No evidence that prefrontal HD-tDCS influences cue-induced food craving

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Abstract

This study investigated whether the application of high definition transcranial direct current stimulation (HD-tDCS) to the dorsolateral prefrontal cortex reduces cue-induced food craving when combined with food-specific inhibitory control training. Using a within-subjects design, participants ($N = 55$) received both active and sham HD-tDCS across two sessions while completing a Go/No-Go task in which foods were either associated with response inhibition or response execution. Food craving was measured pre and post stimulation using a standardised questionnaire as well as desire to eat ratings for foods associated with both response inhibition and response execution in the training task. Results revealed no effect of HD-tDCS on reducing state food craving or desire to eat. Due to the COVID-19 pandemic, we were unable to achieve our maximum preplanned sample size or our minimum desired Bayesian evidence strength across all *a priori* hypotheses; however 6 of the 7 hypotheses converged with moderate or stronger evidence in favour of the null hypothesis over the alternative hypothesis. We discuss the importance of individual differences and provide recommendations for future studies with an emphasis on the importance of cognitive interventions.

Keywords: transcranial direct current stimulation, brain stimulation, food craving, inhibitory control

1. Introduction

Food cravings are an overwhelming desire to consume a specific food, experienced by 60- 100% of the Western adult population (Pelchat, 1997; Taylor, 2019). Given the established link between cravings, increased food consumption and weight gain (Boswell & Kober, 2016; Gendall et al., 1998; Lafay et al., 2000), understanding the neurocognitive mechanisms underlying food craving presents an important goal for basic and translational cognitive

neuroscience. The present study tests whether electric stimulation of prefrontal cortex can be effective in modulating food cravings.

Neuroimaging research has indicated that differences in both cortical structure and function may play a role in the regulation of food-related behaviours (Lowe et al., 2019). Functional differences in prefrontal brain regions such as the dorsolateral prefrontal cortex (DLPFC), have been linked to differences in dietary self-regulation (Gluck et al., 2017). For example, hypo-activity of the DLPFC in response to food images has been identified in obese participants (Brooks et al., 2013), whereas hyper-activity of the DLPFC has been associated with successful self-control when making food choices (Hare et al., 2009). Structural differences have also been revealed; increased grey matter volume in the DLPFC has been linked to dietary self-regulatory success (Schmidt et al., 2018), whereas reduced grey matter volume is associated with increased weight (Brooks et al., 2013) .

Non-invasive brain stimulation research has supported these findings, indicating that increasing activity within the DLPFC can lead to a decrease in both food craving and food consumption (Lowe et al., 2017). Transcranial direct current stimulation (tDCS) is a form of non-invasive brain stimulation that involves passing a weak electrical current through the cortex via scalp electrodes (Nitsche et al., 2003). tDCS has been utilised across multiple studies, modulating the DLPFC in order to investigate its efficacy for modifying food-related behaviours.

In the first study to investigate the effect of tDCS on food craving and consumption, (Fregni et al., 2008) found 20 minutes of stimulation using an anode right/ cathode left montage significantly reduced food craving and food consumption. Using the same montage and

outcome measure, Goldman et al. (2011) and Lapenta et al. (2014) also found a significant reduction in food craving, although, Goldman et al. (2011) did not replicate the effects on food consumption. However, later studies employing very similar tDCS parameters have produced inconsistent findings (Lowe et al., 2017) reporting that effects may be specific to food type, gender and different facets of impulsivity (Kekic et al., 2014). Furthermore, nonsignificant effects have also been reported (Ray et al., 2019; Sedgmond et al., 2019).

In a recent study, Sedgmond et al. (2019) combined the same 20-minute tDCS protocol with a food specific Go/No-Go training task to investigate whether these two interventions could have a cumulative effect on reducing both food craving and consumption. Previous research has indicated that such training tasks can result in decreased consumption of unhealthy foods and weight loss (Adams et al., 2017; Houben & Jansen, 2011; Lawrence, O'Sullivan, et al., 2015; Lawrence, Verbruggen, et al., 2015) and it has been suggested that effects of tDCS may be augmented when coupled with such training (Alonso-Alonso, Miguel & Pascual-Leone, 2007). However, Sedgmond et al. found no reliable effect of tDCS on either food consumption or food craving measured using a standardised state craving questionnaire.

One possible explanation for these null results is the lack of focality when using conventional tDCS. In a recent meta-analysis looking at the effects of non-invasive brain stimulation on food craving and food consumption, Lowe et al. (2017) found no significant effect of tDCS on food craving, but did find a significant effect of transcranial magnetic stimulation (TMS). TMS differs to tDCS in that it has the ability to deliver far greater spatial focality (Wagner et al., 2009). To our knowledge, all tDCS studies within this field have used conventional tDCS with electrodes typically measuring 5x7cm. Electrical field modelling has indicated that large areas of the cortex are disrupted during conventional stimulation (Datta et al., 2008), leading

to the development of more focal applications of tDCS, specifically high definition (HD) tDCS which involves the use of much smaller electrodes (typically 1cm). One electrode is placed over the region of interest, with the remaining four arranged in a ring around the outside of the central electrode. Comparisons of the two methods reveal that the smaller HD electrodes result in a more focal area of stimulation (Datta et al., 2009; see Fig 1).

