Modulating eating behaviour with transcranial direct current stimulation (tDCS): A systematic literature review on the impact of eating behaviour traits

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Abbreviations

AU, arbitrary unit; BED, binge eating disorder; BF_{10}, Bayes factor; BMI, body mass index; CBIT, computer-based image task; CBM, cognitive bias modification; CI, confidence interval; cm, centimetre; COMT, catechol-o-methyl transferase; DLPFC, dorsolateral prefrontal cortex; EBA, extrastriate body area; EDNOS, eating disorder not otherwise specified; F, female; FCI, Food Craving Inventory; FCQ-S, Food Craving Questionnaire-State; GABA, gamma-aminobutyric acid; IAT, implicit association task; IFG, inferior frontal gyrus; kcal, kilocalorie; kg, kilogram; LFPQ, Leeds Food Preference Questionnaire; M, male; mA, milliampere; met, methionine; min, minute; NR, not reported; PFC, prefrontal cortex; PICO, Population, Intervention, Control and Outcome; PWS, Prader Willi syndrome; RoB, risk of bias; SE, standard error; SEM, standard error of the mean; subBED, subthreshold binge eating disorder; tDCS, transcranial direct current stimulation; tnM1, tongue muscle representation of the primary motor cortex; VAS, visual analogue scale; VNS, visual numeric scale

ABSTRACT

Transcranial direct current stimulation (tDCS) is becoming an increasingly popular technique for altering eating behaviours. Recent research suggests a possible eating behaviour trait-dependent effect of tDCS. However, studies recruit participant populations with heterogeneous trait characteristics, including “healthy” individuals who do not present with eating behaviour traits suggesting susceptibility to overconsumption. The present review considers the effects of tDCS across eating-related measures, and explores whether a trait-dependent effect is evident across the literature. A literature search identified 28 articles using sham-controlled tDCS to modify eating-related measures. Random effects meta-analyses were performed, with subgroup analyses to identify differences between “healthy” and trait groups. Trivial overall effects (g = -0.12 to 0.09) of active versus sham tDCS were found. Subgroup analyses showed a more consistent effect for trait groups, with small and moderate effect size (g = -1.03 to 0.60), suggesting tDCS is dependent on participants’ eating behaviour traits. Larger effect sizes were found for those displaying traits associated with study outcomes (e.g. heightened food cravings). “Healthy” individuals appear to be unresponsive to stimulation. Based on this meta-data, future work should recruit those with eating behaviour trait susceptibilities to overconsumption, focussing on those who present with traits associated with the outcome of interest.

1. INTRODUCTION

Obesity is a global health epidemic that is predicted to affect 20% of the worldwide adult population by 2030 [1], with a higher prevalence predicted for both the United Kingdom (35 to 48%) and United States of America (45 to 52%) [2, 3]. This condition is associated with many comorbid diseases, such as type 2 diabetes and coronary heart disease, which places greater emphasis on the treatment of obesity [4, 5]. Although it is often diminished to the notion of “eat less, move more”, obesity is multi-faceted and driven by the complex relationship between behavioural, biological and environmental factors [6, 7]. Despite this complexity, the treatment of obesity typically involves simple changes to the diet and/or physical activity [8, 9]. Although these treatment modalities produce initial weight loss of up to 10%, this weight loss is not maintained long-term [9]. Additional treatment options such as behavioural therapy, medications and surgeries also do not result in successful or maintained weight loss for many individuals [10-12], with extreme forms of treatment such as bariatric surgery associated with 10 to 27% of individuals experiencing weight regain [11, 13]. These weight loss interventions typically target the symptoms of obesity, such as excess adiposity, and often ignore the important underlying brain-dependent factors that contribute to energy balance [14].

The consumption of food is associated with a pleasure response that stimulates reward and motivation circuits within the brain, which can often override the physiological need for energy and promote overconsumption and weight gain [15-18]. Such a response is relevant in the current obesogenic environment, where energy-dense, palatable foods are readily available [19, 20]. This hedonic-driven appetite is heightened following calorie restricted diets, and the pervasiveness of heightened hedonic appetite can lead to weight regain following bariatric surgery [21-23]. Consequently, a lack of maintained weight loss following current treatment modalities may be driven by an individual’s inability to resist highly rewarding foods [24]. The control of hedonic appetite involves executive brain functions, which are strongly associated with activity in regions such as the prefrontal cortex (PFC) and allow goal-directed behaviours through the inhibition of impulsive actions [25-27]. Individuals with

binge eating behaviour or obesity appear to have hypo-activation of the dorsolateral PFC (DLPFC) [28, 29], and show impaired executive functioning [30-32]. This dysregulation of the DLPFC has been linked with greater impulsive behaviours, often leading to overconsumption of energy-dense foods [14, 33, 34]. Of note, those with greater executive functioning following bariatric surgery show more improved weight loss outcomes [35]. By modulating activity within cortical regions associated with executive functioning, it may be possible to improve hedonic appetite control through the inhibition of the rewarding valuation of foods, which may be beneficial for weight management [15].

