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REVIEW

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The use of non-invasive brain stimulation techniques to reduce body weight and food cravings: A systematic review and meta-analysis

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Summary

Several studies demonstrated non-invasive brain stimulation (NIBS) techniques such as transcranial direct current stimulation (tDCS) and transcranial magnetic stimulation (TMS) are safe and simple techniques that can reduce body weight, food cravings, and food consumption in patients with obesity. However, a systematic to evaluate the efficacy of active NIBS versus sham stimulation in reducing body weight and food cravings in patients with obesity is not available. We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) using PubMed, Embase, MEDLINE, and Cochrane Central Register of Control Trial between January 1990 and February 2022. Mean differences (MDs) for continuous outcome variables with 95% confidence intervals (95% CIs) were used to examine the effects of NIBS on body weight and body mass index (BMI), whereas the hedges's g test was used to measure the effects on food craving. Nineteen RCTs involving 571 participants were included in this study. Active neurostimulation (TMS and tDCS) was significantly more likely than sham stimulation to reduce body weight (TMS: −3.29 kg, 95% CI [−5.32, −1.26]; $I^2 = 48\%$; $p < .001$; tDCS: −0.82 kg, 95% CI [−1.01, −0.62]; $I^2 = 0.0\%$; $p = .00$) and BMI (TMS: −0.74, 95% CI [−1.17, −0.31]; $I^2 = 0\%$ $p = .00$; tDCS: MD = −0.55, 95% CI [−2.32, 1.21]; $I^2 = 0\%$ $p = .54$) as well as food cravings (TMS: $g = -0.91$, 95% CI [−1.68, −0.14]; $I^2 = 88$ $p = .00$; tDCS: $g = -0.32$, 95% CI [−0.62, −0.02]; $p = .04$). Compared with sham stimulation, our findings indicate that active NIBS can significantly help to reduce body weight and food cravings. Hence, these novel techniques may be used as primary or adjunct tools in treating patients with obesity.

KEYWORDS
dorsolateral prefrontal cortex, dTMS, neuromodulation, obesity, rTMS, tDCS

1 | INTRODUCTION

The prevalence of obesity is increasing worldwide among both adults and children, exceeding other preventable causes of mortality globally. According to the World Obesity Federation,[1] 1 in 5 women and 1 in 7 men will be overweight or obese by 2030, which represents 1 billion people worldwide. This alarming rise in prevalence is also projected to contribute to the increase population risk of developing cardiovascular disease, diabetes mellitus, some malignancies, musculoskeletal disorders, and other disabling conditions.[2] Additionally, obesity has been linked to increases in annual health care expenditure and prescription costs by 36% and 77%, respectively with the global economic costs of obesity stand at $2 trillion every year.[3]

Although excess energy consumption relative to energy expenditure is the most common cause of obesity, the aetiology of obesity is highly complex and includes multi-factorial factors, which include genetic, physiologic, environmental, psychological, social, economic, and political factors.[4,5] Hedonistic responses to food, such as strong cravings and a difficult-to-resist need to consume certain food items, are characterized by their intensity and specificity.[6,7]

Of relevance to this discourse is the neurobiological underpinning of obesity, which regulates certain brain areas to play an essential role in controlling hunger and eating habits.[8,9] The prefrontal cortex (PFC), sometimes known as the 'control' region of the brain, exerts vital controls on behavioural inhibition, impulsive tendencies, and decision-making in response to environmental stimuli.[8] It represents a crucial node in a fronto-limbic neuronal network responsible for inhibitory control.[10] The limbic system, a group of subcortical brain neurons linked to the PFC, plays an important role in influencing people's motivational actions.[8,11] There is evidence that the hedonic components of eating and incentive salience in food-motivated behaviours are regulated by the brain's mesolimbic structures and mesocorticolimbic circuitry, sometimes known as the 'reward pathway'.[12] The anterior insula, middle frontal gyrus, supplementary motor cortex, parietal cortices, and fronto-stratrial region are other key brain areas linked to nutritional self-control.[13] Additionally, through their connections to the gut-brain reward axis, hormones like leptin and ghrelin influence neurological processes involved in regulating people's eating habits.[8,14] Compared with non-binge eaters, adult binge eaters tend to have lower fronto-striatal (limbic) brain activity, higher trait impulsivity, and weaker inhibitory control abilities.[15] In addition, hypoactivation of brain regions that limit control has been reported in teenagers with food addiction.[16]

A number of management strategies for obesity have been offered, ranging from lifestyle, cognitive behavioural intervention, pharmacotherapies to bariatric surgery[17] with variable outcomes of weight loss.[18] Therefore, there is still need to develop new adjunctive or alternative interventions for treating patients with obesity. Existing evidence suggests that deficits in brain functional connectivity are linked to both bariatric surgery and weight-loss dietary treatments.[19,20] These deficits are characterized by impaired decision-making and inhibitory control, particularly in the PFC.[21,22] The crucial role that cognition and reward play in the cognitive regulation of food intake in humans[23–25] could explain the obese right brain hypothesis which posits that a right PFC impairment may be a key factor in the development of human obesity and positive swing in energy balance.[26] This in conjunction with appetite dysregulation and overactivity of food-related reward and motivation loops, favour a gain in body weight in contemporary societies.[26]

Non-invasive brain stimulation (NIBS) techniques have been used to modulate brain activity safely with neuromodulation techniques like transcranial magnetic stimulation (TMS) in different modalities such as deep TMS (dTMS) or repetitive TMS (rTMS), and transcranial direct current stimulation (tDCS) without the need for a neurosurgical intervention.[27] TMS involves the delivery of rapidly varying magnetic pulses using a magnetic coil placed over the participant's scalp. It can be administered in single or repetitive pulses. These shifting magnetic fields induce secondary currents in the nearby cortex, which in turn initiate neuronal action potentials.[27] In contrast, tDCS involves delivering weak electric currents (usually 1–2 mA) to the brain through a pair of saline-soaked electrode pads placed on the scalp. While a simplistic view and dependent on tDCS parameters, anodal stimulation is considered excitatory, while cathodal is considered inhibitory.[28] Around 50% of the current generated in anodal or cathodal tDCS stimulation pierce the scalp and influence the resting membrane potential of neurons beneath the stimulation sites.[27] The significant benefits of tDCS over rTMS are its low cost, mobility, simplicity of successful blinding, and tolerance.[29]

Several studies have found that stimulation of the dorsolateral prefrontal cortex (DLPFC) can reduce body weight, food cravings, and food consumption.[20,30–32] However, no systematic reviews exploring the effect of brain neuromodulation on body weight have been conducted to date. Such a review could help determine the ideal stimulation parameters required for effective weight loss and the treatment of food addiction in clinical settings. We therefore conducted a systematic review and meta-analysis to investigate the efficacy of NIBS techniques in reducing body weight, body mass index (BMI), and food cravings.

