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Brief Report: Cumulative and Booster Effects of tDCS Sessions on Drug Cravings, Lapse, and Cognitive Impairment in Methamphetamine Use Disorder: A Case Study Report

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Background and Objectives: Transcranial Direct Current Stimulation (tDCS) is a non-invasive brain stimulation method, which shows promising therapeutic effects in controlling drug cravings.

Methods: In this study, we present cumulative and booster effects of tDCS sessions on methamphetamine cravings, lapse, and cognitive impairment in a methamphetamine dependent subject.

Results: Our study shows cumulative effects of continuous anodal tDCS sessions on right dorsolateral prefrontal cortex (DLPFC) could reduce drug cravings and their consequences.

Discussion and Conclusions: Moreover, booster tDCS treatments might be helpful in controlling psychological stress and drug cravings. (Am J Addict 2016;25:264–266)

BACKGROUND

Transcranial Direct Current Stimulation (tDCS) is a non-invasive brain stimulation method, which shows promising therapeutic effects on different aspects of neuropsychiatric disorders. tDCS works on the basis of delivering a weak and continuous current to the subject's scalp via electrodes. According to the placement of the electrodes the current either reduces or enhances neuronal firing in a specific area. Studies have shown administration of tDCS is both safe and warranted; only minor adverse effects, such as mild tingling sensations, has

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been reported.² Recent studies have demonstrated tDCS may be effective in modulating drug cravings.³ In fact, reduction in cravings is an important objective of addiction treatment. Studies have shown altered functioning of dorsolateral prefrontal cortex (DLPFC) is one of the underlying factors for relapse in substance use disorder.¹ DLPFC stimulation using tDCSs may be effective in modulating cravings in alcohol,⁴ cigarette,⁵ and methamphetamine addiction.¹ Moreover, tDCS could modulate risk taking behaviors, and possibly even drugseeking process, in cocaine users.⁶ Also, repeated tDCS stimulation for 5 days appears to be more effective than a single session in reducing cue-induced cravings.⁵

CASE REPORT

A 24-year-old patient participated in this case study after reading, understanding, and signing the consent form. Study was approved by ethics committee of Tehran University of medical sciences, international campus. The patient was diagnosed with methamphetamine use disorder based on DSM-V criteria. He had no family history of psychosis or depression. He also did not have past history of any major psychiatric disorder before substance use.

This patient had a 3 year history of multidrug substance abuse (opium, heroin, alcohol, and tramadol) before enrolling in an outpatient methadone maintenance treatment (MMT) program. In this program, he received 100 mg methadone daily for 4 years. During the, same 4 year period, he also abused methamphetamine (1 g/day) and completed three intensive outpatient psychotherapy programs for substance use (Matrix

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model; 45 minutes sessions, twice weekly, 3 months each). Seven months prior to the tDCS intervention, he was diagnosed with methamphetamine induced psychotic disorder by a psychiatrist. He was suffering from auditory hallucinations, paranoid delusions, suicidal ideations, and mood instability; with a history of three occasions of committing self-injury. Clonazepam (1 mg at bed time) and olanzapine (5 mg twice a day) was prescribed for him. According to his family, he shortly stopped taking his medications and switched back to daily methamphetamine use while on MMT. Simultaneous methadone and methamphetamine use is a novel multidrug abuse regimen in Iran. 8

In order to help the patient to achieve abstinence, we administered 20 tDCS sessions (5 days a week, for 4 weeks; 2 mA, 20 min per day, anode over right DLPFC, and cathode over right arm) for him and followed him up for 6 months. During the study, we did not require the patient to stop using methadone or methamphetamine. He did not receive any other psychological or pharmacological interventions. He was also suffering from paranoia, auditory hallucination, and depressed mood. We measured his drug cravings using Desire for Drug Questionnaire (DDQ)⁹ and also we used the Leeds Dependence Questionnaire (LDQ)10 to measure the severity of substance use related symptoms at the start of the study and monthly afterwards. His cognitive performances were assessed every 2 months using Cognitive Abilities Questionnaire (CAQ)¹¹ and his depression levels were assessed using Beck Depression Inventory at baseline and every 3 months. Side effects check list was completed by the patient after each tDCS session. We tested methamphetamine in his urine by 10-agent rapid urinary tests (amphetamine, methamphetamine, cocaine, morphine, methadone, buprenorphine, tramadol, benzodiazepine, THC, TCA) three times a week for the first 3 months of the study and weekly thereafter.