The modulation of cortical activity is possible through the use of non-invasive brain stimulation techniques such as transcranial direct current stimulation (tDCS) [36]. This technique involves the application of a constant weak electrical current to the brain through electrodes that are connected to a battery-powered device [37, 38]. Although the current strength is not sufficient to cause neuronal firing, it appears able to modulate resting membrane potentials in a polarity-dependent manner [39, 40]. The electric current is delivered through an anode (positive charge) electrode, where it is passed through the brain to a cathode (negative charge) electrode and is returned to the device. Under the anode, resting membrane potentials are depolarised through the inhibition of neurotransmitters such as gamma-aminobutyric acid (GABA), increasing the likelihood of spontaneous neuron firing. In comparison, resting membrane potentials are hyperpolarised under the cathode electrode which decreases the likelihood of spontaneous firing through the inhibition further neurotransmitters (e.g. glutamate) [39]. This technique is considered safe for healthy and patient populations [41], and is increasingly popular as it is a simple, scalable and cost-effective method for altering cortical activity [36].

The ability of tDCS to alter eating behaviours, such as food craving and consumption, has been of great interest for researchers due to its potential use in the treatment of obesity [42], amongst other conditions such as eating disorders and addiction-related conditions [39, 43].

Since the first study using tDCS to alter food craving was published over a decade ago [44], the potential for this technique to improve hedonic appetite control has seen an increase in published data. However, despite the promising effects outlined in this early study, more recent data shows more equivocal effects [45-48]. If tDCS is to be used as an additional or adjunctive treatment modality for weight management, it is important that inconsistencies are addressed [49].

One source of such inconsistency across studies are the participants recruited, which include those who are healthy weight [47, 50], and individuals with overweight or obesity [14, 48]. The eating behaviour traits of these participants also appear to differ across studies. For instance, two recent studies compared the effects of tDCS on food craving and consumption in participants with and without binge eating symptomatology and only found an effect of tDCS in those displaying binge-type behaviours [51, 52]. Indeed, our own data highlights a lack of effect in participants with a healthy weight who appear to show low susceptibility to hedonic-driven overconsumption [53]. Recent data shows improved task performance (e.g. verbal learning, working memory) only in low-cognitive groups [54-56]. As such, only those with impaired PFC activity and poor executive control may benefit from tDCS modulation. Together, this suggests a trait-dependent effect of tDCS but further data are required to support this assumption. The present review will consider the effects of tDCS across measures of eating behaviour, and will discuss the impact of behavioural traits on these measures.

2. METHODS

2.1 Search Strategy

This literature review was performed in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [57] (Table S1). An electronic literature search was conducted across four databases; MEDLINE, PsycINFO, Scopus and Science Direct. Literature searches were performed in March 2019 and repeated in July 2020 to

capture additional articles published during this time. Search terms were: (*"noninvasive brain stimulation" OR "non-invasive brain stimulation" OR "transcranial direct current stimulation" OR "transcranial current stimulation" OR tDCS) AND (appetit* OR food OR "food crav*" OR "food reward" OR "food preference*" OR "food cue" OR "food consumption" OR eat* OR calorie* OR "calorie intake" OR "calorie consumption" OR energy OR "energy intake" OR "energy consumption" OR bing* OR "binge eat*" OR snack**). Due to the limitation on Boolean terms and wildcards (*) in Science Direct, adjusted search terms were used for this database: *("transcranial direct current stimulation" OR tDCS) AND ("food craving" OR "food reward" OR "food preference" OR "food consumption")*.

2.2. Inclusion and Exclusion Criteria

In line with the Population, Intervention, Control and Outcome (PICO) model [58]; articles were included if they were peer-reviewed intervention studies that recruited adult human participants *(population)*, applying conventional (i.e. one anode and one cathode) tDCS procedures *(intervention)* using a sham-controlled design *(control)* to determine the effects on hedonic-related eating behaviours (subjective appetite, food craving, consumption or reward) *(outcome)*. Results were limited to those written in English and published after 1998 to coincide with the development of modern tDCS procedures [38, 59]. Any further articles known to the authors were also considered for inclusion.

2.3. Data Extraction

After removing duplicates (n = 248), titles and abstracts were assessed for inclusion. Full-text articles were then retrieved and assessed for inclusion in the final sample. Reviews, abstracts (where full-text articles were unavailable), editorials/commentaries, book chapters, theses, study protocols, case reports and animal studies were not included in the present review (total n = 68). Two authors (JDB and DS) performed study selection independently. For each eligible study, the following data were extracted: names of authors; year of publication; participant characteristics; montage and electrode size; current intensity and

density; stimulation duration; ramp duration; sham protocol; number of sessions; blinding efficacy; use of online and offline protocols; outcome measures; main findings. Data were extracted as reported in the original article(s) by JDB.

