

## Prefrontal tDCS for Smoking Cessation: Focus on the Number of Sessions and Motivation to Quit

Marta Rebull<sup>1</sup>, Marien Gadea<sup>1,2\*</sup>, Raúl Espert<sup>1,3</sup>, and Álvaro Pascual-Leone<sup>4</sup>

<sup>1</sup>University of València, Department of Psychobiology, Valencia, Spain

<sup>2</sup>Centro de Investigación Biomédica en Red de Salud Mental (CIBERSAM), Madrid, Spain

<sup>3</sup>Hospital Clínico Universitario de València, Neuropsychology Unit, Valencia, Spain

<sup>4</sup>Hinda and Arthur Marcus Institute for Aging Research, Boston, Massachusetts, USA

### Abstract

Neuromodulation through transcranial direct current stimulation (tDCS) has a *B* recommendation for the treatment of addiction according to therapeutic evidence guidance. We present an intervention, with randomization and placebo, to test the effectiveness of 10 tDCS sessions, without other treatment, spaced over 2 weeks, on tobacco consumption and craving, in 26 healthy smokers. The influence of motivation to quit, self-perceived efficacy, and previous physical dependence was assessed. Active dorsolateral prefrontal cortex (DLPFC, cathode F3/anode F4) tDCS (20 min at 2 mA) was compared to sham through pre–post design with 1-month follow-up. Data analysis included AUCg formulas, ANOVA's and linear regressions. The experimental group showed significantly less consumption than sham during intervention ( $p = .02$ ,  $d = .95$ ) but not at follow-up, as well as a significant decrease in craving ( $p = .04$ ,  $\eta^2 = .15$ ). The most prominent predictors of effectiveness were the number of cigarettes regularly smoked ( $B = 4.27$ ,  $p = .001$ ) and self-reported motivation to quit ( $B = -6.48$ ,  $p = .05$ ). In sum, tDCS helps to reduce tobacco consumption and craving, but its benefits are not maintained over time. It would be necessary to increase the number of sessions and control motivation and the level of previous consumption.

**Keywords:** tDCS; smoking; craving; motivation; sham

**Citation:** Rebull, M., Gadea, M., Espert, R., & Pascual-Leone, Á. (2024). Prefrontal tDCS for smoking cessation: Focus on the number of sessions and motivation to quit. *NeuroRegulation*, 11(4), 327–337. <https://doi.org/10.15540/nr.11.4.327>

**\*Address correspondence to:** Marien Gadea, PhD, Departamento de Psicobiología, Facultad de Psicología (Universitat de València), Avda. Blasco Ibañez 21, 46010, Valencia, Spain. Email: marien.gadea@uv.es

**Edited by:** Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA

**Reviewed by:** Rex L. Cannon, PhD, Currents, Knoxville, Tennessee, USA  
Randall Lyle, PhD, Mount Mercy University, Cedar Rapids, Iowa, USA

**Copyright:** © 2024. Rebull et al. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (CC-BY).

Smoking is a leading preventable cause of disease and death, causing over 8 million deaths annually, including 1.3 million nonsmokers who are exposed to second-hand smoke (World Health Organization [WHO], 2023). Tobacco use disorder (TUD) is a chronic disorder characterized by compulsive tobacco-seeking and a loss of control over its use (5th ed.; DSM-5; Appendix A; American Psychiatric Association [APA], 2013). Noninvasive brain stimulation (NIBS) methods, such as transcranial direct current stimulation (tDCS), can target addiction neurocircuitry network and may help treat TUD and other substance use disorders (SUDs; (Mehta et al., 2024). NIBS targeting a central node of the addiction network as the dorsolateral prefrontal cortex (DLPFC) could improve the control of impulsive and risky behavior, allowing more

functional decisions related to smoking. This could be possible since reward-based motivation is thought to be processed in the left DLPFC, while self-control is processed in the right DLPFC; so, many of the actual protocols seek to balance both sides (Balconi et al., 2014; Fecteau et al., 2014). In consonance with this, tDCS has shown evidence of being likely effective (level B) in treating SUDs by modulating DLPFC (cathode on left frontal, anode on right) according to therapeutic evidence guidance from Lefaucheur et al. (2017) and Fregni et al. (2021).

Recent meta-analyses have focused on tobacco consumption and craving. Kang et al. (2019) analyzed 12 studies and found significant improvements in cue-induced craving and smoking

rates with tDCS. Another meta-analysis by Chen et al. (2020) included eight studies and demonstrated significant benefits of tDCS on craving, showing decreased craving and improved quality of life compared to a placebo group. Mehta et al. (2024) reviewed 11 studies on tDCS in TUD ( $n = 448$  participants including controls) showing positive outcomes (in tobacco craving and/or consumption) in seven studies, mainly with right anodal DLPFC stimulation and multisession tDCS protocols. However, the overall effect size was moderate though still considered clinically relevant (Hedge's  $g$  of .50) and nonsignificant due to high variability among studies. Chan et al. (2024) examined 13 studies (327 participants receiving active tDCS and 284 sham) and found a modest reduction in craving with tDCS, but variability in study conditions affected significance. Overall, while tDCS shows potential for treating TUD, more research is needed to clarify which variables influence treatment outcomes. The meta-analysis by Mehta et al. (2024) examined multisession tDCS protocols, with most applying five sessions of active tDCS (Boggio et al., 2009; Fecteau et al., 2014; Müller et al., 2021; Smith et al., 2015). Two studies found no effects on consumption or craving, while the other two showed positive effects, with one showing effects up to 4 days after stimulation ended. Other clinical trials with interventions of only three sessions showed either no results for smoking cessation (Falcone et al., 2018) or a temporary reduction in consumption with no long-term effects (Alghamdi et al., 2019). A study by Perri and Perrotta (2021) applied five sessions and found a reduction in craving but not in consumption. These inconclusive results suggest that more than 3–5 sessions may be necessary for reliable tDCS outcomes. Additionally, while psychological factors such as motivation and self-efficacy are crucial for smoking cessation, little research has explored their influence on tDCS outcomes. These are important to address given neuroimaging work showing the state of DLPFC is different depending on subjective motivation and resolve to stop addictive behavior (Silvanto & Pascual-Leone, 2008). Most studies also did not measure the long-term effects of tDCS beyond a few days. In sum, more research is needed to understand the interaction between nicotine addiction and tDCS and to develop an optimal treatment strategy.

