The effect of transcranial direct current stimulation (tDCS) on food craving, reward and appetite in a healthy population.

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ABSTRACT

The ability to control hedonic appetite is associated with executive functioning originating in the prefrontal cortex (PFC). The rewarding components of food can override homeostatic mechanisms, potentiating obesogenic behaviours. Indeed, those susceptible to overconsumption appear to have PFC hypo-activation. Transcranial direct current stimulation (tDCS) over the dorsolateral PFC (DLPFC) has been shown to reduce food craving and consumption, potentially via attenuating this reward response. We examined the effects of stimulation on food reward and craving using a healthy-weight cohort. This study is amongst the first to explore the effects of tDCS on explicit and implicit components of reward for different food categories. Twenty-one healthy-weight participants (24 ± 7 years, 22.8 ± 2.3 $kg \cdot m^{-2}$) completed two sessions involving double-blind, randomised and counterbalanced anodal or sham tDCS over the right DLPFC, at 2 milliampere for 20 minutes. Food craving (Food Craving Questionnaire-State), reward (Leeds Food Preference Questionnaire), and subjective appetite (100 mm visual analogue scales) were measured pre- and post-tDCS. Eating behaviour trait susceptibility was assessed using the Three Factor Eating Questionnaire-Short Form, Control of Eating Questionnaire, and Food Craving Questionnaire-Trait-reduced. Stimulation did not alter food craving, reward or appetite in healthy-weight participants who displayed low susceptibility to overconsumption, with low trait craving, good craving control, and low uncontrolled eating and emotional eating behaviour. Implicit and explicit reward were reliable measures of hedonic appetite, suggesting these are robust targets for future tDCS research. These findings suggest that applying tDCS over the DLPFC does not change food reward response in individuals not at risk for overconsumption, and future work should focus on those at risk of overconsumption who may be more responsive to the effects of tDCS on hedonic appetite.

KEYWORDS

Appetite control; Dorsolateral prefrontal cortex; Neuromodulation; Food craving; Food reward

HIGHLIGHTS

- We consider the effects of tDCS on implicit and explicit reward using a validated task
- High reliability in reward measures suggest a robust target for future tDCS studies
- Previously findings are limited by high variation within food-related variables
- Effects of tDCS may be dependent on participant eating behaviour traits
- Future work should screen participants using validated psychometric questionnaires

1. INTRODUCTION

Obesity is a global health epidemic that affects more than 650 million adults worldwide, and is associated with an increased risk of developing many other health conditions (World Health Organisation, 2020). The aetiology of obesity involves a complex relationship between behavioural, biological and environmental factors, contributing to the dysregulation of energy balance (Hill, 2006). Hedonic appetite can potentiate this dysregulation, with the rewarding components of food overriding homeostatic mechanisms (Boswell & Kober, 2016; Kober & Boswell, 2018). The ability to control hedonic appetite is associated with executive functioning, which originate in the prefrontal cortex (PFC) and inhibit impulsive actions in favour of goal-directed behaviours (Joseph, Alonso-Alonso, Bond, Pascual-Leone, & Blackburn, 2011). Altered PFC activity in response to food stimuli has been identified in individuals with obesity, especially those displaying binge eating symptoms (Boeka & Lokken, 2011; Karhunen, et al., 2000). It is proposed that a reduction of activity in the right dorsolateral PFC (DLPFC) could facilitate obesogenic behaviours through poor appetite control (Alonso-Alonso & Pascual-Leone, 2007). Indeed, dysregulation of the DLPFC has been linked with greater impulsive behaviours, often leading to overconsumption (Gluck, Viswanath, & Stinson, 2017). Increasing DLPFC activity may improve the ability to control hedonic appetite, providing a novel paradigm in the treatment of obesity (Alonso-Alonso, 2013).

The modulation of cortical activity is possible through the use of non-invasive brain stimulation techniques, such as transcranial direct current stimulation (tDCS). This form of stimulation involves the application of a weak electrical current, typically up to 2 milliampere (mA), to a specific region of the brain via two electrodes that are placed over the scalp (Nitsche & Paulus, 2000). The current is emitted from a battery-powered device, where it is delivered to the brain through an anode electrode and returns to the device through a cathode electrode. The current intensity is not sufficient to cause neuronal firing, but results in the polarity-dependent subthreshold modulation of resting membrane potentials (Filmer,

Dux, & Mattingley, 2014; Jamil & Nitsche, 2017). Although the exact mechanisms are not fully understood, it appears the current inhibits neurotransmitters at the synapse; the anode is associated with the inhibition of gamma-aminobutyric acid (GABA) whereas the cathode is associated with the inhibition of glutamate (Filmer, et al., 2014; Stagg, Antal, & Nitsche, 2018). The inhibition of these neurotransmitters increases or decreases the likelihood of spontaneous neuronal firing, respectively. In addition to these acute effects, tDCS also appears to elicit changes in cortical activity beyond the stimulation duration. For example, in an early study by Nitsche and Paulus (2001), anodal tDCS lasting 13 minutes resulted in greater activity in the motor cortex for up to 90 minutes post-stimulation.

When identifying the effects of tDCS on hedonic appetite, many studies have focussed on measuring state food craving. The first study to identify the impact of tDCS on hedonic appetite compared anodal stimulation to the left and right DLPFC in 21 healthy-weight individuals with frequent food cravings, defined as experiencing 3 or more strong urges to consume high-calorie foods per day (Fregni, et al., 2008). When applying 2 mA stimulation for 20 minutes, a significant reduction in food craving was observed following tDCS over the right DLPFC, but not when applied to the left hemisphere. This reduction in state craving score was replicated in a second study that used the same stimulation parameters and recruited a similar participant cohort (n = 19) (Goldman, et al., 2011).