2.4. Study Quality Assessment

Study quality was determined using the Cochrane Collaboration's Risk of Bias (RoB) tool [60]. Judgements were made by two independent authors (JDB and NCS) at the study level, with high agreement between authors (κ = 0.93).

2.5. Statistical Analysis

Mean, standard deviation (SD) and sample size were extracted for measures of subjective appetite (hunger, fullness, prospective consumption, desire to eat), food craving, food consumption, and food reward (implicit wanting, explicit wanting and explicit liking). If standard error (SE) was reported, SD was estimated using the equation $SD = SE \times \sqrt{n}$ [58]. Where data were not reported in text, means and SD or SE were extracted from available figures using WebPlotDigitizer (version 4.4) [61], through correspondence with study authors, or estimated using Practical Meta-Analysis Effect Size Calculator [62] by inputting *t* or *F* statistic and sample size. Where data or effect sizes were estimated, validation of these measures was independently completed by two authors (JDB and NCS). Standardised mean difference was calculated for each of the extracted variables, and adjusted using Hedges' *g* bias correction due to the small sample size (n < 20) across many of the reviewed studies.

Only data following single-session active and sham tDCS were included to provide comparison across studies. Four studies did not measure the effects of single-session tDCS [63-66]; these were excluded from the analysis. The study by Ljubisavljevic et al. [67] was excluded as all participants received active tDCS for the first stimulation session. A further study was removed due to missing data [68]. A total of 22 studies (total n = 817 participants; "healthy" group n = 490, trait group n = 327) were included in the meta-analysis.

Individual effect sizes are not statistically independent due to differences in comparisons within experiments, articles and research groups. Such dependencies can result in narrow confidence intervals (CI) and small estimates of SE [69, 70]. To account for this, multilevel modelling was completed to estimate the influence of several dependencies on effect size variance. Separate levels for comparison within participant samples, experiments within studies, and studies within research groups were included in the modelling. Akaike information criteria and likelihood ratio test outcomes did not indicate that the addition of each level improved model fit (Table S3).

Meta-analyses were performed using R [71] with the meta package [72]. Random effects models were used due to the variability in study design and outcomes. A negative effect size indicates that active tDCS reduced the outcome measure compared to sham tDCS, whereas a positive effect size indicates an increase in the outcome measure following active versus sham tDCS. Effect sizes were interpreted as trivial (g <0.20), small (g = 0.20), moderate (g = 0.50) or large (g >0.80) [73]. The heterogeneity of effect sizes were assessed using the I^2 index, and interpreted as might not be important (0 to 40%), may represent moderate heterogeneity (30 to 60%), may represent substantial heterogeneity (50 to 90%), or considerable heterogeneity (75 to 100%) [74]. Subgroup analyses were conducted to identify whether participant behaviour traits were moderating the effects of tDCS on eating-related measures. Forest and funnel plots were produced using the meta package for R. To test for publication bias, Egger's regression was used [75]. Where meta-analysis was not possible, a systematic review of the literature is included.

3. RESULTS AND DISCUSSION

3.1 Study Characteristics

The literature search identified 1,135 records, with 28 of these included in the present review after removing duplicates and assessing eligibility (Figure 1). In line with the PICO model, all

included studies used conventional sham-controlled tDCS procedures (i.e. one anode, one cathode), with 12 between-participant and 16 within-participant designs (Table 1). Eight studies involved repeated sessions of tDCS. Across the reviewed studies, a total of 996 participants were recruited, which ranged from 9 to 172 individuals per study. This included individuals with healthy weight (n = 14 studies, 576 participants), overweight or obesity (n = 15 studies, 393 participants). One study included those with healthy weight and overweight (n = 27), but the authors did not provide a breakdown for each weight category [67].

***** INSERT FIGURE 1 HERE ******

***** INSERT TABLE 1 HERE *****

Many studies recruited participants described as "healthy" (n = 14 studies, 576 participants) (Table 1). The consensus definition of "healthy" related to a lack of medical or behavioural conditions, and was irrespective of weight status [14, 48, 63]. It should be noted that 4 of these studies did not measure participants' wider eating behaviour traits, but reported that participants were "healthy" regardless of weight status [48, 67, 76, 77]. Thirteen studies recruited participants (n = 403) with differing eating behaviour traits or medical conditions, including Prader Willi syndrome (PWS) [78], catechol-O-methyl transferase (COMT) Val158Met polymorphism [65, 66], frequent food cravings [44, 45, 79, 80], restrained eating [81, 82], binge eating disorder (BED) [51, 83], and anorexia or bulimia nervosa [84, 85]. Heterogeneity across studies (I^2 range = 0 to 48%) suggests it might not be important. However, potential moderate to substantial heterogeneity is evident for some measures, particularly in trait subgroup analyses. Inspection of funnel plots showed good symmetry across measures (see Supplementary Material); Egger's regression showed little evidence of publication bias for overall analyses ($p > 0.07$) (see Table S4).