[Insert Figure 1 here]

The present study sought to further the findings of previous literature with improved tDCS methodologies to investigate effects on food craving. Using a within-subjects design, participants received active and sham HD-tDCS across two separate testing sessions. Based on previous findings all participants received anodal right-hemisphere stimulation due to the inconsistent results produced using anodal left-hemisphere stimulation (Carvalho et al., 2019; Fregni et al., 2008). The stimulation was paired with food-related Go/No-Go training and food craving was measured before and after stimulation. Most studies that have reported a significant effect of tDCS on food craving have recruited participants identified as high food cravers (e.g. Fregni et al., 2008; Goldman et al., 2011; Lapenta et al., 2014; Ljubisavljevic et al., 2016), whereas those reporting non-significant effects did not include any measures of self-reported trait food craving (Ray et al., 2019; Sedgmond et al., 2019). Trait food craving is known to be positively associated with a loss of control around craved foods, often leading to excessive consumption (Taylor, 2019); furthermore, scores on measures of trait food craving have been positively related to BMI (Meule et al., 2012) and symptoms of food addiction (Meule & Kübler, 2012). As such, trait craving was assessed before stimulation using a standardised questionnaire, and changes in *state* food craving were measured before and after stimulation using a desire to eat scale and a standardised questionnaire. Differences

in inhibitory control between stimulation conditions were investigated with a speeded Go/No-Go task (see Sedgmond et al., 2019).

Broadly consistent with previous research (Goldman et al., 2011; Lapenta et al., 2014; Montenegro et al., 2012) we expected active prefrontal HD-tDCS to reduce desire to eat for foods associated with response inhibition (H1a) but not for foods associated with response execution (H1b). We also expected a decrease in overall state food craving for active, compared to sham stimulation (H2). Independently of HD-tDCS, we expected to observe effects of training: in particular, any reduction in craving (H3a) or liking (H3b) before vs. after training should be greater for foods associated with response inhibition than for foods associated with response execution. Further evidence of training effects were expected in the speeded task, where reaction times to no-go foods should be greater than reaction times to novel foods (H3c; see Best et al., 2016). Finally, if prefrontal stimulation boosts inhibitory control then we expected to see fewer commission errors in the speeded task following active HD-tDCS (H4).

1.1.Hypotheses

Primary Hypotheses:

- H1a. Effect of HD-tDCS on desire to eat for inhibited foods: Participants will show a greater reduction in desire to eat no-go foods (unhealthy foods that are associated with the inhibition of a response during Go/No-Go training) from pre-post HD-tDCS following active stimulation compared to sham stimulation. Desire to Eat: $(NoGop_{OST} NoGop_{RE}$) $Acitive < (NoGop_{OST} - NoGop_{RE})$ Sham
- H1b. Effect of HD-tDCS on desire to eat for non-inhibited foods: Participants will show no change in desire to eat go foods (healthy foods associated with a response during

Go/No-Go training) from pre-post HD-tDCS following active stimulation compared to sham stimulation. Desire to Eat: $(G_{OPOST} - G_{OPRE})_{Active} = (G_{OPOST} - G_{OPRE})_{Sham}$

- H2. Main effect of HD-tDCS on craving: Participants will show a greater decrease in state food craving from pre-post HD-tDCS following active stimulation compared to sham stimulation. State Food Craving: (POST–PRE)Active < (POST–PRE)Sham
- H3a. Effect of training on desire to eat, independent of HD-tDCS: For sham stimulation, any reduction in desire to eat scores for no-go foods from pre-post stimulation should be greater than the corresponding difference in desire to eat scores for go foods. Desire to Eat: $(NoGop_{OST} - NoGop_{RE})_{Sham} < (Go_{POST} - Go_{PRE})_{Sham}$
- H3b. Effect of training on liking, independent of HD-tDCS: For sham stimulation, any reduction in liking for no-go foods from pre-post stimulation should be greater than the corresponding difference in liking for go foods. Liking: $(NoGop_{OST} NoG^{O}}$ Bham $<(G^{O}P$ OST – G^{O} PRE)Sham
- H3c. Training effects independent of HD-tDCS: Reaction time (RT) on correct trials for nogo foods should be greater than reaction time for novel foods during the speeded Go/No -go task. RT: $NoGo_{RT} > Novel_{RT}$
- H4. Effect of HD-tDCS on commission errors after training: Participants receiving active HD-tDCS will make fewer commission errors during a subsequent speeded Go/No-go task compared to those receiving sham HD-tDCS. % Errors: Active < Sham