Our general aim is to study the effects of repeated tDCS sessions on smoking consumption pattern and tobacco craving in people with TUD, through an improved design (a longitudinal randomized placebo-controlled trial) which will include the effect

of the neurostimulation at the time of the intervention and after a follow-up of a month. In addition, we wanted to analyze the influence of certain psychophysiological variables on the tDCS outcome regarding tobacco consumption. Finally, with the additional aim to obtain more descriptive information about the subjective reception of the stimulation, we recorded all sensations after the application of tDCS and evaluated their influence on the outcome.

## Method

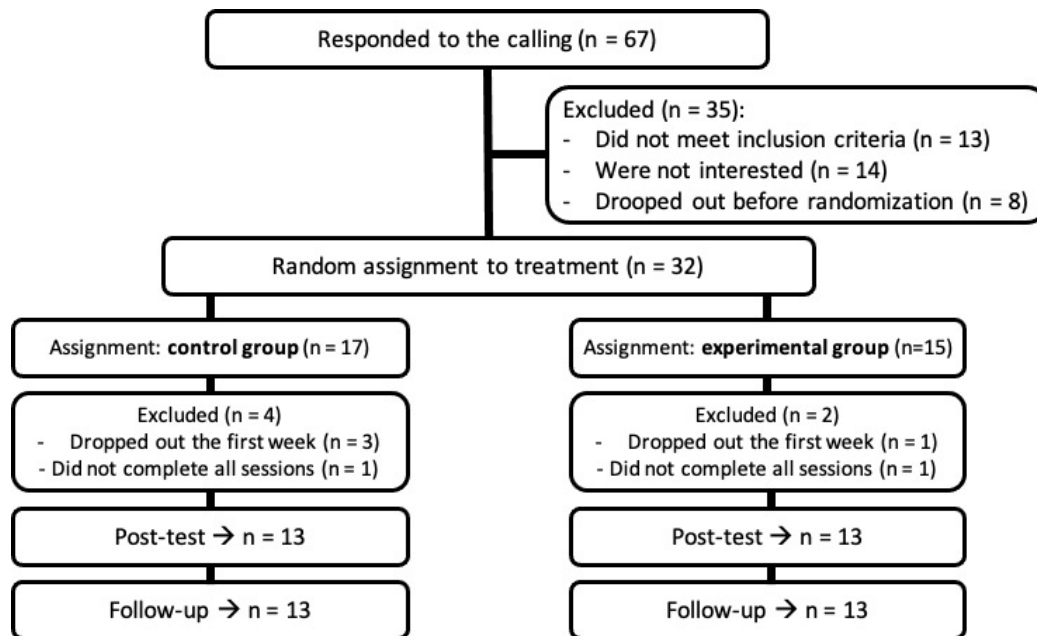
### Participants

From an initial pool of 67 individuals, 26 adults aged 23–69 participated in the study, including 14 women and 12 men equally randomly divided between experimental and placebo groups (each  $n = 13$ ). Participants were recruited via email following promotions with posters and social media ads. All met DSM-5 criteria for TUD and had smoked for at least a year. Safety measures excluded those who were pregnant; had significant clinical, psychiatric, or neurological illnesses (such as epilepsy or traumatic brain injury); had metallic brain or skull implants, a history of stroke with cerebral stent placement or in carotid arteries, dermatological sensitivities, or pacemakers. The design standardized participants' physical dependence, motivation to quit smoking, and perceived self-efficacy. The flowchart for the selection of the participants according to CONSORT guidelines (Schulz et al., 2010) can be consulted in Figure 1. Descriptive data for demographical and all other variables of interest can be consulted in Table 1.

### Materials

**TDCS Apparatus.** The study used the Brain Premier E1 tDCS device for neuromodulation, approved by the European Union for medical use and equipped with safety features. The device can provide a current output of 0.5 to 2 mA for 20 or 30 min, depending on the settings. For safety, stimulation starts with a gradual current increase over 30 s (ramp in) and decreases similarly before the session ends (ramp out). The study used round sponge electrodes measuring 1.5 in. in diameter.

**Psychometric Measures.** The psychometric assessment instruments used in this protocol were as follows: (a) a smoking interview (adapted from Becoña, 1994): this is a semi-structured interview to ascertain sociodemographic data, smoking history and current tobacco use; (b) a self-recording weekly template (from Monday to Sunday) which facilitates the recording of the total number of cigarettes smoked each day; (c) a visual analog scale for

**Figure 1.** Flowchart for the Selection of the Participants According to CONSORT Guidelines.**Table 1**  
Descriptive Data for Demographical and All Other Variables

	ACTIVE tDCS Mean (SD)	SHAM tDCS Mean (SD)	<i>t</i> , <i>p</i>
Gender	7 W & 6 M	7 W & 6 M	
Age	46 (13.08)	42.15 (11.16)	<i>t</i> < 1 n.s.
Years of Smoking	22.15 (13.70)	21.7 (10.28)	<i>t</i> < 1 n.s.
No. Cigarettes a Day	13.53 (4.09)	13.46 (4.74)	<i>t</i> < 1 n.s.
Physical Dependence	5.23 (1.96)	4.53 (2.56)	<i>t</i> < 1 n.s.
Motivation	7.46 (1.26)	7.69 (1.60)	<i>t</i> < 1 n.s.
Autoefficacy	5.38 (2.32)	6.46 (1.33)	<i>t</i> (gl 24) = 1.44, <i>p</i> = .08

**Note.** Descriptive data in means and standard deviations (SD) for demographic and other variables of interest at baseline, separated for the active tDCS group and the sham tDCS group. W = women, M = men.

craving (VAS-C), that measures the desire to smoke, where 0 corresponds to the total absence of desire and 10 to the maximum; (d) the Richmond Test (Richmond et al., 1993) to evaluate the motivation to quit smoking, which consists of four items with two or three response alternatives and classifies motivation as low (0–6 points), medium (7–9 points) and high (10 points); (e) the Fagerström Test of Nicotine Dependence (FTDN; Heatherton et al., 1991) to evaluate the physical dependence of smoking, which consists of six items with two or four response alternatives whose score ranges between

0 and 10, where it is considered a high degree of nicotine dependence from 6 or more points, although low scores do not necessarily indicate a low degree of dependence; (f) a visual analog scale for the perceived autoefficacy (VAS-EFI) to quit the smoking habit, where 0 corresponds to zero perceived efficacy and 10 is the maximum; and finally, (g) the tDCS-Related Feelings Questionnaire (Antal et al., 2017), a questionnaire that assesses the patient's possible sensations of distress after the application of tDCS, according to four degrees of intensity. Please note that some of the dependent

measures were taken in a slightly different time of the entire experiment, according to the design detailed below.