3.2 Study Quality

Only 7 of the 28 studies showed low risk of bias across all domains and therefore overall low risk of bias (Figure S2). In the remaining studies, bias arose from issues with the blinding protocol (Figure 2). Insufficient detail around the blinding of both participants and researchers was given across studies, particularly the process in which researcher were made blind. Most studies (n = 18; Table 1) maintained a double-blind protocol through the use of pin-protected stimulation devices or an independent researcher completing stimulation protocols. Seven studies used a single-blind design, with a further three studies providing insufficient detail.

***** INSERT FIGURE 2 HERE *****

It should be noted that Ray et al. [76] included a source of intended bias around blinding of participants, with the aim of assessing the impact of expecting to receive active versus sham tDCS on eating-related measures. Although this study received an overall high risk of bias, the study was high-quality and this source of bias provides important considerations around the information shared with participants. Some bias arose due to the post-randomisation exclusion of participants (n = 14 studies). Many studies do not provide a sample size calculation, which makes it difficult to identify the impact of these exclusions. The exclusion of participants is particular problematic where this leads to a relatively small sample size, which is an important consideration as this area of research repeatedly uses small sample size that are not linked to achieving satisfactory statistical power [36, 86, 87].

3.3 Subjective Appetite

The subjective rating of hunger, fullness, desire to eat and prospective consumption are the most consistently measured variable in the reviewed research, particularly the rating of hunger, and are assessed across 18 of the 28 studies (Table 2). There is an overall lack of tDCS-related effect shown for measures of appetite across the reviewed studies (g = -0.12 to 0.09) (Figure 3). This trivial effect size can also be seen for “healthy” groups (g = 0.06 to

0.15) (Figure S7), where a lack of change in scores [14, 46, 47, 52, 53, 63, 64, 76, 78, 88], or increase in measures of hunger [77, 89], is often shown. Although Heinitz et al. [64] found no difference in subjective appetite scores when delivering daily inpatient tDCS, they did observe reductions in hunger and the urge to eat following outpatient treatment and after adjusting for age and sex. This suggests that long stimulation duration (40 minutes) and regular repetition (15 sessions) may affect the subjective appetite sensations of individuals with obesity. A similar effect was shown in participants who were overweight, with reduced desire to eat following single-session active versus sham tDCS, which was further reduced following isocaloric exercise [68]. Although these studies include participants either considered or assumed to be "healthy", neither fully measure or report the behaviour traits of their participants, and so it is difficult to identify what impact these traits may have on the change in subjective appetite scores.

***** INSERT FIGURE 3 HERE *****

***** INSERT TABLE 2 HERE *****

When we compare these effects to those studies using populations with specific behavioural traits or conditions relating to a heightened hedonic response to food, an overall trivial effect size is seen (g = -0.08 to 0.08) (Figure S7). However, greater effects are observed when we look at those displaying specific traits associated with the subjective appetite measure. For example, in individuals with PWS who experience hyperphagia [78], and appear to have hypoactivation of the DLPFC in response to food stimuli [90], a large effect size can be seen for hunger scores (g = -1.03; 95% CI = -2.50, 0.43). Additionally, the desire to eat is reduced in those who display frequent food cravings (g = -0.43; 95% CI = -1.11, 0.25) (Table S2). A similar comparison between "healthy" and trait populations cannot be made for fullness or prospective consumption scores, as all studies included in our analyses recruited "healthy" individuals.

There appears to be an influence of COMT Val158Met polymorphism, whereby those who are carriers of the methionine (met) allele showed reduced appetite following 16 sessions of active tDCS compared to no change in scores for non-carriers [66]. The COMT enzyme is important for dopaminergic neurotransmission [91], and absence of the met allele is associated with reduced dopamine degradation which can increase the sensitivity to rewarding cues [92]. This altered dopamine transmission impacts activity within the DLPFC and executive functioning capabilities [93, 94]. The findings by Fassini et al. [66] suggest that absence of the met allele can inhibit the modulatory influence of tDCS. Indeed, COMT Val158Met polymorphism has previously been shown to impact the effects of stimulation [95]. However, when Fassini et al. repeated their study in a further cohort of met carrier and non-carriers, they did not find a difference in subjective appetite scores [65]. Further data are required to fully understand the influence of COMT Val158Met polymorphism on the modulation of eating behaviour by tDCS.

