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A systematic review on transcranial direct current stimulation (tDCS) in the treatment of obesity

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Abstract:
Introduction: *This review aimed to investigate the effects of transcranial direct current stimulation (tDCS) on appetite, food intake, food craving, and body weight in people with obesity.*
Methods: *Two independent reviewers conducted a systematic search in PubMed, Science Direct, and Bibiolteca Virtual em Saúde databases. All randomized controlled clinical trials that studied the effects of tDCS in at least one of the following outcomes: appetite, body weight changes, food intake, and food craving in adults with overweight or obesity, were included.*
Results: *Fourteen studies were identified. Of those, six analyzed appetite, nine analyzed food intake, five analyzed food craving, and six analyzed body weight changes. All the studies considered the dorsolateral prefrontal cortex (DLPFC) as a target. The results reinforce the safety of this technique and point to a positive effect of the association of tDCS with other strategies for the management of obesity. Furthermore, they highlight the importance of understanding individual variability to promote beneficial results.*
Conclusions: *This systematic review shows promising results regarding the use of tDCS in the treatment of obesity. However, the current literature is still controversial and differs between the tDCS protocols and the methods for evaluating the analyzed outcomes. Further studies are needed to better understand the mechanisms of action and individual effects of tDCS in people with obesity to enable its use in clinical practice.*

Keywords: *Obesity - Transcranial direct current stimulation - Body weight - Appetite - Food intake - Food craving*

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Abbreviations
BIS: Barratt Impulsiveness Scale
COMT: Catechol-O-methyl transferase
CT: cognitive training
DEBQ-R: Dutch Eating Behavior Questionnaire-Restraint
DLPFC: dorsolateral prefrontal cortex
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SFTT: snack food taste test
SMC: sensorimotor cortex
tDCS: transcranial direct current stimulation
VAS: visual analog scale

INTRODUCTION

Obesity is defined by the World Health Organization (WHO) as the excess body fat that harms health. It is classified by the Body Mass Index (BMI) which is calculated as body weight (in kilograms) divided by the square of height (in meters), having obesity those adults who have a BMI ≥ 30 kg/m^2. It is a chronic and multifactorial disease that affects people of all genders, social classes, ethnicities, and ages. all over the world. The world prevalence of obesity has grown alarmingly, having tripled between 1975 and 2006, and is considered a public health problem, once it is a risk factor for cardiovascular diseases, type 2 diabetes mellitus, and some types of cancer (WHO, 2020). Obesity is preventable, but it faces challenges to be treated. Current treatment focuses on lifestyle change, which includes diet, physical activity, and behavior modification. Drug therapy, medical devices, and bariatric surgery may also be indicated, although not exempt from side effects. (Gadde et al., 2018). In addition, long-term weight loss maintenance remains a challenge.

The regulation of food intake is highly complex, involving neural, hormonal, and nutritional control. Food intake is regulated by the hedonic and the homeostatic systems consisting of the cortico-limbic structures and by the hypothalamus and brainstem, respectively. The energy imbalance present in obesity may reflect the overlap of the hedonic over the homeostatic system (Berthoud, 2011; Ribeiro et al., 2013). Neuroimaging studies have identified structural and functional differences in the brain regions that participate in cognitive control between individuals with normal weight or obesity. Especially in the prefrontal cortex, which performs cognitive and executive functions and is associated with an increase in appetite, food craving, and consequent ingestion of foods that may be a potent risk for the development and maintenance of obesity (Dendy et al., 2019; Gluck et al., 2017; García-García et al., 2019; Verzijl et al., 2018). The hypoactivity of the dorsolateral prefrontal cortex (DLPFC) found in people with obesity can be reversed by neuromodulation. Among the neuromodulation techniques, the present study aimed to investigate the effects of Transcranial Direct Current Stimulation (tDCS) on appetite, food intake, food craving, and body weight in the field of obesity, as it presents itself as a non-invasive, safe, inexpensive, and easy to apply technique when compared to other techniques of neuromodulation. (McClelland et al., 2013).