2 | MATERIALS AND METHODS

2.1 | Registration

The protocol of this systematic review and meta-analysis has been registered with PROSPORO (registration number: CRD42022336477).

2.2 | Search strategy

The literature was systematically reviewed to identify randomized controlled trials (RCTs) of NIBS techniques involving patients with obesity using PubMed, Embase, MEDLINE, and Cochrane Central Register of Controlled Trials electronic databases from January 1990 to February 2022. The list of references of included studies was searched for potentially eligible papers that were no picked up by the

electronic searches. The grey literature was search using the Google search engine.

The following key terms were searched in PubMed ('Transcranial Magnetic Stimulation'[MeSH Terms] OR ('Transcranial Magnetic Stimulation'[MeSH Terms] OR ('transcranial'[All Fields] AND 'magnetic'[All Fields] AND 'stimulation'[All Fields]) OR 'Transcranial Magnetic Stimulation'[All Fields] OR 'rtms'[All Fields]) OR ('Transcranial Direct Current Stimulation'[MeSH Terms] OR ('Transcranial Direct Current Stimulation'[MeSH Terms] OR ('transcranial'[All Fields] AND 'direct'[All Fields] AND 'current'[All Fields] AND 'stimulation'[All Fields]) OR 'Transcranial Direct Current Stimulation'[All Fields] OR 'tdcs'[All Fields]))) AND ('Obesity'[MeSH Terms] OR 'Overweight'[MeSH Terms]), Cochrane Central Register of Control Trial (('Transcranial Magnetic Stimulation'[Mesh] OR rTMS) OR ('Transcranial Direct Current Stimulation'[Mesh] OR tDCS)) AND (('Obesity'[Mesh]) OR 'Overweight'[Mesh]), Embase and MEDLINE (('Transcranial Magnetic Stimulation' OR rTMS) OR ('Transcranial Direct Current Stimulation' OR tDCS)) AND (('Obesity') OR 'Overweight').

2.3 | Inclusion criteria

The inclusion criteria were RCTs that: (1) evaluated the efficacy of active NIBS techniques versus sham stimulation in human participants with overweight or obesity; (2) involved adults aged >18 years or older; and (3) These measures were changes from baseline across body weight (kg), BMI, and food cravings.

The exclusion criteria were: (1) non-RCTs; (2) studies involving animals; (3) absence of a sham group; (4) studies that recruited participants without obesity; (5) studies that did not report on the outcomes of interest; and (6) studies written in languages other than English. There are no specific restrictions on the brain regions targeted by NIBS during the inclusion criteria.

2.4 | Study selection and data extraction

The articles were evaluated for inclusion according to the inclusion and exclusion criteria. Eligible articles were examined further to extract data on first author names, year of publication, sample size, duration of follow-up, types of interventions, and baseline and post-intervention measures of food cravings, BMI, and body weight. Data on the number of stimulation sessions, stimulation parameters, and stimulation sites were also extracted.

2.5 | Publication bias

Publication bias was assessed using funnel plots,[33] Egger's regression test was used to measure funnel plots asymmetry[34] and Begg and Mazumdar rank correlation test.[35] If publication bias was observed, a non-parametric trim-and-fill analysis of publication bias was applied to modify the effect size caused by publication bias.

2.6 | Dealing with missing data (means and SD)

No attempts were made to contact the corresponding authors of the studies to obtain any missing data. However If the median, upper, and lower interquartile were reported, we estimated mean and SD using the sample size, median, range, and/or interquartile range as described in Ref. 36. Alternatively, the mean and standard deviation (SD) were estimated directly from figures or graphs using the following App: https://www.digitizeit.xyz/.

2.7 | Quality assessment

The Cochrane Collaboration tool for RCTs[37] was used to evaluate the quality of the studies included in this review. Random sequence generation, allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other biases were all evaluated for risk of bias. Every potential source of bias was assigned a risk of bias rating of high, low, or unclear. If the domain could not be adequately assessed due to lack of sufficient information, it was assigned an uncertain risk of bias. The Review Manager (RevMan) was used to create the risk of bias figures.

2.8 | Statistical analysis

Statistical analysis was performed using Stata SE 16.1 software (Stata Corp LLC. 2019. Stata Statistical Software: Release 16). Mean differences (MDs) for continuous outcome variables with 95% confidence intervals (95% CIs) were used to examine magnitude of the effect of NIBS on body weight and BMI for standard meta-analysis and subgroup meta-analysis. To measure the difference in food cravings levels, the Hedges's g with a corresponding 95% CIs was calculated because variations in the scales used across studies. The calculation of Hedges's g was performed using the 'meta' command in Stata, which incorporates the necessary formulas and adjustments for small sample sizes. This command automatically computes the mean difference, pooled SD, correction factor, and Hedges's g based on the provided data. The magnitude of g is commonly interpreted as indicating a low ($g = 0.2$–0.5), medium ($g = 0.5$–0.8), or high ($g > 0.8$) effect size. A random-effect model was used to pool the data. Heterogeneity among studies was assessed using the I^2 test as low (I^2 was ≤40%), moderate (I^2 > 30% to <60%), substantial (I^2 > 50% to <90%), or considerable (I^2 ≥ 75% to 100%).

2.9 | Subgroup meta-analysis

Subgroup meta-analyses were performed based on device type (TDCs, rTMS, and dTMS), duration of session (e.g., 20, 30, or 40 min) and stimulation site (left or right). Moreover, meta-regression was analysed using body weight and food cravings as dependent variables while age, gender percentage, and the number of sessions as an independent variable. Also, the number of pulses and frequencies (10 or 18 Hz) as an independent variable was used in TMS studies.

3 | RESULTS

3.1 | Study selection

Of the 472 potentially relevant studies identified by the initial searches, 81 duplicate records were removed, and 362 records were excluded after reviewing the title and applying filters. Twenty-nine studies were assessed for eligibility, of which 10 studies were excluded due to involving patients who are non-obese or reporting irrelevant outcomes. Nineteen RCTs, involving 571 participants, published between 2015 and 2021, focusing on the use of NIBS interventions in patients with obesity met the inclusion criteria and were included in this review and meta-analysis (Figure 1).