2. Methodology

2.1. Participants

A total of 67 participants aged 18-45 were recruited from a university staff and student population as well as participant databases. We recruited male and female participants. To comply with our ethics for brain stimulation techniques participants were required to have no contraindications to tDCS safety. Participants were excluded if they were currently dieting (with the aim to lose weight), if they had any history of clinically diagnosed eating disorders, if they were fasting or had any allergies to the foods used in the experiment, or if they had a clinical diagnosis of bipolar disorder. All participants were reimbursed for their time at a rate of £10 per hour. The study was approved by the Research Ethics Committee at the School of Psychology, Cardiff University. All participants provided informed consent and were debriefed at the end of the study.

2.2. Sampling Plan

A Sequential Bayes Factor design with maximal n was utilised. We planned for data collection to continue until the desired level of evidence was obtained for all primary hypotheses or until the resource limit was reached (Schönbrodt & Wagenmakers, 2018); however, due to the COVID-19 pandemic and consequent university closure, we were required to terminate data collection before either condition was met. Analyses began when a minimum of 40 datasets had been collected (n_{min}) and analyses were then conducted for every ~10 participants from that point. We planned for data collection to continue until BF₁₀ was \geq 6 or \leq 1/6 for all primary and secondary hypotheses, or a maximum of 100 participants (n_{max}) was reached, whichever happened first. $BF_{10} \ge 6$ will indicate moderate evidence for H₁, while $BF_{10} \le 1/6$ will indicate moderate evidence for H₀ (Lee & Wagenmakers, 2013).

[Insert Figure 2 here]

A Bayes Factor design analysis was conducted to plan for the probability of obtaining the target level of evidence while also controlling for the probability of generating misleading evidence (Schönbrodt & Wagenmakers, 2018a). For H1 an informative prior was used based on all available data from studies investigating the effects of conventional tDCS on food craving (specifically desire/urge to eat; Goldman et al., 2011; Lapenta et al., 2014;

Montenegro et al., 2012). The raw mean effect and standard error of each study was entered into a meta-analysis to produce a posterior mean of 0.6367, which was then used as the prior (Dienes, 2014); see Figure 2). For H2, H3 and H4, previous data was not available, therefore a default scale parameter of $\sqrt{2}/2$ for the half-Cauchy distribution was used (Rouder et al., 2009; see Figure 3).

[Insert Figure 3 here]

2.3. Procedure

Prior to the study, participants were electronically screened for eligibility criteria and were asked to complete the Food Craving Questionnaire – Trait Reduced (FCQ-T-r; (Meule, Hermann, et al., 2014) and the Barratt Impulsiveness Scale (BIS; (Patton et al., 1995). These instruments were included for the purposes of exploratory analyses (see Section 3.3). Participants were informed that they were taking part in a study investigating the effects of personality type on food preferences and were instructed to eat three hours before the study and then refrain from eating. During the first session, participants were required to initially pass safety screening for HD-tDCS and provide their consent. Participants were then additionally required to pass pre-session screening before both sessions (e.g. to exclude recent use of caffeine and/or alcohol). At the beginning of each session participants completed scales measuring their hunger (three visual analogue scales rating on a 100mm scale a. how hungry they feel, b. how full they feel and c. their current desire to eat) and mood (Positive and Negative Affect Schedule; PANAS; (Watson et al., 1988); including measures of discomfort/pain and nausea to rule out differences in food craving due to these

potential influences of HD-tDCS). Participants then completed the General Food Craving Questionnaire – State Version (G-FCQ-S; (Nijs et al., 2007) before completing a further twelve visual analogue scales to measure food-specific desire to eat and liking (see section 2.4 below). After this, participants received HD-tDCS in isolation for 5 minutes before beginning the Go/No-Go training task for a further 15 minutes (see sections 2.7 and 2.8 below). Following HD-tDCS and training, participants completed all scales again before completing the speeded Go/No-Go task (see Figure 4 for the experimental procedure).

[Insert Figure 4 here]

The above procedure was repeated for the second session with the exception that participants did not need to complete HD-tDCS safety screening. The second session was at least seven days after the initial session and efforts were made to ensure that testing took place at the same time for both sessions. At the end of the second session participants were probed for their awareness of the HD-tDCS condition (participants were asked whether they believed they received active or sham HD-tDCS in each session) and the experimenter also recorded participants' height and weight to calculate body mass index $(BMI; kg/m²)$ and probed for awareness of the study's aims. During the debrief participants were asked directly if they were aware of the aim of the study. If they answered 'no' they were reminded of the cover story (that we were interested in the effects of personality types on food preferences). In addition, they were probed for awareness of the stimulus mappings; specifically, they were asked whether they noticed anything in particular in the computer task. If they answered 'no' they were asked whether they thought the signals were distributed evenly, randomly or whether they thought they were grouped. Finally, participants were asked to confirm that they were not currently dieting, and that they had no history of eating disorders.

