Efficacy of transcranial direct current stimulation (tDCS) in tobacco use: a PRISMA systematic review

Eficacia de la estimulación transcraneal con corriente directa (tDCS) en el consumo de tabaco: una revisión sistemática PRISMA

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Abstract

Introduction: Transcranial direct current stimulation (tDCS) is an emerging, non-invasive, and safe brain neuromodulation technique intended to relieve symptoms associated with psychiatric disorders, including addiction. Research on tobacco consumption offers promising results; however, at the same time, a lack of replicability is evident among current studies. Objective: To offer an overview of the effectiveness of the tDCS intervention in tobacco consumption over the last 10 years (2014-2024). Method: Systematic review of controlled, double-blind, and randomized empirical studies registered in Science Direct, Scopus, and PubMed between 2014 and 2024. Results: Thirteen empirical studies have been examined that aim to investigate the effects of tDCS stimulation associated with tobacco consumption, highlighting a heterogeneity between the results, since depending on the variable evaluated and the parameters of the stimulation protocol, its effectiveness may vary. Conclusion: The present systematic review shows that tDCS continues to be a promising technique as an alternative for the treatment of tobacco consumption, showing effective results in reducing craving and consumption patterns.

Keywords

Transcranial direct current stimulation (tDCS); tobacco; quit smoking.

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Resumen

Introducción: La estimulación transcraneal de corriente continua (tDCS) es una técnica emergente de neuromodulación cerebral no invasiva y segura, destinada a aliviar los síntomas asociados con los trastornos psiquiátricos, incluida la adicción. Las investigaciones en el consumo de tabaco ofrecen resultados prometedores, no obstante, a su vez se evidencia una falta de replicabilidad entre los estudios actuales. Objetivo: ofrecer una visión general sobre la eficacia de la intervención de tDCS en el consumo de tabaco, en los últimos 10 años (2014-2024). Método: Revisión sistemática de estudios empíricos controlados, doble ciego y aleatorizados, registrados en Science Direct, Scopus y PubMed, entre los años 2014 y 2024. Resultados: Se han examinado 13 estudios empíricos que tienen como propósito investigar los efectos de la estimulación de tDCS asociado al consumo de tabaco, destacando una heterogeneidad entre sus resultados, pues dependiendo de la variable evaluada y de los parámetros del protocolo de estimulación su eficacia puede variar. Conclusión: la presente revisión sistemática evidenció que la tDCS continúa siendo una técnica prometedora como alternativa para el tratamiento del consumo de tabaco, mostrando resultados efectivos en la reducción del ansia y patrón de consumo.

Palabras clave

Estimulación transcraneal de corriente continua (tDCS); tabaco; dejar de fumar.

INTRODUCTION

Addiction is defined as a chronic, repetitive disease or disorder characterized by a compulsive experience of drug use and pursuit, loss of inhibitory control, a significant increase in consumption, and the presence of both physical and psychological symptoms upon withdrawal from the drug (Koob and Volkow, 2016). Therefore, a person with this type of condition makes drugs their primary objective, prioritizing consumption over any interests or daily activities important for their survival or reproduction, persisting despite the harmful consequences for their physical and mental health.

In this way, addictive disorders represent a public health problem, leading to a high probability of diseases associated with chronic pain, poisoning, and/or overdose (Bahorik et al., 2017), as well as negative consequences across all dimensions of the individual's life. Additionally, substance use disorder (SUD) encompasses a variety of causal factors—genetic, neurobiological, psychological, economic, and social—that render it a heterogeneous psychiatric condition, altering important brain circuits involved in the regulation of behavior and cognitive processes (Abellaneda-Pérez, Lusilla-Palacios & Gual, 2023).

According to Koob and Schulkin (2019), addiction can be understood neurobiologically as a repeated cycle of three stages that activate brain circuits involved in salience processes, emotional states, and executive functions: 1) Intoxication/binge: drugs, when consumed, are inherently rewarding, producing reinforcing effects by activating neurocircuits such as the basal ganglia, which are responsible for releasing reward neurotransmitters, such as dopamine and opioid peptides; 2) Withdrawal/negative affect: upon cessation of drug use, a negative emotional state manifests, activated

by the extended amygdala and its projections to the hypothalamus and brainstem, which release corticotropins, norepinephrine, and dynorphins—neurotransmitters that play important roles in the negative reinforcement of behavior; 3) Craving: the main brain structures involved in the subjective effects caused by the drug are the cortex and allocortex, responsible for processing conditioned reinforcement (basolateral amygdala), contextual information (hippocampus), executive control (prefrontal cortex or PFC), and craving (orbital cortex, anterior cingulate cortex, temporal lobe, amygdala). Additionally, structures responsible for metacognitive functions (dorsolateral prefrontal cortex or DLPFC, dorsal anterior cingulate cortex or dACC, and inferior frontal gyrus or IFG), as well as those involved in the regulation of emotions, conditioning, and incentive allocation (ventromedial prefrontal cortex or vmPFC and medial orbitofrontal cortex or mOFC), and in automatic response tendencies and impulsivity (ventrolateral prefrontal cortex or vlPFC and lateral orbitofrontal cortex or lOFC), are also implicated (Nakamura-Palacios et al., 2021).

According to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) (American Psychiatric Association [APA], 2013), Tobacco Use Disorder (TUD) or smoking is defined as a chronic disorder characterized by the compulsive seeking and consumption of tobacco, which leads to limitations in self-control and changes in emotional state upon cessation of use. This disorder is manifested by various factors over a period of 12 months, including physical dependence (tolerance and withdrawal syndrome) and psychological dependence (craving). Smoking represents a global epidemic that threatens public health, with nearly 1.3 billion people consuming tobacco and more than 8 million deaths occurring annually, either from direct use or exposure to smoke (World Health Organization [WHO], 2023). According to the 2023 Report on Alcohol, Tobacco, and Illegal Drugs in Spain, in 2022, 70% of the population aged 15 to 64 years reported having used tobacco at some point in their lives, 39% in the past year, 37% in the past month, and 33% on a daily basis in the last month (Spanish Observatory of Drugs and Addictions [OEDA], 2023).

Nicotine is the primary active ingredient in tobacco, associated with various neurotransmitters released in the central nervous system (CNS), such as acetylcholine. The main effect of nicotine is the stimulation of nicotinic cholinergic receptors, which are found throughout the mesolimbic system. Additionally, it affects the noradrenergic, serotonergic, vasopressin, and glutamatergic systems, as well as the pituitary-adrenal axis (Leone et al., 2022). Similarly, nicotine influences dopaminergic systems by activating brain areas that constitute the reward system: the Ventral Tegmental Area (VTA), Nucleus Accumbens (NAcc), Prefrontal Cortex (PFC), hypothalamus, and amygdala, thereby reinforcing drug administration, as these areas are involved in motivation, memory, and learning. The increase in nicotinic receptors causes the brain to adapt to the regular use of the drug, leading to tolerance and helping to alleviate the discomfort caused by withdrawal syndrome (Corvalán, 2017).

Currently, there are various treatments available for quitting tobacco use, both pharmacological and non-pharmacological. When combined with the type and severity of dependence, as well as the individual's motivation, these treatments can bring significant benefits to health and quality of life (Espert-Tortajada, Rebull-Monje & Gadea-Doménech, 2021).

Non-pharmacological treatments aim to support and enhance the individual's process of quitting (Choi et al., 2021). These include: 1) Cognitive Behavioral Therapy (CBT): an approach that helps patients adapt by reinforcing motivation to abstain, learning coping techniques for risky situations, modifying conditioned reinforcing behaviors, promoting effective emotional management, and improving personal and social functioning; 2) Contingency Management: a procedure based on operant conditioning that reinforces and maintains abstinence by using rewards or incentives tailored to the individual; 3) Motivational Interviewing: a person-centered intervention designed to increase motivation to quit by focusing on inhibitory control, resolving ambivalence about change, and managing impulses and associated cues.

Regarding pharmacological treatments for tobacco use, which have shown evidence of effectiveness and safety (Giulietti et al., 2020), these include: 1) Nicotine Replacement Therapy (NRT): a treatment that provides non-combustible nicotine to alleviate withdrawal symptoms and cravings, available in forms such as gum, patches, inhalers, or lozenges; 2) Bupropion: a non-nicotinic agent that functions as an atypical antidepressant by inhibiting the reuptake of neurotransmitters like dopamine and norepinephrine, thereby reducing withdrawal and craving symptoms; 3) Varenicline: a partial nicotinic agonist that decreases withdrawal and craving symptoms while maintaining dopamine levels in the brain.

In addition to these common treatments, new therapeutic alternatives, such as neuromodulation techniques, are emerging, as they modify brain networks and enhance homeostatic functioning (Abellaneda-Pérez, Lusilla-Palacios & Gual, 2023). In the field of addictive disorders, non-invasive techniques include transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS).

tDCS is a noninvasive neuromodulation technique that uses electrodes to apply a small electrical charge (between 1 and 2 mA) to the scalp, modulating the resting membrane potential of cortical neurons in specific brain areas. It consists of two poles: 1) the cathode, which hyperpolarizes neurons and decreases cortical excitation; and 2) the anode, which depolarizes the threshold, increasing the firing rate of neurons and enhancing cortical excitability (Zhang et al., 2019).