3.2 | Study characteristics

Table 1 summarizes the study characteristics. All the included studies used NIBS techniques (11 tDCS, 4 rTMS, and 4 dTMS). The number of stimulation sessions ranged from 1 to 20 sessions and the duration of each session ranged from 20 to 40 min. Only six studies used hypocaloric diet alongside the intervention (Gluck et al. two studies).[29,30,38–40] Duration of intervention ranged from 4 to 28 days however, most of the studies with 4–5 weeks of intervention. In the TMS group, there was one study that reported only body weight, excluding BMI. In the tDCS group, there were four studies that reported only body weight, excluding BMI, and one study that specifically reported BMI. Cathodal stimulation has been consistently used in seven studies to reduce food cravings and intake. It effectively suppresses cravings and consumption, resulting in decreased caloric intake. Specifically, it reduces cravings for sweet foods while leaving savoury cravings unaffected. Additionally, it decreases hunger and increases feelings of satiety, leading to an overall reduction in food intake.[25,29,31,38,41–43]

3.3 | Risk of bias assessment

The Cochrane Collaboration tool for RCTs was used to evaluate the risk of bias for each included study. The overall risk of bias ratings was judged as low risk for three studies,[38,44,45] as having some concerns for three studies[20,46,47] and as high for the remaining 13 (Supplementary File S1).[25,29,48,49,30–32,39–43]

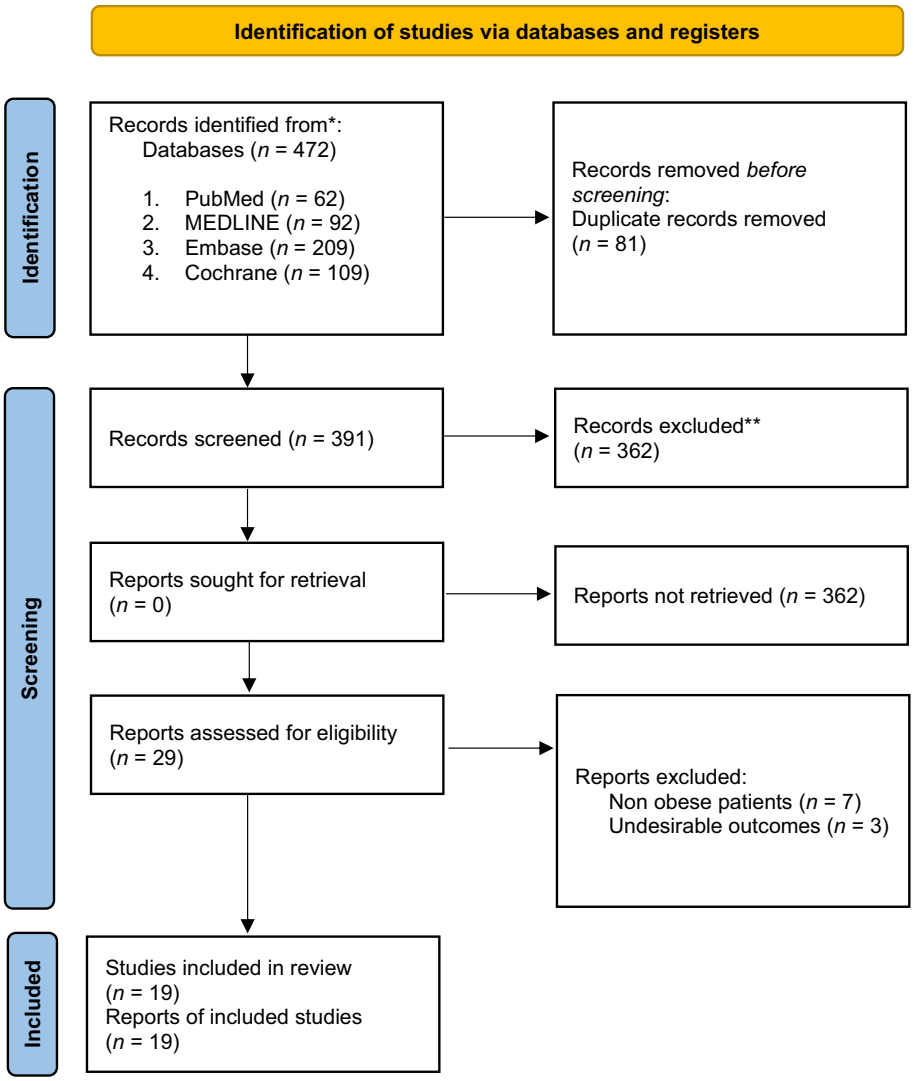

FIGURE 1 Preferred reporting items for systematic reviews and meta-analyses: The PRISMA Statement.[67]

TABLE 1 Summary of study characteristics.

Study ID	Sample size	Control	Intervention	Duration of sessions (min)	BMI/I	BMI/C	No. sessions	Type of device	Craving measure	Population	Frequency/mA	Stimulation site
Devoto (2021)	17	8	9	30	34.3	36.5	15	dTMS	FCQ-T	Adults obese/some have T2D	18 Hz	Bilaterally PFC and the insula
Ferrulli (2019)	33	13	10	30	36.7	36.3	15	dTMS	FCQT and a self-report inventory	Adults, obese	18 Hz	Bilaterally PFC and the insula
Ferrulli (2021)	22	7	9	30	37.3	35.5	15	dTMS	NR	Adults, obese	18 Hz	Bilaterally PFC and the insula
Luzi (2021)	45	19	26	30	34.7	36.51	15	dTMS	FCQ-T	Adults, obese	18 Hz	Bilaterally PFC and the insula
Alvarado Reynoso (2019)	37	19	18	__	32.6	33.14	17	rTMS	FCI	Adults, overweight or obese	10 Hz	Left DLPFC
Encarnacion (2020)	29	14	15	20	36	35.9	4	rTMS	VAS	Adults, obese	10 Hz	Left DLPFC
Kim (2017)	60	28	29	20	30.6	27.9	4	rTMS	NR	Adults, obese	10 Hz	Left DLPFC
Kim (2019)	43	22	21	20	31	29.2	8	rTMS	NR	Adults, obese	10 Hz	Left DLPFC
Burgess (2016)	30	30	30	20	36	36	1	tDCS	VAS	Adults, overweight or obese	2 mA	Cathode, left, Anode right of DLPFC
de Araujo (2020)	28	14	14	20	31.8	31.3	20	tDCS	NR	Adults, overweight or obese	2 mA	Cathode, left, Anode right of DLPFC
Fassini (2020)	38	18	20	30	33.3	32.9	10	tDCS	FCQ-S and FCQ-T	Adults, obese, only female	2 mA	Cathode, right, Anode left of DLPFC
Forcano (2020)	18	9	9	20	43.2	41.9	4	tDCS	NR	Adults, obese	2 mA	Cathode, left, Anode right of DLPFC
Gluck (2015)	9	4	5	40	35	42	6	tDCS	NR	Adults, obese	2 mA	Cathode, left DLPFC, Anode on the left forearm
Gluck (2015 [2])	9	4	5	40	34	35	6	tDCS	NR	Adults, obese	2 mA	Anode, left DLPFC, Cathode above the right eye
Heinitz (2017)	23	14	9	40	39.1	38	12	tDCS	NR	Adults, obese	2 mA	Anode, left, Cathode right of DLPFC
Ljubisavljevic (2016)	30	14	13	20	26	24.9	5	tDCS	FCQ-S, FCQ-T and FCI	Adults: Normal, overweight	2 mA	Anode, right, Cathode left of DLPFC
Ray (2017)	18	18	18	20	37.4	37.4	1	tDCS	VAS	Adults, obese	2 mA	Cathode, left, Anode right of DLPFC
Ray (2019)	74	35	39	20	31	29.2	1	tDCS	FCT	Adults, overweight or obese	2 mA	Cathode, left, Anode right of DLPFC
Usanos (2019)	38	18	20	20	31.5	31.9	8	tDCS	FCQ-T and FCQ-S	Adults: overweight or obese only female	2 mA	Anode, left, Cathode right of DLPFC