Twenty-four hours after the completion of each session, participants were emailed a postmonitoring form consisting of 15 questions aimed to monitor whether participants experienced any adverse effects following stimulation. Effects include dizziness, headaches, and skin irritation.

2.4. Food Liking and Desire to Eat

Participants completed twelve 100mm visual analogue scales to measure liking and desire to eat for task-specific foods (from 'not at all' to 'very much'). As in Rogers & Hardman (2015), participants were asked to taste one piece of each of the six foods used in the Go/No-Go task and rate their desire to eat the remaining portion (see Table 1 for foods and quantities). Foods were presented in a pseudorandom order.

[Insert Table 1 here]

2.5. The General Food Craving Questionnaire – State Version

The G-FCQ-S includes 15 statements to measure food craving in the current moment, for example "I'm craving tasty food" (Nijs et al., 2007). There are five subscales: desire to eat, anticipation of positive reinforcement from eating, anticipation of relief from negative feelings from eating, lack of control over eating and craving as a physiological state. Participants were asked to indicate how much they agreed with each statement 'at this very moment' using a five-point scale (from 1 'strongly disagree' to 5 'strongly agree'). Scores can be calculated for specific subscales or a total score can be calculated (ranging from 15 to 75). As the G-FCQ-S measures food craving as a transient state, retest reliability is low

(Taylor, 2019) and construct validity is high with scores correlating with when food was last consumed (Meule et al., 2012).

2.6. The Food Craving Questionnaire – Trait Reduced

The FCQ-T-r measures trait food craving generally (Meule, Hermann, & Kübler, 2014) across 15 statements, for example "I find myself preoccupied with food". There are five subscales: intentions and plans to consume food, lack of control over eating, thoughts or preoccupation with food, emotions before or during food craving and environmental cues that may trigger craving. Participants respond on a six-point scale (from 1 'never or not applicable' to 6 'always') indicating how frequently each of the statements would be true for them in general. Scores can be calculated for specific subscales or a total score can be calculated (ranging from 15 to 90). The FCQ-T-r has been shown to have high retest reliability and high construct validity, confirming that it does assess craving as a trait (Meule, Teran, et al., 2014). Scores on the FCQ-T-r have also been correlated with external eating, emotional eating and body weight (Hormes & Meule, 2016; Innamorati et al., 2016).

2.7. HD-tDCS

Participants received both active and sham stimulation across two separate sessions (order counterbalanced). Four circular electrodes, 1cm in diameter were positioned in the 4x1 HDtDCS montage with the centre electrode (anode) placed over the right DLPFC (F4), positioned according to the international 10-20 EEG system. The four return electrodes (cathodes) were placed at AF4, F2, F6 and FC4. For active stimulation a 1.5mA¹ current was

 1 We originally proposed to use a 2mA current with a 10-second ramp-up time, but pilot testing revealed this to be intolerable with participants reporting pain underneath the site of the anode. We considered increasing the ramp-up time to 30 seconds (while maintaining current at 2mA), but as the pain was still being reported midway through the stimulation, we decided instead to apply a lower and more commonly used current of 1.5mA. Participants still reported some discomfort during pilot sessions when stimulating at 1.5mA using a 10 second ramp-up, but stimulation was tolerable with 1.5 mA and a 30-second ramp-up. We therefore modified

applied using a battery-driven constant-current stimulator (Neurconn DC-STIMULATOR PLUS with the DC-S Equaliser Kit, neuroConn GmbH, Illmenau, Germany) for 20 minutes (with a 30 second ramp up and down). For sham stimulation the stimulator delivered a 1.5mA current for 30 seconds following a 30 second ramp up, before being slowly ramped down to 0mA over a 1-minute period. The experimenter was provided with a study code for each participant that generated either active or sham stimulation, ensuring that the experimenter was blinded to the condition.

2.8. Go/No-Go Task

All tasks were programmed in Matlab (Mathworks, Natick, MA) using Psychophysics Toolbox (www.psychtoolbox.org) and all stimuli will be presented on a 24-inch widescreen LED monitor. The training task was largely identical to that used in Sedgmond et al. (2019) but with some of the stimuli changed to improve the design. Specifically, filler images were changed from clothes to household items to avoid associations between clothes and dieting. Some food images were also replaced to make food categories clearer e.g. various fruit images were replaced with three images of grapes to enhance category-level learning. The training task lasted approximately 15 minutes and consisted of eight blocks of 36 trials with a 15 second break between each block. The blocks randomly presented nine images of unhealthy foods (three images each of chocolate, crisps and biscuits), nine images of healthy foods (three images each of grapes, rice cakes and carrots) and 18 filler images (three each of books, pens, buckets, baskets, chairs and candles). All images were close-up views of the food item against a white background; images were carefully selected on the basis that there were no additional ingredients or packaging, and they were matched for size and complexity.

the protocol in line with these parameters prior to data collection. Previous research has found no significant difference between intensities of 1.5mA and 2mA (Shekhawat & Vanneste, 2018) and there is a substantial body of evidence suggesting that stimulation of the DLPFC at 1.5mA can influence behaviour (Guo et al., 2018; He et al., 2016; Ke et al., 2019; Naka et al., 2018).