tDCS promotes a low-intensity electrical current that modifies the resting membrane potential of neurons through electrodes placed on the head. The effect of tDCS depends on the direction of the applied current, it can facilitate neural activity by increasing the resting membrane potential of neurons with anodal stimulation or inhibit activity by reducing the potential with cathodal stimulation. In addition, the after-effects could be controlled by the current intensity and duration as well as by the number of sessions and the interval between those (Lefaucheur et al., 2017; Nitsche et al., 2000). By analyzing different time intervals between two stimulation sessions, one study highlighted the importance of a specific time window between stimulations for the duration of the after-effects. The after-effects of stimulations combined and lasted up to 24h after the end of tDCS when the interval was 3 or 20 minutes between sessions. The interval between 3 and 24 hours caused the after-effects of stimulation to be abolished. Furthermore, stimulations without a time interval between them resulted in reduced motor cortex excitability (Monte-Silva et al., 2013). Furthermore, in order to achieve the intended distribution and intensity, it was important that the electrodes had an adequate size and shape, that they were stable and correctly positioned on the brain targets, and that the contact medium was adequate (Woods et al., 2016).

Although the number of studies investigating the effects of tDCS has increased in the past years, suggesting a potential new therapeutic intervention that could benefit patients with obesity, some gaps to be explored includes the inter and intraindividual factors, such as the genotype and cognitive-based traits, the different protocols diversifying the duration and intensity, number of sessions and montages that can modify the tDCS effects. These gaps must be clarified to generate adequate knowledge of the real impact of tDCS as a technique to contribute to the treatment of obesity (Alonso-Alonso, 2013; Fassini et al., 2020). Thus, a systematic review is needed to analyze the results found in the studies using different tDCS protocols in individuals with obesity.

Materials and methods

The present review follows the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). To identify pertinent studies, a two-staged literature search was carried out.

Search strategy

First, an online search was conducted in PubMed, Science Direct, and Biblioteca Virtual em Saúde databases in February 2021. Second, to search for more potential studies, an additional literature search was performed using the reference lists of the identified studies, other reviews, and several meta-analytical studies.

The online search on the databases was performed following the PICO method (Patient/Population, Intervention, Comparison, and Outcome). By the acronym, the guide question was determined: "What are the effects of neuromodulation by transcranial direct current stimulation on appetite, food intake, food craving, and body weight in a population with obesity?".

The following search query was used: ("obesity" OR "obesity management") AND ("body weight changes" OR "weight loss" OR "appetite" OR "eating" OR "food intake" OR "craving") AND ("transcranial direct current stimulation" OR "tDCS").

No time limitations or language restrictions were included.

Selection criteria

Studies that met the following criteria were included in the review: (1) randomized controlled clinical trials; (2) transcranial direct current stimulation (tDCS) as an intervention; (3) overweight or obesity population; (4) who has analyzed the effect of tDCS in at least one of the following contexts: (a) appetite; (b) body weight changes; (c) food intake; (d) food craving as an outcome.

Study selection

Initially, all duplicates were removed. Each title and abstract were screened and filtered to meet the selection criteria. In the last step, the full text of the remaining studies was reviewed in detail.

RESULTS

The search resulted in 262 studies. After screening, 23 records required full-text review. **Figure 1** illustrates the study selection process. The remaining 14 articles were included in the analyses for data extraction (**Tables 1 and 2**).

Appetite

There were six studies evaluating the effect of Transcranial Direct Current Stimulation (tDCS) on appetite using the visual analog scale (VAS). They applied the anodal tDCS to the left dorsolateral prefrontal cortex (Amo Usanos et al., 2020; Fassini et al., 2019; Fassini et al., 2020; Heinitz et al., 2017; Marron et al., 2019; Montenegro et al., 2012).