In two recent publications, Burgess and colleagues highlight a potential eating behaviour trait-dependent effect of tDCS (Burgess, et al., 2016; Ray, et al., 2017). Thirty participants who were obese and met the diagnostic criteria for binge eating disorder (BED) underwent 20 minutes of 2 mA tDCS to the right DLPFC, which resulted in a significant decrease in state food craving and in-laboratory food consumption (Burgess, et al., 2016). In contrast, these effects were not significant when this protocol was replicated in 18 participants with frank obesity (i.e. non-binge eating) (Ray, et al., 2017). This suggests that the effects of tDCS may be dependent on individual variation in the level of susceptibility to reward-driven

overconsumption. Consistent with this, previous research has demonstrated that individuals with BED are hyper-responsive to the rewarding aspects of food (Davis, 2013; Davis, et al., 2009). The estimated prevalence of BED in the general population ranges from 0.7 – 3.0%, and is commonly comorbid with overweight and obesity (Kessler, et al., 2013). Recurrent episodes of binge eating behaviour are estimated to occur in 10 – 20% of individuals who are healthy weight, overweight or obese, and constitutes a trait that can be assessed psychometrically and applied to a non-clinical population. Similar to findings in individuals with BED, individuals with eating behaviour trait susceptibility to overconsume (i.e. binge eating and emotional eating) have been found to be hyper-responsive to the rewarding aspects of food (Dalton, Blundell, & Finlayson, 2013a). Therefore, including validated measures of food reward and eating behaviour trait susceptibility may be important when considering the effect of tDCS on food consumption, reward and craving. To date, no study has identified the effects of tDCS on implicit and explicit components of reward across different food categories.

Although there are many promising findings, not all studies have found an effect of tDCS on measures of hedonic appetite. This may be due to the inconsistent application of stimulation parameters (e.g. variation in target electrode placement and current intensity), inadequate experimental blinding, and large variation in experimental measures (Hall, Vincent, & Burhan, 2018; Tremblay, et al., 2014). The most consistently used measure of hedonic appetite in tDCS research is food craving, which is commonly assessed using the Food Craving Questionnaire-State (FCQ-S) (Cepeda-Benito, Gleaves, Williams, & Erath, 2000). Although significant effects of tDCS on food craving have been identified (Fregni, et al., 2008; Goldman, et al., 2011), this has not been consistently shown (Georgii, Goldhofer, Meule, Richard, & Blechert, 2017; Sedgmond, et al., 2019). Across studies there is large variation in state food craving scores, ranging from 0.40% to 41.67% following the active condition (Fregni, et al., 2008; Goldman, et al., 2011; Kekic, et al., 2014; Ljubisavljevic, Maxood, Bjekic, Oommen, & Nagelkerke, 2016), which may be due to the poor reliability of

these measures. Developmental publications of the FCQ-S suggest low-to-moderate reliability (r = 0.39 – 0.56) (Cepeda-Benito, et al., 2000; Meule, Teran, et al., 2014). Measures of food consumption have also been utilised, primarily using *ad libitum* buffets of highly palatable foods (Burgess, et al., 2016; Georgii, et al., 2017; Gluck, et al., 2015; Ray, et al., 2017; Sedgmond, et al., 2019). Although greater craving control is associated with improved weight loss outcomes (Dalton, et al., 2017), the effects of tDCS on craving and consumption are not correlated (Burgess, et al., 2016), suggesting other targets are required to validate tDCS as an intervention to alter eating behaviour. Food reward plays a more pivotal role in the dysregulation of energy balance (Boswell & Kober, 2016; Kober & Boswell, 2018). Therefore, it is important to look beyond the measure of food craving and identify the role of tDCS in modulating food reward.

The present study examined how measures of food craving, reward and appetite would change following the inducement of hyper-activity of the right DLPFC through tDCS in a healthy-weight cohort. We hypothesised stimulation would reduce state food craving and subjective appetite, based on previous findings utilising healthy participant groups (Fregni, et al., 2008; Goldman, et al., 2011; Kekic, et al., 2014; Lapenta, Sierve, de Macedo, Fregni, & Boggio, 2014). We also hypothesised that participants' preference for and perceived rewarding value of high-fat and sweet foods would be diminished following anodal tDCS. We also looked to establish the reliability of these measures, including both implicit and explicit components of reward, prior to tDCS with a view to establishing the viability of their future use in our research.

2. METHODS

2.1 Participants

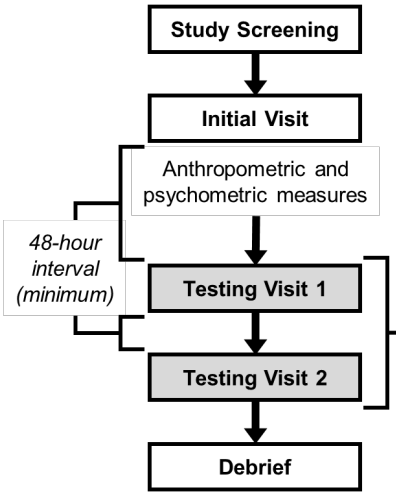
The study was approved by an institutional ethics committee, and all participants provided written informed consent. Sample size was determined using G*Power 3.0.10 (Faul, Erdfelder, Lang, & Buchner, 2007). An effect size f of 0.33 was based on mean percentage

difference from baseline in food craving scores following single session tDCS (mean difference between conditions -22.22 ± 33.68%) (Fregni, et al., 2008; Goldman, et al., 2011; Kekic, et al., 2014; Ljubisavljevic, et al., 2016). Using α error probability of 0.05, 1 group with 2 measurements, a correlation among repeated measures equal to 0.5, and non-sphericity correlation Є of 1, sample size calculations determined a minimum sample size of 21, with actual power of 0.82, was required. Twenty-one participants (24 ± 7 years, 22.8 ± 2.3 $kg \cdot m^{-2}$) were recruited via email and poster advertisements. Interested individuals were initially screened with an online questionnaire. Eligible participants were male or female between 18 and 60 years of age who presented with a body mass index (BMI) between 18.5 and 24.9. All participants were free of neurological, cardiovascular, metabolic and joint disease, and potential participants were excluded if they presented with low mood or depressive symptoms, as indicated using the Centre for Epidemiologic Studies Short Depression Scale (CESD-10) (Andresen, Malmgren, Carter, & Patrick, 1994; Radloff, 1977). Female participants who were pregnant or wishing to conceive were also excluded from the study. Participants were naïve to tDCS protocols, non-smokers and were not recreational drug users or taking any medications at the time of data collection.

2.2 Experimental Design

The study utilised a double-blind, within-participant, repeated measures design. Participants attended the laboratory on three separate occasions (Figure 1). During the first visit, participants completed a series of psychometric questionnaires, and height and body composition were measured. Visits 2 and 3 were experimental trials where all participants received either active or sham tDCS in a randomised and counterbalanced order. Randomisation was determined using a permuted block paradigm and completed by an independent party. The participants and researcher conducting stimulation were blind to the tDCS condition, adhering to a double-blind design, which was maintained using a pin-protected device. All sessions were scheduled at the same time of day within-subject, occurring between 09:00 and 15:00, and with a minimum interval of 48 hours between

sessions to prevent any residual effects of stimulation (Alonzo, Brassil, Taylor, Martin, & Loo, 2012).