### Design and Procedure

The study was a longitudinal randomized placebo-controlled trial with participants divided equally between a control group (sham tDCS) and an experimental group (active tDCS). Three phases were evaluated: a baseline phase, an intervention phase, and a follow-up 1 month after intervention ended. Participants who responded to the call were invited to an initial interview to obtain general and nonspecific information about their habit, check inclusion criteria, receive information about the study, and sign consent documents where appropriate. During the following week, the selected participants completed the self-recording weekly template for daily cigarette consumption (baseline: seven measurements preintervention phase). Immediately after this, the participants attended a second interview, in which most of the above-listed psychometric measures were collected (smoking interview, Fagerström test, Richmond test, VAS-EFI scale). From this moment, the intervention phase started and lasted for 2 weeks. Participants received a total of 10 tDCS sessions at 2 mA for 20 min, one session at the same time every working day for 2 weeks (see details of the protocol below). For the placebo condition, the same protocol was applied, but the tDCS device was disconnected (see details for the protocol below). During this intervention phase, we took two types of measures: on the one hand, the number of smoked cigarettes, which was recorded every day during the 2nd week of intervention (seven measurements, on-intervention phase); on the other hand, the level of craving, which was recorded with the VAS-C scale along the 2 weeks of intervention (three measures each week, six measures in total). Right after the completion of this intervention phase, the participants fulfilled the Antal test to explore sensations after the tDCS. The follow-up phase occurred 1 month after intervention and involved recording cigarette consumption over a week (seven measures) and assessing craving levels and the psychometric measures of physical dependence, motivation, and perceived self-efficacy again (note that, while these follow-up measures were recorded, they were not included in the statistical analyses for the current study aims and objectives).

### TDCS Protocol

The study involved placing electrodes over the DLPFC following the international 10–20 system of Jasper, with the anode on the right frontal (F4) and

the cathode on the left frontal (F3). The electrodes (of 6 cm diameter) were soaked in a 0.9% sodium chloride saline solution and positioned on the scalp after the area was cleaned with 96% alcohol. Participants received 10 sessions of tDCS at 2 mA for 20 min each, one session per day (Monday to Friday) for 2 weeks. For the placebo group, the same protocol was followed, but the tDCS device was turned off. To match the somatosensory effects of tDCS, we used a saline solution with a small amount of capsaicin (0.75 mg/g cream, Viñas laboratories) to simulate the slight itching or burning sensation of tDCS (capsaicin is a cream indicated for the relief of moderate to severe pain in painful diabetic neuropathy, and it causes a slight sensation of itching or burning on the skin). During neurostimulation, participants sat comfortably in a chair and listened to relaxing music through earphones. At the end of the tDCS protocol, all participants, whether in the sham or active groups, completed the Antal questionnaire (2017) to assess sensations and possible side effects of the intervention.

### Ethics

All participants were provided with information about the study and signed several consent forms, including the Informed Consent Document, Confidentiality Commitment, tDCS Protocol Consent, and Informed Consent for the Use of Clinical Data. The Human Research Ethics Committee of our university approved the project (H1549015474557), ensuring it adhered to the fundamental principles of the Declaration of Helsinki and the Council of Europe Convention on Human Rights. The study also complied with legal and ethical standards in biomedical research and bioethical data protection as established by local legislation. The research was conducted in accordance with the ethical and legal standards in force, including the Declaration of Helsinki. The raw data collected for the study have been deposited in an open repository according to the DORA and CoARA agreements, and can be consulted in <https://doi.org/10.5281/zenodo.10960954>.

### Statistical Analysis

Statistical analyses were performed using SPSS statistical software version 28.0.1.1. Descriptive statistics were calculated for all variables, and Spearman  $\rho$  correlations were conducted to explore relationships among demographic and psychometric variables at baseline. To assess cigarette consumption, a single representative measure was calculated for each phase (baseline, intervention, and follow-up). For this purpose, the area under the

curve with respect to the ground (AUC<sub>g</sub>) was calculated as a dependent measure according to the formula of Pruessner et al. (2003) for each phase. Such measure has been previously applied mainly for the analyses of hormonal response, especially cortisol (Fekedulegn et al., 2007) but also for behavioral variables related to addiction (Amlung et al., 2015), and it is useful to analyze data sets comprised of repeated measurements over time where the researcher wants to explore whether any changes occurred (Rodriguez, 2023). Thus, all posterior analyses for smoking behavior were based on this measure. Mean differences were tested using repeated-measures ANOVA. Normality was assessed with the Shapiro-Wilk test, and sphericity with Mauchly's test. Adjustments were made using the Greenhouse-Geisser correction when necessary. Post-hoc comparisons used robust *t*-tests with bootstrapping ( $n = 1,000$ ) or comparisons with estimated marginal means difference and Bonferroni corrections. Effect sizes were reported using  $\eta^2$  or Cohen's *d*. For craving, six raw scores were analyzed during the 2 weeks of tDCS using repeated-measures ANOVA with the same assumptions and post-hoc tests. Backward stepwise regression analyses were performed to assess the influence of baseline psychometric variables and the intervention on immediate and 1-month smoking outcomes. Data are reported in means and standard deviations (*SD*) or 95% confidence intervals when relevant.

## Results

### Descriptive Data and Relations Among Baseline Variables

Table 1 provides descriptive data for the sample, divided by groups. At the beginning of the trial, there were no significant differences between the groups in terms of mean age, years of smoking, number of cigarettes smoked per day, physical dependence, motivation to quit smoking, and perceived self-efficacy (though the placebo group had a slightly higher mean for this last variable). Spearman's  $\rho$  revealed significant correlations among some variables. Age was positively correlated with years of smoking ( $\rho = .66, p = .001$ ), but not with the number of cigarettes smoked per day. Additionally, the number of cigarettes smoked per day was positively related to physical dependence ( $\rho = .50, p = .008$ ). Finally, the initial motivation to quit smoking was positively related to perceived self-efficacy ( $\rho = .59, p = .001$ ). No other significant relationships were observed at baseline.