The general state of hunger had a relative elevation after the active tDCS when compared with sham tDCS in the study that applied a single session of tDCS using a left DLPFC/right cerebellum tDCS montage. Furthermore, active tDCS caused an increase in cue-triggered desire to eat and hunger. (Marron et al., 2019)

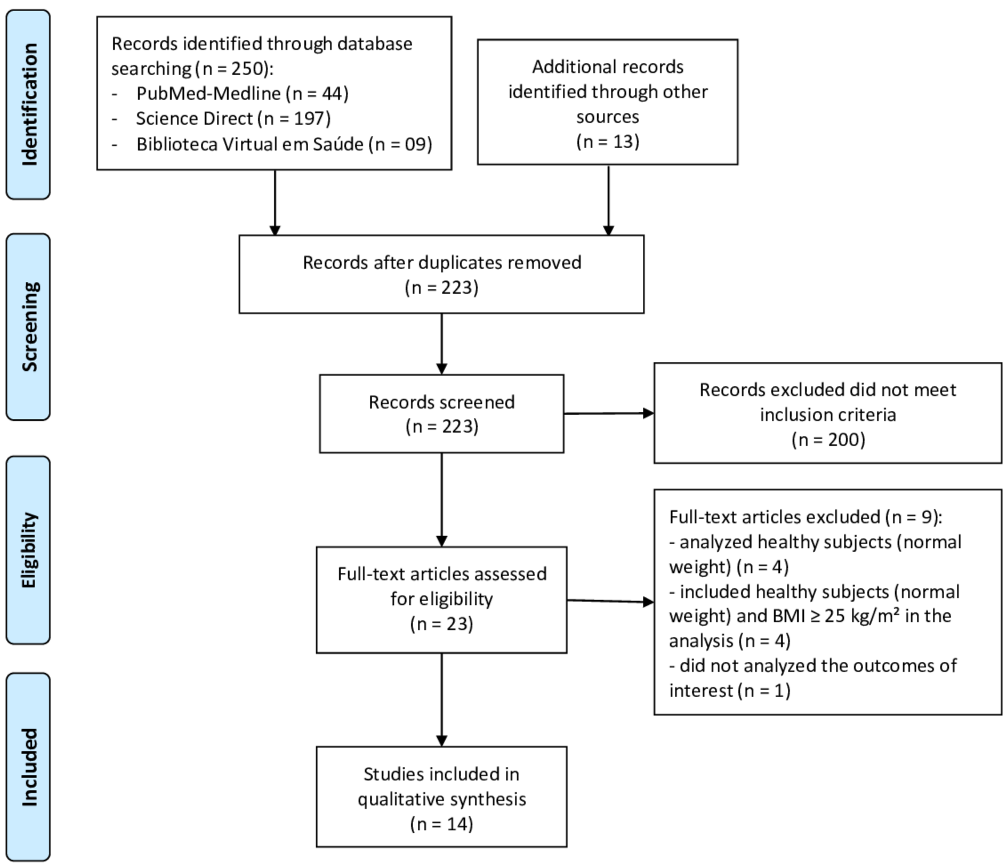

Figure 1. Prisma flow chart of study selection

First author (year)	Population	Study characteristics	Outcome measured
Montenegro et al. (2012)	n=9 (mean age: 24 years; mean BMI: 28.2 kg/m²; 44.4% women)	single session; crossover design; randomized, single-blind, sham-controlled	Appetite (VAS)
Gluck et al. (2015)	n=9 (mean age: 42 ± 8 years; mean BMI1: 38 ± 7 kg/m²; mean BMI2: 34 ± 4 kg/m²; 66.7% women)	3 sessions; crossover design; randomized, single-blind, sham-controlled	Food intake (VM) Body weight changes
Grundeis et al. (2017)	n=25 (mean age: 28.8 ± 6 years; mean BMI: 36.5 ± 4.1 kg/m²; 100% women)	single session; crossover design; randomized, double-blind, sham-controlled	Food intake (Buffet)
Heinitz et al. (2017)	n=23 (range age 32.7 ± 12.0–43.9 ± 5.63 years; mean BMI: 39.3 ± 8.42 kg/m²; 47.8% women)	15 sessions; parallel design; randomized, single-blinded, sham-controlled	Appetite (VAS) Food intake (VM and SFTTs) Body weight changes
Ray et al. (2017)	n=18 (mean age: 22.7 ± 7.9 years; mean BMI: 37.4 ± 9.1 kg/m²; 55.6% women)	single session; crossover design; double-blind, sham-controlled	Food intake (In-lab eating test) Food craving (Food photo "wanting" test)
Fassini et al. (2019)	n=38 (range age: 20–40 years; range BMI 30–35 kg/m²; 100% women)	17 sessions; parallel design; randomized, double-blind, sham-controlled	Appetite (VAS)
Marron et al. (2019)	n=12 (mean age: 41.6 ± 4.8 years; mean BMI: 32.7 ± 1.9 kg/m²; 75% women)	single session; crossover design; randomized, single-blind, sham-controlled	Appetite (VAS)