After 20 sessions of tDCS, there was a considerable reduction of drug cravings. The subject reported he only had slight cravings and he was able to control them. He reported he had used methamphetamine only two times during the initial 4 weeks period (during initial 20 sessions of therapy). He used methamphetamine during booster tDCS sessions occasionally.

We decided to administer booster tDCS sessions during follow up period according to the following criteria: 1) if the patient reports three episodes of cravings since last treatment, 2) if he reports three episodes of cravings in a single day, 3) or if he reports a very difficult to control single episode of craving. He also provided twice weekly progress reports during his visits or called in whenever he experienced an uncontrollable episode of craving.

The patient received four booster tDCS treatments during 6 months follow up on days 67, 70, 72, and 88 of the study. Rapid urine tests were positive for methamphetamine three times on days 5, 25, and 67 of the study. The patient reported slight headache on the first session of tDCS treatment. Based on semi-structured interviews with the patient, he did not experience any paranoid delusions or hallucinations in the follow up period. Results are illustrated in Table 1.

DISCUSSION

We administered tDCS booster doses whenever the subject experienced uncontrolled cravings. During the follow up period, the participant experienced severe methamphetamine cravings due to emotional stress after a break up he went

TABLE 1. The scores of drug craving intensity, leeds dependence questionnaire, depression severity, and the qualification of different cognitive functions of the case during tDCS sessions and follow up period

				F	Booste	er dose	es				
	Baseline	Month 1 (30th day)	Month 2 (60th day)			72nd day			Month 4 (120th day)	Month 5 (150th day)	Month 6 (180th day)
DDQ	68	61	62					66	37	37	37
LDQ	25	11	12					9	9	9	8
BDI	38		_					19	 -		21
CAQ											
Memory	17		23					_	25		28
Inhibitory control and selective attention	7		17					_	16	_	17
Decision making	8	_	17					_	15	_	16
Planning	5		12					_	12		10
Sustain attention	7		11					_	11		9
Social cognition	15		5					_	14		3
Cognitive flexibility	4		10					_	11		13
Total number of cognitive tasks	63	_	95					_	99	_	94

DDQ, desire for drug questionnaire; LDQ, leeds dependence questionnaire; BDI, Beck's depression inventory; CAQ, cognitive abilities questionnaire.

through; but this severe methamphetamine craving was reduced gradually after administering four booster tDCS treatments. It is well known that psychological stress is associated with drug cravings and high rates of relapse,³ and that patients will engage in stressful situations during their treatment programs. In this situation, repeated therapy was probably able to control psychological stress and therefore might be able to control drug cravings.

Cognitive impairment is one of the serious consequences of methamphetamine use. ¹² Studies show tDCS is associated with cognitive improvement and might have a positive effect on executive functions. ¹³

According to the results, there were notable changes in executive functions such as memory, inhibitory control, selective attention, decision making, planning, and sustaining attention as well as cognitive flexibility. In the present case, we detected lapses on days 5 and 25 (interval of 20 days) of the treatment. The other lapse happened on day 67, an interval of 6 weeks from the last lapse. So, it seems multiple sessions of tDCS could be effective in methamphetamine use reduction and cognitive functions improvement. In fact, best behavioral effects could be attained after several sessions of tDCS treatments⁵ which could lead to reduction in drug cravings.

To the best our knowledge there are no documented studies on the minimum effective number of sessions for controlling drug cravings. Some studies are suggesting 20 Trans Magnetic Stimulation (TMS) sessions for depression and schizophrenia treatment, hence, the 20 tDCS sessions in our study. More studies are needed in order to determine the optimum number of tDCS treatment sessions for controlling drug cravings.

It is worth mentioning although stimulation of right DLPFC appears to be effective in modulating methamphetamine craving, both left and right DLPFC have significant roles in drug cravings and no significant differences have been found between left and right DLPFC stimulation using tDCS. It seems cathode stimulation of left DLPFC might in fact suppress this area and be associated with negative outcomes in relation to drug cravings. Therefore, in contrast to other studies, we used only anode stimulation of right DLPFC and connected cathode electrode to right arm.