### Cigarette Consumption

The study aimed to evaluate whether daily tobacco consumption was reduced in the active tDCS group compared to the placebo group. Figure 2 displays daily cigarette consumption for each experimental phase, showing similar baseline consumption between groups. During the intervention phase, active tDCS caused a significant reduction in daily cigarette consumption, followed by a partial rebound during follow-up after the end of the intervention. To analyze the data, an AUC<sub>g</sub> was calculated for each phase and group. A repeated-measures ANOVA with Greenhouse-Geisser correction showed no significant main effect of the group ( $F < 1$ ), but there was a significant main effect of the time of intervention,  $F(1, 62; 38, 9) = 47.49, p = .001, \eta^2 = .66$ . Most interesting, the interaction between the time and group,  $F(1, 62; 38, 9) = 16.61, p = .001, \eta^2 = .40$ , was significant, as shown in Figure 3. Post-hoc analysis using independent samples *t*-tests with bootstrapping revealed a significant difference between groups during the intervention phase,  $t(24) = 2.43, p = .02, d$  Cohen = .95, with the active tDCS group (Mean = 36.07; *SD* = 28.17) showing a greater reduction in cigarette consumption compared to the sham tDCS group (Mean = 61.80; *SD* = 25.74). No significant differences were found between groups at baseline (active tDCS: Mean = 84.11; *SD* = 25.70 vs. sham tDCS: Mean = 74.65; *SD* = 30.80) or follow-up (active tDCS: Mean = 54.88; *SD* = 34.93 vs. sham tDCS: Mean = 69.96; *SD* = 28.44). Further analysis of each group's data with estimated marginal means differences and Bonferroni corrections showed that the active tDCS group had significantly different means across all phases: baseline to intervention (I-J = 48.03;  $p = .001$ ), intervention to follow-up (I-J = 18.80;  $p = .001$ ), and baseline to follow-up (I-J = 29.23;  $p = .001$ ) indicating a reduction in cigarette consumption during intervention and a partial increase during follow-up, although they did not recover the same level of consumption as in the baseline, maintaining a significantly lower level. In contrast, the sham tDCS group showed a different mean from baseline to intervention (I-J = 12.8;  $p = .04$ ), and from intervention to follow-up (I-J = 8.15;  $p = .05$ ) but no significant difference between baseline and follow-up, indicating some reduction during intervention but an increase back to baseline levels during follow-up.

### Craving

The study's second objective was to evaluate whether craving for tobacco consumption decreased during intervention and whether there were differences between groups. A repeated-measures

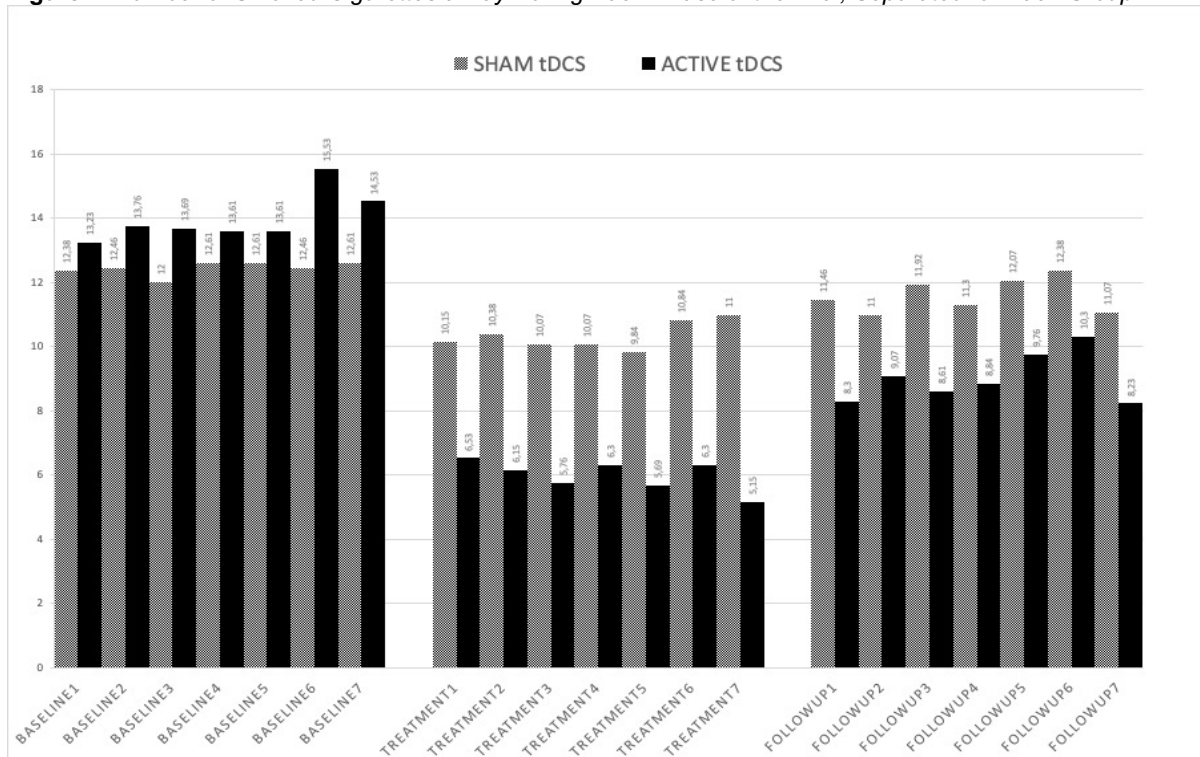
ANOVA showed a significant main effect for the factor “group,”  $F(1, 24) = 4.51, p = .04, \eta^2 = .15$ , due to a higher overall level of craving in the control group (Mean = 6.87; 95% IC [6.15, 7.59]) compared with the active tDCS group (Mean = 5.82; 95% IC [5.09, 6.54]). The ANOVA also revealed a significant main effect,  $F(5, 120) = 9.29, p = .001, \eta^2 = .27$ , for the factor “time” (six measures obtained across 2 weeks) that was nuanced by a significant interaction between the time and the group,  $F(5, 120) = 7.58, p = .001, \eta^2 = .24$ . Post-hoc analyses with separate ANOVAs for each group found no significant differences among the six measures for the control group,  $F(5, 60) = 1.87, p = .11$ . In contrast, the active tDCS group showed a significant effect of “time,”  $F(5, 60) = 11.04, p = .001, \eta^2 = .47$ . In the active tDCS group, estimated marginal means difference with Bonferroni corrections showed a significant decrease in craving from the initial measure (Monday of the 1st week of intervention) to later points in the intervention phase. Significant decreases were observed when comparing the initial craving to timepoint 4 (Monday

of the 2nd week:  $I-J = 2.15; p = .01$ ), as well as timepoint 4 to 5 (I-J = 2.15;  $p = .009$ ) and to 6 (end of intervention, Friday of the 2nd week;  $I-J = 2.84; p = .002$ ). Comparisons among measures taken during the 2nd week of intervention did not reach statistical significance.