Natividade et al. (2019)	n=28 (range age: 20–50 years; range BMI 25–35 kg/m²; 50% women)	20 sessions; parallel design; randomized, double-blind, sham-controlled	Body weight changes
Ray et al. (2019)	n=74 (mean age: 19.9 ± 3.4 years; mean BMI: 31.8 ± 5.5 kg/m²; 59.5% women)	single session; parallel design; randomized, double-blind, sham-controlled	Food intake (In-lab eating test) Food craving (Food photo-rating task)
Amo Usanos et al. (2020)	n= 38 (range age: 45–65 years; range BMI: 25–35 kg/m²; 100% women)	8 sessions; parallel design; randomized, double-blind, sham-controlled	Appetite (VAS) Food craving (FCQ-S and FCQ-T) Body weight changes
de Araujo et al. (2020)	n=28 (range age: 20-50 years; range BMI: 25–35 kg/m²; 50% women)	20 sessions, parallel design; randomized, double-blind, sham-controlled	Food intake (3-day WDR) Body weight changes
Fassini et al. (2020)	n=38 (range age: 20–39 years; range BMI: 30–35 kg/m²; 100% women)	17 sessions; parallel design; randomized, double-blind, sham-controlled	Appetite (VAS) Food intake (Dietary recalls) Food craving (FCQ-S and FCQ-T) Body weight changes
Forcano et al. (2020)	n=18 (mean age: 43.2 ± 5.7 years; mean BMI: 42.56 ± 4.9 kg/m²; 66.7% women)	4 sessions; parallel design; randomized, double-blind, sham-controlled	Food intake (4-day dietary record)
Stevens et al. (2020)	n=28 (mean age: 21.0 years; mean BMI: 34.0 ± 7.05 kg/m²; 67.9% women)	single session; crossover design; sham-controlled	Food intake (In-lab food consumption) Food craving (Food image craving ratings)

Note: BMI, body mass index; VAS, visual analogue scale; VM, vending machine; SFTTs, snack food taste test; FCQ-S, Food Craving Questionnaire-State; FCQ-T, Food Craving Questionnaire-Trait; WRD, weighted dietary records.