Time (min)	Task
0	Baseline Questionnaire (adherence to fasting criteria)
2	Questionnaires (pre-tDCS): Appetite VAS → LFPQ → FCQ-S
17	tDCS preparatory procedures (see 2.4)
22	Active or Sham tDCS (randomised and counterbalanced)
42	Adverse Events Questionnaire
45	Questionnaires (post-tDCS): Appetite VAS → LFPQ → FCQ-S
60	Adverse Events Questionnaire
75	Adverse Events Questionnaire
90	Adverse Events Questionnaire

Figure 1 Study Procedure

FCQ-S, Food Craving Questionnaire-State; LFPQ, Leeds Food Preference Questionnaire; tDCS, transcranial direct current stimulation; VAS, visual analogue scales.

2.3 Procedure

Participants were required to fast for a minimum of 4 hours prior to each visit, where they were asked to refrain from consuming any food or drink other than water. In addition, they were asked to refrain from consuming products containing caffeine and alcohol in the 12 or 24 hours prior to each visit, respectively. Adherence to this fasting criteria was self-reported at the start of each visit. On arrival at the laboratory, participants were instructed to turn off their mobile phones and remove any metallic objects from their person in adherence with our tDCS protocol.

During visit 1, participants completed the Three Factor Eating Questionnaire-Short Form (TFEQ-r18), Control of Eating Questionnaire (CoEQ), and Food Craving Questionnaire-Trait-reduced (FCQ-T-r); see 2.5.1. Height was measured using a portable stadiometer (SECA

Limited, Birmingham, UK) to the nearest mm. Measurements were taken following inhalation, with the participant standing straight, their back to the rule, and their eyeline level with ear canal. Body composition, including weight and BMI, was assessed using a Tanita BC-418MA analyser (Tanita Europe B.V., Amsterdam). Weight was measured to the nearest 0.1 kg, and body fat percentage to the nearest 0.1%. Participants were then shown the food images used in the Leeds Food Preference Questionnaire (LFPQ; see 2.5.4), and their familiarity and acceptance of each food item was assessed. Any food items that were unfamiliar or had low acceptance (i.e. disliked or not consumed in the normal diet) were substituted with images from a database of additional items with similar nutritional and sensory properties (Oustric, et al., 2020).

During visits 2 and 3, participants completed a series of questionnaires immediately pre-tDCS (Figure 1). These included appetite visual analogue scales (VAS), the FCQ-S and the LFPQ; see 2.5. Each participant then underwent 20 minutes of active or sham tDCS. Questionnaires were then repeated immediately post-stimulation. Visits 2 and 3 were identical, apart from the stimulation condition. At the end of visit 3, participants were debriefed. They were informed of the sham stimulation condition and were asked whether they were able to differentiate between the active and sham conditions, and in which visit they believe active tDCS was delivered.

2.4 Stimulation Protocol

Stimulation was delivered using the HDCstim direct current stimulator (Newronika s.r.l., Milan, Italy) by a trained researcher. Anodal stimulation was used to target the right DLPFC, in accordance with the International Standards for Electroencephalography 10-20 system (Klem, Lüders, Jasper, & Elger, 1999). A 25 cm^2 anode electrode was placed over the frontal area 4 (F4) and a 51 cm^2 cathode electrode placed over occipital zero point (Oz). Cathode placement over the Oz reduces the impact of associated inhibitory effects on study measures (Bestmann, de Berker, & Bonaiuto, 2015; Galetta, 2017), and decreases the

likelihood of current shunting across the scalp (Rush & Driscoll, 1968). Rubber electrodes were housed in sponge pads, pre-soaked in 0.9% sodium chloride. A constant current of 2 mA was delivered through the anode electrode, culminating in a current density of 0.08 $mA \cdot cm^{-2}$. The current was ramped up over a 30-second period, and active tDCS was then delivered for 20 minutes, with a 30-second ramp down. Stimulation was delivered offline (i.e. no task was performed during tDCS), and participants were instructed to remain seated, relaxed and awake. Sham stimulation involved the same setup as active tDCS, but the current was only delivered for 36 seconds (3% active tDCS duration). This is associated with similar sensations (e.g. itching, tingling) (Brunoni, et al., 2011; Nikolin, Huggins, Martin, Alonzo, & Loo, 2018), but has a limited neuromodulatory effect (Gandiga, Hummel, & Cohen, 2006).

The effectiveness of sham as a blinding technique was assessed during debrief. Impedance was measured at the start of stimulation, and periodically checked thereafter. It is recommended that impedance should remain below 5 kilo-ohm (kΩ) (DaSilva, Volz, Bikson, & Fregni, 2011; Thair, Holloway, Newport, & Smith, 2017). The occurrence of sensations and adverse events were measured using a standardised questionnaire (Brunoni, et al., 2011) immediately following stimulation and at regular intervals for a minimum of 45 minutes, in accordance with our standardised procedure.

2.5 Measurements

2.5.1 Psychometric Questionnaires

A series of psychometric questionnaires were used to assess eating behaviour traits of participants in the screening session (Figure 1). The TFEQ-r18 (Karlsson, Persson, Sjöström, & Sullivan, 2000) measures three subscales of eating behaviour; cognitive restraint, uncontrolled eating, and emotional eating. Scores range from 0 to 100 for each subscale, with higher scores indicating a greater presence of problematic eating behaviour. The TFEQ-r18 has good internal validity, with a Cronbach's alpha (α) of 0.82, and

comparable construct validity to the full TFEQ (r = 0.71 – 0.99) (Karlsson, et al., 2000). The CoEQ (Dalton, Finlayson, Hill, & Blundell, 2015) considers the frequency, intensity and severity of food cravings experienced over the previous 7 days. Items are assessed using 100 mm VAS, with scores averaged across items to provide an individual score for craving control, craving for sweet foods, craving for savoury foods, and positive mood. Cronbach's α highlighted acceptable internal validity; craving control α = 0.88, craving for sweet foods α = 0.67, craving for savoury foods α = 0.66, positive mood α = 0.74. Finally, general and habitual food cravings were measured using the 15-item FCQ-T-r (Meule, Hermann, & Kübler, 2014). This questionnaire assesses lack of control over eating, emotions experienced before or during food craving and consumption, and guilt from cravings and/or giving in to cravings. A higher score suggests more frequent cravings and a total score greater than 50 highlights clinically relevant trait cravings (Meule, 2018). The FCQ-T-r has high internal validity (α = 0.94).