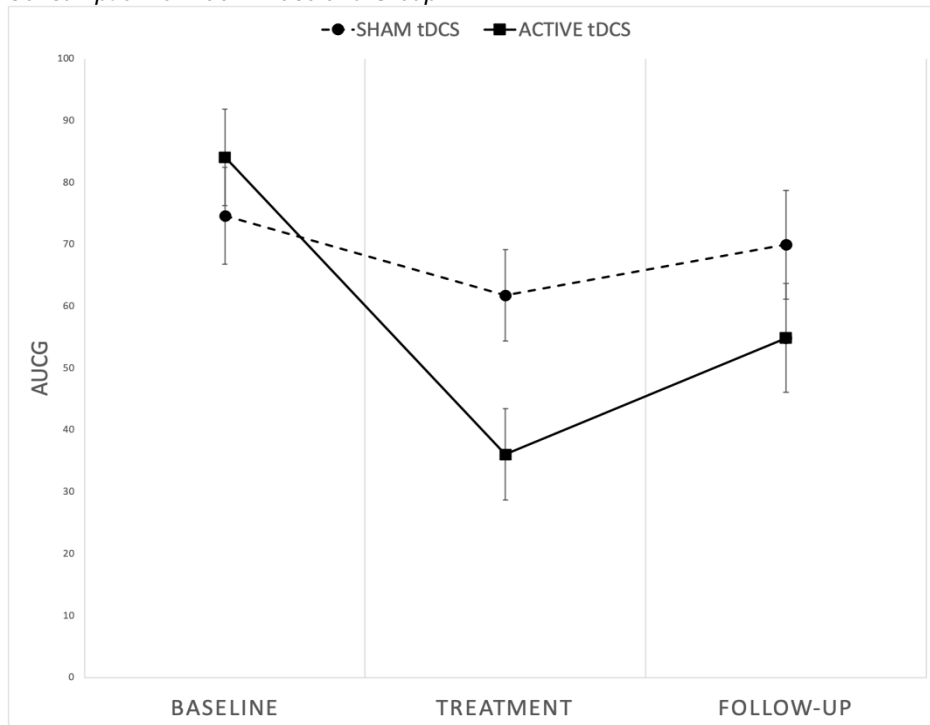
**Regression Analysis on Smoking Behavior**

The study explored the influence of initial baseline measures (age, years of smoking, number of cigarettes smoked per day, physical dependence, motivation to quit smoking, and perceived self-efficacy) along with tDCS intervention (active or sham) on smoking consumption. Backward stepwise regression analyses were performed on the AUCgINTERVENTION (outcome during the 2nd week of intervention) and AUCgFOLLOW-UP (outcome after a month) dependent variables. For the AUCgINTERVENTION outcome, the best-fitting significant mode,  $F(5, 20) = 9.65; p = .001; R^2 = .63$ , included intervention, age, number cigarettes smoked per day, and motivation to quit smoking.

**Figure 2.** Number of Smoked Cigarettes a Day During Each Phase of the Trial, Separated for Each Group.

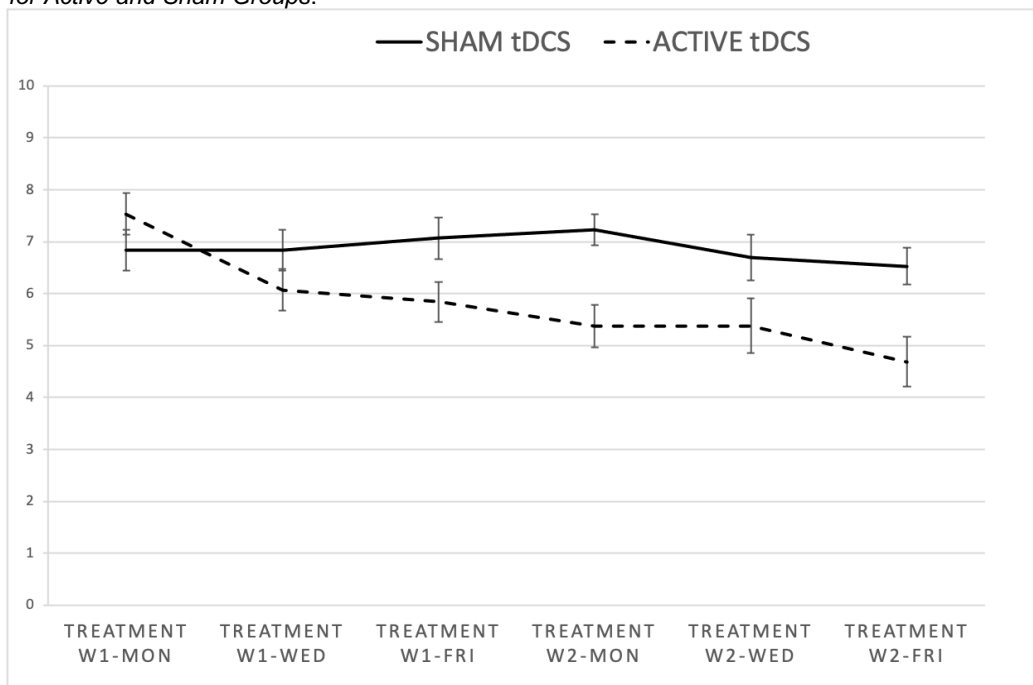


**Figure 3.** Mean AUCg (Area Under the Curve From the Ground) Regarding Cigarette Consumption for Each Phase and Group.



**Note.** Comparison between groups was significant just for the intervention (see text).

**Figure 4.** Evolution for Craving Experience Along the 2 Weeks of tDCS Intervention, Separated for Active and Sham Groups.