Table 1. Characterization of the studies included in the review

First author (year)	Active tDCS protocol	Sham tDCS protocol
Montenegro et al. (2012)	anode over the left DLPFC/cathode over the supraorbital contralateral area 20 min, 2 mA	anode over the left DLPFC/cathode over the supraorbital contralateral area 30 s, 2 mA
Gluck et al. (2015)	anode over the left DLPFC/cathode above the right eye 40 min, 2mA	anode over the left DLPFC/cathode above the right eye 75 s, 2 mA
Grundeis et al. (2017)	anodal: anode over the left DLPFC/cathode over the right frontal operculum; cathodal: anode over the right frontal operculum/cathode over the left DLPFC 20 min, 2 mA	anodal: anode over the left DLPFC/cathode over the right frontal operculum; cathodal: anode over the right frontal operculum/cathode over the left DLPFC 1 min, 2 mA
Heinitz et al. (2017)	anode over the left DLPFC/cathode over the right supraorbital region 40 min, 2 mA	anode over the left DLPFC/cathode over the right supraorbital region 10 s, 2 mA
Ray et al. (2017)	anode over right DLPFC)/cathode over the left DLPFC 20 min, 2 mA	anode over right DLPFC)/cathode over the left DLPFC 2 min, 2 mA
Fassini et al. (2019)	anode over the left DLPFC/cathode over the right supraorbital area 30 min, 2 mA	anode over the left DLPFC/cathode over the right supraorbital area 30 s, 2 mA
Marron et al. (2019)	anode over the left DLPFC/cathode over the right cerebellum 20 min, 2 mA	anode over the left DLPFC/cathode over the right cerebellum 20 min, 2 mA
Natividade et al. (2019)	anode over the right DLPFC/cathode over the left DLPFC 20 min, 2 mA	anode over the right DLPFC/cathode over the left DLPFC 1 min, 2 mA
Ray et al. (2019)	anode over the right DLPFC/cathode over the left DLPFC 20 min, 2 mA	anode over the right DLPFC/cathode over the left DLPFC 2 min, 2 mA
Amo Usanos et al. (2020)	anode over the left DLPFC/cathode over the right supraorbital area 20 min, 2 mA	anode over the left DLPFC/cathode over the right supraorbital area 75s, 2 mA
de Araujo et al. (2020)	anode over the right DLPFC/cathode over the left DLPFC 20 min, 2 mA	anode over the right DLPFC/cathode over the left DLPFC 1 min, 2mA
Fassini et al. (2020)	anode over left DLPFC/cathode over the right supraorbital area 30 min, 2 mA	anode over left DLPFC/cathode over the right supraorbital area 30 s, 2 mA
Forcano et al. (2020)	anode over the right DLPFC/cathode over the left DLPFC 20 min, AF3(−1,093 µA), AF4(1,178 µA), F3(−1,161 µA), F4(1,104 µA), F7(−414 µA), F8(530 µA), FC5(1,189 µA), and FC6(−1,332 µA).	anode over the right DLPFC/cathode over the left DLPFC 6 s, AF3(−1,093 µA), AF4(1,178 µA), F3(−1,161 µA), F4(1,104 µA), F7(−414 µA), F8(530 µA), FC5(1,189 µA), and FC6(−1,332 µA).
Stevens et al. (2020)	anode over right DLPFC/cathode over left DLPFC 20 min, 2 mA	anode over the left sensorimotor cortex/cathode over the right sensorimotor cortex 20 min, 2 mA

Note: tDCS, transcranial direct current stimulation; DLPFC, dorsolateral prefrontal cortex.

Table 2. Characterization of the tDCS protocols

A reduction in desire to eat was observed in the active group, after eight sessions of tDCS (Amo Usanos et al., 2020), while a study found a greater daily reduction in VAS ratings for hunger and urge to eat, adjusted for age and sex, in the active group relative to the sham group, after 15 tDCS sessions (Heinitz et al., 2017).

In addition to these controversial findings, a paradoxical effect of tDCS on appetite related to the genotype was identified in a study that analyzed the Catechol-O-methyl transferase (COMT) Val158Met polymorphism where Met non-carries subgroup presented an increased appetite as a result of tDCS intervention. (Fassini et al., 2019)

The tDCS associated with aerobic exercise showed significant differences in the within-group comparison. Appetite was evaluated in sham and active conditions in four different moments: baseline, after tDCS, immediately after exercise, and 30 min after exercise. When tDCS was associated with exercise a greater decrease in desire to eat was observed compared to either tDCS or exercise alone. On the other hand, significantly higher VAS scores for the desire to eat were found 30 min after exercise when compared to the moments after tDCS and immediately after exercise for both sham and active tDCS (Montenegro et al., 2012).