2.5.2 Appetite Visual Analogue Scales (VAS)

Four 100 mm VAS were used to assess subjective ratings of appetite (Blundell, et al., 2010), which are sensitive to experimental manipulation and considered reliable and valid measures of subjective appetite (Beechy, Galpern, Petrone, & Das, 2012). Scales measured hunger ("*How hungry do you feel right now?*"), fullness ("*How full do you feel right now?*"), prospective consumption ("*How much food could you eat right now?*"), and the desire to eat ("*How strong is your desire to eat right now?*"). Scores range from 0 to 100, with higher scores indicating greater prevalence of the appetite measure.

2.5.3 Food Craving Questionnaire-State (FCQ-S)

The FCQ-S (Cepeda-Benito, et al., 2000) measures subjective food craving, and is responsive to situational changes (Cepeda-Benito, et al., 2000; Meule, Teran, et al., 2014). This questionnaire assesses the desire to eat, craving for food, and emotional responses to food and consumption over 15 statements. Participants rate each statement on a 5-point

scale, where 1 corresponds with "*Strongly disagree*" and 5 corresponds with "*Strongly agree*". Corresponding scores are totalled, with a minimum score of 15 and a maximum of 75; higher scores equating to greater momentary craving. Similar to the FCQ-T-r, the state FCQ has good internal validity (Cronbach's α = 0.94) (Cepeda-Benito, et al., 2000).

2.5.4 Leeds Food Preference Questionnaire (LFPQ)

The LFPQ (Dalton & Finlayson, 2014; Finlayson, King, & Blundell, 2007) is a validated computer-based assessment of hedonic preference for food, measuring explicit liking and wanting and implicit wanting as components of reward. "Liking" can be defined as the subjective pleasure elicited by food or related cues, whereas "wanting" is the motivational component of reward that refers to subjective desire or craving for foods (see Finlayson and Dalton (2012) for review). Liking operates at an explicit level (i.e. conscious, introspective), and wanting at both explicit and implicit (i.e. subconscious, automatic) levels (Finlayson & Dalton, 2012). The task uses a standardised set of 16 images depicting ready-to-eat foods that are common in the diet (Table 1), and reward is assessed according to the fat content and taste of these foods. Food images illustrate items that are either high (>40% energy) or low (<20% energy) in fat, and either sweet or savoury. Food items are split into four categories; high-fat savoury (HFSA), high-fat sweet (HFSW), low-fat savoury (LFSA), and low-fat sweet (LFSW). The food items are comparable in protein content, palatability and familiarity (Oustric, et al., 2020).

Table 1 Standardised food images used in the LFPQ.

HFSA	HFSW	LFSA	LFSW
Garlic bread	Chocolate biscuits	Green salad	Mixed berry salad
Fries	Glazed doughnut	Broccoli	Skittles
Crisps	Blueberry muffin	Vegetable rice	Haribo
Sausage roll	Milk chocolate	Bread roll	Banana

HFSA, high-fat savoury; HFSW, high-fat sweet; LFSA, low-fat savoury; LFSW, low-fat sweet

The LFPQ involves two tasks, where food items are displayed in pairs (forced-choice task) or individually (single-food task). The forced-choice task measures the implicit wanting for foods. Participants are required to choose the food they most want to consume "right now" from two items presented on a computer screen. Scores for implicit wanting are calculated using a frequency-weighted algorithm, by combining reaction time and the frequency of choosing or avoiding a food (Dalton & Finlayson, 2014). In the single-food task, participants are presented with each of the 16 food items individually and asked to rate "*How much do you want some of this food right now?*" and "*How pleasant would it be to taste some of this food right now?*" on 100 mm VAS. This second task measures explicit wanting and liking, respectively, for each food item. In addition, fat appeal bias (FAB) and taste appeal bias (TAB) scores are calculated by subtracting mean scores across food groups (e.g. mean low-fat scores subtracted from mean high-fat scores), and provide scores for explicit liking, explicit wanting and implicit wanting.

2.6 Data Analysis

Mean and standard deviations (SD) were calculated at each time point (pre- and post-stimulation) under active and sham tDCS conditions. Normality of data were assessed using Shapiro-Wilks test, and reliability of baseline measures were determined using Pearson's *r*

correlations. The effects of tDCS on FCQ-S and LFPQ scores were evaluated using a 2 (condition; active or sham) * 2 (time point; pre-stimulation vs post-stimulation scores) repeated-measures analysis of variance (ANOVA). Post-hoc significant effects were determined using pair-wise comparisons with Bonferroni correction. Although fasting protocols were standardised, significant differences in baseline scores across all appetite VAS measures were found. To control for this difference, scores were transformed to difference from baseline and analysed using a paired-samples t-test. To determine the impact of difference in baseline hunger scores on other test variables, analysis of covariance (ANCOVA) were performed with baseline hunger as a covariate. ANCOVA were additionally performed to control for behaviour trait scores. Adverse events were compared using further paired-samples t-tests. Statistical analyses were performed using SPSS version 21 and 26 (IBM, New York, USA). Data are presented as mean ± SD to an alpha level of 0.05.

To interpret the null findings and assess the strength of evidence, Bayesian statistics were computed using JASP (version 0.13.1; University of Amsterdam). The classification scheme by Lee and Wagenmakers (2013) provides descriptive labels for Bayes factors (BF_{10}), and was used to interpret values. In brief, scores greater than 1 provide evidence in favour of the alternative hypothesis, whereas scores below 1 provide evidence in favour of the null hypothesis. Scores are labelled as anecdotal (score between 1 and 3 or 1 and 0.33), moderate (score between 3 and 10 or 0.33 and 0.10), strong (score between 10 and 30 or 0.10 and 0.03), very strong (score between 30 and 100 or 0.03 and 0.01), or extreme (score greater than 100 or lesser than 0.01).

3. RESULTS

Participant anthropometric and psychometric characteristics are displayed in Table 2. Participants were weight stable (±5%) for 3 months prior to the study, and displayed “healthy” eating behaviour trait profiles as identified by FCQ-T, CoEQ and TFEQ-r18 scores. Scores for the FCQ-T-r were below the 50-point cut-off for clinically relevant trait craving

(Meule, 2018), with CoEQ and TFEQ-r18 scores comparable to healthy-weight individuals in other studies (Anglé, et al., 2009; De Lauzon-Guillain, et al., 2009; Fleurbaix Laventie Ville Sante Study, 2004; Wardle, et al., 2018).