Across studies, the fasting period and baseline subjective appetite levels were not well controlled. Fasting duration ranged from 2 to 7 hours, with 7 studies either not measuring/reporting fasting duration or not asking participants to fast [52, 64, 76, 78, 80, 84, 96]. Longer fasting periods can lead to heightened appetite and greater hedonic response to foods and related cues [97, 98]. No study has assessed the effects of differing fasting durations on eating-related outcome measures following tDCS, but the impact of these uncontrolled fasting periods cannot be excluded. It may be that the equivocal effects following tDCS are driven by greater baseline appetite levels, but only two papers have included subjective appetite scores as covariates in statistical analyses [52, 53]. To identify a more consistent effect of tDCS on subjective appetite and other eating-related behaviours, greater control of fasting duration and baseline appetite is required [99].

Across the reviewed studies, the effects of tDCS on measures of subjective appetite are not consistent, although our meta-analysis shows a more promising effect in some populations.

This may be due to these individuals experiencing abnormal levels of appetitive sensations or being unable to appropriately respond to these sensations [100-103], with tDCS stabilising the response. It should also be noted that these subjective sensations, particularly hunger, are largely under homeostatic control [19], and may be outside the modulatory influence of tDCS [104]. Instead, other behaviours may be more important variables, particularly where these behaviours are related to the hedonic response to foods and require executive control mediated by the PFC. These potentially more malleable behaviours include food craving, food reward, and food consumption and will be discussed in the following sections.

3.4 Food Craving

Here we focus specifically on the measure of in-the-moment food craving as assessed via the Food Craving Questionnaire-State (FCQ-S) [105]. Food craving was measured in 8 of the reviewed studies (Table 2). An additional 6 studies measured food craving as a proxy of explicit wanting [44, 45, 51, 52, 76, 79]; these studies will be discussed in the following section. As with subjective appetite, there is a lack of a consistent overall effect of stimulation on measures of food craving across studies (g = -0.08; 95% CI = -0.28, 0.12) (Figure 4). Where these studies recruited those participants considered “healthy”, no change in food craving scores was observed when comparing anodal versus sham tDCS (g = -0.06; 95% CI = -0.29, 0.17) (Figure 4). Of interest, although Ljubisavljevic et al. [67] recruited “healthy” individuals they demonstrated that repeated sessions of tDCS were able to reduce food craving scores, and particularly the craving for fast-food, sweet and high-fat food groups. This may highlight a beneficial impact of multi-sessions designs on eating behaviour measures, which was also demonstrated for subjective appetite [64] (see 3.2). Again, the authors did not fully describe the behavioural traits of their participants, and so the impact of these traits cannot be fully identified.

***** INSERT FIGURE 4 HERE *****

The overall effect for trait groups shows only a trivial effect size (*g* = -0.16; 95% CI = -0.57, 0.26) (Figure 4). When we consider the effects of tDCS on state food craving in a population who experience frequent food cravings, there is a more consistent reduction in craving intensity when applying active versus sham stimulation (*g* = -0.43; 95% CI = -1.11, 0.25) (Table S2). However, this effect was not extended to those with disinhibited and restrained eating behaviour (*g* = 0.00; 95% CI = -0.52, 0.52). Finally, COMT Val158Met polymorphism did not appear to influence the effects of repeated-session tDCS on food craving scores, with no change in scores for met carriers and non-carriers when comparing active versus sham tDCS [65].

A large proportion (62.5%) of studies recruited "healthy" individuals, with only single studies recruiting those experiencing frequent food cravings [80], disinhibited restrained eaters [81], or those with COMT Val158Met polymorphism [65]. Across populations there are equivocal findings, with a more consistent effect in those experiencing frequent food cravings. When we consider explicit wanting, which incorporates the sensation of food craving [106], the reduction in craving score in those who experience frequent food cravings is consistently shown (*g* = -0.45; 95% CI = -1.03, 0.11) (Table S2; see 3.5). This highlights the importance of recruiting participants who show specific behavioural trait susceptibility to the particular behavioural outcome of interest; for example, recruiting those who experience heightened food cravings if we are looking to reduce food cravings intensity. The lack of effect in "healthy" populations should not be surprising as these individuals are likely to experience infrequent food cravings, and when they do experience a craving they are likely able to sufficiently control their response to these [20, 27].

3.5 Food Reward

Food reward can be measured as "liking" (perceived impact of a food or related cue on subject affect or pleasure) and "wanting" (subjective motivation that encompasses the desire, craving or awareness of the 'lack of something desirable') responses to food [106].