Food Intake

Food intake was assessed in nine studies that applied multiple (de Araujo et al., 2020; Fassini et al., 2020; Forcano et al.,2020; Gluck et al., 2015; Heinitz et al., 2017) or single (Grundeis et al.,2017; Ray et al., 2017; Ray et al., 2019; Stevens et al., 2020) anodal stimulation in the DLPFC, ranging from right to left. Only one of the studies also analyzed cathodal stimulation.

None of the studies that applied a single session of tDCS found a significant difference in food intake between sham and active groups. In addition, a study that controlled the trait scores found some significant differences in males. Compared to the control, the active group had a higher reduction in kcal consumed of their preferred food when Dutch Eating Behavior Questionnaire-Restraint (DEBQ-R) Intent scores were considered in the analyzes, being the reduction higher in men with lower scores of DEBQ-R Intent. Additionally, men in the active group had a significantly reduced total food consumption, primarily for preferred vs. less-preferred food, compared to sham, when covaried for Barratt Impulsiveness Scale (BIS) Nonplanning scores were included in the analysis. Moreover, men whose BIS Nonplanning scores were higher had a greater reduction in total food consumption (Ray et al., 2017).

Analyzing the direction of the current, a study found that after three tDCS sessions, the group that received anodal stimulation over the left DLPFC consumed significantly fewer calories from fat and soda when compared to the group that received the cathodal stimulation. Between the active and sham groups, no significant difference was found (Gluck et al., 2015).

A relatively lower total energy intake in satiated individuals was observed by the snack food taste test (SFTT) after long-term tDCS (fifteen sessions) although no influence of tDCS on food intake was found in the short-term tDCS (three sessions) assessed by vending machines (Heinitz et al., 2017).

Nonetheless, other studies that applied a long-term tDCS (seventeen and twenty sessions) didn't find a significant difference in energy consumption or macronutrient distribution between the sham and active groups (de Araújo et al., 2020; Fassini et al., 2020). The tDCS associated with cognitive training (CT) presented a small positive effect on the total calories consumed post-intervention, mainly by a reduction in lipid intake. An additional increase in this effect was found in the follow-up period, despite the consumption of calories from sugar being higher in the active group than in the control (Forcano et al., 2020).

Food Craving

In this systematic review, five studies evaluated food craving after anodal tDCS on the DLPFC. Three studies applied a single session on the right side (Ray et al., 2017; Ray et al., 2019; Stevens et al., 2020) while two applied multiple sessions on the left side (Amo Usanos et al., 2020; Fassini et al., 2020). No study found a main effect of stimulation. However, when considering BIS Attentional scores in the analysis, the active tDCS promoted a reduced food craving for sweets, fatty proteins, mixed foods, and the all-foods category in females. A significant BIS Attention × stimulation condition interaction was also found such that tDCS reduced food craving for mixed foods in females with lower attention-type impulsiveness compared to control tDCS (Ray et al., 2017). When BMI was controlled, a reduced craving for sweets was observed in the control group that received stimulation over the sensorimotor cortex (SMC) (Stevens et al., 2020).

The food craving factor 3 (anticipation of relief from negative states and feelings as a result of eating) had a borderline significant reduction in the active group compared to the control (Amo Usanos et al., 2020).

Body weight changes

Six articles evaluated the change in body weight as an outcome. All of them applied multiple sessions of tDCS on DLPFC, four studies targeted the left side (Amo Usanos et al., 2020; Fassini et al., 2020; Gluck et al., 2015; Heinitz et al., 2017), and two targeted the right side (de Araujo et al., 2020; Natividade et al., 2019). Only one study investigated a diet for weight maintenance (Gluck et al., 2015), while the remaining studies applied a hypocaloric diet (HD). Amo Usanos et al. observed a greater weight loss in the active group, at the end of the intervention, compared to the control. (Amo Usanos et al., 2020). Comparing the current direction, the anodic stimulation over the left dorsal prefrontal cortex revealed a greater weight reduction than the cathodic one (Gluck et al., 2015). A 6-month follow-up identified a weight regain in the active tDCS compared to the sham group (Fassini et al., 2020).