Table 2 Mean, standard deviation and range for participant anthropometric and eating behaviour trait characteristics

	Female	Male	All
N	11	10	21
Age (years)	25 ± 9 (19 – 52)	23 ± 4 (20 – 29)	24 ± 7 (19 – 52)
Height (cm)	165 ± 6 (155 – 175)	179 ± 6 (170 – 189)	172 ± 9 (155 – 189)
Weight (kg)	60.1 ± 7.4 (49.6 – 71.4)	76.5 ± 7.1 (66.6 – 88.9)	67.9 ± 11.0 (49.6 – 88.9)
BMI ($kg \cdot m^{-2}$)	22.0 ± 2.1 (18.5 – 25.0)	23.8 ± 2.2 (20.1 – 27.7*)	22.8 ± 2.3 (18.5 – 27.7*)
Body fat (kg)	16.3 ± 4.3 (10.9 – 23.3)	12.9 ± 4.9 (6.4 – 20.7)	14.7 ± 4.8 (6.4 – 23.3)
Body fat (%)	26.8 ± 4.3 (20.6 – 33.1)	16.6 ± 5.5 (9.2 – 26.0)	21.9 ± 7.1 (9.2 – 33.1)
CESD-10 (AR)	5 ± 3 (0 – 10)	5 ± 4 (0 – 10)	5 ± 3 (0 – 10)
FCQ-T-r (AR)	36 ± 8 (22 – 49)	34 ± 10 (20 – 47)	35 ± 9 (20 – 49)
TFEQ-r18 Cognitive Restraint (AR)	34 ± 19 (5.6 – 61.1)	33 ± 21 (11.1 – 77.8)	40 ± 20 (5.6 – 77.8)
TFEQ-r18 Uncontrolled Eating (AR)	33 ± 11 (7.4 – 44.4)	34 ± 18 (3.7 – 66.7)	33 ± 14 (3.7 – 66.7)
TFEQ-r18 Emotional Eating (AR)	24 ± 24 (0.0 – 66.7)	20 ± 23 (0.0 – 66.7)	22 ± 22 (0 – 66.7)
CoEQ Craving Control (mm)	66 ± 18 (36.0 – 96.2)	68 ± 18 (36.4 – 94.1)	65 ± 18 (36.0 – 96.2)
CoEQ Craving for Sweet Foods (mm)	30 ± 16 (3.0 – 59.7)	28 ± 21 (2.3 – 67.0)	29 ± 18 (2.3 – 67.0)
CoEQ Craving for Savoury Foods (mm)	54 ± 19 (16 – 78)	46 ± 26 (2.0 – 79.3)	51 ± 23 (2.0 – 79.3)
CoEQ Positive Mood (mm)	51 ± 16 (20 – 84)	54 ± 13 (31.0 – 68.3)	52 ± 14 (20 – 84)

* n = 1 with BMI >24.9 due to high fat-free mass (weight 88.9 kg, fat-free mass 74.2 kg, fat mass 14.7 kg / 16.5%).

BMI, Body Mass Index; CESD-10, Centre for Epidemiologic Studies Short Depression Scale; FCQ-T-r, Food Craving Questionnaire-Trait reduced form; TFEQ-r18, Three Factor Eating Questionnaire 18-item version; CoEQ, Control of Eating Questionnaire.

3.1 Appetite Visual Analogue Scales (VAS)

Baseline hunger scores were significantly higher in the active session (63.1 ± 21.4 mm), when compared to the sham session (51.9 ± 25.8 mm) ($t_{(20)}$ = 2.567, p = 0.018). Similarly, scores for fullness ($t_{(20)}$ = 2.925, p = 0.008), prospective consumption ($t_{(20)}$ = 3.196, p = 0.005), and desire to eat ($t_{(20)}$ = 2.756, p = 0.012) were greater at baseline in the active versus sham session. Baseline hunger scores did not significantly affect fullness, prospective consumption or desire to eat (p's > 0.05). There were no significant changes in subjective hunger ($t_{(20)}$ = 0.572, p = 0.574, BF_{10} = 0.264), fullness ($t_{(20)}$ = 0.146, p = 0.886, BF_{10} = 0.230), prospective consumption ($t_{(20)}$ = 0.969, p = 0.344, BF_{10} = 0.345), or desire to eat ($t_{(20)}$ = 1.772, p = 0.092, BF_{10} = 0.858) when comparing pre- and post-stimulation in the active and sham tDCS conditions (Figure 2). Bayes factors show moderate evidence in favour of the null hypothesis over the alternative hypothesis for hunger and fullness, whereas prospective consumption and the desire to eat were supported only by anecdotal evidence in favour of the null hypothesis. When controlling for behaviour traits scores, the effects of tDCS on the desire to eat only neared significance (p = 0.062 – 0.076), and remained non-significant for other subjective appetite measures (p's > 0.32).