**Note.** There were some statistical differences only in the evolution of the active tDCS group (see text). Bars: standard error of the mean.

The stronger predictors were for number of cigarettes smoked per day ( $B = 4.27$ ,  $t = 5.15$ ,  $p = .001$ ) and the intervention itself ( $B = -27.49$ ,  $t = -3.62$ ,  $p = .002$ ). Motivation to quit smoking ( $B = -6.48$ ,  $t = -2.06$ ,  $p = .05$ ) and age ( $B = 0.661$ ,  $t = 2.08$ ,  $p = .05$ ) were also modestly significant predictors. Regarding the AUCgFOLLOW-UP outcome, the best-fitting significant model,  $F(4, 21) = 8.28$ ,  $p = .001$ ,  $R^2 = .53$ , included the intervention, age, number of cigarettes smoked per day and years of smoking as predictors. In this case, the number of cigarettes smoked per day ( $B = 5.74$ ,  $t = 5.35$ ,  $p = .001$ ) was the most significant predictor, with intervention ( $B = -20.36$ ,  $t = 2.31$ ,  $p = .03$ ) and age ( $B = 1.39$ ,  $t = 2.44$ ,  $p = .02$ ) also being significant predictors.

### Sensations After the tDCS

In both groups, most participants reported sensations just below the electrode (84.6% in the active group and 92.3% in the control group). A higher percentage of the control group (84.6%) experienced discomfort from the beginning compared to the active group (76.9%). However, for the active group, discomfort mostly persisted until the end (92.3%) compared to the control group (76.9%). Despite these differences, the discomfort did not affect more than half of the sample (53.8% in the active group and 61.5% in the control group) or affected them very little (46.1% in the active group and 38.4% in the control group). Proportions were similar between groups, and  $t$ -tests showed no significant differences in controlled variables such as itching, pain, burning, heat, metallic taste, fatigue, and dizziness. These results indicate the absence of significant differences between the two groups regarding neuromodulation sensations in our design using capsaicin.

### Discussion

The study aimed to test the efficacy of DLPFC tDCS for treating tobacco consumption and craving during the intervention and after a 1-month follow-up. The findings revealed a significant reduction in self-reported daily tobacco consumption in the experimental group compared to the sham control group during the tDCS intervention, which consisted of 10 repeated sessions over 2 weeks at 20 min each and 2 mA. While the sham group also reduced their consumption, thus probing a certain placebo effect in the mechanism of the technique, the active tDCS group experienced a significantly greater reduction. However, this positive outcome was not sustained over time, as both groups experienced some rebound in smoking after a month. However,

note that such rebound was not the same for both groups, since the experimental group recovered their addiction, but they did not do so at the baseline level, while the placebo group did return to their initial level of tobacco consumption. On the other hand, and regarding the craving experimented during the neuromodulation, we found it progressively decreasing along the 2 weeks of intervention only for the active tDCS group. When comparing the results to similar studies with multisession protocols, there were both similarities and differences. For instance, in the study of Verveer et al. (2020), participants received six tDCS sessions in 1 week (twice a day), and found the number of smoked cigarettes a day progressively decreased up to 1 week after the last tDCS session, though in both sham and active conditions and with no additional benefits for the active tDCS for the consumption neither for craving. Other studies, such as Hajloo et al. (2019), reported positive results for both cigarette consumption and craving, even after a month, with a protocol involving 10 sessions over 5 weeks. On the other hand, Mondino et al. (2018) applied 10 sessions on 5 consecutive days (twice a day) and found active tDCS significantly reduced craving but with no differences with sham tDCS in the number of smoked cigarettes during the intervention or after a month. Maybe a decisive factor is, apart from the number of sessions, the timing at which the sessions are delivered. It appears from the published studies the efficacy might be greater when the sessions are more spread over time. For instance, Ghorbani Behnam et al. (2019) applied 20 sessions over 4 or 12 weeks and found that the longer duration led to the highest abstinence rate (25.7%) at 6 months. Overall, the findings suggest the need for a minimum of 10 sessions, spaced out over time, to achieve stable benefits. Our study's design included 2 weeks of stimulation, but measured tobacco consumption during the 2nd week, with the intention of accumulating some neuromodulation prior to the assessment of the result. Anyway, it seems that 10 sessions may not have been sufficient for lasting effects, in line with the findings of Mondino et al. (2018) and Verveer et al. (2020). Longer duration protocols, such as Ghorbani Behnam et al. (2019), may lead to more sustained benefits even after 6 months. This raises the interesting possibility that aside from the potential biological effects of the tDCS, the psychological factors associated with an intervention which is sustained over many weeks might be critical to disrupt the addiction-sustaining habits.



The study also aimed to assess the influence of certain variables on the outcome of the tDCS intervention. Apart from the intervention itself, the number of cigarettes smoked per day was the best predictor of success both during intervention and in maintaining abstinence after a month. This suggests that the tDCS technique may be more effective for light smokers (around 10 cigarettes per day). Interestingly, motivation to quit smoking was also an important predictor of success during intervention, supporting the findings of Vitor de Souza Brangioni et al. (2018), who observed that tDCS coupled with high motivation significantly reduced cigarette consumption up to 4 weeks postintervention. Similarly, Fecteau et al. (2014) found benefits from five tDCS sessions in participants who wanted to quit smoking, and Verveer et al. (2020) suggested that the lack of positive results in their study might be partly due to participants' low motivation to quit smoking. Motivation appears to be a critical factor for immediate success in reducing or quitting smoking. As we commented in the introduction, neurostimulation can have state-dependent effects, thus pointing to a "motivated DLPF cortex" more prone to control addictive behavior. However, in this study, motivation did not influence the outcome after a month. Instead, age emerged as a significant predictor for maintaining abstinence, with older participants showing better restraint in consumption after a month (note that the study included participants up to around 60 years old). Factors such as years of smoking, physical dependence, and perceived self-efficacy to quit smoking were not strong predictors of outcome, at least as measured in this study.