In the treatment of addictive disorders, the primary purpose of tDCS is to enhance the activity of neural circuits associated with inhibitory control and craving, thereby modulating cortical excitability (Zhao et al., 2017) and reducing processes that increase the likelihood of addiction, such as physical and psychological dependence.

Recent scientific evidence indicates a growing interest in the use of tDCS as a therapeutic alternative, due to its non-invasive nature, low cost, and ease of application (Espert-Tortajada, Rebull-Monje & Gadea-Doménech, 2021). It has also been effectively utilized in neuropsychiatric conditions such as major depressive disorder (Razza et al., 2020), anxiety disorder (Chen et al., 2022), post-traumatic stress disorder (Gouveia et al., 2020), obsessive-compulsive disorder (Silva et al., 2021), and schizophrenia (Sun et al., 2021).

In the context of addictive behaviors, evidence has been found regarding the consumption of various substances, including cocaine, alcohol, nicotine, crack, methamphetamine, and cannabis (Lapenta et al., 2018; Lupin et

al., 2017). Specifically, concerning tobacco use, tDCS has been studied in relation to variables associated with craving, motivation to quit smoking, resistance to smoke, attention bias, and decision-making (Camacho-Conde et al., 2023).

Taking into account the heterogeneity in effect size evaluations from recent systematic reviews and meta-analyses, studies like those by Kang, Kim, and Kim (2019) demonstrate that tDCS can be a high-impact alternative for reducing smoking dependence symptoms and facilitating brain neuroplasticity. After applying stimulation to the DLPFC in 392 participants, they observed improvements in cognitive processes and a decrease in markers of nicotine addictive behavior, with significant changes in craving triggered by associated cues and a reduction in nicotine consumption rates.

Conversely, studies such as Lapenta et al. (2018) indicate a moderate effect size (0.476) from tDCS application on the DLPFC to diminish cravings, yet they highlight a notable lack of replicability across studies. This underscores the need for a broader approach to systematic investigations, incorporating double-blind trials and long-term follow-ups to better understand the stimulation parameters (Lupi et al., 2017).

This recent evidence regarding the efficacy of tDCS in tobacco consumption continues to generate significant scientific interest, prompting questions such as: What factors determine the effectiveness of tDCS as an alternative treatment for tobacco use? Therefore, the main objective of this systematic review is to provide an overview of the efficacy of tDCS interventions in tobacco consumption over the last 10 years (2014-2024).

METHODS

A systematic review was conducted to examine the most recent literature on the efficacy of transcranial direct current stimulation (tDCS) treatment in tobacco users. The PRISMA statement guidelines (Moher et al., 2009) for conducting systematic reviews were followed. The initial search was performed between November and December 2023 across three main databases: PubMed, Scopus, and ScienceDirect. The search combined the main terms "tDCS" and "drugs of abuse" to identify a greater number of studies. However, the results did not yield a significant number of relevant studies, prompting a shift to focus on legal drugs (alcohol and tobacco). Given the limited evaluation of consumption patterns associated with alcohol, the search was narrowed to studies exclusively addressing tobacco consumption. A definitive search was then conducted in April 2024 using the same databases. English was selected for the keyword search to maximize results, using Boolean connectors such as OR and AND, resulting in the following syntax: [("Transcranial direct current stimulation" OR tDCS) AND ("tobacco" OR "nicotine")]. This combination of terms, along with filters for study type (clinical trials), language (English and, where appropriate, Spanish), and the time range (2014-2024), yielded a substantial number of results.

The criteria for selecting studies were as follows:

Inclusion criteria: Empirical studies, including Randomized Clinical Trials (RCT) or Randomized Controlled Clinical Trials, published in English or Spanish, between 2014 and 2024 (both inclusive), with a population sample size of at least 15 participants (either

total or divided into subgroups). The studies had to involve tobacco or tobacco consumption treatment (TCT) and demonstrate considerable methodological quality, achieving at least a score of 5 on the PEDro scale and at least a score of 3 on the Jadad scale.

Exclusion criteria: Non-experimental studies, such as systematic reviews, narrative reviews, editorials, meta-analyses, case reports, intervention protocols, expert opinions, preclinical studies with non-human samples, pathophysiological studies, or other studies that were not RCTs or equivalent controlled clinical trials (ECCCs). Studies that combined pharmacological treatments with tDCS, had small sample sizes (fewer than 15 participants), involved substances other than tobacco or nicotine (such as alcohol, cocaine, crack, heroin, methamphetamine, cannabis, opioids), or included participants with physiological comorbidities, dual pathology, or behavioral addictions were also excluded. Additionally, studies that did not meet the methodological quality criteria on the PEDro (scores below 5) and Jadad (scores below 3) scales were excluded.

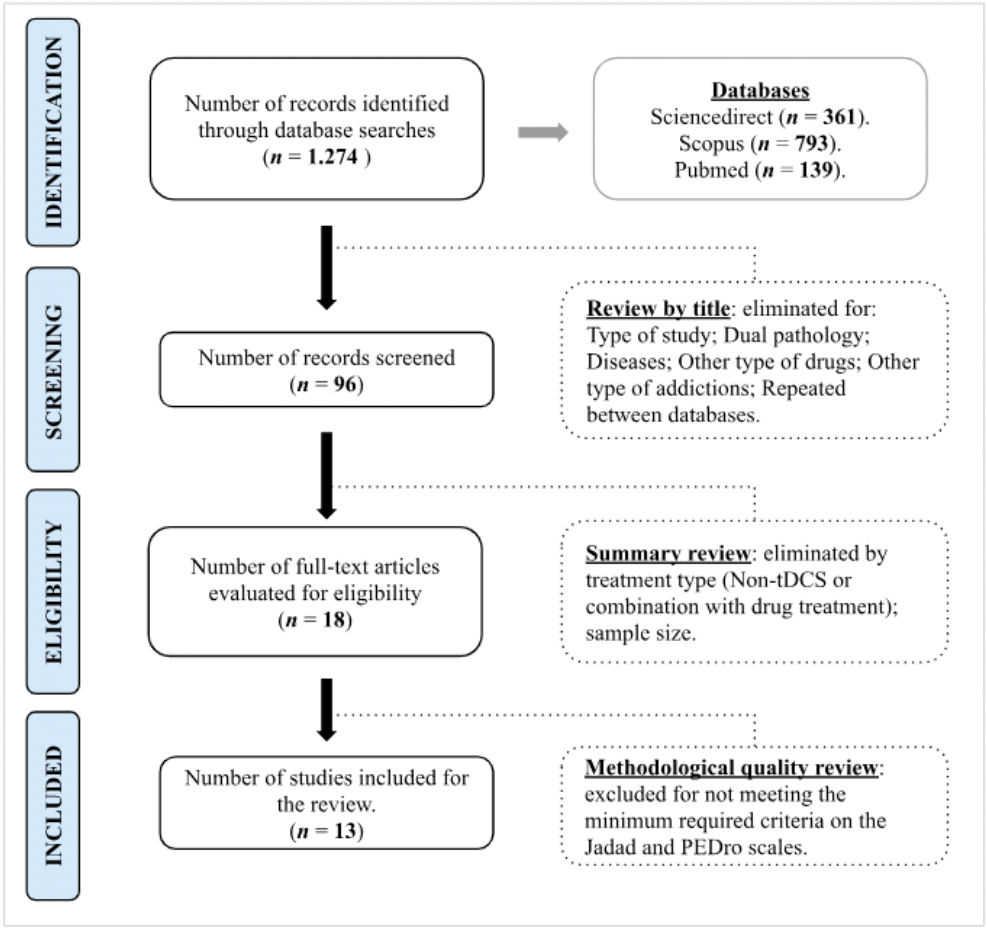
Selection Process

According to the flow diagram (Figure 1), the selection process was conducted in four stages: 1) Identification: the total number of results identified from the information gathered in each of the databases; 2) Screening: filtering of studies based on search criteria regarding title review; 3) Eligibility: further filtering of studies based on a more comprehensive review of abstracts; and 4) Inclusion: selection of studies for the review based on the assessment of methodological quality.