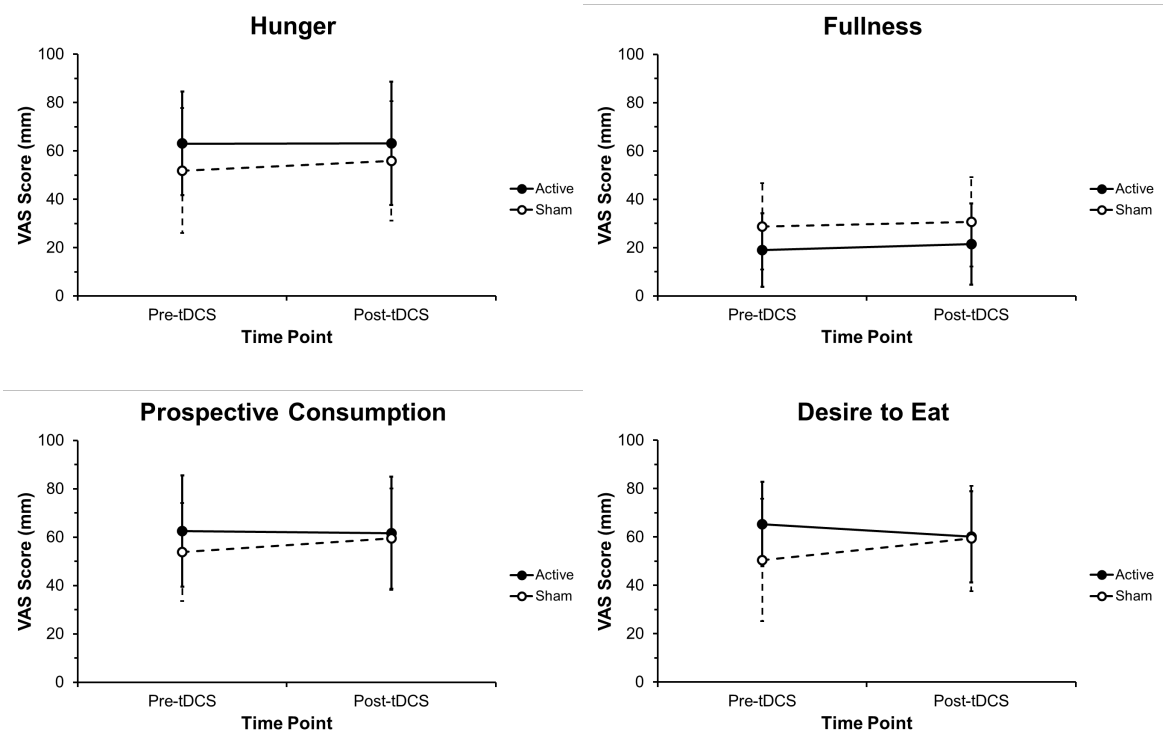


Figure 2 Mean ± SD appetite visual analogue scale (VAS) scores prior to and following tDCS intervention (*n* = 21).

3.2 Food Craving Questionnaire-State (FCQ-S)

There were no significant differences in state food craving from pre- to post-stimulation under active (pre-tDCS 47.2 ± 9.9 AU, post-tDCS 47.8 ± 12.2 AU) or sham conditions (pre-tDCS 43.8 ± 10.2 AU, post-tDCS 44.9 ± 9.0 AU) ($F_{(1, 19)}$ = 0.069, p = 0.797). Bayes factor highlights moderate evidence in favour of the null hypothesis over the alternative hypothesis (BF_{10} = 0.272). In addition, this effect remained non-significant when controlling for baseline hunger ($F_{(1, 38)}$ = 0.037, p = 0.849) and behaviour trait scores (p > 0.74).

3.3 Leeds Food Preference Questionnaire (LFPQ)

Stimulation did not alter measures of implicit or explicit food reward, with the condition * time point interactions for the liking and wanting of HFSA, LFSA, HFSW and LFSW categories showing no significant effect (p > 0.05) (Table 3), which is supported by moderate-to-strong evidence in favour of the null hypothesis over the alternative hypothesis (BF_{10} = 0.041 –

0.168). The interactions remained non-significant when controlling for baseline hunger (p's > 0.10) and behaviour trait scores (p's > 0.11). In addition, tDCS did not significantly change implicit or explicit TAB, with non-significant condition * time point interactions for explicit liking ($F_{(1, 18)}$ = 0.079 p = 0.782, BF_{10} = 0.030), explicit wanting ($F_{(1, 18)}$ = 0.902, p = 0.355, BF_{10} = 0.078), and implicit wanting ($F_{(1, 17)}$ = 0.786, p = 0.388, BF_{10} = 0.076). Again, this is supported by strong evidence in favour of the null hypothesis over the alternative hypothesis and the effects remained non-significant when controlling for baseline hunger (p's > 0.40) and behaviour trait scores (p's > 0.42). Similar non-significant condition * time point interactions were seen for FAB explicit wanting ($F_{(1, 18)}$ = 0.136, p = 0.716, BF_{10} = 0.183) and implicit wanting ($F_{(1, 17)}$ = 0.646, p = 0.433, BF_{10} = 0.111). These scores remained non-significant when controlling for baseline hunger (p = 0.823 and 0.236, respectively) and behaviour trait scores (p's > 0.24). However, there was a significant time point ($F_{(1, 18)}$ = 6.785, p = 0.018) and condition * time point interaction for FAB explicit liking ($F_{(1, 18)}$ = 7.374, p = 0.014, BF_{10} = 0.545); scores increased following both active and sham tDCS, and to a greater extent following active stimulation (Table 3). After controlling for baseline hunger scores this effect was no longer significant ($F_{(1, 36)}$ = 2.944, p = 0.095, BF_{10} = 0.313). Similarly, when controlling for baseline behaviour trait scores no significant effects were identified (p's > 0.08).

Table 3 Pre-stimulation and post-stimulation LFPQ scores (*n* = 21).

		Explicit Liking (mm)		Explicit Wanting (mm)		Implicit Wanting (AU)	
		Pre-tDCS	Post-tDCS	Pre-tDCS	Post-tDCS	Pre-tDCS	Post-tDCS
Active	HFSA	52.9 ± 23.9	64.7 ± 25.1	49.9 ± 23.8	59.9 ± 25.7	-0.7 ± 31.0	15.7 ± 47.7
	LFSA	54.0 ± 20.9	53.7 ± 22.0	53.3 ± 22.1	53.6 ± 19.3	-1.4 ± 24.9	-15.1 ± 38.7
	HFSW	48.2 ± 24.6	54.6 ± 23.0	48.0 ± 24.2	48.8 ± 24.4	-6.5 ± 27.9	-3.6 ± 26.6
	LFSW	60.2 ± 20.8	60.5 ± 21.8	60.0 ± 19.5	57.1 ± 19.5	10.8 ± 28.7	3.8 ± 26.5
	FAB	**-6.6 ± 24.1***	**2.5 ± 21.4***	-7.8 ± 25.0	-1.0 ± 23.3	-7.1 ± 45.3	12.1 ± 53.7
	TAB	0.7 ± 18.2	-1.6 ± 20.0	2.4 ± 15.5	-3.9 ± 19.3	3.8 ± 20.2	-9.5 ± 39.1
Sham	HFSA	53.8 ± 26.6	57.2 ± 25.2	51.8 ± 27.7	55.1 ± 25.8	9.6 ± 33.1	14.4 ± 28.5
	LFSA	49.7 ± 18.4	49.8 ± 18.1	49.7 ± 20.1	49.8 ± 18.2	-2.3 ± 25.2	-3.6 ± 23.5
	HFSW	49.0 ± 27.6	47.1 ± 26.4	42.6 ± 28.0	45.9 ± 26.1	-9.5 ± 29.5	-6.9 ± 30.9
	LFSW	57.4 ± 22.3	55.4 ± 19.0	56.8 ± 20.1	53.5 ± 20.5	5.5 ± 30.0	-0.6 ± 29.4
	FAB	**-2.1 ± 26.3***	**-0.4 ± 23.2***	-6.1 ± 29.6	-1.1 ± 23.8	0.2 ± 45.0	7.6 ± 41.9
	TAB	1.4 ± 18.9	-2.3 ± 12.9	-1.0 ± 16.3	-2.8 ± 11.6	-5.3 ± 29.4	-8.7 ± 25.6

Mean ± SD. HFSA, high-fat savoury; LFSA, low-fat savoury; HFSW, high-fat sweet; LFSW, low-fat sweet; FAB, fat appeal bias; TAB, taste appeal bias. * Indicates significant difference between active and sham conditions ($p < 0.05$).