Participants in the study reported no significant side effects from tDCS, and no one withdrew due to discomfort during intervention. The most common sensations related to tDCS were mild burning, itching, and heat under the electrode, consistent with previous research. A systematic review by Matsumoto and Ugawa (2017) confirmed that the most common side effects from tDCS are mild skin-related issues that dissipate after electrode removal. The placebo strategy used in the study (using physiological saline solution with a small amount of capsaicin 0.75 mg/g cream) proved effective, as there were no significant differences in sensations between the active and sham groups. This strategy helped ensure that the participants' experiences during the study were similar regardless of the intervention group.

The study's results should be interpreted cautiously due to the small sample size and the fact that there

were no objective measures such as expired CO<sub>2</sub>, although, on the other hand, efforts were made to maintain homogeneity and a well-designed experiment. Several indicators were used to assess the therapeutic effects of tDCS as a smoking cessation treatment, such as self-recording, craving, and motivation to quit smoking. A follow-up measure was also included to evaluate the evolution of tDCS effects. The study's results partially align with previous research on tDCS for nicotine dependence, which found improvements in tobacco consumption habits following tDCS neuromodulation of DLPFC, especially when a minimum of 10 sessions is applied, preferably spread over time. This may be due to the modulation of cognitive control circuits involved in decision-making, self-control, and craving regulation, which promote executive function and enhance control over impulsive behaviors motivated by nicotine reward (Kang et al., 2019). In conclusion, tDCS targeting the DLPFC (anode F4 and cathode F3) at 2 mA for 10 sessions over 2 weeks significantly reduces self-reported tobacco consumption and craving. However, the effects are not stable, suggesting that extending the tDCS protocol beyond 10 sessions could enhance long-term outcomes.

#### Author Disclosure

Authors have no grants, financial interests, or conflicts to disclose.

#### References

- Alghamdi, F., Alhussien, A., Alohal, M., Alatawi, A., Almusned, T., Fecteau, S., Habib, S. S., & Bashir, S. (2019). Effect of transcranial direct current stimulation on the number of smoked cigarettes in tobacco smokers. *PLoS ONE*, *14*(2), Article e0212312. <https://doi.org/10.1371/journal.pone.0212312>
- American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders* (5th ed.). <https://doi.org/10.1176/appi.books.9780890425596>
- Amlung, M., Yurasek, A., McCarty, K. N., MacKillop, J., & Murphy, J. G. (2015). Area under the curve as a novel metric of behavioral economic demand for alcohol. *Experimental and Clinical Psychopharmacology*, *23*(3), 168–175. <https://doi.org/10.1037/pha0000014>
- Antal, A., Alekseichuk, I., Bikson, M., Brockmüller, J., Brunoni, A. R., Chen, R., Cohen, L. G., Douthwaite, G., Ellrich, J., Flöel, A., Fregni, F., George, M. S., Hamilton, R., Haeisen, J., Herrmann, C. S., Hummel, F. C., Lefaucheur, J. P., Liebetanz, D., Loo, C. K., ... Paulus, W. (2017). Low intensity transcranial electric stimulation: Safety, ethical, legal regulatory and application guidelines. *Clinical Neurophysiology*, *128*(9), 1774–1809. <https://doi.org/10.1016/j.clinph.2017.06.001>
- Balconi, M., Finocchiaro, R., & Canavesio, Y. (2014). Reward-system effect (BAS rating), left hemispheric "unbalance" (alpha band oscillations) and decisional impairments in drug addiction. *Addictive Behaviors*, *39*(6), 1026–1032. <https://doi.org/10.1016/j.addbeh.2014.02.007>