In the first stage of identification, the results obtained from each of the three selected databases for the study (Scopus, PubMed, and ScienceDirect) were recorded, yielding a total of 1,274 studies. Subsequently, in the screening phase, we reviewed the titles, applying the inclusion and exclusion criteria, resulting in a total of 96 results. Studies were discarded for being systematic reviews or meta-analyses of clinical trials, preclinical experimental studies (animal studies: rats, zebrafish), future projection protocols, dual pathology (having a mental disorder, such as depression and anxiety, in addition to tobacco use disorder), comorbid diseases such as schizophrenia, behavioral addictions (e.g., gambling, video game addiction, or food addiction), and other drugs besides tobacco or nicotine. Additionally, duplicate studies that appeared across the databases were removed. Following this, in the eligibility phase, we reviewed the abstracts, resulting in a total of 18 studies. Studies were excluded due to sample size (fewer than 15 participants) and treatment type (TMS and/or combinations with other treatments such as pharmacological ones). Thus, out of the 353 results found in the ScienceDirect database, 7 remained for review; in Scopus, 7 out of 767; and in PubMed, 4 out of 145 results found. Finally, to comply with the last phase regarding inclusion, the selected articles were evaluated for their methodological quality using two scales:

- Physiotherapy Evidence Database (PEDro) Scale: This tool assesses the methodological quality of clinical designs, such as physiotherapy interventions or clinical trials, used in systematic reviews to evaluate both internal and external validity of the studies, as well as the correct inclusion of statistical information (Maher et al., 2003). It consists of 11 items that serve as criteria for analyzing the methodological quality of each study. Each item is scored

Figure 1. PRISMA flow chart for the selection of the studies



dichotomously (1 point if the criterion is met, 0 if not), yielding a maximum score of 10 (noting that item 1 does not score as it measures external validity, and the minimum score is 0). Therefore, scores lower than 5 points in the evaluation criteria are considered to indicate low methodological quality and high risk of bias in the design, execution, and analysis of the data (Moseley et al., 2002). The assessment using the PEDro scale excluded 5 of the 18 studies reviewed in depth for scoring below 5 points. Most studies did not specify the processes related to blinding and randomization. Consequently, the 13 articles included in the review scored between 7 and 10 points.

- Jadad Scale: Also known as the Jadad score or the Oxford quality scoring system, this validated and user-friendly tool assesses the methodological quality of controlled clinical trials, measuring validity and reliability. It consists of 5 items that evaluate criteria in the form of questions related to the blinding of study interventions, random assignment of interventions, and accounting for losses during participant follow-up, addressing potential validity biases in controlled clinical trials, such as selection, performance, follow-up, and detection biases (Clark et al., 1999).

The total score is calculated by awarding 1 point for each criterion met (up to a total of 5 points); if not met, it receives 0 points, except for two questions confirming randomization and blinding, which may incur a negative score (-1 point). Therefore, a study is considered of high quality if it scores 3 points or higher. The evaluation results from the Jadad scale aligned with those of the PEDro scale, as 5 out of the 18 studies were excluded for failing to meet certain criteria, obtaining very low scores below 3 points, indicating that the studies were not double-blind or did not report the randomization process. In total, 13 articles were included in the review, with scores ranging from 3 to 5 points.

RESULTS

Through the detailed search strategy, 13 studies were reviewed, revealing an increase in empirical research regarding the use of tDCS in recent years, particularly in relation to various clinical phenomena, including the field of addictions, with a focus on the consumption of legal drugs, specifically tobacco.

The main objective of the 13 studies (see Table 1) primarily involved measuring, examining, or investigating the effects of tDCS stimulation on tobacco consumption. This included evaluating variables related to consumption patterns, such as the number of cigarettes consumed (Alghamdi et al., 2019; Falcone et al., 2016; Falcone et al., 2019; Meng et al., 2014; Mondino et al., 2018; Verveer et al., 2020a; Victor de Souza et al., 2018) and the latency to smoke (Falcone et al., 2016; Falcone et al., 2019). Additionally, they assessed variables such as exposure to cues associated with consumption (Kroczek et al., 2016; Meng et al., 2014; Mondino et al., 2018), craving or desire to consume (Hajloo et al., 2019; Kroczek et al., 2016; Mondino et al., 2018; Palm et al., 2023; Perri & Perrotta, 2021; Verveer et al., 2020a).

As a treatment for smoking cessation, variables such as the number of days abstinent or the abstinence rate were measured (Falcone et al., 2019; Palm et al., 2023; Victor de Souza et al., 2018). In addition, cognitive processes such as inhibitory control (Verveer et al., 2020b) and motivation to quit smoking (Verveer et al., 2020a; Victor de Souza et al., 2018) were also evaluated as modulators in specific brain areas (Fischell et al., 2020).

On the other hand, the methodological strategies implemented to evaluate both the use and maintenance of brain stimulation and modulation, as well as abstinence from tobacco consumption—through smoking cessation paradigms or brief interventions—highlight a variability in results. While some studies showed favorable outcomes (Falcone et al., 2016; Fischell et al., 2020; Hajloo et al., 2019; Meng et al., 2014; Mondino et al., 2018; Palm et al., 2023; Perri & Perrotta, 2021; Verveer et al., 2020a; Victor de Souza et al., 2018), other studies did not reveal any significant differences between their groups (Alghamdi et al., 2019; Falcone et al., 2019; Kroczek et al., 2016; Verveer et al., 2020b).

Table 1. General characteristics of the studies

Authors	Aim	Measure	Instruments	Methodology	Results
Alghamdi et al., 2019	Evaluate whether tDCS over the DLPFC modulate ciga-rette smoking in tobacco smokers.	Total number of cigarettes smoked.	Smoking diary; FTND; tDCS side effects question-naire.	Bilateral stimula-tion of DLPFC with tDCS.	No significant difference between active and sham tDCS.
Falcone et al., 2016	To examine the effects of tDCS on the ability to resist smoking.	Latency to smoke; total number of cigarettes smoked.	Exhaled CO reading; QSU-B; Smoking cessation paradigm; FTND; tDCS ad-verse effects ques-tionnaire.	tDCS stimulation in a smoking ces-sation para-digm.	Active tDCS significantly in-creased smoking latency and decreased the total number of cigarettes smoked.
Falcone et al., 2019	Test the effects of tDCS on smoking cessation for 7 days.	Number of days abstinent; Laten-cy to smoke; Number of cigarettes smoked.	FTND; Exhaled CO reading; Smoking cessation paradigm.	tDCS stimulation in a smoking ces-sation para-digm, in a supervised 7-day cessation period.	No evidence of effects of tDCS on maintenance of abstinence, and change in average number of ciga-rettes smoked per day during the quit period.
Fischell et al., 2020	To assess the impact of tDCS on trait and state aspects of smoking.	Smoking Ha-bit; Nicotine Status.	WASI; n-back task, Flanker, modified face-shape matching task; fMRI.	tDCS modula-tion in 3 brain networks: ECN; DMN; and SN.	tDCS has a main effect to partially alleviate large-scale network dys-function asso-ciated with DMN.
Hajloo et al., 2019	Investigate the effects of tDCS on smoking desire.	Craving.	DDQ.	tDCS stimulation on the bilateral DLPFC.	Active tDCS significantly reduced nicotine craving, also at follow-up.
Kroczek et al., 2016	To examine whether tDCS affects cortical hemodynam-ic indi-cators of functional connectivity, craving, and heart rate variability during cue-related exposure.	Craving;	FTND; fNIRs.	In vivo exposure to smoking cues supported by tDCS stimulation.	No significant difference in stimulation on craving and cue exposure. Active tDCS increased connectivity between the orbitofrontal and dorsolateral prefrontal cortex.
Meng et al., 2014	To examine the effects of FPT area inhibition on atten-tional bias to smoking-related cues and smoking behavior.	Attentional bias to smo-king cues; Number of cigarettes smoked.	TMS; tDCS sensa-tion questionnaire; Ciga-rette smoking Diary; eye tracking system.	Eye-tracking system to assess visual attention bias towards related cues, and measure the number of daily ciga-rettes consumed before and after tDCS treat-ment.	Bilateral cathodal stimulation of FPT areas significantly reduced attention to smoking-related cues and daily cigarette consumption the following day. Anodal stimulation in the left FPT and cathodal stimulation in the right did not reduce smoking behav-ior or attention to smoking cues.
Mondino et al., 2018	To investigate the effects of repeated tDCS sessions on smoking, craving, and brain reactivity to smoking cues..	Con-sumption; Craving to smoke; Bra-in reactivity to smoking cues.	Cigarette Diary; CO reading; BDI; Q-MAT; fMRI.	Repeated tDCS stimula-tion of the right dorsolat-eral cortex.	Active tDCS significantly reduced smoking craving and increased brain reacti-vity to smoking cues.

