and get motivated for treatment because they can easily identify the negative future of their behavior as harmful and costly (Chauchard et al., 2013). In this regard, Joyce, & Meador-Woodruff (1997) suggested that the cortical distribution of dopaminergic cortex and nerve receptors may lead to various patterns of cognitive disorders among drug abusers. For example, dopaminergic receptor D1 is present primarily in the anterior neocortex, especially in the prefrontal cortex. Although addictive substances have distinct effects on brain functions, they are common in some activities, such as the increase of the dopamine system. Given cognitive processes that are disrupted by narcotics through their impacts on hippocampus and prefrontal cortex structures, it has been shown that narcotics may increase apoptosis process (scheduled cell death) and neurogenesis inhibition (neural tissue formation) (Nyberg, 2012). The apoptosis process is associated with morphine-based tolerance, and the morphine apoptotic effect is blocked by naloxone (an opioid receptor antagonist) (Hu, Sheng, Lokensgard & Peterson, 2002). Therefore, electrical stimulation can mitigate the cognitive defects by coping with the apoptosis process and also facilitating the neurogenesis process.

This research had some limitations, such as the employment of self-reporting tools for data collection, the lack of a sham group (sham stimulation), and the conduct of the research on one gender (men). Therefore, it is suggested that future studies employ other data gathering tools, sham group, and both genders. In addition, according to the obtained results, therapists are recommended to use direct transcranial electrical stimulation as an intervention method for the treatment of addicted people. The consideration of biological and neurological infrastructures can act as a step towards improving the treatment of substance abuse and identifying precise neurological pathways by means of advanced and advanced systems, such as functional magnetic resonance imaging and CT scan in order to determine the effectiveness of this method.

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