- Becoña, E. (1994). Tratamiento del tabaquismo. In J. L. Graña (Ed.), *Conductas adictivas. Teoría, evaluación y tratamiento*. Madrid: Debate.
- Boggio, P. S., Liguori, P., Sultani, N., Rezende, L., Fecteau, S., & Fregni, F. (2009). Cumulative priming effects of cortical stimulation on smoking cue-induced craving. *Neuroscience Letters*, 463(1), 82–86. <https://doi.org/10.1016/j.neulet.2009.07.041>
- Chan, Y.-H., Chang, H.-M., Lu, M.-L., & Goh, K. K. (2024). Targeting cravings in substance addiction with transcranial direct current stimulation: Insights from a meta-analysis of sham-controlled trials. *Psychiatry Research*, 331, Article 115621. <https://doi.org/10.1016/j.psychres.2023.115621>
- Chen, J., Qin, J., He, Q., & Zou, Z. (2020). A meta-analysis of transcranial direct current stimulation on substance and food craving: what effect do modulators have? *Frontiers in Psychiatry*, 11, Article 598. <https://doi.org/10.3389/fpsy.2020.00598>
- Falcone, M., Bernardo, L., Ashare, R., Hamilton, R., Faseyitan, O., McKee, S. A., Loughhead, J., & Lerman, C. (2016). Transcranial direct current brain stimulation increases ability to resist smoking. *Brain Stimulation*, 9(2), 191–196. <https://doi.org/10.1016/j.brs.2015.10.004>
- Fecteau, S., Agosta, S., Hone-Blanchet, A., Fregni, F., Boggio, P., Ciraulo, D., & Pascual-Leone, A. (2014). Modulation of smoking and decision-making behaviors with transcranial direct current stimulation in tobacco smokers: A preliminary study. *Drug and Alcohol Dependence*, 140, 78–84. <https://doi.org/10.1016/j.drugalcdep.2014.03.036>
- Fekedulegn, D. B., Andrew, M. E., Burchfiel, C. M., Violanti, J. M., Hartley, T. A., Charles, L. E., & Miller, D. B. (2007). Area under the curve and other summary indicators of repeated waking cortisol measurements. *Psychosomatic Medicine*, 69(7), 651–659. <https://doi.org/10.1097/PSY.0b013e31814c405c>
- Fregni, F., El-Hagrassy, M. M., Pacheco-Barrios, K., Carvalho, S., Leite, J., Simis, M., Brunelin, J., Nakamura-Palacios, E. M., Marangolo, P., Venkatasubramanian, G., San-Juan, D., Caumo, W., Bikson, M., Brunoni, A. R., & Neuromodulation Center Working Group (2021). Evidence-based guidelines and secondary meta-analysis for the use of transcranial direct current stimulation in neurological and psychiatric disorders. *International Journal of Neuropsychopharmacology*, 24(4), 256–313. <https://doi.org/10.1093/ijnp/pyaa051>
- Ghorbani Behnam, S., Mousavi, S. A., & Emamian, M. H. (2019). The effects of transcranial direct current stimulation compared to standard bupropion for the treatment of tobacco dependence: A randomized sham-controlled trial. *European Psychiatry*, 60, 41–48. <https://doi.org/10.1016/j.eurpsy.2019.04.010>
- Hajloo, N., Pouresmali, A., Alizadeh Goradel, J., & Mowlaie, M. (2019). The effects of transcranial direct current stimulation of dorsolateral prefrontal cortex on reduction of craving in daily and social smokers. *Iranian Journal of Psychiatry*, 14(4), 291–296.
- Heatherston, T. F., Kozlowski, L. T., Frecker, R. C., & Fagerström, K. O. (1991). The Fagerström Test for nicotine dependence: A revision of the Fagerström Tolerance Questionnaire. *British Journal of Addiction*, 86(9), 1119–1127. <https://doi.org/10.1111/j.1360-0443.1991.tb01879.x>
- Kang, N., Kim, R. K., & Kim, H. J. (2019). Effects of transcranial direct current stimulation on symptoms of nicotine dependence: A systematic review and meta-analysis. *Addictive Behaviors*, 96, 133–139. <https://doi.org/10.1016/j.addbeh.2019.05.006>
- Lefaucheur, J.-P., Antal, A., Ayache, S. S., Benninger, D. H., Brunelin, J., Cogiamanian, F., Cotelli, M., De Ridder, D., Ferrucci, R., Langguth, B., Marangolo, P., Milius, V., Nitsche, M. A., Padberg, F., Palm, U., Poulet, E., Priori, A., Rossi, S., Sackellmann, M., ... Paulus, W. (2017). Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). *Clinical Neurophysiology*, 128(1), 56–92. <https://doi.org/10.1016/j.clinph.2016.10.087>
- Matsumoto, H., & Ugawa, Y. (2017). Adverse events of tDCS and tACS: A review. *Clinical Neurophysiology Practice*, 2, 19–25. <https://doi.org/10.1016/j.cnp.2016.12.003>
- Mehta, D. D., Praecht, A., Ward, H. B., Sanches, M., Sorkhou, M., Tang, V. M., Steele, V. R., Hanlon, C. A., & George, T. P. (2024). A systematic review and meta-analysis of neuromodulation therapies for substance use disorders. *Neuropsychopharmacology*, 49(4), 649–680. <https://doi.org/10.1038/s41386-023-01776-0>
- Mondino, M., Luck, D., Grot, S., Januel, D., Suaud-Chagny, M. F., Poulet, E., & Brunelin, J. (2018). Effects of repeated transcranial direct current stimulation on smoking, craving and brain reactivity to smoking cues. *Scientific Reports*, 8(1), Article 8724. <https://doi.org/10.1038/s41598-018-27057-1>
- Müller, T., Shevchenko, Y., Gerhardt, S., Kiefer, F., & Vollstädt-Klein, S. (2021). The influence of perceived stress and self-control on efficacy of repeated transcranial direct current stimulation in non-treatment-seeking smokers. *Drug and Alcohol Dependence*, 226, Article 108861. <https://doi.org/10.1016/j.drugalcdep.2021.108861>
- Perri, R. L., & Perrotta, D. (2021). Transcranial direct current stimulation of the prefrontal cortex reduces cigarette craving in not motivated to quit smokers: A randomized, sham-controlled study. *Addictive Behaviors*, 120, Article 106956. <https://doi.org/10.1016/j.addbeh.2021.106956>
- Pruessner, J. C., Kirschbaum, C., Meinlschmid, G., & Hellhammer, D. H. (2003). Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. *Psychoneuroendocrinology*, 28(7), 916–931. [https://doi.org/10.1016/s0306-4530\(02\)00108-7](https://doi.org/10.1016/s0306-4530(02)00108-7)
- Richmond, R. L., Kehoe, L. A., & Webster, I. W. (1993). Multivariate models for predicting abstinence following intervention to stop smoking by general practitioners. *Addiction*, 88(8), 1127–1135. <https://doi.org/10.1111/j.1360-0443.1993.tb02132.x>
- Rodríguez, D. (2023). Area under the curve as an alternative to latent growth curve modeling when assessing the effects of predictor variables on repeated measures of a continuous dependent variable. *Stats*, 6(2), 674–688. <https://doi.org/10.3390/stats6020043>
- Schulz, K. F., Altman, D. G., Moher, D., & the CONSORT Group. (2010). CONSORT 2010 Statement: Updated guidelines for reporting parallel group randomised trials. *BMC Medicine*, 8, Article 18. <https://doi.org/10.1186/1741-7015-8-18>
- Silvanto, J., & Pascual-Leone, A. (2008). State-dependency of transcranial magnetic stimulation. *Brain Topography*, 21, 1–10. <https://doi.org/10.1007/s10548-008-0067-0>
- Smith, R. C., Boules, S., Mattiuz, S., Youssef, M., Tobe, R. H., Sershen, H., Lajtha, A., Nolan, K., Amiaz, R., & Davis, J. M. (2015). Effects of transcranial direct current stimulation (tDCS) on cognition, symptoms, and smoking in schizophrenia: A randomized controlled study. *Schizophrenia Research*, 168(1–2), 260–266. <https://doi.org/10.1016/j.schres.2015.06.011>
- Verveer, I., Remmerswaal, D., Jongerling, J., van der Veen, F. M., & Franken, I. H. A. (2020). No effect of repetitive tDCS on daily smoking behaviour in light smokers: A placebo-controlled EMA study. *PLoS ONE*, 15(5), Article e0233414. <https://doi.org/10.1371/journal.pone.0233414>
- Vitor de Souza Brangioni, M. C., Pereira, D. A., Thibaut, A., Fregni, F., Brasil-Neto, J. P., & Boechat-Barros, R. (2018). Effects of prefrontal transcranial direct current stimulation and motivation to quit in tobacco smokers: A randomized, sham controlled, double-blind trial. *Frontiers in Pharmacology*, 9, Article 14. <https://doi.org/10.3389/fphar.2018.00014>

World Health Organization (WHO). (2023). WHO report on the global tobacco epidemic, 2023: Protect people from tobacco smoke. Geneva: World Health Organization.

**Received:** May 24, 2024

**Accepted:** June 4, 2024

**Published:** December 20, 2024