Abbreviations: BMI, body mass index; C, control; DLPFC, dorsolateral prefrontal cortex; FCI, The food-craving inventory; FCQ-S, Food Craving Questionnaire State; FCQ-T, Food Cravings Questionnaire-Trait; FCT, Food craving task; I, intervention; no, number; NR, not reported; PFC, prefrontal cortex; VAS, visual analogue scales.

3.4 | TMS studies

3.4.1 | Body weight

The results indicate a significant overall effect for TMS on body weight in participants with obesity (MD = −3.29 kg, 95% CI [−5.32, −1.26]; I^2 = 48%; p < .001) favouring active over sham TMS in reducing body weight (Figure 2A).

Subgroup analysis by the duration of sessions (20 [132 participants] and 30 min [117 participants]) indicated that 30 min of active stimulation was more effective (MD = − 2.59 kg, 95% CI [−4.91, −0.27]; I^2 = 0% p < .05) than 20 min (MD = − 1.68 kg, 95% CI [−3.28,

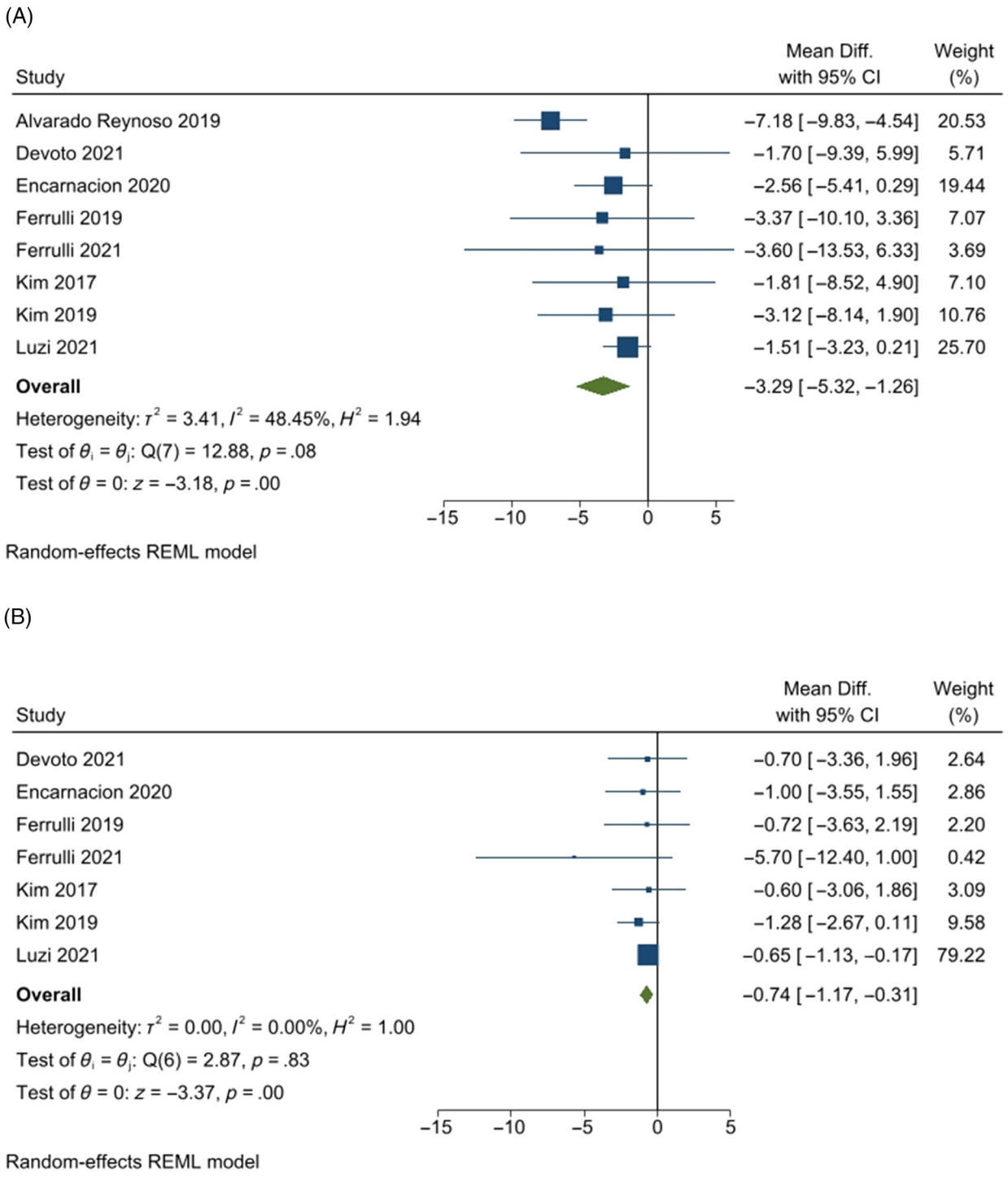

FIGURE 2 (A) The overall effect of transcranial magnetic stimulation (TMS) brain stimulation on body weight. (B) The effect of TMS brain stimulation on body mass index.