Each trial began with the presentation of a central rectangle (inter-trial interval; 1250ms). A stimulus was then presented within this rectangle randomly, and with equal probability, to either the left- or right-hand side (1250ms). Participants were required to respond to the location of the stimulus as quickly and accurately as possible using their left and right index fingers (using the 'C' and 'M' keys, respectively). A signal (the fixation rectangle turns bold for the duration of the trial) was presented on 50% of trials indicating that the participant must withhold their response for that trial. All of the unhealthy food images were presented with a signal (100% mapping), while none of the healthy foods were presented with a signal (0% mapping) and half of the filler images were presented with a signal (50% mapping). Instructions were presented electronically before the task and read verbatim by the experimenter.

2.9. Speeded Go/No-Go Task

To investigate whether HD-tDCS has any effect on inhibitory control we included a second Go/No-go task. The commission error rate (the percentage of erroneous responses made on no-go trials) on the training task is typically very low $(-5%)$ making it difficult to detect any potential improvements in inhibitory control. This second, speeded GNG task, was very similar to the training task but with a faster presentation time (500ms ITI and stimulus presentation time compared to 1250ms) and a lower percentage of no-go trials (33.3% compared to 50%). It has been shown that these changes encourage rapid responding and, as a result of the speed-accuracy trade-off, also increase the rate of commission errors (see Collins & Mullan, 2011; Sedgmond et al., 2019). The speeded GNG task consisted of 15 blocks of 45 trials (a total of 675 trials, lasting ~15 minutes with a 15 second break between each block). Each block randomly presented nine healthy foods, nine unhealthy foods and 18 filler images (identical to those in the training task) as well as nine novel unhealthy foods (three images each of chips, pastries and doughnuts). Three images for each food category and 6 filler images were presented alongside a no-go signal (33.3% mapping). This task also allowed us to compare inhibitory control towards images previously associated with inhibition and novel images. The instructions for this task were presented electronically at the beginning. Participants were informed that this was the same task that they previously performed and were warned about the faster presentation time.

3. Statistical Analyses

3.1. Data Screening

The training data were checked for the percentage of incorrect/ missed responses on no-signal trials and the commission error rate for signal-trials to allow for exclusions based on failure to comply with task instructions (see section 4).

3.2. Analyses

All primary analyses were conducted with the primary investigator still blinded to the HDtDCS conditions. All analyses were tested using Bayesian paired samples t-tests (see Table 2). Frequentist statistics are also reported.

[Insert Table 2 here]

3.3. Exploratory Analyses

Several measures in the design were included for the sole purpose of exploratory analyses and we therefore broadly summarise those analyses here.

Several studies have shown an effect of conventional tDCS on food craving when participants were frequent food cravers (Fregni et al., 2008; Goldman et al., 2011; Lapenta et al., 2014), we therefore explored whether trait food craving (measured using the FCQ-T-r (Meule, Hermann, et al., 2014) acted as a moderator. Research has also indicated that different facets of impulsivity may influence the efficacy of tDCS (Ray et al., 2017) so we also used scores from the BIS (Patton et al., 1995) to assess this.

Exploratory analyses were also undertaken using BMI to assess whether HD-tDCS is more effective in participants with a higher BMI, as has been suggested in previous research (Forcano et al., 2018).

Awareness of HD-tDCS condition was also investigated.

4. Exclusion Criteria

All excluded participants were replaced.

Participants were excluded from the analysis if any of the following preregistered criteria were met:

- Failure to comply with the study's eligibility requirements including:
	- o Not having a current/ history of eating disorders
	- o Not currently being on a diet
- Inability to perform the training task correctly based on the following:
	- o >15% error rate for no-signal trials, including incorrect responses (judging the stimulus to be on the incorrect side of the screen) and missed responses, within either session (sham or active HD-tDCS)
	- o RTs for no-signal trials exceed 3SDs from the group mean within either session (sham or active HD-tDCS)
- o Commission error rate for signal trials in either session (sham or active HD-tDCS) is >3SDs from the group mean within the relevant HD-tDCS condition
- Any reason to discontinue with HD-tDCS based on adverse reaction during the session
- The participant exercised their right to withdraw from the study or their right to withdraw data
- The participant correctly guessed the aim of the study during debrief, when probed for knowledge of the study's aims
- Any unforeseen errors resulting in the loss of any data or inability to complete the entire session

5. Results

5.1. Data exclusions

Based on the preregistered exclusion criteria (see section 4), 12 participants were excluded from data analyses. Of those excluded, 4 participants failed to perform the training task correctly, including 2 for a commission error rate exceeding 3 SDs from the group mean for signal trials, 1 for their reaction times for no-signal trials exceeding 3 SDs from the group mean, and 1 for a 54% error rate for no-signal trials in their second session. The remaining 8 participants were excluded due to the inability to complete their second session due to the COVID-19 lockdown. As noted, due to the COVID-19 pandemic, data collection was terminated prior to the original stopping rule.