3.4 Test-Retest Analysis

With the exception of desire to eat (r = 0.382, p = 0.088), all variables were significantly correlated between baseline assessment. Twelve of the 23 variables assessed (across measurement instruments) displayed a strong correlation (r = >0.7), with LFPQ implicit wanting and FAB appearing most consistent. Some baseline measures, particularly FCQ-S and appetite VAS measures, indicated only moderate reliability (r = 0.5 to 0.7; Table 4).

Table 4 Correlations between baseline (pre-tDCS) measures during visits 2 and 3 (n = 21).

			r	p
Food Craving Questionnaire-State			0.549	0.010
Appetite VAS	Hunger		0.654	0.001
	Fullness		0.588	0.005
	Prospective Consumption		0.841	<0.001
	Desire to Eat		0.382	0.088
LFPQ	Implicit Wanting	HFSA	0.837	<0.001
		LFSA	0.795	<0.001
		HFSW	0.882	<0.001
		LFSW	0.718	0.001
	Explicit Liking	HFSA	0.652	0.002
		LFSA	0.664	0.002
		HFSW	0.781	<0.001
		LFSW	0.784	<0.001
	Explicit Wanting	HFSA	0.698	0.001
		LFSA	0.751	<0.001
		HFSW	0.712	0.001
		LFSW	0.668	0.002
	Fat Appeal Bias	Explicit Liking	0.853	<0.001
		Explicit Wanting	0.887	<0.001
		Implicit Wanting	0.677	0.001
	Taste Appeal Bias	Explicit Liking	0.536	0.018
		Explicit Wanting	0.555	0.014
		Implicit Wanting	0.737	<0.001

HFSA, high-fat savoury; HFSW, high-fat sweet; LFPQ, Leeds Food Preference Questionnaire; LFSA, low-fat savoury; LFSW, low-fat sweet; VAS, visual analogue scale.

3.5 Responses to tDCS

Successful delivery of the electric current occurred across all 42 stimulation sessions, with mean impedance levels of 8 ± 4 kΩ at the start of stimulation which reduced to 3 ± 2 kΩ within the initial five minutes of current delivery. Stimulation was well-tolerated by participants with only common adverse events, particularly cutaneous sensations, experienced during tDCS. The most common sensations reported were tingling, itching, sleepiness and a burning sensation (Table 5). Tingling ($p = 0.016$), itching ($p = 0.021$) and sleepiness ($p = 0.021$) were reported by significantly more participants following active tDCS, when compared with sham stimulation. No other sensations were significantly different between conditions. Despite experiencing more minor adverse events, participants were unable to identify the active tDCS session above the level of chance, with only 38% (8/21) of participants able to successfully distinguish between conditions.

Table 5 Frequency of adverse events experienced immediately post-stimulation.

	Active	Sham	p
Headache	7 (33%)	4 (19%)	0.186
Neck pain	0 (0%)	0 (0%)	-
Scalp pain	3 (14%)	1 (5%)	0.329
Tingling	14 (67%)	7 (33%)	**0.016***
Itching	11 (52%)	6 (29%)	**0.021***
Burning sensation	9 (43%)	2 (10%)	0.267
Skin redness	5 (24%)	2 (10%)	0.186
Sleepiness	12 (57%)	7 (33%)	**0.021***
Trouble concentrating	5 (24%)	3 (14%)	0.329
Acute mood change	2 (10%)	2 (10%)	1.000

* Indicates significant difference between active and sham conditions.

4. DISCUSSION

The current study examined the effect of induced hyper-activity of the right DLPFC through tDCS on food craving, reward and subjective appetite measures in a healthy-weight cohort. It is important to note that the sample used in the current study appeared to show low susceptibility to hedonic-driven overconsumption, evidenced by their scores on several measures of eating behaviour traits linked to overconsumption. We also sought to examine the reliability of measures prior to tDCS with a view to establishing the viability of their future use in our research. We report strong relationships between key variables, particularly implicit wanting and FAB, when preparatory procedures prior to tDCS were standardised. These variables may prove to be sensitive targets for detecting significant effects in future eating behaviour-focussed tDCS research. Other variables, particularly food craving measures, proved less stable and may require tighter experimental control or larger sample sizes to reveal differences. Collectively our findings are novel to tDCS research.

Prior work has mainly focussed on measuring food craving and in-laboratory consumption with equivocal findings (Fregni, et al., 2008; Georgii, et al., 2017; Goldman, et al., 2011; Sedgmond, et al., 2019). The present study is favourable by comparison in sample size, study design (i.e. sham-controlled and double-blind) and stimulation parameters (Burgess, et al., 2016; Fregni, et al., 2008; Goldman, et al., 2011; Ray, et al., 2017). Recently published meta-analyses have cast doubt in the ability of tDCS to alter measures of food craving (Hall & Lowe, 2018; Lowe, Vincent, & Hall, 2017), which may be due to the poor test-retest reliability of food craving measures (Cepeda-Benito, et al., 2000; Meule, Teran, et al., 2014). This is in agreement with our data which highlighted only moderate reliability of baseline FCQ-S scores. In comparison, our data show strong relationships between baseline measures of implicit and explicit reward. In developing the LFPQ, Dalton and Finlayson (2014) reported a reliability coefficient of 0.6 – 0.7 for implicit wanting and 0.8 – 0.9 for explicit liking measures, with our data supporting this moderate-to-strong reliability. The LFPQ has been utilised in several settings, and is considered a sensitive measure for individual eating behaviour traits (Dalton, et al., 2013a; Dalton, Blundell, & Finlayson, 2013b; Finlayson, Arlotti, Dalton, King, & Blundell, 2011), and a good predictor of in-laboratory and real-world food choice and consumption (French, Mitchell, Finlayson, Blundell, & Jeffery, 2014; Griffioen-Roose, Mars, Finlayson, Blundell, & de Graaf, 2011). The present study is the first to extend the use of the LFPQ to include tDCS procedures, and the reliability of this questionnaire suggests it is a robust measure and should be explored in future research.