0.07]; $I^2 = 0\%$ $p < .05$; Figure S5). Subgroup analysis by type of stimulation device, revealed that rTMS (169 participants) resulted in more weight loss (MD = − 4.17 kg, 95% CI [−7.00, −1.33]; $I^2 = 54\%$ $p < .05$) than dTMS (117 participants; MD = − 1.68 kg, 95% CI [−3.28, −0.07]; $I^2 = 0\%$ $p < .05$; Figure S6). The results also showed that a frequency of 10 Hz (169 participants) led to greater weight loss (MD = −4.17 kg, 95% CI [−7.00, −1.33]; $I^2 = 54\%$, $p < .05$) compared with a frequency of 18 Hz (117 participants; MD = −1.68 kg, 95% CI [−3.28, −0.07]; $I^2 = 0\%$, $p < .05$; Figure S7).

3.4.2 | Body mass index

All studies that used TMS reported changes in BMI except one.[30] The pooled results revealed a significant effect for TMS on BMI in patients with obesity (MD = − 0.74, 95% CI [−1.17, −0.31]; $I^2 = 0\%$ $p = .00$) favouring active TMS over sham interventions (Figure 2B). Subgroup analysis by duration of stimulation indicated that 20 min of neuromodulation was superior (132 participants; MD = − 1.09, 95% CI [−2.19, −0.00]; $I^2 = 0\%$ $p < .05$) to 30 min of intervention (117 participants; MD = − 0.68, 95% CI [−1.15, −0.21]; $I^2 = 0\%$ $p < .05$; Figure S8). Furthermore, subgroup analysis by stimulation device indicated that rTMS resulted in more reduction in BMI (MD = − 1.09, 95% CI [−2.19, −0.00]; $I^2 = 0\%$ $p < .05$) than dTMS (MD = − 0.68, 95% CI [−1.15, −0.21]; $I^2 = 0\%$ $p < .05$; Figure S9).

3.4.3 | Food cravings

All TMS studies reported changes in food cravings except one.[46] However, the mean difference was difficult to obtain due to differences in measurement scales across the studies. Therefore, a standardized mean difference was used to measure the effect size (Hedges's g). The analysis revealed a statistically significant high effect for TMS neuromodulations on food cravings in participants with obesity ($g = -0.91$, 95% CI [−1.68, −0.14]; $p = .00$) favouring active TMS over sham intervention. The test for heterogeneity was significant ($I^2 = 88\%$; $Q_{(6)}$ 33.84, $p = .00$; Figure 3). Subgroup analysis by the duration of sessions revealed a significant, albeit small, effect size for TMS neurostimulation intervention (20 min, 132 participants; $g = -0.49$, 95% CI [−0.84, −0.15]; $p < .05$) and a medium effect for 30 min (95 participants; g = −0.56, 95% CI [−1.13, −0.02]; $p > .05$). The change for 30 min sessions was not significant and with there was heterogeneity between the studies ($I^2 = 40\%$ $Q_{(3)} = 5.91$; $p = .12$; Figure S10). Subgroup analysis by the type of stimulation device revealed a large effect size for rTMS (169 participants; $g = -1.16$, 95% CI [−2.55, 0.22]; $I^2 = 94\%$ $p > .05$), and a medium effect for dTMS (95 participants; $g = -0.56$, 95% CI [−1.13, 0.02]; $I^2 = 40\%$ $p > .05$; Figure S11). The findings also revealed that a frequency of 10 Hz (169 participants) resulted in greater reduction in food cravings ($g = -1.16$, 95% CI [−2.55, 0.22]; $I^2 = 94\%$, $p > .05$) compared with a frequency of 18 Hz (117 participants; $g = -0.56$, 95% CI [−1.13, 0.02]; $I^2 = 40\%$, $p > .05$; Figure S12).

3.5 | tDCS studies

3.5.1 | Body weight

The seven studies that used tDCS reported significant changes in weight.[25,29,38–40,48] The results revealed a significant overall effect for tDCS brain stimulation on reducing body weight in participants with obesity (MD = −0.82 kg, 95% CI [−1.01, −0.62]; $I^2 = 0.0\%$; $p = 0.00$) favouring active tDCS over sham intervention (Figure 4A). Moreover,

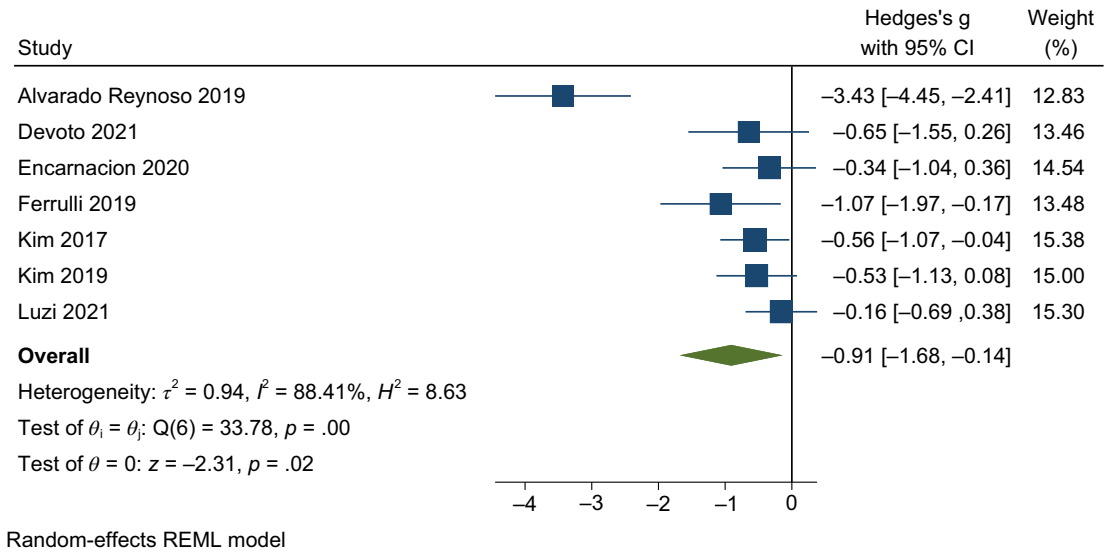

FIGURE 3 The overall effect of transcranial magnetic stimulation brain stimulation on food cravings.