(Table continued on next page)

Authors	Aim	Measure	Instruments	Methodology	Results
Palm et al., 2023	To investigate the effects of tDCS as an adjunctive treatment to a standardized brief smoking cessation intervention.	Abstinence rate; Craving for cigarettes.	QSU; CRQ; Cigarette Diary; CO Reading; Specific Questionnaire for Withdrawal; FTND.	tDCS stimulation of the DLPFC and brief inter-vention for smoking cessation.	Active tDCS reduced the urge to smoke. No significant difference in smoking cessation rate between active and sham tDCS. No effect at follow-up.
Perri & Perrotta, 2021	Evaluate the role of multiple tDCS sessions on cigarette craving and consumption.	Craving; Ciga-rette consumption.	QSU-B; VAS; FTND; Q-MAT.	Bilateral tDCS stimulation of the DLPFC with right anode/left cathode.	Active tDCS decreased craving to smoke. No significant difference between active and sham tDCS in the number of cigarettes smoked.
Verveer et al., 2020a	Measure smoking behavior using EMA.	Number of cigarettes smoked; Craving to smoke; Positive affect.	FTND; CO reading; EMA.	Repeated bilateral tDCS stimulation of the right DLPFC.	Active tDCS had no effect on cigarette consumption, craving, and affect; and together with sham, it decreased the number of cigarettes smoked.
Verveer et al., 2020b	Evaluate the effects of tDCS on measures of cognitive control.	Inhibitory con-trol; Error processing.	FTND; CO reading; Go-NoGo Task; EMA; QSU; BSSS; BIS-BAS; RR.	Adaptive modulation of tDCS on smoking behav-ior.	No significant effect of active tDCS on behavioral and neurophysiologi-cal measures of cognitive control. However, there was a significant effect at follow-up.
Victor de Souza et al., 2018	To assess the direct effects of tDCS and motivation to quit smoking on average cigarette consumption.	Number of cigarettes smoked; Motiva-tion to quit smoking.	Smoking history questionnaire; FTND; VAS.	tDCS stimulation in the left DLPFC.	tDCS together with high motivation significantly reduced cigarette con-sumption.

FTND (Fagerström Test of Nicotine Dependence); DLPFC (Dorsolateral Prefrontal Cortex); CO (Carbon Monoxide); QSU-B (Smoking Urge Questionnaire – Short Form); WASI (Wechsler Abbreviated Scale of Intelligence); fMRI (Functional Magnetic Resonance Imaging); ECN (Executive Control Network); DMN (Default Mode Network); SN (Salience Network); FPT (Frontal-Parietal-Temporal Association Area); DDQ (Desires for Drug Questionnaire); fNIRs (Functional Near Infrared Spectroscopy); TMS (Transcranial Magnetic Stimulation); BDI (Beck Depression Index); Q-MAT (Smoking Quit Motivation Questionnaire); CRQ (Side Effects Questionnaire); VAS (Visual Analogue Scale); EMA (Ecological Momentary Assessment); BSSS (Brief Sensation Seeking Scale); BIS (Behavioral Inhibition Scale); BAS (Behavioral Activation Scale); RR (Response to Reward).

Regarding the characteristics of the participants (see Table 2), a total of 556 individuals (337 males and 219 females) participated in the research. Of these, 75%, or a total of 412, are smokers, categorized into mild (Verveer et al., 2020a; Verveer et al., 2020b), moderate, and severe risk levels (Falcone et al., 2019; Fischell et al., 2020; Hajloo et al., 2019; Kroczek et al., 2016; Meng et al., 2014; Perri & Perrotta, 2021; Victor de Souza et al., 2018). According to the WHO classification (2013), mild-risk consumers smoke fewer than 5 cigarettes a day, moderate consumers smoke between 6 and 15, and severe consumers smoke more than 16. Additionally, 20% of participants are diagnosed with tobacco consumption disorder (TCD) (Alghamdi et al., 2019; Falcone et al., 2016; Mondino et al., 2018; Palm et al., 2023), while the remaining 5% are non-smokers (Fischell et al., 2020).

In terms of demographic characteristics, there is heterogeneity among the studies regarding gender. Out of the 13 studies, 10 include both genders. Among these, women participate in greater numbers in 3 studies (Mondino et al., 2018; Palm et al., 2023; Victor de Souza et al., 2018), in fewer numbers in 4 studies (Falcone et al., 2016; Falcone et al., 2019; Kroczek et al., 2016; Perri & Perrotta, 2021), and in similar numbers in 3 studies (Fischell et al., 2020; Verveer et al., 2020a; Verveer et al., 2020b). In the remaining 3 studies, only men participated, representing almost 17% of the total population sample (Alghamdi et al., 2019).

Regarding motivation to quit smoking, 54% of the studies (6 out of 13) considered it (Alghamdi et al., 2019; Falcone et al., 2019; Hajloo et al., 2019; Meng et al., 2014; Mondino et al., 2018; Victor de Souza et al., 2018), while the remaining studies did not address this aspect (Falcone et al., 2016; Fischell et al., 2020; Kroczek et al., 2016; Palm et al., 2023; Perri & Perrotta, 2021; Verveer et al., 2020a; Verveer et al., 2020b).

As for age, participants range from 18 to 65 years. Specifically, in 8 studies, participants are between 20 and 30 years old (Alghamdi et al., 2019; Fischell et al., 2020; Hajloo et al., 2019; Kroczek et al., 2016; Meng et al., 2014; Perri & Perrotta, 2021; Verveer et al., 2020a; Verveer et al., 2020b), while in the other 5 studies, the population is over 40 years old (Falcone et al., 2016; Falcone et al., 2019; Mondino et al., 2018; Palm et al., 2023; Victor de Souza et al., 2018).

Table 2. Characteristics of the participants

Authors	Number	Level of consumption	Gender	Age	Motivation*
Alghamdi et al., 2019	22	TCT	M.	Range 19 to 29 years. Mean: 24,3; SD: 5,03.	Yes
Falcone et al., 2016	25	TCT	10 F y 15 M.	Range 18 to 60 years. Mean: 42,1; SD: 11,2.	No
Falcone et al., 2019	106	Smokers.	38 F y 68 M.	Range 18 to 60 years. Mean: 45,3; SD: 9,9.	Yes
Fischell et al., 2020	43	15 smokers and 28 non-smokers.	Smokers (7 F; 8 M), and non-smokers (14 F; 14 M).	Range 18 to 60 years. Smokers (Mean: 39,3; SD: 10,3) and non-smokers (Mean: 40,1; SD:12,0).	No
Hajloo et al., 2019	40	Daily and social smokers.	M	Range 18 to 30 years. Mean: 21,58; SD: 0,43.	Yes
Kroczek et al., 2016	25	Smokers	10 F y 15 M.	Mean: 25; SD: 5.	No
Meng et al., 2014	30	Smokers.	M	Mean: 23,7; SD:7,2	Yes
Mondino et al., 2018	29	TCT	20 F y 9 M.	Range 18 to 55 years. Mean: 41; SD: 9,1.	Yes.
Palm et al., 2023	36	TCT	22 F y 14 M.	Mean: 50,97; SD: 13,89.	No.
Perri & Perrotta, 2021	20	Smokers	5 F y 15 M.	Mean: 32,63; SD: 17,35.	No.
Verveer et al., 2020a	71	Smokers	36 F y 35 M.	Range 19 to 53 years. Mean: 22,3; SD: 4,7	No.
Verveer et al., 2020b	73	Smokers	36 F y 37 M.	Mean: 22,3; SD: 4,7.	No.
Víctor de Souza et al., 2018	36	Smokers	21 F y 15 M.	Range 18 to 65 years. Mean: 45; SD: 11.	Yes

TCT (Tobacco Use Disorders); M: male; F: female; SD: Standard Deviation; (*) Motivation to quit smoking.

Regarding the tDCS implementation protocol (see Table 3), all reviewed studies were randomized, double-blind, and controlled. They included comparisons between active groups (direct current stimulation of specific brain areas) and sham conditions (placebo conditions that mimic the active stimulation by providing similar skin sensations), ensuring minimal or no differences between participants. The duration of the intervention varied depending on the number of sessions implemented. Some studies conducted sessions on consecutive days (Alghamdi et al., 2019; Falcone et al., 2016; Fischell et al., 2020; Kroczek et al., 2016; Mondino et al., 2018; Perri & Perrotta, 2021; Victor de Souza et al., 2018), while others held sessions on strategic days (Falcone et al., 2019; Palm et al., 2023) or conducted two daily sessions (Hajloo et al., 2019; Meng et al., 2014; Verveer et al., 2020a; Verveer et al., 2020b).

In terms of session characteristics, the number and duration showed heterogeneous results. This included a single session of 15 minutes (Kroczek et al., 2016), two or three sessions lasting between 20 minutes (Alghamdi et al., 2019; Falcone et al., 2016; Falcone et al., 2019; Meng et al., 2014) and 25 minutes (Fischell et al., 2020), five or six sessions lasting between 13 minutes (Verveer et al., 2020a; Verveer et al., 2020b) and 20 minutes (Palm et al., 2023; Perri & Perrotta, 2021; Victor de Souza et al., 2018), and up to ten sessions of 20 minutes each (Hajloo et al., 2019; Mondino et al., 2018).

Regarding the stimulated area, all studies examined stimulation at intensities ranging from 1 to 2 mA in the bilateral DLPFC (Alghamdi et al., 2019; Hajloo et al., 2019; Perri & Perrotta, 2021), the left DLPFC (Falcone et al., 2016; Falcone et al., 2019; Fischell et al., 2020; Kroczek et al., 2016; Palm et al., 2023; Victor de Souza et al., 2018), or the right DLPFC (Mondino et al., 2018; Verveer et al., 2020a; Verveer et al., 2020b). The only exception was Meng et al. (2014), who chose to stimulate the bilateral FPT cortex, justified as an area related to attention bias toward cues associated with smoking behavior.