It is logical that the significant interaction between tDCS condition and time point for FAB explicit liking was removed when controlling for baseline hunger as the excitatory effects of anodal tDCS are not associated with increased preference for high-fat foods (Goldman, et al., 2011; Jauch-Chara, et al., 2014). In addition, healthy individuals are likely to have a normative response to food stimuli and are able to sufficiently integrate rewarding signals with other appetitive signals to select appropriate eating behaviours (see Alonso-Alonso and

Pascual-Leone (2007) for review). Healthy individuals are also unlikely to have structural deficits observed in obesity and binge eating, which are associated with alteration in reward response (Balodis, Grilo, & Potenza, 2015; Lowe, Reichelt, & Hall, 2019). It is probable that stimulation would have no additive effects in healthy individuals (Burgess, et al., 2016). The greater baseline hunger score likely heightened the rewarding value of high-calorie foods, particularly those high in fat, that participants were exposed to during the computer-based task (Cameron, Goldfield, Finlayson, Blundell, & Doucet, 2014; Finlayson, King, & Blundell, 2008; Mehta, et al., 2012).

In addition to the equivocal findings for food craving and consumption, previous work has been inconsistent in the recruitment of participants and some of the variation in results may be due to participants' eating behaviour traits. Two previous studies have directly linked tDCS effects as occurring in those with abnormal eating behaviours (Burgess, et al., 2016; Ray, et al., 2017), and when comparing further studies that utilise similar tDCS parameters (i.e. 2 mA for 20 minutes over the right DLPFC), a trait-dependent effect is evident. Studies that recruited participants with frequent food cravings found a consistent reduction in measures of state food craving (Fregni, et al., 2008; Goldman, et al., 2011; Kekic, et al., 2014; Lapenta, et al., 2014). In comparison, studies that did not measure behaviour traits or report comparable traits between healthy and overweight populations, fail to find a significant effect of stimulation on craving (Bravo, et al., 2016; Sedgmond, et al., 2019). Our data supports the robustness of healthy eating behaviours against perturbation in cortical activity within the DLPFC, which is assumed to occur in populations that are obese or with BED (Boeka & Lokken, 2011; Karhunen, et al., 2000). We therefore speculate that there is a diminishing return for attempting to increase neuronal activity within the DLPFC when participants are already able to control their eating behaviours. Hyper-activity in this cortical region may have a ceiling effect beyond which no further improvement is seen. This may account for the null effect we found for food craving, reward and appetite following tDCS,

and can be supported by the moderate-to-strong evidence in favour of the null hypothesis as highlighted by our Bayesian statistical approach.

The present study is not without limitation. It is understood that males and females experience different eating behaviours, and may express differing behavioural traits (Rolls, Fedoroff, & Guthrie, 1991). The present study recruited both male and female participants, which may have influenced the effects of tDCS, and provided an additional source of variation across data. However, this is not without precedent as prior studies that recruited male and female participants have shown an experimental effect (Burgess, et al., 2016; Carvalho, et al., 2019; Goldman, et al., 2011). Given the novelty of using the LFPQ it was important to consider the wider effects of tDCS on this variable before focussing on specific sex. Second, our original hypotheses did not consider the impact of eating behaviour traits and as such these were not controlled for during screening. Our inclusion criteria focussed on weight status, but the participants recruited displayed behaviour traits that do not suggest susceptibility to overconsumption, as discussed above; notably, all participants scored below the 50-point cut-off for trait food craving. Third, prior studies have induced hyperactivity in the DLPFC through bilateral and unilateral stimulation of the cortex (Carvalho, et al., 2019; Fassini, et al., 2019; Lapenta, et al., 2014; Ljubisavljevic, et al., 2016). Although these montages have been shown to improve measures of hedonic appetite (Fregni, et al., 2008; Goldman, et al., 2011), the efficacy of such electrode placement has been debated due to the simultaneous effects of anodal and cathodal stimulation on the same cortical region (Bestmann, et al., 2015). The inhibitory effects associated with cathodal stimulation during traditional montages may also impact hedonic appetite measures, as the left DLPFC is implicated in dietary control and food choice behaviour (Higuera-Hernández, et al., 2018). Similar to the right DLPFC, there is some support for reduced activity in the left DLPFC in response to food, when comparing individuals who are lean with those who are obese (Le, et al., 2006; Le, et al., 2007). In the present study, a prefrontal-occipital montage was used, utilising a similar montage seen in previous work (Marron, et al., 2018; Vitor-Costa, et al.,

2015). The ability of this montage to induce hyperactivity in the DLPFC has been confirmed in several recent computational models (Marron, et al., 2018; Zheng, et al., 2016; Zheng, et al., 2017). Moreover, we verified that the electric current was being delivered in a consistent manner across all 42 stimulation sessions by checking impedance. Finally, the effectiveness of common sham procedures as a blinding technique has been debated due to significantly greater sensations often reported following active tDCS (Horvath, 2015). Indeed, in the present study participants reported significantly greater itching, tingling and sleepiness following active stimulation. However, the inability of participants to identify the active protocol beyond the level of chance, despite these heightened sensations, provides further support for the use of standardised sham protocols as a blinding technique in tDCS research (Ambrus, et al., 2012).

5. CONCLUSION

Our study is the first to report the effects of tDCS on components of food reward in sample of healthy individuals with no susceptibility to overconsume, and we show no significant change in these measures. Prior to examining these effects, we established an indication of data reliability and revealed some plausible targets for future effects through tDCS exposure. In the present sample these effects were transient for the most part and, in line with the work by Burgess and colleagues (Burgess, et al., 2016; Ray, et al., 2017), this highlights a behaviour trait-dependent effect of stimulation. Future work should focus on populations who are at risk of reward-driven overconsumption and weight gain, such as those showing recurrent binge eating behaviours, as these individuals may be responsive to the effects of tDCS on hedonic appetite.

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AUTHOR CONTRIBUTIONS

Jordan Beaumont: Conceptualisation, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review and editing, Visualisation, Project administration.

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DECLARATION OF INTEREST

None.

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