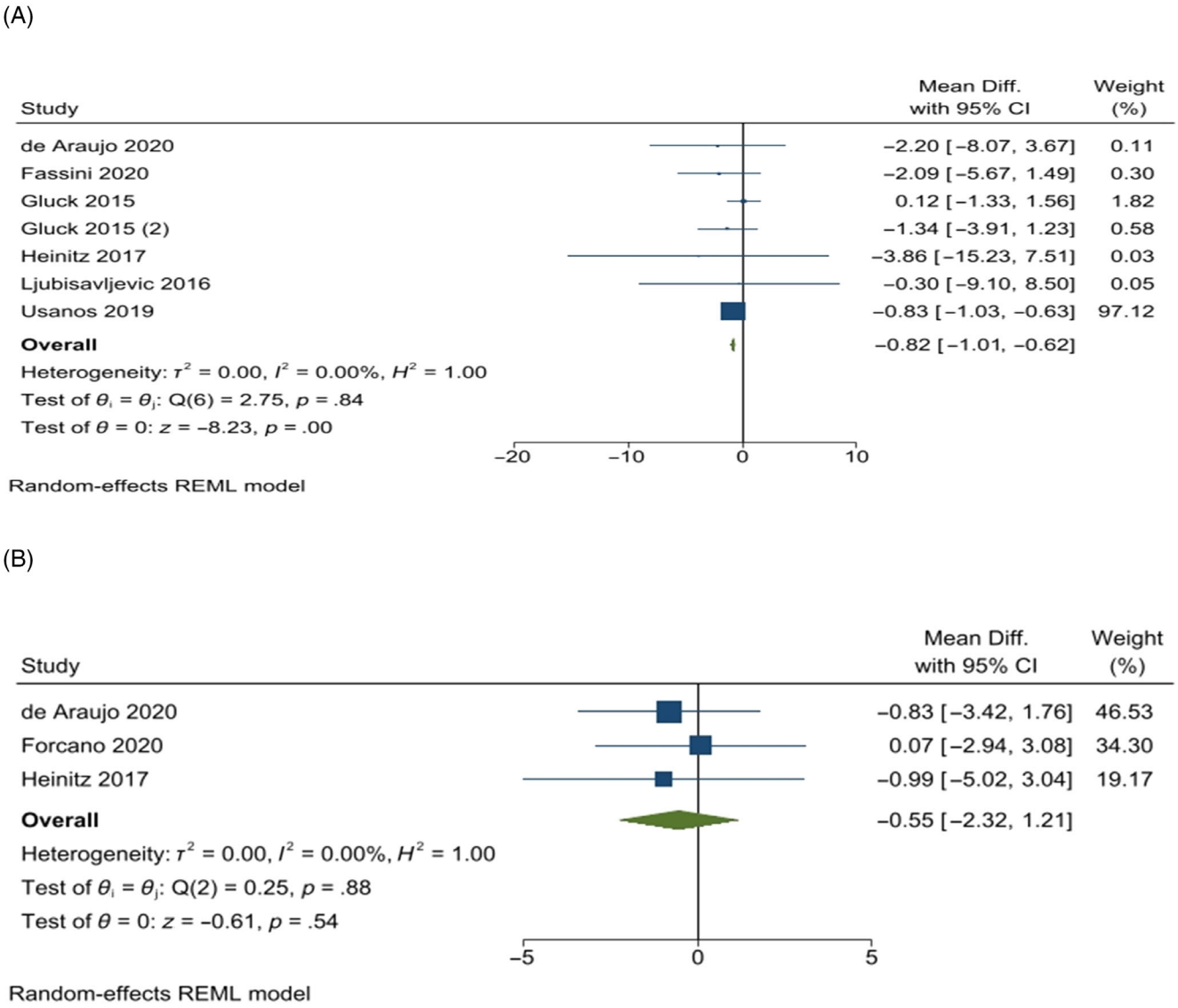

FIGURE 4 (A) The overall effect of transcranial direct current stimulation (tDCS) brain stimulation on body weight. (B) The effect of tDCS brain stimulation on body mass index.

subgroup analysis by the duration of sessions (20 and 40 min) indicated that 20 min of active tDCS stimulation was more effective (96 participants; MD = − 0.83 kg, 95% CI [−1.03, −0.63]; I^2 = 0% p < .05) than 40 min (41 participants; MD = − 0.28 kg, 95% CI [−1.53, 0.97]; I^2 = 0% p > .05; Figure S13). Furthermore, subgroup analysis by the stimulation site (left DLPFC or right DLPFC) indicated that stimulation of the right DLPFC was superior (67 participants; MD = − 0.84 kg, 95% CI [−1.03, −0.62]; I^2 = 0.00% p < .05) to left DLPFC in reducing body weight (108 participants; MD = − 0.02 kg, 95% CI [−1.41, −1.36]; I^2 = 0% p > .05; Figure S14). Cathodal stimulation of the right DLPFC (67 participants) resulted in a greater reduction in body weight (MD = −0.84 kg, 95% CI [−1.03, −0.62]; I^2 = 0.00%, p < .05) compared with the left DLPFC (108 participants; MD = −0.02 kg, 95% CI [−1.41, −1.36]; I^2 = 0%, p > .05; Figure S15).

3.5.2 | Body mass index

The three studies that used tDCS reported changes in BMI,[38,41,48] but the results were not statistically significant (MD = − 0.55, 95% CI [−2.32, 1.21]; I^2 = 0% p = .54; Figure 4B).

3.5.3 | Food cravings

The five studies that used tDCS reported changes in food cravings.[25,31,39,42,43] However, the mean difference could not be obtained due to differences in measurement scale among included studies. Therefore, a standardized mean difference was used to measure the effect size (Hedges's *g*). The analysis revealed a significant, albeit small, effect for tDCS neuromodulations on food cravings in participants with obesity

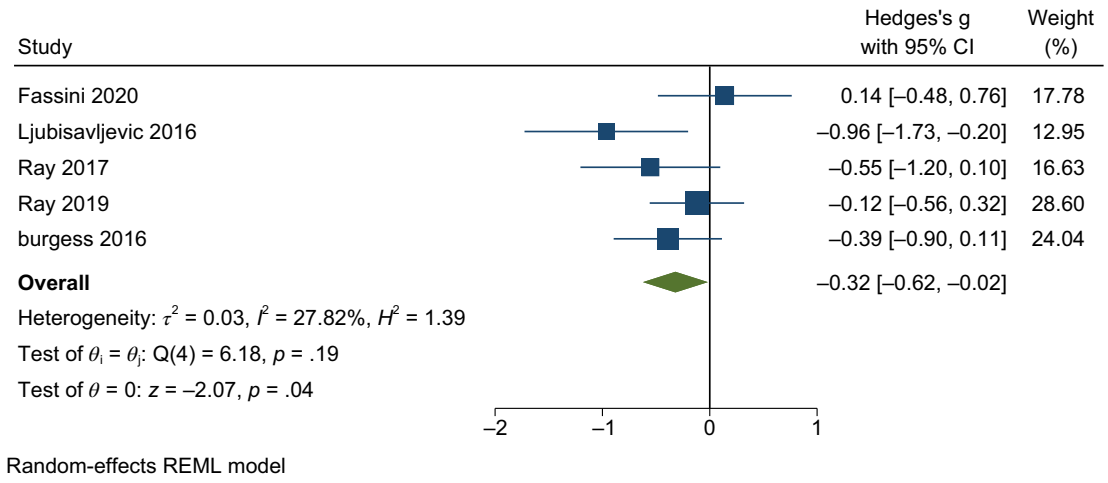

FIGURE 5 The overall effect of transcranial direct current stimulation brain stimulation on food cravings.