Finally, regarding the long-term effects, 8 of the 13 studies conducted follow-up assessments after the tDCS intervention, with most choosing to do so one or more months later (Alghamdi et al., 2019; Hajloo et al., 2019; Mondino et al., 2018; Palm et al., 2023; Verveer et al., 2020a; Verveer et al., 2020b) or weeks later (Falcone et al., 2019; Victor de Souza et al., 2018).

DISCUSSION

The present systematic review aims to examine the effectiveness of tDCS in tobacco use in the scientific literature (RCTs or RCCTs published in the last ten years). We found heterogeneity among the results (see Table 4), since it varies depending on the variable evaluated (consumption pattern, craving to smoke, associated cues, abstinence or motivation) and the characteristics of the tDCS protocol (stimulation parameters, stimulated area, number and frequency of sessions, study population or follow-up); thus, the effectiveness may vary.

Effects of tDCS on smoking patterns

According to the scientific literature, previous research has evaluated the effectiveness of tDCS on smoking patterns (Facteau et al., 2014; Muller et al., 2021; Qin et al., 2023); however, the conditions of the studies regard-

Table 3. Characteristics of the tDCS protocol of the studies

Authors	Groups	Duration	Sessions	Stimulated zone	Intensity	follow-up
Alghamdi et al., 2019	Active (***n*** = 12); Sham (***n*** = 10).	3 days.	***Nº***: 3. ***Time***: 20 minutes.	Bilateral DLPFC. ***Electrode position***: right at F4 (cathode) and F3 (return electrode).	***Active***: 1.5 mA; ***Sham***:10 sec ramp at the start and end of session. ***Stimulator***: StarStim 8 (NE Neuroelectrics, Barcelona, Spain).	4 months.
Falcone et al., 2016	Active and sham.	2 days.	***Nº***: 2. ***Time***: 20 minutes.	Left DLPFC. ***Electrode position***: F3 (anode) and FP2 (cathode).	***Active***: 1 mA; ***Sham***: 1,0 mA during the first 30 sec. ***Stimulator***: DC Magstim Eldith 1 channel Plus.	No.
Falcone et al., 2019	tDCS 1 mA (***n*** = 35); tDCS 2 mA (***n*** = 36); tDCS sham (***n*** = 35).	3 days.	***Nº***: 3. ***Time***: 20 minutes.	Left DLPFC. ***Electrode position***: F3 (anode) and FP2 (cathode).	***Active***: 1 mA and 2 mA; ***Sham***: 2 mA 30 sec at start and end of session. ***Stimulator***: NeuroConn DC-Stimulator Plus.	4 visits (days 6, 8, 10 and 12).
Fischell et al., 2020	tDCS An-dlPFC; tDCS An-vmPFC; sham.	2 days.	***Nº***: 3. ***Time***: 25 minutes.	Left DLPFC. ***Electrode position***: (L) dlPFC (anode) and (R) vmPFC (cathode).	***Active***: 2 mA; ***Sham***: impedance reading. ***Stimulator***: NeuroConn DC-Stimulator Plus-MR; neuroCare, Munich, Germany.	No
Hajloo et al., 2019	Active (***n*** = 20); Sham (***n*** = 20).	5 weeks.	***Nº***: 10. ***Time***: 20 minutes.	Bilateral DLPFC. ***Electrode position***: F3 (left anode) and F4 (right cathode).	***Active***: 2 mA; ***Sham***: not applied. ***Stimulator***: Not specified.	1 month.
Kroczek et al., 2016	Active (***n*** = 13); Sham (***n*** = 12).	20 minutes.	***Nº***: 1. ***Time***: 15 minutes.	Left DLPFC. ***Electrode position***: F3 (anode) and Fp2 (cathode).	***Active***: 2 mA; ***Sham***: impedance reading. ***Stimulator***: NeuroConn GmbH, Ilmenau, Germany.	No
Meng et al., 2014	Single cathode (***n*** = 10); Double cathode (***n*** = 10); Sham (***n*** = 10).	1 day.	***Nº***: 3. ***Time***: 20 minutes.	FPT bilateral. ***Electrode position***: left (anode) and right (cathode); FPT (double cathode); and LO (double anode).	***Active***: 1 mA; ***Sham***: impedance reading. ***Stimulator***: Not specified.	No
Mondino et al., 2018	Active (***n*** = 17); Sham (***n*** = 12).	5 days.	***Nº***: 10. ***Time***: 20 minutes.	Right DLPFC. ***Electrode position***: F4 (anode), and on LO left on Fp2 (cathode).	***Active***: 2 mA; ***Sham***: 2 mA first 40 sec. ***Stimulator***: Eldith DC (NeuroConn, GmbH, Germany).	1 month.
Palm et al., 2023	Active (***n*** = 17); Sham (***n*** = 17).	9 days.	***Nº***: 5. ***Time***: 20 minutes.	Left DLPFC. ***Electrode position***: F3 (anode) and Fp2 (cathode).	***Active***: 2 mA; ***Sham***: 20 minutes shutdown interval at the start and end of the session. ***Stimulator***: Eldith DC (neuroConn GmbH, Ilmenau, Germany).	3 months.
Perri & Perrotta, 2021	Active (***n*** = 10); Sham (***n*** = 10).	5 days.	***Nº***: 5. ***Time***: 20 minutes.	Bilateral DLPFC. ***Electrode position***: F4 (right anode) and F3 (left cathode).	***Active***: 2 mA; ***Sham***: 2 mA first 10 sec. ***Stimulator***: BrainStim (EMS srl, Bolonia, Italia).	No.

(Table continued on next page)

Authors	Groups	Duration	Sessions	Stimulated zone	Intensity	follow-up
Verveer et al., 2020a	Active (***n*** = 35); Sham (***n*** = 36).	3 days.	***Nº***: 6. ***Time:*** 13 minutes.	Right DLPFC. ***Electrode position***: F4 (anode) and F3 (cathode).	***Active***: 2 mA; ***Sham***: 2 mA first 30 sec. ***Stimulator***: DC-plus (NeuroConn, Ilmenau, Germany).	3 months.
Verveer et al., 2020b	Active (***n*** = 34); Sham (***n*** = 35).	3 days.	***Nº***: 6. ***Time***: 13 minutes.	Right DLPFC. ***Electrode position***: F4 (anode) and F3 (cathode).	***Active***: 2 mA; ***Sham***: 2 mA 30 sec at start and end of session. ***Stimulator***: DC-plus (NeuroConn, Ilmenau, Germany).	3 months.
Víctor de Souza et al., 2018	Active (***n*** = 19); Sham (***n*** = 17).	5 days.	***Nº***: 5. ***Time***: 20 minutes.	Left DLPFC. ***Electrode position***: F3 (anode) and right supraorbital area (cathode).	***Active***: 1 mA; ***Sham***: simulated mode. ***Stimulator***: Not specified.	1 and 4 weeks

Nº: Number; DLPFC (Dorsolateral prefrontal cortex); FPT (Frontal-parietal-temporal association area); LO (Occipital lobe); (L) dlPFC (Left dorsolateral prefrontal cortex); (R) vmPFC (Right ventromedial prefrontal cortex); mA: milliamperes.

ing their internal validity, as well as the parameters of the protocol used or the sample size, mean that their findings do not have the appropriate relevance. These investigations have associated the modulation of brain circuits that are involved in smoking behavior, such as the DLPFC, a cortex responsible for regulating cognitive processes, for example, social and behavioral control, decision-making, and planning (Mostafavi et al., 2020), as a strategy to prevent addictive behavior. However, the recent results found in this review evaluate the tobacco consumption patterns; in their findings, they do not find significant differences. Alghamdi et al. (2019), when evaluating the effect of three repeated sessions of tDCS in the bilateral DLPFC and a 4-month follow-up in adults with TCT, found no difference between the active and sham tDCS groups, as cigarette consumption was reduced in both. Similarly, Verveer et al. (2020a), in an exploratory study to reduce smoking by stimulating the right DLPFC with tDCS in six sessions (on three different days), in low-risk smokers, used a different methodology (ecological momentary assessments or EMA), which allows the variables to be measured ecologically, taking into account the person's mood and context, and avoiding biases from retrospective memories; they found no difference in cigarette consumption and craving to smoke between the groups. For their part, Verveer et al. (2020b) assessed the neurophysiological and behavioral effects of anodal tDCS on the right DLPFC, using measures of cognitive control (inhibitory control and error processing), which are important for the maintenance of addictive behavior, as well as the duration of such effects. The results did not show significant evidence in the early processes of both inhibitory control and error processing in the groups of smokers. However, positive findings were observed in inhibitory control during the follow-up three months later, since, in active tDCS, a decrease in P3 amplitudes in images linked to smoking was evident after the tDCS sessions, according to the tests on inhibitory control (Go No Go), and it was also associated with faster reaction times compared to sham tDCS. They conclude that the delayed result in the

follow-up indicates a long-term learning effect on the inhibition of motor responses to cues that attract motivational attention to smoking cues, and not a specific improvement, as stated in the studies by Deweese et al. (2018) and Piasecki et al. (2017). From another point of view, other studies have chosen to stimulate other brain areas involved in the same direction. Meng et al. (2014) demonstrated a reduction in attention to cues associated with nicotine consumption and daily cigarette consumption the following day in a single session of bilateral cathodal stimulation in the frontal-parietal-temporal (FPT) area. Likewise, in double cathodal stimulation, they showed a positive correlation between changes in visual attention and cigarette consumption, indicating the possibility that tDCS reduces the need to smoke and, in turn, prevents consumption. On the other hand, Kroczek et al. (2016), when measuring prefrontal hemodynamics, found an increase in connectivity between DLPFC—important in inhibitory control of automatic responses—and OFC—which is in charge of processing the reinforcing value of a stimulus—in smokers during exposure to smoking cues, thus demonstrating that tDCS stimulation between these two brain areas associated with addiction causes hemodynamic coupling during exposure to smoking cues.

