Brain Stimulation 9 (2016) 191–196

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.brainstimjrnl.com

Transcranial Direct Current Brain Stimulation Increases Ability to Resist Smoking

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ARTICLE INFO

Article history:
Received 13 July 2015
Received in revised form 28 August 2015
Accepted 15 October 2015
Available online 23 October 2015

Keywords:
tDCS
Nicotine addiction
Smoking relapse

ABSTRACT

Background: The ability to exert self-control over temptation is a fundamental component of smoking behavior change. Transcranial direct current stimulation (tDCS) of the dorsolateral prefrontal cortex (DLPFC) has been shown to modulate cognitive control circuits. Although prior studies show that stimulation reduces cigarette craving and self-reported smoking, effects on ability to resist smoking have not been investigated directly.

Objectives: We assessed effects of a single 20-minute session of 1.0 mA anodal stimulation over the left DLPFC with cathodal stimulation over the right supra-orbital area (vs. sham stimulation) on ability to resist smoking in a validated smoking lapse paradigm.

Methods: Twenty-five participants completed two tDCS sessions (active and sham stimulation) in a within-subject, double-blind, randomized and counterbalanced order with a 2-week washout period. Following overnight abstinence, participants received tDCS in the presence of smoking related cues; they had the option to smoke at any time or receive $1 for every 5 minutes they abstained. After 50 minutes, they participated in a 1 hour ad libitum smoking session. Primary and secondary outcomes were time to first cigarette and cigarette consumption, respectively.

Results: In multiple regression models, active tDCS (compared to sham) significantly increased latency to smoke ($p = 0.02$) and decreased the total number of cigarettes smoked ($p = 0.014$) during the session.

Conclusion: These findings suggest that acute anodal stimulation over the left DLPFC (with cathodal stimulation over the right supra-orbital area) can improve ability to resist smoking, supporting the therapeutic potential of tDCS for smoking cessation treatment.

Introduction

Tobacco use accounts for over six million deaths each year worldwide [1] and takes a significant economic toll [1,2]. Even with the best treatments available, most people revert to their former smoking practices [3]. While currently available treatments may address symptoms of nicotine withdrawal or alter the reinforcing effects of nicotine, they do not address the disruptive brain processes that may undermine attempts to quit smoking [4].

Abstinence from smoking produces cognitive impairments and altered brain functions that can make it more difficult to resist temptations to smoke (e.g., smoking cessation) [5]. For example, working memory performance and associated neural activity in the dorsolateral prefrontal cortices (DLPFC) are downregulated during nicotine withdrawal, compared to smoking satiety [6–9]. Reductions in working memory-related DLPFC activity predict smoking relapse above and beyond clinical and performance measures, with 81% accuracy [10]. The DLPFC is at the core of the brain's cognitive control network which supports behavioral self-control [11–14], suggesting that targeting DLPFC functions may be a therapeutic strategy to support smoking behavior change.

Emerging evidence shows that activity in the DLPFC and cognitive control circuits can be modulated using a noninvasive and safe intervention: direct current transcranial stimulation (tDCS) [15–17]. Active anodal tDCS administered to the DLPFC has been shown to increase task-related activity in the DLPFC during a risk sensitivity task, and to increase resting state functional connectivity in the attention network [18,19]. In smokers, tDCS has been shown to reduce

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1935-861X/
http://dx.doi.org/10.1016/j.brs.2015.10.004

smoking cue-induced craving and self-reported cigarette intake [20–22]. However, these studies examined minimally-abstinent (1.5 hrs or less) smokers. Another study found that active tDCS versus sham reduced negative affect but not cigarette craving in smokers after overnight abstinence [23], but this study did not examine subsequent smoking behavior.

Given the relevance of DLPFC activity for smoking relapse, we tested the hypothesis that anodal tDCS over the left DLPFC (with cathodal stimulation over the right supra-orbital area) after overnight abstinence will increase ability to resist temptations to smoke. This preliminary study employed a within-subject crossover design to compare active versus sham stimulation, such that each participant served as his/her own control, and utilized a validated smoking lapse paradigm that is sensitive to the effects of efficacious smoking treatments [24,25]. We predicted that active stimulation (versus sham) would increase latency to first cigarette and decrease the total number of cigarettes smoked during the session.