TABLE 2 Summary of meta-regression results.

Dependent variable	Intervention	Independent variable	Coefficient	Std. err.	*t*-test	$p > \|t\|$
Body weight	tDCS	Number of sessions	−0.21	0.189	−1.11	.316
		Age	−0.004	0.049	−0.09	.934
		Women to men %	−0.01	0.015	−0.70	.513
	TMS	Number of sessions	−0.16	0.17	−0.90	.405
		Age	0.14	0.020	0.70	.512
		Women to men %	−0.079	0.049	−1.61	.158
		Frequency (10 or 18 GHz)	2.32	1.91	1.21	.270
		Number of pulses	0.001	0.001	1.33	.232
Food cravings	tDCS	Number of sessions	0.035	0.048	0.72	.524
		Age	0.002	0.014	0.19	.860
		Women to men %	0.008	0.006	1.30	.286
	TMS	Number of sessions	−0.09	0.072	−1.30	.251
		Age	0.14	0.206	0.70	.512
		Women to men %	−0.07	0.049	−1.61	.158
		Frequency (10 or 18 GHz)	2.32	1.91	1.21	.270
		Number of pulses	0.000	0.0004	0.84	.440

Abbreviations: tDCS, transcranial direct current stimulation; TMS, transcranial magnetic stimulation.

($g = -0.32$, 95% CI [−0.62, −0.02]; $p = .04$) favouring active tDCS over sham intervention. The test for heterogeneity was not statistically significant ($I^2 = 25\%$; $Q_{(4)}$ 6.04, $p = .20$; Figure 5).

3.6 | Hypocaloric diet

Only six studies used hypocaloric diet alongside the intervention.[29,30,38–40] One study has used TMS[30] and five studies have used tDCS.[28,37–39] When hypocaloric studies were excluded from the analysis the results for TMS still have shown effect on body weight (MD = −1.93 kg, 95% CI [−3.17, −0.68]; $I^2 = 0\%$; $p < .00$) and on food cravings ($g = -0.48$, 95% CI [−0.74, −0.21]; $I^2 = 0\%$; $p < .00$; Figures S16 and S17). Moreover, tDCS has shown an effect on food craving ($g = -0.40$, 95% CI [−0.71, −0.09]; $I^2 = 0\%$; $p < .00$; Figure S18). Due to the limited number of studies that did not employ a hypocaloric diet, there is a lack of available data regarding the impact of tDCS on body weight.

3.7 | Meta-regression

The meta-regression indicated that there is no significant relationship between the outcomes and age, number of sessions, women to men percentage, number of pulses or TMS frequency. Table 2 summaries the regression results.

3.8 | Publication bias

The assessment for publication bias indicates that no publication bias was observed in body weight outcome. However, publication bias was observed in food craving for TMS studies ($p = .02$) there we ran trim-and-fill test to adjust the effect size which indicates that there are two studies missing from the left side of funnel plot. The test shown an average effect size ($g = -1.19$) which is comparable to our original results (publication bias figures, Supplementary File S1).

4 | DISCUSSION

Based on 19 studies, a meta-analysis was performed to examine the effects of non-invasive neurostimulation on body weight, BMI, and food cravings. The main analysis showed significant effects on reducing body weight, BMI, and food cravings for both TMS and tDCS, although the effect of tDCS on food cravings was relatively small. The results also showed significant effects for 20 and 30 min of TMS stimulation on body weight, while only 20 min of stimulation showed a significant effect on cravings. Although results from tDCS studies showed that 20 and 40 min of tDCS intervention had an effect on body weight, the effect was only significant for 20 min stimulation sessions. More importantly, among all the intervention devices (rTMS, dTMS, and tDCS), tDCS is the only device that had a significant effect on both body weight and food cravings. This is in agreement with the study by Chen et al.,[50] which reported a small effect size for tDCS on food craving. After excluding studies involving hypocaloric diet interventions, it is evident that both TMS and tDCS still have a significant impact on food cravings. Due to the limited number of studies that have specifically examined the effects of tDCS on participants with obesity without the inclusion of a low-caloric diet, it is currently not possible to establish conclusive findings regarding the isolated impact of tDCS on body weight.

These results are in disagreement with Song et al.,[51] who reported that compared with sham, NIBS resulted in a significant, albeit small, reduction in food cravings ($g = -0.456$; CI: 0.328–0.583). This might be due to the inclusion of studies that measured craving to various other substances such as alcohol, food, nicotine, and drugs. Also, it is notable that the authors pooled the effects of TMS and tDCS together although these are different interventions. However, when the results of our study were combined, a significant effect was observed ($g = -0.66$; CI: -1.10, -0.21; $p = .00$; Figure S19). Our findings are in agreement with those of Lowe, Vincent, and Hall[52] which demonstrated a moderate effect in reducing food cravings through the stimulation of DLPFC when all techniques were combined (effect size: $g = -0.52$, CI: -1.00, -0.03). However, it is important to highlight that our findings differ from the study conducted by Lowe, Vincent, and Hall, as our results indicate a significant effect of tDCS on reducing food cravings, whereas their study did not find a statistically significant effect when analysing the techniques separately.

The processes that inhibit food cravings following stimulation are not fully understood. Many studies have supported the hypothesis that the inhibition of food craving might be related to changes in reward valuation or improved cognitive control abilities.[52] There is evidence that excessive food cravings might be explained by reduced activation of the DLPFC.[53] It is possible that enhancing DLPFC activity through brain stimulation aided in the effective suppression of food cravings via stimulation-induced cognitive control improvements.[52] Also, DLPFC stimulation could play a role in reduction of the values assigned to food stimuli which support the theory that the DLPFC is involved in the computation of values at the moment of choice, possibly by sending signals to the medial orbitofrontal cortex that are combined with other signals to compute values for stimuli at the time of decision-making.[54] This hypothesis also supported by Amo Usanos et al.[40] who found a link between improved inhibitory control and lower levels of food craving. They suggested that neuromodulation has improved underlying brain circuitry connected to eating behaviour cognitive control, resulting in a greater capacity to resist the effect of food signals. In addition to that Chen et al.[50] have suggested that increased cognitive control is one putative method by which DLPFC activation reduces craving as the executive control network, which includes the DLPFC, orbitofrontal cortex, and anterior cingulate cortex, is crucial for human executive control, including craving management. Neural plasticity can be induced and regulated by neuromodulation.