Effects of tDCS on smoking craving

Unlike the consumption pattern, the effectiveness of tDCS on smoking craving is consistent with the scientific literature, with the DLPFC being the protagonist as the most frequently used stimulation area, as it is also responsible for mediating desire, regulating the reward system (Volkow et al., 2017), inhibition (Metzuyanim-Gorlick & Mashal, 2016), and emotional control (Perri et al., 2014). According to the results in this review, the number of sessions available for stimulation reinforces the controversy over the effectiveness of tDCS, since while Meng et al. (2014) found positive results in the consumption pattern and smoking craving in a single session, the research by Kroczek et al. (2016), who measured craving and heart rate variability in a single session by stimulating the DLPFC (left anode) and OFC (cathode) in smokers, found no significant evidence of craving or change in heart rate when exposed to associated signals between the active and sham tDCS groups. However, research that opted to conduct more sessions managed to find favorable findings. Mondino et al. (2018) evaluated the effects of tDCS on smoking, desire, and brain activity in ten repeated sessions (two per day) with a one-month follow-up in adults with TCT. They showed that when evaluating craving between active and sham tDCS, a decrease in the desire to smoke was observed after the active sessions compared to the sham sessions, although there was no cumulative effect between sessions. Similarly, active tDCS resulted in increased brain reactivity to smoking-associated cues before and after sessions compared to sham tDCS. These brain areas are associated with the posterior cingulate cortex (PCC), which plays an important role in intrinsic control and craving resistance networks. Meanwhile, Hajloo et al. (2019) investigated the effects of ten sessions of tDCS on the bilateral DLPFC to examine smoking craving in everyday and social smokers and demonstrated significant findings by evidencing a decrease in craving and the number of cigarettes consumed after active tDCS stimulation and during follow-up one month later. Likewise, Perri & Perrotta (2021) tested the efficacy of five sessions of tDCS on the DLPFC in smokers not motivated to quit smoking. The findings showed a reduction in smoking craving by 47%.

Effects of tDCS and motivation to quit smoking

Regarding the effects on smoking cessation, rather than the number and frequency of sessions, recent review results show that motivation is a factor that could be important to achieve satisfactory results in the efficacy of tDCS (Jones, Gözenman & Berryhill, 2015). The study by Victor de Souza et al. (2018) confirmed positive effects of tDCS on cigarette smoking, influenced by motivation to quit smoking. They observed that active tDCS over the left DLPFC, compared to sham, showed a significant reduction in the number of cigarettes consumed during the follow-up four weeks later in smokers with an above-average smoking pattern, i.e., more than seven cigarettes per day. The authors argue that the interaction between the effects of tDCS and motivation may be mediated by the cognitive functioning of the participants, since those who had higher levels of motivation from the beginning of the intervention were those who showed a greater reduction in cigarette consumption, unlike those who had less motivation to quit smoking. However, some studies found positive findings in non-motivated populations. Falcone et al. (2016), in a crossover study, demonstrated a significant effect of two sessions (one active and one sham) of anodal tDCS in the left DLPFC on the ability to resist smoking in the presence of smoking cues in vivo, since their findings showed an increase in the latency to smoke, delaying consumption by nine minutes, as well as a 17% decrease in cigarette intake in a validated model of smoking lapse in a session of active tDCS. For their part, Fischell et al. (2020) decided to stimulate the DLPFC (left anode) and vmPFC (right cathode) in three sessions, important areas for the performance of cognitive tasks, and three brain networks (Executive Control Network or ECN; Default Mode Network or DMN; Salience Network or SN), comparing smokers with no motivation to quit smoking and non-smokers. Their findings suggest that tDCS stimulation can modify the dysregulation of cognitive control circuits involved in nicotine withdrawal syndrome, since they showed an improvement in the suppression of the DMN network during a working memory task and activation in the SN network during an error monitoring task. This indicates that stimulation can prevent the cognitive and affective alterations produced by withdrawal syndrome, which in turn predicts the prevention of smoking relapses. Regarding this, Palm et al. (2023) used tDCS stimulation in the DLPFC (five sessions) combined with a brief smoking cessation intervention to assess the effects on quit rate and urge to smoke in adults with TCT who had no intention to quit. The findings indicated that active versus sham tDCS decreased urge to smoke but found no significant differences in quit rate or long-term effects over three months of follow-up. This latest study calls into question whether the motivation factor plays a crucial role for the effectiveness of tDCS as a treatment, as Falcone et al. (2019) contradicted the study by Falcone et al. (2016) by stimulating the same brain area, the left DLPFC (anodal electrode over F3, cathodal over the contralateral supraorbital area), increasing the sample size (n = 106; 38 M and 68 F), with similar mean ages (mean 45.3 years; SD: 9.9), and adding one session of active tDCS (1 mA tDCS; 2 mA tDCS; sham tDCS). The results concluded that three sessions were not sufficient as a treatment to quit smoking over a period of seven days, showing no significant evidence in the number of cigarettes smoked per day or the ability to remain abstinent during a validated smoking lapse paradigm in motivated smokers.

Table 4. Summary of the studies.

Authors	Subjects	Methodology			Results
		Instruments	tDCS	follow-up	
Alghamdi et al., 2019	***Participants:*** 22 smokers with TCT. ***Age:*** Range 19 to 29 years; Mean 24,3; SD: 5.03. ***Gender:*** M.	Smoking diary; FTND; tDCS side effects questionnaire.	***Groups:*** Active (*n* = 12) and Sham (*n* = 10). ***N° sessions:*** 3. ***Session duration:*** 20 minutes. ***Treatment duration:*** 3 consecutive days. ***Stimulated zone:*** DLPFC. ***Electrode position:*** F3 (anode) and F4 (cathode). ***Intensity:*** 1.5 mA.	4 months	No significant difference between active and sham tDCS.
Falcone et al., 2016	***Participants:*** 25 smokers with TCT. ***Age:*** Range 18 to 60 years; Mean 42,1; SD: 11,2. ***Gender:*** 10 F and 15 M.	CO reading; QSU-B; FTND; tDCS adverse effects questionnaire.	***Groups:*** Active and Sham. ***N° sessions:*** 2. ***Session duration:*** 20 minutes. ***Treatment duration:*** 2 days. ***Stimulated zone:*** Left DLPFC. ***Electrode position:*** F3 (anode) and in the right supraorbital area (cathode). ***Intensity:*** 1 mA.	No	Active tDCS significantly increased smoking latency and decreased the total number of cigarettes smoked.
Falcone et al., 2019	***Participants:*** 106 smokers. ***Age:*** Range of 18 to 60 years. Mean 45,3; SD: 9,9. ***Gender:*** 38 F and 68 M.	FTND; Exhaled CO reading.	***Groups:*** **1)** tDCS 1 mA (*n* = 35); **2)** tDCS 2 mA (*n* = 36); **3)** tDCS sham (*n* = 35). ***N° sessions:*** 3. ***Session duration:*** 20 minutes. ***Treatment duration:*** 1 week. 3 stimulation days (days 1, 3, 5). ***Stimulated zone:*** Left DLPFC. ***Electrode position:*** F3 (anode) and in the right supraorbital area (cathode). ***Intensity:*** 1 mA and 2 mA.	4 visits (days 6, 8, 10 and 12)	No evidence of effects of tDCS on maintenance of abstinence, and change in average number of cigarettes smoked per day during the quit period.
Fischell et al., 2020	***Participants:*** 43 (15 smokers and 28 non-smokers). ***Age:*** Range from 18 to 60 years. Smokers (Mean: 39,3; SD: 10,3) and non-smokers (Mean: 40,1; SD:12). ***Gender:*** Smokers (7 F and 8 M) and non-smokers (14 F and 14 M).	WASI; n-back task, Flanker, modified face-shape matching task; fMRI.	***Groups*****: 1)** tDCS An-dlPFC; **2)** tDCS An-vmPFC; **3)** Sham**.** ***N° sessions:*** 3. ***Session duration:*** 25 minutes. ***Treatment duration:*** 2 days. ***Stimulated zone:*** Left DLPFC. ***Electrode position:*** (L) dlPFC (anode) and (R) vmPFC (cathode). ***Intensity:*** 2 mA.	No	tDCS has a main effect to partially alleviate large-scale network dysfunction associated with DMN.
Hajloo et al., 2019	***Participants:***40 daily and social smokers. ***Age:*** Range 18 to 30 years. Mean: 21,58; SD: 0,43. ***Gender:*** M.	DDQ.	***Groups:*** Active (*n* = 20) and Sham (*n* = 20). ***N° sessions:*** 10. ***Session duration:*** 20 minutes. ***Treatment duration:*** 5 weeks. ***Stimulated zone:*** Bilateral DLPFC. ***Electrode position:*** F3 (left anode) and F4 (right cathode). ***Intensity:*** 2 mA.	1 month.	Active tDCS significantly reduced nicotine craving, also at follow-up.