[Insert Table 3 here]

5.2. Baseline measures

Following exclusions, the final sample consisted of 55 participants (76.36% female, mean age $= 22.25$, $SE = 0.76$, mean BMI = 23.34, $SE = 0.43$). State variables were analysed to test for any statistically significant differences between active and sham conditions at baseline. We found no statistically significant differences in hunger, fullness, desire to eat, state craving, positive affect, negative affect, nausea or discomfort/pain at baseline (all $B_{JZS} < 0.68$, all *t*s < 1.82, all *p*s > 0.07; see Table 3).

5.3. Primary analyses

The results of all primary hypothesis tests are summarised in Table 4.

[Insert Table 4 here]

5.3.1. Effect of HD-tDCS on desire to eat for inhibited and non-inhibited foods (H1a and H1b)

A paired samples t-test was conducted to assess whether participants showed a greater reduction in desire to eat no-go foods after receiving active stimulation in comparison to sham stimulation (H1a). Despite active stimulation resulting in a numerical decrease in desire to eat ($M = -0.12$, $SE = 0.6$) compared to sham stimulation ($M = 0.81$, $SE = 0.48$), there was no statistically significant difference, with a BF indicating anecdotal evidence for H0 (B_{JZS} = 0.53, $t(54) = 1.22$, $p = 0.11$, $dz = 0.17$). In line with H1b, we also found no evidence for a change in desire to eat go foods following active $(M = 0.51, SE = 0.46)$ compared to sham stimulation ($M = 0.71$, $SE = 0.44$), with analyses suggesting moderate evidence for H0 (B_{JZS}) $= 0.16$, $t(54) = 0.4$, $p = 0.69$, $dz = 0.06$; see Fig. 5).

[Insert Figure 5 here]

5.3.2. Main effect of HD-tDCS on craving (H2)

A paired samples t-test comparing the difference in state craving score from pre to post stimulation (H2) indicated no significant difference between active ($M = 0.46$, $SE = 0.92$) and sham stimulation (M = -0.07, SE = 0.97; B_{JZS} = 0.11, $t(54) = 0.43$, $p = 0.66$, $dz = 0.06$), indicating moderate evidence for H0 (see Fig. 6).

[Insert Figure 6 here]

5.3.3. Training effects independent of HD-tDCS (H3a, H3b, H3c)

Differences in changes in desire to eat and liking in the sham sessions were analysed to assess the effects of the training task, independently of HD-tDCS. For H3a, no significant differences were found in desire to eat no-go food from pre-post sham stimulation ($M = 0.81$, $SE = 0.48$) in comparison to go foods (M = 0.71, $SE = 0.44$; $B_{JZS} = 0.13$, $t(54) = 0.18$, $p =$ 0.57, $dz = 0.02$). Similarly, for H3b, no significant difference was found in liking of no-go foods from pre to post sham stimulation ($M = 0.35$, $SE = 0.35$) in comparison to go foods (M $= 0.64$, SE = 0.39; B_{JZS} = 0.34, $t(54) = 0.87$, $p = 0.2$, $dz = 0.12$). These outcomes provide anecdotal-to-moderate evidence that the training task had no reliable effect on changes in desire to eat or liking.

For H3c, a paired samples t-test found no significant difference in reaction time on correct trials for no-go foods ($M = 348.9$, $SE = 3.78$) in comparison to novel foods ($M = 352$, $SE =$ 3.67) when performance from both active and sham trials was collapsed (H3c; $B_{JZS} = 0.04$, $t(54) = 2.99$, $p = 1$, $dz = 0.4$). This outcome provides strong evidence that participants did not learn the association between the no-go foods and stopping a response; thus the preregistered manipulation check did not succeed.

5.3.4. Effect of HD-tDCS on commission errors after training (H4)

The final confirmatory analysis (H4) investigated the number of commission errors made during the speeded Go/No-Go task following active vs. sham stimulation. No statistically significant difference was observed (Sham: $M = 8.11$, $SE = 0.47$ vs Active: $M = 8.53$, $SE =$ 0.55; $B_{JZS} = 0.07$, $t(54) = 1.15$, $p = 0.87$, $dz = 0.16$), providing strong evidence that active HD-tDCS did not reliably decrease commission errors.