Where liking operates on an explicit level (i.e. conscious, introspective), wanting can be expressed on both explicit and implicit (i.e. subconscious, automatic) levels [106, 107]. These reward measures are important in the control of eating behaviour, as the presence of food cues or consumption of food results in a pleasure response that stimulates reward and motivation circuits within the brain that can override physiological need and promote overconsumption [15-18, 106]. Across the reviewed studies, food reward was typically measured using a computer-based image task (CBIT), where participants were shown food images and asked to respond to questions across VAS (e.g. "*Which food do you most want to eat now?*"). Fifteen studies measured food reward, mainly through measures of explicit wanting (Table 2). It should be noted that many of these tasks are not validated measures, but are often created ad-hoc in response to study needs. The exception is our use of the Leeds Food Preference Questionnaire (LFPQ) [53], a validated and widely used measure of implicit and explicit food reward [107].

The overall effect of active versus sham tDCS on measures of explicit wanting (g = -0.10; 95% CI = -0.31, 0.11), explicit liking (g = 0.08; 95% CI = -0.05, 0.21), and implicit wanting (g = -0.06; 95% CI = -0.50, 0.37) show only trivial effect sizes (Figure 5, Figure S9). These effect sizes are mirrored in "healthy" participant populations (g = 0.00 to 0.09) (Figure S8). Although no effect of tDCS was found, Ray et al. [76] did show that the expectation of receiving active tDCS led to reduced explicit wanting for foods. When this effect was removed from analyses, the effect size for overall (g = -0.01; 95% CI = -0.16, 0.14) (Figure 5) and "healthy" groups (g = 0.09; 95% CI = -0.04, 0.22) increased, although remained trivial (Figure S8). This emphasises the importance of controlled study designs and limiting the information shared with participants, with the aim of reducing the bias that expectation may have on the dataset.

***** INSERT FIGURE 5 HERE *****

A more consistent pattern of effects on food reward measures appears when we assess trait groups. A small effect size can be seen for both explicit (*g* = -0.12; 95% CI = -0.42, 0.19) and implicit wanting (*g* = -0.19; 95% CI = -1.66, 1.29) (Figure S8). These effects are driven by individuals with binge eating or frequent food craving trait characteristics (Table S2), again who appear to have altered activity within the DLPFC [28, 29]. Burgess et al. [51] showed reduced craving (explicit wanting) scores for desserts, savoury proteins and all-foods categories in those with BED. In addition, Goldman et al. [45] found reduced explicit liking and wanting, particularly for sweet foods, and highlighted an improved ability to resist foods in participants with frequent food cravings. Of note, there does not appear to be an effect of active tDCS in a heterogeneous sample of individuals with anorexia, bulimia or eating disorders not otherwise specified (EDNOS), with a small positive effect size (Table S2).

Here we also include studies that measure eye tracking [44, 79, 83], as this can be used as a measure of reward sensitivity [97, 108]. Two studies tracked participants' eye movement while they were presented with a series of food and non-food images on a computer screen, and recruited those with frequent food cravings [44, 79]. Although both studies showed reduced food craving intensity (*g* = -0.54; 95% CI = -1.23, 0.15) (Table S2), the significant reduction in fixation on food by Fregni et al. [44] was not replicated by Lapenta et al. [79]. An additional study used an anti-saccade task, where participants were sat in front of a computer screen displaying a central cross; a food image was displayed on either the left or right side of the screen, and participants were required to look in the opposite direction as fast as possible [83]. The authors found a current intensity-dependent effect, where faster latency of anti-saccades were shown following 2.0 mA, but not 1.0 mA, tDCS in participants with BED.

Although there appears to be a more consistent effect of tDCS on food reward, when compared to craving and subjective appetite, there are only a limited number of studies confirming these effects. A greater number of studies incorporating reward-based measures is needed, and these studies should focus on recruiting participants with deficits in the

control of this reward, as these individuals are likely to be responsive to the modulatory effects of stimulation [15]. In addition, studies should focus on a more comprehensive measure of explicit and implicit components of reward, and use validated measure such as the LFPQ.

3.6 Food Consumption

Total food consumption, often reported as caloric intake, was measured across 15 studies. Intake was primarily assessed through *ad libitum* buffets, with some studies using a vending machine paradigm [48, 64] or food recall [65]. The *ad libitum* buffets vary in quality, with many studies only providing participants with energy-dense, high-sugar and high-fat foods (e.g. chocolate, potato chips, cookies) [44, 45, 51, 52, 76, 79, 80, 82]. Although this type of buffet can be used to measure the amount of food consumed, it ignores the more qualitative nutrient and sensory aspects of food choice [109]. Studies that use these highly palatable foods also typically only provide 3 to 4 different food options, with only two studies providing a greater variety of 9 to 11 options [44, 79]. Only a small number of studies included a greater selection of foods, incorporating healthier items (e.g. fruits, vegetables) with the more energy-dense foods (e.g. chocolate, potato chips), and providing 8 to 29 options [14, 46, 47, 88]. It should be noted that providing a large variety of foods can lead to overconsumption through delayed satiation [110]; the number of food options should be carefully considered. As well as providing a greater variety of foods, it is important to consider the liking for each food made available as this will likely drive the amount of the food consumed [109, 111]; many of the studies included in this review do not measure participants' liking of the test foods.