(Table continued on next page)

Authors	Subjects	Methodology			Results
		Instruments	tDCS	follow-up	
Kroczek et al., 2016	***Participants:*** 25 smokers. ***Age:*** Mean 25; SD: 5. ***Gender:*** 10 F and 15 M.	FTND; fNIRs.	***Groups:*** Active (*n* = 13) and Sham (*n* = 12). ***N° sessions:*** 1. ***Session duration:*** 15 minutes. ***Treatment duration:*** 20 minutes. ***Stimulated zone:*** DLPFC. ***Electrode position:*** F3 (anode) and Fp2 (cathode). ***Intensity:*** 2 mA.	No	No significant difference in stimulation on craving and cue exposure. Active tDCS increased connectivity between the orbitofrontal and dorsolateral prefrontal cortex.
Meng et al., 2014	***Participants:*** 30 smokers. ***Age:*** Mean 23,7; SD:7,2 ***Gender:*** M.	TMS; tDCS sensation questionnaire; Cigarette smoking diary; eye tracking system.	***Groups: 1)*** single cathodic stimulation (***n*** = 10); **2)** double cathodic stimulation (***n*** = 10); **3)** sham (***n*** = 10). ***N° sessions:*** 3. ***Session duration:*** 20 minutes. ***Treatment duration:*** 1 day. ***Stimulated zone:*** FPT. ***Electrode position:*** **1)** left (anode) and right (cathode). **2)** FPT (double cathode) and LO (double anode). ***Intensity:*** 1 mA.	No	Bilateral cathodal stimulation of FPT areas significantly reduced attention to smoking-related cues and daily cigarette consumption the following day. Anodal stimulation in the left FPT and cathodal stimulation in the right did not reduce smoking behavior or attention to smoking cues.
Mondino et al., 2018	***Participants:*** 29 smokers with TCT. ***Age:*** Range 18 to 55 years; Mean 41; SD: 9,1. ***Gender:*** 20 F and 9 M.	Cigarette diary; CO reading; BDI; Q-MAT; fMRI.	***Groups:*** Active (n = 17) or sham (n = 12). ***N° sessions:*** 10. ***Session duration:*** 2 sessions each day for 5 consecutive days. ***Treatment duration:*** 20 minutes. ***Stimulated zone:*** Right DLPFC. ***Electrode position:*** F3 (anode) and Fp2 (cathode). ***Intensity:*** 2 mA.	1 month.	Active tDCS significantly reduced smoking craving and increased brain reactivity to smoking cues.
Palm et al., 2023	***Participants:*** 34 smokers with TCT. ***Age:*** Mean 50,97; SD: 13,89. ***Gender:*** 22 F and 14 M.	QSU; CRQ; Cigarette diary; CO reading; Quit smoking cessation questionnaire; Saliva cotinine test; FTND.	***Groups:*** Active (*n* = 17) and Sham (*n* = 17). ***N° sessions:*** 5. ***Session duration:*** 20 minutes. ***Treatment duration:*** 9 days. ***Stimulated zone:*** Left DLPFC. ***Electrode position:*** F3 (anode) and Fp2 (cathode). ***Intensity:*** 2 mA.	3 months.	Active tDCS reduced the urge to smoke. No significant difference in smoking cessation rate between active and sham tDCS. No effect at follow-up.

(Table continued on next page)

Authors	Subjects	Methodology			Results
		Instruments	tDCS	follow-up	
Perri & Perrotta, 2021	***Participants:*** 20 smokers. ***Age:*** Mean 32,63; SD: 17,35. ***Gender:*** 5 F and 15 M.	QSU-Brief; EVA; FTND; Q-MAT.	***Groups:*** Active (*n* = 10) and Sham (*n* = 10). ***Nº sessions:*** 5. ***Session duration:*** 20 minutes. ***Treatment duration:*** 5 days. ***Stimulated zone:*** Bilateral DLPFC. ***Electrode position:*** F4 (right anode) and F3 (left cathode). ***Intensity:*** 2mA.	No.	Active tDCS decreased craving to smoke. No significant difference between active and sham tDCS in the number of cigarettes smoked.
Verveer et al., 2020a	***Participants:*** 71 smokers. ***Age:*** Range: 19 to 53 years. Mean: 22,3; SD: 4.7. ***Gender:*** 36 F and 35 M.	FTND; CO Reading; EMA.	***Groups:*** Active (*n* = 35) and Sham (*n* = 36). ***Nº sessions:*** 6. ***Session duration:*** 13 minutes. ***Treatment duration:*** 3 days in a week. ***Stimulated zone:*** Right DLPFC. ***Electrode position:*** F4 (anode) and F3 (cathode). ***Intensity:*** 2 mA.	3 months.	Active tDCS had no effect on cigarette consumption, craving, and affect; and together with sham, it decreased the number of cigarettes smoked.
Verveer et al., 2020b	***Participants:*** 69 smokers. ***Age:*** Mean 22,3; SD: 4,7. ***Gender:*** 36 F and 37 M.	FTND; CO Reading; Go-NoGo Task; EMA; QSU; BSSS; BIS-BAS Scales, plus RR Ability.	***Groups:*** Active (*n* = 34) and Sham (*n* = 35). ***Nº sessions:*** 6. ***Session duration:*** 13 minutes. ***Treatment duration:*** 3 days in a week. ***Stimulated zone:*** Right DLPFC. ***Electrode position:*** F4 (anode) and F3 (cathode). ***Intensity:*** 2 mA.	3 months.	No significant effect of active tDCS on behavioral and neurophysiological measures of cognitive control. However, there was a significant effect at follow-up.
Víctor de Souza et al., 2018	***Participants:*** 36 smokers. ***Age:*** Range 18 to 65 years. Mean 45 years; SD: 11. ***Gender:*** 21 F and 15 M.	Smoking History Questionnaire; FTND; VAS.	***Groups:*** Active (*n* = 19) and sham (*n* = 17). ***Nº sessions:*** 5. ***Session duration:*** 20 minutes. ***Treatment duration:*** 5 days. ***Stimulated zone:*** Left DLPFC. ***Electrode position:*** F3 (anode) and in the right supraorbital area (cathode). ***Intensity:*** 1 mA.	1 and 4 weeks	tDCS together with high motivation significantly reduced cigarette consumption.

TCT (Tobacco Use Disorders); F: female; M: male; DLPFC (Dorsolateral prefrontal cortex); FPT (Frontal-parietal-temporal association area); LO (occipital lobe); (L) dlPFC (left dorsolateral prefrontal cortex); (R) vmPFC (right ventromedial prefrontal cortex); FTND (Fagerström test for nicotine dependence); EMA (Ecological Momentary Assessments); QSU (Smoking Urges Questionnaire); BSSS (Brief Sensation Seeking Scale); RR (Response to Reward); VAS (Visual Analogue Scale); CRQ (Side Effects Questionnaire); BDI (Beck Depression Index); Q-MAT (Motivation to Quit Smoking Questionnaire); fMRI (Functional Magnetic Resonance Imaging); DDQ (Drug Craving Questionnaire); WASI (Wechsler Abbreviated Scale of Intelligence); BIS (Behavioral Inhibition Scale); BAS (Behavioral Activation Scales); fNIRs (Functional Near Infrared Spectroscopy); TMS (Transcranial Magnetic Stimulation); CO (Carbon Monoxide).