The second possible hypothesis is that dopamine excretion in the corpus striatum can be induced by neurostimulation of the DLPFC. Fonteneau et al.[55] have shown that the dopamine release generated by a tDCS session causes an increase in extracellular dopamine. They have suggested that the changes in dopamine could be explained by a direct pathway, via corticostriatal projections, and an indirect pathway, via cortical projections on mesostriatal dopamine neurons in the midbrain, both include glutamatergic cortical projections. According to animal studies that revealed that stimulation of the PFC promotes activity in both the striatal and ventral tegmental areas, suggesting that both direct and indirect pathways may be implicated in tDCS effects.[56,57] Moreover, Ceccanti et al.[58] have shown that deep rTMS have rebalanced of the dopamine-cortisol equilibrium during alcohol withdrawal with significant reduction in cortisolemia and prolactinemia. They have also revealed a reduction in VAS for craving and number of alcoholic drinks per day after the deep rTMS intervention. Indeed, the significance of DA in inhibitory control is widely understood, and its disturbance might lead to behavioural discontrol disorders such as obesity.[59] Wang et al.[60] have shown that the availability of dopamine D2 receptors reduced in proportion to the BMI in individuals with obesity. They conclude that dopamine regulates motivation and reward circuitry, therefore dopamine deficit in obese people may cause pathological eating to compensate for reduced activity of these circuits. Thus, obesity therapy may benefit from strategies targeted at enhancing dopamine function.[60] Whereas satiety and desire to eat were linked with the lower activity of the DLPFC which could encouraging weight-gain-promoting habits.[61,62] As a result, it possible

that individuals with food craving and /or obesity may benefit from dopamine regulation which can be induced by non-invasive brain modulation.

As discussed above, the improvements in cognitive control abilities, changes in reward valuation or enhancing dopamine function may not only help to supress food craving but they could also help to body weight reduction. Moreover, Kim et al.[47,49] have shown that reduction of Food cravings can lead to a reduction in food consumption and weight loss. Several studies that have employed tDCS have observed acute reductions in self-reported food cravings and appetite, as measured by the visual analogue scale. Furthermore, improvements in the ability to resist food and immediate decreases in caloric intake have been reported.[25,63–65] Alongside these findings, tDCS has been associated with improvements in impulsivity. A meta-analysis conducted by Yang et al.[63] examined the effects of tDCS on impulsivity, incorporating 12 effect sizes from nine studies. This analysis revealed a statistically significant small effect size. Supporting these results, Mayer et al.[64] also reported promising outcomes of tDCS on impulsivity in both healthy individuals and clinical populations, indicating overall positive effects. By enhancing these cognitive control abilities, individuals may exhibit better restraint in their eating behaviours, making healthier choices and resisting impulsive or emotional eating episodes, thus contributing to weight loss. In addition to that, Luzi et al.[45] have found a significant positive relation between the variation of leptin and Barratt impulsiveness scale-11 after brain stimulation with dTMS. Leptin is a hormone produced mostly in enterocytes and originates from adipose tissue and the small intestine, which helps to control energy balance by reducing appetite, resulting in lower fat mass in adipocytes.[65,66] Thus, regulation of leptin level may have impact on reduction of appetite and food consumption, as leptin resistance may lead to overeating and obesity.[65] Moreover, Ferrulli et al.[46] suggest that 5 weeks of rTMS has promote beneficial change in gut microbiota composition in individuals with obesity. They state that the relevant changes in gut microbiota composition happened in the same group where a considerable weight loss was also seen. They also concluded that Only 5 weeks of HF dTMS therapy was found to be successful in altering gut microbiota composition in participants with obesity, correcting obesity-associated microbiota changes, and boosting bacterial species with anti-inflammatory capabilities that were indicative of healthy people. From all hypotheses above it is hard to say which theory may explain the results of this review regarding body weight reduction. However, the leptin imbalance and change in gut microbiota composition have less literature support.

In the majority of our analysed results, heterogeneity does not pose a significant concern. The observed heterogeneity is within an acceptable range, indicating that the included studies are relatively consistent in terms of methodology, participant characteristics, and outcome measures. However, in the analysis of TMS results, it was observed that the study conducted by Alvarado Reynoso et al contributed to the observed heterogeneity. This heterogeneity may be attributed to the fact that Alvarado Reynoso et al combined a hypocaloric diet with the TMS intervention. The inclusion of a hypocaloric diet alongside TMS may introduce additional factors that influence the outcomes and contribute to the observed variation among studies.

In this review, there are some limitations worth to mention. First, the lack of research examining the impact of neuromodulation on food intake and body weight does not assist to investigate the long-term outcomes of neurostimulation as most studies have 5 weeks or less of follow-up. Moreover, the limited studies in the literature did not allow this review from provide clear evidence about the effect on BMI and food craving regarding the duration of sessions and stimulation site. Finally, the heterogeneity between studies was high in overall food craving and moderate in body weight, which could affect the quality of finding in this systematic review and meta-analysis. While this review has found significant findings of NIBS on body weight and food cravings, it is important to note that the number of studies included in this review was limited. Therefore, it is important to be careful when drawing any conclusions from this review and network meta-analysis. In future studies, there are several areas that could be improved, including randomization and allocation procedures, reporting of results using diverse formats beyond graphs only, and increasing sample sizes.

5 | CONCLUSION

The primary investigation did reveal a hedge decrease in body weight and BMI. The results also showed a significant benefit of NIBS on lowering food cravings. The finding also exposed that whereas only 20 min of TMS intervention had a significant impact on cravings, both 20 and 30 min had an impact on body weight. Surprisingly, tDCS is the only intervention device that significantly affects both body weight and cravings of food. Insufficient studies examining tDCS without a low-caloric diet limit our ability to draw definitive conclusions about its effects on body weight.

Overall, The findings of this report potentially lend support to the growing evidence of the efficacy of NIBS approaches on body weight and food cravings and suggested that the improvements in cognitive control abilities, changes in reward valuation or enhancing dopamine function may supress food craving and they could also lead to body weight reduction. Moreover, our results suggest that NIBS could be a promising technique for treating patients with obesity especially combined with food cravings.

AUTHOR CONTRIBUTIONS

Najat Khalifa, Waleed Al-Khyatt, and Iskandar Idris conceived and designed the study, Yousef Abdullah Alhindi carried out data collection, undertook analysis and prepared the first draft of the article. All authors were involved in the revision of the draft article and have agreed to the final content.

CONFLICT OF INTEREST STATEMENT

None declared for all authors.

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