DISCUSSION

This systematic review aimed to investigate the effects of the transcranial direct current stimulation technique on appetite, food intake, food craving, and body weight in the adult population with obesity.

Studies carried out in populations other than those targeted in this review pointed to a positive effect of the tDCS on some outcomes analyzed, whether in a normal-weight population (Fregni et al., 2008; Jauch-Chara et al., 2014; Lapenta et al., 2014), with binge-eating disorder (BED) (Burgess et al., 2016) or frequent food craving (Goldman et al., 2011; Ljubisavljevic et al., 2016).

Although we found promising results regarding the use of tDCS to treat obesity, to date the literature is still controversial. The studies differ regarding the subjects' characteristics, tDCS protocol, and the methods used for the outcomes assessment.

Many of the studies included in this review did not find a main effect of stimulation, but when considering the group individualities in the analysis, promising results were found, showing that neurostimulation presents different effects depending on the subpopulation in which it is applied.

The genetic variability seemed to affect the results of tDCS since higher levels of appetite after active tDCS were found for the Met non-carriers of COMT Val158Met polymorphism and an opposite effect for the Met carriers subgroup. To our knowledge, this was the first study to show that genetic variability impacts tDCS effects in women with obesity. Despite having considered only one gene, this result highlights the need to assess inter-individual differences that may affect the effect of tDCS on an individual basis (Fassini et al., 2019). Furthermore, controlling cognitive-based traits differences seems to affect the tDCS effects on food consumption and food craving (Ray et al., 2017). This result was also observed in a study that found a higher calorie intake in predominantly healthy-weight women with higher impulsivity receiving active tDCS (Georgii et al., 2017). Another study also explored the influence of the inter-individual characteristics in women that received prefrontal tDCS. Among women self-identified as food cravers, those who exhibited more reflective choosing behavior had a greater reduction in desire to eat, when compared to the participants who exhibited more impulsive choosing behavior (Kekic et al. 2014).

Regarding the tDCS protocol, we highlighted the differences found in the analyzed studies, in which seven enhanced the excitability of the left DLPFC (Amo Usanos et al., 2020; Gluck et al., 2015; Grundeis et al., 2017; Heinitz et al., 2017; Fassini et al., 2019; Fassini et al., 2020; Montenegro et al., 2012), one study aimed enhancing the activity of the prefrontal cortex and decreasing the activity of the cerebellum simultaneously (Marron et al., 2019), and six studies performed bilateral tDCS, enhancing the activity of the right DLPFC and decreasing the activity of the left DLPFC (de Araujo et al., 2020; Forcano et al., 2020; Natividade et al., 2019; Ray et al., 2017; Ray et al., 2019; Stevens et al., 2020). Despite the variety of protocols, the studies did not show conclusive results regarding which tDCS protocol is the most promising target for the treatment of obesity. Also, half of the studies applied a single session of tDCS (Grundeis et al., 2017; Marron et al., 2019; Montenegro et al., 2012; Ray et al., 2017; Ray et al., 2019; Stevens et al., 2020), while the other half carried out tDCS' sessions from 3 to 20 (Amo Usanos et al., 2020; de Araujo et al., 2020; Fassini et al., 2019; Fassini et al., 2020; Forcano et al., 2020; Gluck et al., 2015; Heinitz et al., 2017; Natividade et al., 2019). All studies applied a 2 mA current and the tDCS sessions lasted between 20 to 40 minutes. The results were also not conclusive regarding the number of sessions that could promote the best results. In addition, they differ in the study design and the methodology for outcomes assessment.