In line with the measures discussed above, there is a lack of overall effect of active versus sham tDCS on food consumption measures (g = -0.09; 95% CI = -0.31, 0.14), with a similar trivial effect in the "healthy" group (g = -0.08; 95% CI = -0.32, 0.16) (Figure S10). As with explicit wanting, the expectation effect observed by Ray et al. [76] led to greater effect sizes in favour of active tDCS. When this effect was removed, the effect in favour of active tDCS was reduced for both the overall (g = 0.01; 95% CI = -0.18, 0.20) and "healthy" groups (g = 0.05;

95% CI = -0.07, 0.17) (Figure 6). In comparison, a greater effect of active versus sham tDCS can be seen in trait groups (g = -0.12; 95% CI = -0.76, 0.51) (Figure 6), driven particularly by participants displaying frequent food cravings (g = -0.30; 95% CI = -1.32, 0.72) and binge eating traits (g = -0.23; 95% CI = -0.74, 0.28) (Table S2).

***** INSERT FIGURE 6 HERE *****

Although two studies found reduced *ad libitum* consumption when comparing active to sham tDCS in those who experience frequent food cravings [44, 79], this effect was not shown across further studies recruiting similar populations [45, 80], with an increase in chocolate consumption in a cohort with specific cravings for chocolate [82]. It is important to note that food craving is not correlated with food consumption [51]. However, where specific behavioural traits are evident (e.g. binge-type behaviour), heightened food cravings can lead to greater food intake [112]. Therefore, it is possible that other eating behaviour traits are also influencing this discrepancy in effects. Burgess et al. [51] recruited participants with BED or subthreshold BED (i.e. meet all BED criteria with the exception of binge eating frequency), and found an 11% reduction in food consumption. However, when the authors replicated their study in participants with frank (non-binge eating) obesity, they did not find a main effect of active versus sham tDCS on food consumption [52]. Only when specific behaviour traits were included as covariates in statistical analyses did an effect appear; males with intent to restrict or non-planning impulsiveness traits had a 13% reduction in the consumption of preferred foods. The studies that recruited participants experiencing frequent food cravings did not measure wider eating behaviour traits, and so a definitive effect of these wider traits on food consumption is not clear.

This effect on preferred versus less-preferred foods has been demonstrated across several studies [51, 52, 76]. Sedgmond et al. [46] also found that the consumption of familiar healthier foods (carrots, grapes, rice cakes, breadsticks) was greater following active tDCS in a “healthy”

cohort. This again demonstrates the need for providing wider food options as part of an *ad libitum* buffet to account for differences in individual taste, preference and familiarity [109, 111]. It is particularly difficult to determine the impact of behaviour traits on tDCS-mediated changes in food consumption across different food groups, as the studies that include a more varied buffet only recruit those participants deemed "healthy" (i.e. do not report a susceptibility to overconsumption). Future studies should identify the effects of a varied *ad libitum* buffet in a population susceptible to overconsumption, to determine whether the effects of tDCS on consumptive behaviours are specific to highly palatable foods or can modulate the consumption of wider food groups.

The vending machine paradigm involved unrestricted and *ad libitum* access to an automated vending machine for 23.5 hours per day as part of an inpatient facility [48, 64]. The vending machines were filled with 40 foods that were pre-selected by each participant as the most preferred items from a larger group of foods. Participants were also given access to soda, juice, milk and condiments in addition to the pre-selected foods, and any food not consumed by the participant was recorded. This method of measuring food consumption is considered accurate, particularly in comparison to self-reported measures such as a food diary, with an intra-class correlation coefficient of 0.84 to 0.90 [113]. In this vending machine paradigm, Gluck et al. [48] and Heinitz et al. [64] were able to demonstrate reduced food consumption when comparing active to sham tDCS. However, this was only for particular food groups, being candy [64] or fat and soda [48], and there was no repetition of effect for these specific food groups across the studies. Although both studies report successful blinding, 75% of those in the active group were able to correctly identify the condition they received [48] and the effect of this bias on food consumption cannot be ruled out. This is an important consideration, as Ray et al. [76] found that the expectation of receiving active tDCS resulted in a 37.4% reduction in consumption, regardless of which condition the participants actually received.

