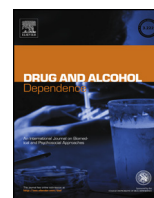




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Modulation of smoking and decision-making behaviors with transcranial direct current stimulation in tobacco smokers: A preliminary study

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ABSTRACT

Background: Most tobacco smokers who wish to quit fail to reach their goal. One important, insufficiently emphasized aspect of addiction relates to the decision-making system, often characterized by dysfunctional cognitive control and a powerful drive for reward. Recent proof-of-principle studies indicate that transcranial direct current stimulation (tDCS) over the dorsolateral prefrontal cortex (DLPFC) can transiently modulate processes involved in decision-making, and reduce substance intake and craving for various addictions. We previously proposed that this beneficial effect of stimulation for reducing addictive behaviors is in part mediated by more reflective decision-making. The goal of this study was to test whether nicotine intake and decision-making behaviors are modulated by tDCS over the DLPFC in tobacco smokers who wished to quit smoking.

Methods: Subjects received two five-day tDCS regimens (active or sham). Stimulation was delivered over the right DLPFC at a 2 mA during 30 min. Nicotine cravings, cigarette consumption and decision-making were assessed before and after each session.

Results: Main findings include a significant decrease in the number of cigarettes smoked when participants received active as compared to sham stimulation. This effect lasted up to four days after the end of the stimulation regimen. In regards to decision-making, smokers rejected more often offers of cigarettes, but not offers of money, after they received active as compared to sham stimulation at the Ultimatum Game. No significant change was observed at the Risk Task with cigarettes or money as rewards.

Conclusion: Overall, these findings suggest that tDCS over the DLPFC may be beneficial for smoking reduction and induce reward sensitive effects.

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1. Introduction

Most tobacco smokers who would like to quit smoking fail to achieve such goal (National Institute on Drug Abuse, 2012). Experimental studies have reported impaired decision-making processes in nicotine smokers. For instance, smokers as compared

to non-smokers tend to take more risk (Lejuez et al., 2003, 2005), and such behaviors seem to be reward sensitive: smokers display greater self-interest motives when dealing with cigarettes as compared to money at the Ultimatum Game (Takahashi, 2007). It has been suggested that such decision-making dysfunction is associated to addictive behaviors. More specifically, an unbalance between a weakened inhibitory control and an excessively powerful reward system would push the addict, when experiencing an urge to smoke, to balance his decision toward maladaptive options (Goldstein and Volkow, 2002; Hyman, 2007).

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Decision-making processes, such as self-interest motives (Sanfey, 2003; Knoch et al., 2010) and risk taking (Rogers et al., 2004; Ernst et al., 2002), have been repeatedly associated with the dorsolateral prefrontal cortex (DLPFC, among a complex cortical and subcortical network; see also Krain et al., 2006) and can be influenced with noninvasive brain stimulation when applied over this region, independent of smoking habits. For instance, transcranial direct current stimulation (tDCS) over the DLPFC can induce a more conservative response style in the context of risk taking at the Risk Task (Fecteau et al., 2007a) and the balloon analog risk task (BART; Fecteau et al., 2007b), and low-frequency repetitive transcranial magnetic stimulation (rTMS) over the DLPFC can increase risk taking at the Risk Task (Knoch et al., 2006a) and self-centered motives at the Ultimatum Game (Knoch et al., 2006b, 2010). Conversely, high-frequency rTMS over the DLPFC during the delay-discounting task has been shown to modulate delayed discounting of gains and losses, enabling subjects to make less impulsive decisions (Sheffer et al., 2013). When applied to nicotine smokers, tDCS over the DLPFC can reduce cigarette intake (Boggio et al., 2009) and cue-induced nicotine craving (Fregni et al., 2008a,b; Boggio et al., 2009). High-frequency rTMS over the DLPFC can also reduce nicotine smoking (Eichhammer et al., 2003; Amiaz et al., 2009) and craving (Johann et al., 2003; Amiaz et al., 2009; Li et al., 2013). Diminished craving has also been reported with tDCS or rTMS over the DLPFC for alcohol (Boggio et al., 2008), cocaine (Camprodon et al., 2007; Politi et al., 2008), and food (Uher et al., 2005; Fregni et al., 2008a,b). A recent meta-analysis on the noninvasive brain stimulation (NIBS)-induced reduction of drug cravings intensity has determined that active stimulation (tDCS or rTMS) significantly decrease cravings compared to sham (Jansen et al., 2013). Of interest, the meta-analysis points out that there is no significant difference in the reduction of craving between stimulation of the left or right DLPFC, and the effect remains stable across substances. Although further analyses are needed to evaluate the mechanisms of action of tDCS and rTMS and their respective effect magnitude in this perspective, the results are promising.