CONCLUSIONS AND FUTURE PROJECTIONS

Taking into account the findings of the studies in this review, it is possible to highlight aspects that may be promising for future research to address tobacco use. In relation to the consumption pattern, it is interesting to delve deeper into tDCS stimulation in fronto-parieto-temporal areas involved in cognitive control, since it is made up of some structures such as the insula, the hippocampus, and the DLPFC, which are important in reducing addictive behavior related to tobacco (Goldstein & Volkow, 2002). Although the research by Meng et al. (2014) achieved favorable results in bilateral stimulation of FPT, when applying anodal stimulation in the left FPT and cathodal stimulation in the right, a reduction in smoking behavior and attention to smoking signals was not obtained, leaving an unknown to be resolved. Likewise, it was a study that was conducted only on men, so it is necessary to highlight the importance of including sex differences in the studies, since according to the 2023 Report on alcohol, tobacco, and illegal drugs in Spain, in 2022 women represented 42.8% of the population aged 15 to 64 who have consumed tobacco daily (OEDA, 2023). In addition, in the research by Kroczek et al. (2016), connectivity was demonstrated in the DLPFC and OFC, giving rise to future research to investigate the neural bases as mechanisms underlying the prevention of relapses in TUS, since they could facilitate prefrontal stimulation protocols as alternative neurobiological treatments that complement other standard treatments used for addictions. Regarding the craving to smoke, the heterogeneity of the results calls into question two factors: the parameters of stimulation in the DLPFC and the number of sessions. In the first factor, three of the studies that obtained favorable results stimulated the DLPFC using different montages, while Perri & Perrotta (2021) stimulated the brain area bilaterally, placing F4 (right anode) and F3 (left cathode); Hajloo et al. (2019) preferred to change the position of the electrodes, leaving F3 (left anode) and F4 (right cathode); and Mondino et al. (2018) chose to stimulate the left occipital region in Fp2 with the anode at F4 and the cathode at F3. These results demonstrate that the appropriate electrode montage in tDCS intervention has not yet been defined. In the second factor, the number of sessions has generated debate among researchers, since the results do not only depend on this factor. On the other hand, the results examined in this review related to craving show that the multiplicity and frequency of sessions could bring beneficial effects; however, this cannot be confirmed. Regarding the role of motivation in the effectiveness of tDCS to treat tobacco use, it plays an interesting role that could continue to impact the results of future research, agreeing with Fischell et al. (2020) and Victor de Souza et al. (2018) in using tDCS as an alternative therapy that supports other standard treatments used for nicotine use, allowing for personalized treatments that adjust to the level of motivation of smokers. That said, although tDCS shows potential as a treatment for tobacco use, it is essential to continue with detailed and diversified research to optimize its effectiveness and practical application in drug addiction care centers. An example of this is the recent study by Rebull-Monje et al. (2024a), which showed a reduction in tobacco consumption and an improvement in nicotine dependence, motivation, and perceived self-efficacy to quit smoking when evaluating the effects of repeated sessions of tDCS (at 1.5 mA for 20 minutes on the DLPFC: cathode F3 and anode F4) on the consumption pattern, motivation, and perceived self-efficacy to quit smoking in

16 people with TCT using a time series design proposal with four phases A-B-A-B (A: two baselines and B: two treatment phases) and intra-subject replication, a methodology that ensures the verification of behavioral change more effectively. Therefore, although further studies are required to continue investigating the effectiveness of tDCS, it is a technique that may be useful as a complementary therapy. Another recent study that has demonstrated the effectiveness of tDCS treatment and, therefore, expanded future research is the article by Rebull-Monje et al. (2024b), which achieved a significant decrease in daily tobacco consumption in the experimental group compared to the simulated control group, and a progressive decrease in cravings only in the active tDCS group during a tDCS intervention on the DLPFC (anode F4 and cathode F3) at an intensity of 2 mA for 10 sessions applied over two weeks. This study used an effective placebo strategy (saline solution with a minimal amount of capsaicin), since there were no significant differences in the sensations related to tDCS between both groups. Similarly, knowing that the use of tDCS has garnered greater interest in the scientific community, it is important to highlight the use of other alternatives, such as high-definition transcranial direct current stimulation (HD-tDCS), another non-invasive neuromodulation technique used to improve the spatial precision of the original tDCS, as it has been used in cognitive processes (Bender et al., 2017; Martin et al., 2019; Cai et al., 2024). This technique uses a different electrode setup, in which it modulates the part of the brain directly below the central electrode. This 4x1 setup, i.e., one anodal and four cathodal electrodes (Alam et al., 2016), could be beneficial for future research on smoking cessation efficacy. Another alternative to consider is transcranial alternating current stimulation (tACS), which consists of applying oscillating electrical current to modulate brain activity, allowing a different functional interpretation compared to the original tDCS, since in an electrical oscillation, during half of this cycle, the anodal and cathodal electrodes can increase or decrease the intensity, while in the other half cycle, the pattern is reversed, allowing a relevant role in temporal coherence between brain areas (Antal & Paulus, 2012). On the other hand, reviewing the Clinical Trials.gov database (Table 5) of future research currently working with tDCS and tobacco or nicotine consumption, three out of 22 are currently recruiting. These investigations continue to add to those already existing, involving factors that were limited in previous studies, such as the inclusion of both sexes (NCT 04209153) and/or the increase in sample size to evaluate the consumption pattern and craving. In addition, they propose examining other variables of great interest, such as combining tDCS with mindfulness (NCT05460676) in order to find effects in reducing anxiety caused by tobacco consumption. They also propose to examine the reactivity to cues caused by individual factors surrounding the person, both internal (mood) and external (situational), associated with consumption, the number of cigarettes smoked, and immediate nicotine consumption in the 50:50 condition, a condition in which the participant can decide whether to smoke a cigarette or resist it while doing the intervention (NCT05875194). Finally, the present systematic review showed that tDCS continues to be a promising technique as an alternative for the treatment of tobacco consumption, showing effective results in reducing craving and consumption patterns. Therefore, the importance of new research to resolve the existing limitations on the use of this technique in reducing smoking is highlighted.

Table 5. Research on Clinical Trials.gov

Identifier	Responsible	Title	Characteristics	
NCT04209153 Last Update Posted: **2021**-12-07. Estimated year of completion: **2025.**	Sponsor: Assistance Publique - Hôpitaux de Paris. Information provided by: Assistance Publique - Hôpitaux de Paris (Responsible Party).	Evaluation of the Effect of Transcranial Direct Current Stimulation (tDCS) in Nicotine-Dependent Tobacco Users.	**Subjects**	Nicotine-dependent subjects, of both sexes, over 18 years of age.
			Aim	Evaluate the consumption pattern, desire to smoke and tolerance of tDCS.
			Methodology	tDCS- Neuroelectrics sessions.
			Outcome measurement	Fagerström score; Assessment of changes in smoking craving intensity and tolerance of tDCS.
NCT05460676 Last Update Posted: **2023**-11-18. Estimated year of completion: **2024**-09.	Sponsor: Wake Forest University Health Sciences. Information provided by: Wake Forest University Health Sciences (Responsible Party).	Reducing Distress and Tobacco Smoking in Cancer Survivors: a TDCS Telehealth Study.	**Subjects**	46 participants who currently smoke cigarettes and seek to reduce cigarette consumption, of both sexes, between the ages of 21 and 75 years.
			Aim	Evaluate the feasibility of using tDCS in DLPFC as a tool to reduce distress and smoking.
			Methodology	Randomized, double-blind, parallel study. Experimental: active tDCS + Mindfulness. Sham comparator: sham tDCS + Mindfulness.
			Outcome measurement	FTQ score; Kessler Psychological Distress Scale (K10) score; Weekly cigarette consumption.
NCT05875194 Last Update Posted: **2023**-05-25. Estimated year of completion: **2023**-12.	Sponsor: University Hospital Tübingen. Information provided by: University Hospital Tuebingen (Responsible Party).	Investigation of the Influence of Transcranial Direct Current Stimulation (tDCS) on the Brain Activation Measured by fNIRS During the Decision Not to Smoke in High-risk Situations.	**Subjects**	60 tobacco smokers of both sexes, between 18 and 70 years old.
			Aim	Demonstrate how individual factors impact prediction of cue reactivity, including immediate smoking in the 50:50 condition and number of cigarettes smoked within 14 days after tDCS.
			Methodology	Parallel, randomized, triple-blind study. Experimental: A single application of anodal tDCS to left DLPFC positioned (10-20 F3 position) and reference electrode on the arm, intensity 2mA. Sham comparator: A single application of sham tDCS to the same brain area as the active one, at an intensity that increases up to 2mA over a 20-s duration period and then turns off again at the end of the 20-s ramp.
			Outcome measurement	Craving; Prefrontal fNIRS activity; SNS activity; PNS activity; VFC; Functional connectivity of dlPFC and OFC; Extinction learning efficacy; Relationship between impulsivity trait scores and subjective craving; Relationship between impulsivity trait scores and number of cigarettes smoked; Relationship between personality traits and state effects (self-efficacy, control beliefs) and craving; Relationship between general anxiety and worry and number of cigarettes smoked.

tDCS (transcranial direct current stimulation); DLPFC (Dorsolateral prefrontal cortex); FTQ (Feasibility and Tolerability Questionnaire); fNIRS (Functional Near Infrared Spectroscopy); SNS (Sympathetic nervous system); PNS (Parasympathetic nervous system); HRV (Heart rate variability); OFC (Orbitofrontal cortex).

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