5.4. Exploratory analyses

5.4.1. HD-tDCS tolerability and blinding

Tolerability of HD-tDCS was measured following stimulation. There was no significant difference in reported nausea following active $(M = 1.24, SE = 0.07)$ compared to sham stimulation (M = 1.18, SE = 0.06; B_{JZS} = 0.19, $t(54)$ = 0.72, $p = 0.47$, $dz = 0.11$), but there was weak evidence for a difference in discomfort/pain, with participants reporting a higher discomfort/pain level after active stimulation ($M = 1.29$, $SE = 0.08$) than after sham ($M =$ 1.13, $SE = 0.05$; $B_{JZS} = 0.96$, $t(54) = 2.02$, $p = 0.05$, $dz = 0.27$).

To investigate participants' awareness of HD-tDCS condition after each session, they were asked whether they thought they had been receiving active or sham stimulation. Following active stimulation 65.45% of participants correctly guessed in comparison to 47.27% correctly guessing after sham. Inferential analyses revealed no evidence that participants were systematically aware of which type of stimulation they had been receiving $(B_{JZS} = 0.570$, *χ 2* (1) =1.843, *p =* 0.175, *ϕ* = 0.129).

We then investigated whether participants were more likely to correctly identify which type of stimulation they had received in the second session but not in the first. This appeared to be the case, with participants significantly more likely to identify the stimulation condition in the second (B_{JZS} = 3, $\chi^2(1) = 4.56$, $p = 0.03$, $\phi = 0.29$) session compared to the first (B_{JZS} = 0.33, $\chi^2(1) = 0.09, p = 0.76, \phi = 0.04$

5.4.2. Desire to eat

In addition to measuring participants' desire to eat each food item, participants also completed a general measure of desire to eat using a VAS before and after stimulation. The VAS has been a primary outcome measure in several studies reporting an effect of conventional tDCS on reducing food craving (Fregni et al., 2008; Goldman et al., 2011; Lapenta et al., 2014; Montenegro et al., 2012), so we conducted a paired samples t-test to explore whether there was any difference in desire to eat based on stimulation type. We found no significant difference in overall desire to eat after active stimulation $(M = 0.04, SE = 0.31)$ compared to sham stimulation (M = -0.12, SE = 0.31; B_{JZS} = 0.16, $t(54) = 0.41$, $p = 0.68$, $dz =$ 0.06).

5.4.3. Sweet vs savoury foods

Based on findings from previous research that has indicated that food type may play a role on the effect of tDCS (e.g. Goldman et al., 2011; Kekic et al., 2014), we split the foods by sweet and savoury (3 sweet, 3 savoury). We found no effect of HD-tDCS on desire to eat sweet $(B_{JZS} = 0.17, t(54) = 0.54, p = 0.59, dz = 0.07)$ or savoury foods $(B_{JZS} = 0.34, t(54) = 1.34, p = 0.54$ $0.19, dz = 0.18$.

5.4.4. Exploratory training effects

It is notable that our manipulation check for the training task (H3c) failed. To test for additional evidence of learned associations between no-go stimuli and stopping, we therefore examined the rate (%) of successful response inhibition in the speeded task, collapsed across

sham and active sessions. We found that participants were significantly more successful at response inhibition for overall unhealthy food stimuli ($M = 88.12\%$, $SE = 0.53$) in comparison to novel stimuli (M = 85.76%, SE = 0.51; B_{JZS} = 105,642.56, $t(54) = 6.06$, $p <$ 0.001, $dz = 0.82$) and healthy food stimuli (M = 86.08%, SE = 0.62; B_{JZS} = 457.27, $t(54)$ = 4.43, $p < 0.001$, $dz = 0.6$). These results provide *post hoc* evidence that participants learned an association between the no-go stimuli and stopping. Taken together with the lack of support for H3c, it is possible that response inhibition provides a more sensitive measure of the effect of trained associations than reaction time for previously inhibited foods.

To further demonstrate evidence of learning we looked at performance in the training task itself as is typically done in inhibition training studies (e.g. Camp & Lawrence, 2019; Lawrence, O'Sullivan, et al., 2015; Stice et al., 2017). We first collapsed the data across sham and active sessions and found that, consistent with learning, reaction times for healthy foods $(M = 468.4, SE = 7.92)$ were significantly faster than reaction times for filler stimuli $(M = 168.4, SE = 7.92)$ 489.2, SE = 8.93) on go trials (B_{JZS} = 6.715e+10, $t(54)$ = 9.86, $p < 0.001$, $dz = 1.33$). We also found moderate evidence for an effect of learning when analysing performance on no-go trials. Participants exhibited a higher percentage of successful stopping to unhealthy foods (M $= 97.36$, SE = 0.23) in comparison to filler stimuli (M = 96.57, SE = 0.36) on no-go trials $(B_{JZS} = 3.58, t(54) = 2.67, p = 0.01, dz = 0.36).$