We proposed that the beneficial effects of noninvasive brain stimulation over the DLPFC on decreasing addictive behaviors, including nicotine intake, reflect shifts in the role of the DLPFC related to decision-making behaviors (Fecteau et al., 2010). Specifically, we suggested that it might influence the individual's response to smoking triggers, shifting decision-making processes to a more reflective mode, reducing reward seeking and resulting in significant reduction of cigarette intake. The goal of this study was thus to test whether tDCS applied over the DLPFC modulate nicotine intake and decision-making behaviors in tobacco smokers who wished to quit smoking. Based on our previous work (Fregni et al., 2008a,b;

Boggio et al., 2009), we first hypothesized that when smokers receive active as compared to sham stimulation, they will reduce smoking and report a decreased level of nicotine craving. Also, in keeping with our theoretical framework (Fecteau et al., 2010), we predicted that modulation of decision-making processes will be reward sensitive, that is modulation will be greater when the reward consists of cigarettes than money.

2. Materials and methods

2.1. Design

The present study was a crossover, blind at four levels (group allocator, subjects, tDCS provider, outcome assessor), randomized, sham-controlled design in which subjects received two five-day regimens (one active and one sham) of tDCS over the DLPFC. Three months separated the two tDCS regimens to avoid carryover effects. Subjects were asked to fill out a daily cigarette diary during the entire experiment and to perform decision-making tasks before and after each tDCS regimen.

2.2. Participants

Twelve adults (five men; mean age of 36.3; range 21 to 64 years) took part of the study. One participant was categorized as "heavy smoker" (25+ cigarettes per day), seven as "moderate smokers" (15–24 cigarettes per day) and four as "light smokers" (<15 cigarettes per day; Wilson et al., 1999). They were all in the contemplator stage, as assessed by the Prochaska and DiClemente questionnaire (Prochaska and DiClemente, 1983), indicating they wanted to quit smoking. Participants had no history of neurological or psychiatric disorders other than addiction for nicotine smoking and had normal physical and neurological exams. One participant (subject 2) was taking lisinopril for high blood pressure. Participants were also assessed on nicotine dependence (Fagerström Test for Nicotine Dependence; Fagerstrom et al., 1990) impulsivity (Barratt Impulsiveness Scale; Patton et al., 1995), mood (Beck Depression Inventory; Beck et al., 1996), sleep (Pittsburgh Sleep Quality Index; Buysse et al., 1989), food habits (General Food Craving; Cepeda-Benito et al., 2000), and handedness (Edinburgh Handedness Inventory). None of the participants dropped out of the study. Demographic and clinical measures are presented in Table 1.

Participants were screened for noninvasive brain stimulation contraindications (Wassermann, 1998; Rossi et al., 2009). All were naive to brain stimulation, the decision-making tasks, and were not informed about the experimental variables related to the cognitive

Table 1
Demographic and clinical measures.

ID	Gender	Age	Handedness	No. of cigarettes	Time	FTND	BIS	BDI	G-FCQ-T	PSQI
1	F	62	84	25	<5	6	55	0	25	1
2	M	53	100	20	6–30	5	77	10	55	6
3	F	58	40	15	6–30	3	72	2	40	2
4	M	22	100	12	6–30	6	56	2	45	9
5	F	64	100	20	<5	7	68	1	35	2
6	F	21	30	15	6–30	4	54	9	38	9
7	F	20	100	15	31–60	2	73	2	27	12
8	F	21	63	10	31–60	2	73	4	42	5
9	M	25	100	20	<5	6	79	10	57	5
10	M	36	100	7	31–60	2	59	4	40	5
11	F	32	100	10	6–30	2	65	15	23	10
12	M	21	88	17	6–30	5	90	5	37	2

Number of cigarettes: average of cigarettes smoked per day before starting the experiment. Time: laps in minutes between awakening and first cigarette. FTND: Fagerström test for nicotine dependence BIS: Barratt impulsiveness scale 11. BDI: Beck depression inventory. G-FCQ-T: general craving food questionnaire trait. PSQI: Pittsburgh sleep quality index.

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