In conclusion, we administered a 4-week protocol followed up by tDCS booster doses as a symptom-triggered therapy for additional 5 months. Symptom triggered therapy shows promising effects on controlling alcohol withdrawal symptoms¹⁶ and it could be efficacious in the treatment of drug cravings using tDCS.

CONCLUSION

Development of a symptom triggered tDCS protocol with cumulative and booster doses for controlling drug cravings seems to be a sensible approach. A randomized controlled trial in order to investigate the cumulative effects of bi-anodal bipolar tDCS stimulation of DLPFC for controlling drug cravings will provide more evidence for this method of treatment.

Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper. PBF is supported by a NHMRC Practitioner Fellowship (1078567). PBF has received equipment for research from MagVenture A/S, Medtronic Ltd, Cervel Neurotech and Brainsway Ltd and funding for research from Neuronetics and Cervel Neurotech. He is on the scientific advisory board for Bionomics Ltd.

REFERENCES

- Shahbabaie A, et al. State dependent effect of transcranial direct current stimulation (tDCS) on methamphetamine craving. Int J Neuropsychopharmacol 2014;17:1591–1598.
- Feil J, Zangen A. Brain stimulation in the study and treatment of addiction. Neurosci Biobehav Rev 2010;34:559–574.
- Jansen JM, et al. Effects of non-invasive neurostimulation on craving: A meta-analysis. Neurosci Biobehav Rev 2013;37:2472–2480.
- Boggio PS, et al. Prefrontal cortex modulation using transcranial DC stimulation reduces alcohol craving: A double-blind, sham-controlled study. *Drug Alcohol Depend* 2008;92:55–60.
- Boggio PS, et al. Cumulative priming effects of cortical stimulation on smoking cue-induced craving. Neurosci Lett 2009;463:82–86.
- Gorini A, et al. Modulation of risky choices in recently abstinent dependent cocaine users: A transcranial direct-current stimulation study. Front Hum Neurosci 2014;8:661.
- 7. Shoptaw S, et al. The Matrix model of outpatient stimulant abuse treatment: Evidence of efficacy. *J Addict Dis* 1994;13:129–141.
- Shariatirad S, Maarefvand M, Ekhtiari H. Methamphetamine use and methadone maintenance treatment: An emerging problem in the drug addiction treatment network in Iran. *Int J Drug Policy* 2013;24:e115–e116.
- Maarefvand M, Hasani-Abharian P, Ekhtiari H. Measurement of drug craving in persian speaking subjects; a review on current experiences and future perspectives. *Zahedan J Res Med Sci (ZJRMS)* 2012;14:1–7.
- Raistrick D, et al. Development of the Leeds Dependence Questionnaire (LDQ): A questionnaire to measure alcohol and opiate dependence in the context of a treatment evaluation package. *Addiction* 1994;89:563– 572
- Nejati V. Cognitive abilities questionnaire: Development and evaluation of psychometric properties. Adv Cogn Sci 2013;15:12–19.
- King G, et al. Neuropsychological deficits in adolescent methamphetamine abusers. Psychopharmacology (Berl) 2010;212:243–249.
- Minichino A, et al. Prefronto-cerebellar transcranial direct current stimulation improves visuospatial memory, executive functions, and neurological soft signs in patients with euthymic bipolar disorder. Neuropsychiatr Dis Treat 2015;11:2265–2270.
- Levkovitz Y, et al. Efficacy and safety of deep transcranial magnetic stimulation for major depression: A prospective multicenter randomized controlled trial. World Psychiatry 2015;14:64–73.
- Zhao S, et al. Randomized controlled trial of four protocols of repetitive transcranial magnetic stimulation for treating the negative symptoms of schizophrenia. Shanghai Arch Psychiatry 2014;26:15–21.
- Daeppen J, et al. Symptom-triggered vs fixed-schedule doses of benzodiazepine for alcohol withdrawal: A randomized treatment trial. *Arch Intern Med* 2002;162:1117–1121.