Finally, Fassini et al. [65] measured food consumption via recall. To increase the validity of this measure, the authors asked participants to complete a photo record book [65]. The study did not find any difference in food consumption between stimulation groups. This may be due to the issues with accuracy and bias during food recall if not conducted in a standardised manner [114], but may also be due to an inability of tDCS to modulate food consumption beyond the testing period. This technique has been shown to alter cortical activity for up to 90 minutes post-stimulation [37], with the consumption of foods that were recalled likely being outside of this window. The impact of tDCS on food consumption is less clear than other measures discussed in this review, and this efficacy of tDCS to reduce food consumption has previously been questioned [64, 115]. Although there is some evidence to suggest tDCS can modulate energy intake for specific food groups, the method of measuring food intake and other methodological considerations (e.g. participant characteristics, stimulation parameters) vary greatly between studies. In order to identify an effect of tDCS on consumptive behaviours, more consistent and carefully considered use of feeding practices is required.

4. CONCLUSION

The increased interest in tDCS for the modulation of eating behaviours has led to a wealth of methodological approaches. These varying approaches are important for initially identifying the impact of tDCS across measures and populations, but as we start to build a greater research base and look to find consistent effects, it is important that we start to be more consistent in our approach. In this review we have considered how differences in participant characteristics can shape the effects of tDCS, and there appears a more evident and consistent effect of tDCS in those susceptible to hedonic-driven appetite. This is logical as neuroimaging studies of those with specific traits (e.g. binge eating symptomatology) show reduced activity in the PFC [28, 29], and so these individuals will likely benefit from hyper-activation of this cortical region through tDCS. Several recent studies have acknowledged this trait-dependent effect [51-53], and the lack of significant results for participants who do not show susceptibility to the rewarding components of food should not be surprising.

With the aim of improving consistency and identifying a meaningful effect of tDCS, we suggest that future work adhere with the following recommendations:

1. Focus on recruiting participants who are susceptible to hedonic-driven appetite (e.g. those experiencing frequent food craving or presenting with binge-type behaviour).
2. Recruit participants who have trait susceptibilities for the specific outcome measure of interest (e.g. recruit those with binge eating symptomatology when looking to modulate food reward).
3. To elucidate the potential link between enhanced executive functioning and improved appetite control following tDCS, studies should establish participants' baseline executive functioning capabilities and monitor any changes following stimulation.
4. Limit the information provided to participants during recruitment and screening procedures, as this can drive any effects on eating behaviour outcomes.
5. Incorporate a comprehensive group of validated measures, including explicit liking and explicit and implicit wanting.
6. Control fasting duration and measure baseline subjective appetite, even where subjective appetite is not a measure of interest.

We acknowledge that our meta-analysis considers the effects of heterogeneous tDCS parameters on eating behaviours. This may account for some variation in effect sizes, and it is important that the above recommendations are met with the use of effective stimulation parameters and appropriate study design (see [116]). Our understanding of population-based differences in tDCS effects is still limited, and we need more studies to confirm our hypothesis that those with deficits in the control of eating behaviour will be responsive to the effects of tDCS. However, early data suggests this distinction may be apparent. This also highlights the further need for the publication of null effects, which will help identify potential cohorts that are unresponsive to tDCS. This should go hand-in-hand with the reporting of

Bayesian statistics so study results can be quantified in terms of their agreement with the alternative or null hypotheses.

AUTHOR CONTRIBUTIONS

Jordan D. Beaumont: Conceptualisation, Methodology, Validation, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualisation, Project administration. **Natalie C. Smith**: Validation, Data curation. **David Starr**: Validation, Data curation. **Danielle Davis**: Conceptualisation, Writing – review & editing, Supervision. **Michelle Dalton**: Conceptualisation, Writing – review & editing, Supervision. **Alexander Nowicky**: Writing – review & editing. **Mark Russell**: Writing – review & editing. **Martin J. Barwood**: Conceptualisation, Methodology, Validation, Writing – review & editing, Supervision.

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967 **TABLE LEGENDS**

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969 **Table 1** Overview of participant characteristics and study design of included studies.

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971 **Table 2** Overview of appetite-related measures and main results.

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FIGURE LEGENDS

Figure 1 PRISMA flow diagram detailing the search and selection process performed to identify studies applying conventional tDCS for the modulation of eating behaviours.

Figure 2 Risk of bias across the 28 reviewed studies. A colour version of this figure is available in the supplementary material (see Figure S1).

Figure 3 Forest plot of standardised mean difference and 95% CI for the overall effects of tDCS on subjective appetite scores.

Figure 4 Forest plot of standardised mean difference and 95% CI for the overall and subgroup effects of tDCS on food craving (FCQ-S) scores.

Figure 5 Forest plot of standardised mean difference and 95% CI for the overall effects of tDCS on food reward scores.

Figure 6 Forest plot of standardised mean difference and 95% CI for the overall and subgroup effects of tDCS on food consumption (without expectation effect).