Some studies investigated tDCS associated with other two strategies for treating obesity as an intervention. Aerobic exercise presented a synergistic effect (Montenegro et al., 2012), while tDCS combined with cognitive training promoted a beneficial result (Forcano et al., 2020).

The combination of tDCS with diet was investigated in different studies (Amo Usanos et al., 2020; de Araujo et al., 2020; Fassini et al., 2020; Gluck et al., 2015; Heinitz et al. 2017; Natividade et al., 2019). From those, only two were conducted during an inpatient setting (Fassini et al., 2020; Gluck et al., 2015). Although environment control is important to minimize possible confounders in these studies, it is a difficult task. Considering that the use of tDCS does not require hospitalization, methods to assess food consumption are of utmost importance to minimize confounders. Only one study reported the adherence to the hypocaloric diet in the outpatient setting. The authors used the expected weight reduction and the three-day weighted diet records (3-day WDRs), classifying as adherent those who reached at least 80% of their calculated energy goals (de Araujo et al., 2020).

However, regarding the expected effects of tDCS, it was observed in one study that those who believed they were receiving stimulation had less intense food cravings and lower food intake than those who thought they were not receiving tDCS (Ray et al., 2019).

To date, the investigation of the long-term effects of tDCS is scarce in the literature and reveals an important aspect to be considered in future studies. As an innovative technique in the field of obesity, in addition to understanding the tDCS mechanism of action, it is important to understand the tDCS effects over a long-term period. In this review, two studies followed the participants after the end of the intervention. One had a short follow-up evaluation that occurred over one week after the intervention (Forcano et al., 2020) and the other evaluated a longer follow-up period after one, three, and six months following the end of the intervention (Fassini et al., 2020).

The safety of tDCS has been reinforced by the studies included in this review, with no harmful health effects within the period analyzed. Although two studies reported skin redness in the active group compared to the sham group, no other side effects were significantly different between these groups (Gluck et al., 2015; Heinitz et al., 2017).

The studies that analyzed eutrophy individuals in the same overweight and obesity group were not included in this review, as they did not allow us to identify the influence of tDCS on outcomes in our population of interest. Since tDCS has been gaining ground as a possible strategy for the treatment of obesity, future studies need to address the open questions discussed to clarify the interaction between neurostimulation and the different levels of obesity.

Despite the increase of randomized controlled studies in the field of tDCS for the treatment of obesity, the potential effect of tDCS in this population is limited due to the methodology differences. The main methodological variations in the studies: the inclusion of overweight individuals and different degrees of obesity in the same analyzed sample; differences in the tDCS protocol as well as the duration and numbers of sessions and the brain target varying between the left and right side of the DLPFC; different methods of assessing the analyzed outcomes.

Our study has the limitations of not analyzing the risk of bias of the individual studies in this review and not classifying the studies into classes and levels of evidence.

It is also relevant to point out that food craving and drug addiction share common neural mechanisms such as hyperreactivity of the reward system and reduced involvement of the prefrontal cortex, having as its main feature the craving. Since both clinical conditions have complex management, the need to study tDCS as an alternative treatment associated with other interventions in both affections is evident. Furthermore, despite such similarities, future studies of tDCS in the field of obesity need to shed light on the mechanism of action of tDCS in this population specifically.

For a better understanding of the effect of tDCS in the population with obesity, it is important that future studies include a greater sample size. Furthermore, we highlighted the importance of considering the individual characteristics such as genotype, BMI, and cognitive-based traits.

CONCLUSION

Although the current literature presents inconclusive results, the findings in this review point to the potential use of tDCS as an adjunct in the treatment of obesity. The controversial effects can be explained by the difference in tDCS protocols, either in terms of stimulation or analysis of evaluated outcomes. Therefore, future studies should consider the inter-individualities of the target group to increase the comprehension of the tDCS mechanism of action and the possible interference factors. This could contribute to the definition of a more effective tDCS protocol to be used in clinical practice in the field of obesity.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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