Materials and methods

Participants

All procedures were approved by the University of Pennsylvania Institutional Review Board and carried out in accordance with the Declaration of Helsinki. Healthy adults between the ages of 18 and 60 who reported smoking at least 10 cigarettes per day (CPD) for the past year and were not planning to quit smoking in the next 3 months were recruited through mass media. All participants provided written informed consent and completed an in-person eligibility screen including a urine drug screen, a breath alcohol test, and an expired breath carbon monoxide (CO) reading to confirm smoking status; women completed a urine pregnancy test. Individuals who self-reported a history of DSM-IV Axis I psychiatric or substance disorders (except nicotine dependence) and those taking psychotropic medications were excluded. Additional exclusion criteria included: current use of chewing tobacco, snuff, or smoking cessation products; pregnancy, planned pregnancy or breastfeeding; history of brain injury or seizures; presence of metal (other than dental apparatus) in the face or head; low or borderline intelligence (estimated IQ <90 on Shipley Institute of Living Scale [26]); and any impairment that would prevent task performance.

Procedures

Participants in this within-subject cross-over investigation completed two identical laboratory sessions (one session involving active stimulation and the other involving sham stimulation) scheduled at least two weeks apart to minimize carryover effects. Session order was double-blind, randomized and counterbalanced. Sessions started at approximately 9am (+/−1 hr) after overnight abstinence (~12 hours). Participants provided an expired CO reading at the start of the session which was required to be <10 ppm (or at least a 50% reduction from the reading obtained at the eligibility screen) in order to confirm compliance with the abstinence requirement. Following confirmation of eligibility, participants completed the Questionnaire on Smoking Urges – brief version (QSU-B [27]) and then received 20 minutes of active or sham stimulation during a laboratory smoking lapse paradigm.

Smoking lapse paradigm

The smoking lapse paradigm was based on that designed by McKee and colleagues [24] and adapted for co-administration of tDCS. Participants were escorted to a 10×10 room equipped with industrial grade exhaust fans approved for exhaust of cigarette smoke, a comfortable couch, a coffee table, and a portable smoking topography unit (Clinical Research Smoking Systems, Plowshare Technologies/Borgwaldt, Baltimore, MD). A pack of cigarettes of the participant's preferred brand was placed in view on the table along with a lighter and ashtray. Prior to initiating tDCS, participants were instructed that over the next 50 minutes they should try not to smoke. Participants could choose to start smoking at any time, but for each 5 minute period that they were able to delay, they would earn $1.00 (up to a maximum of $10 [24]). Once they decided to smoke, they could smoke as little or as much as they wished through the smoking topography device. Participants were permitted to read books or magazines but were asked to refrain from using smartphones or other electronic devices. Once instructions were delivered, tDCS commenced. The tDCS equipment remained in place until the end of the 50 minute resist period to avoid influencing the participant's smoking behavior; however, stimulation was delivered only for the first 20 minutes. Participants remained in the smoking room for the full 50 minutes, regardless of when they decided to smoke, so that all participants would begin the subsequent ad libitum period at the same time relative to tDCS administration (30 minutes post-stimulation). Time to first cigarette (latency to smoke) and total number of cigarettes smoked were recorded electronically via the smoking topography device.

After the 50 minute resist period ended, the tDCS equipment was removed and participants were given new instructions for a 60 minute ad libitum smoking period. During this period, participants were given eight cigarettes of their preferred brand and informed that they had a $4.00 "tab" with the researchers. Participants were instructed to smoke as much or as little as they wished through the smoking topography device, but that for each cigarette lit, they would "lose $0.50 from their $4.00 tab." Participants received any money left in the tab at the end of the session. Self-reported smoking behavior (number of cigarettes smoked) for the 24 hours following the tDCS session was assessed using a timeline follow-back method during a follow-up call the next day.

tDCS procedures

A Magstim Eldith 1 Channel DC Stimulator Plus was used to apply a constant direct current via two 5 cm × 5 cm electrodes covered in saline-soaked sponges. Electrode placement was determined using the international 10–20 system developed for EEG [28]; the anodal electrode was placed over the F3 area for stimulation over the left DLPFC and the cathode was placed over the right supra-orbital area. During the active condition, current was ramped up to 1.0 mA over 30 s, maintained for 19 minutes and ramped down over 30 s (total stimulation period 20 min). During the sham condition, the current was ramped up to 1.0 mA over 30 s and immediately ramped down at the beginning and end of the 20 minute period. This process mimics the skin sensations experienced during active stimulation; most participants cannot distinguish between real and sham tDCS using this procedure [29].

Measures

Outcomes

The primary outcome was latency to smoke (in minutes) and the secondary outcome was total number of cigarettes smoked during the resist and ad libitum periods. Latency to smoke was set to 110 minutes if a participant did not smoke during either period (i.e. the combined duration of the abstinence period plus the ad libitum smoking period). As exploratory measures, we examined smoking topography (total puff volume) and self-reported smoking behavior for the 24 hours following the tDCS session. Total puff volume was set to zero if a participant did not smoke during either period.