To investigate whether this evidence of learning in the training task was determined by stimulation type, we analysed performance during active and sham sessions separately. During both active and sham stimulation, reaction times for healthy foods were significantly faster than for filler stimuli (active: $B_{JZS} = 1.082e+7$, $t(54) = 7.37$, $p < 0.001$, $dz = 0.99$; sham: $B_{JZS} = 1.281e+9$, $t(54) = 8.72$, $p < 0.001$, $dz = 1.18$). However when looking at successful

response inhibition it seems the significant effect was being driven by performance during sham stimulation (B_{JZS} = 18.04, $t(54)$ = 3.32, $p = 0.002$, $dz = 0.45$); during active stimulation there was no significant difference in successful response inhibition for unhealthy foods compared to filler stimuli (B_{JZS} = 0.15, $t(54) = 0.21$, $p = 0.84$, $dz = 0.03$).

5.4.5. Moderators

Much of the research showing effects of tDCS on food craving has focused on high food cravers (Fregni et al., 2008; Goldman et al., 2011; Lapenta et al., 2014; Ljubisavljevic et al., 2016). We therefore analysed trait craving score as a moderator for the effect of HD-tDCS on state craving score. We used a linear mixed effects analysis in R (R core team, 2016) using the lme4 package (Bates et al., 2015; within-subjects factor: HD-tDCS condition [active or sham]; within-subjects factor: time [pre- or post- stimulation]; continuous factor: trait craving). p-values were calculated from degrees of freedom estimated using Satterthwaite's method (Kuznetsova, Brockhoff & Christensen, 2016). This analysis revealed no significant main effects of HD-tDCS, trait craving or time (all Fs < 3.56, all *p*s > 0.06) and no significant interactions between HD-tDCS and trait craving, HD-tDCS and time, time and trait craving, or the three-way interaction between time, HD-tDCS and trait craving (all Fs < 3.53, all *p*s > 0.06).

Similarly, previous research has indicated that different facets of impulsivity may influence the efficacy of tDCS. Ray et al. (2017) found no main effect of conventional tDCS on food craving in female participants until the BIS attentional subscale was taken into account. A second linear mixed effects analysis was therefore conducted to explore the effects of HDtDCS on food craving in female participants with the attentional subscale as a moderator. However, this revealed no statistically significant main effects or interactions when only

female participants' data was included (all $Fs < 1.14$, all $ps > 0.28$) or when male and female participants were included (all $Fs < 3.77$, all $ps > 0.05$).

Finally, given evidence for an effect of conventional tDCS on craving in both overweight and obese participants (Gluck et al., 2015; Montenegro et al., 2012), we studied BMI as a moderator. Average BMI was 23.3 ($SE = 0.43$); 67.3% of participants were in the healthy weight range, 27.3% were overweight, 3.6% were obese and 1.8% were underweight. A linear mixed effects analysis found no significant main effects or interactions (all $Fs < 1.52$, all $ps > 0.1$).

6. Discussion

Previous studies have provided mixed evidence that brain stimulation – specifically tDCS – may be an effective technique to reduce food craving (Fregni et al., 2008; Goldman et al., 2011; Lowe et al., 2017; Sedgmond et al., 2019). Here we sought to improve upon our previous methods (Sedgmond et al., 2019) by increasing the focality of prefrontal stimulation with HD-tDCS and investigating individual differences thought to play a role in the efficacy of tDCS. Using a double-blind within-subjects design, HD-tDCS was administered alongside inhibition training to assess the combined effect on cue-induced food craving. Overall, results revealed no evidence that prefrontal HD-tDCS influences state food craving or desire to eat, nor did we find any moderating effects of trait craving, BMI, or impulsivity.

Despite our lack of evidence supporting earlier studies displaying an effect of tDCS on craving (e.g. Fregni et al., 2008; Goldman et al., 2011; Lapenta et al., 2014), our findings are consistent with more recent evidence. Combining tDCS with a cognitive bias modification task, Carvalho et al. (2019) found stimulation was not able to reduce craving for chocolate.

Similarly, in a previous study we combined conventional tDCS with a food-specific Go/No-Go training task and found no significant effect of tDCS on reducing craving (Sedgmond et al., 2019). Furthermore, a meta-analysis investigating the findings from published and unpublished data using brain stimulation to modulate food craving and consumption concluded that the effect on food cravings was not significant for tDCS (Lowe et al., 2017). The same meta-analysis did, however, find a significant stimulation effect when TMS was used. A later review also concluded that TMS seems to show more promise than tDCS (Hall et al., 2017). For example, Van den Eynde et al. (2010) found a single session of repetitive TMS (rTMS) to the DLPFC to reduce cue-induced food craving in a clinical group, and in another study rTMS was found to maintain craving level after exposure to food whereas sham stimulation resulted in an increase (Uher et al., 2005). One explanation as to why TMS may produce more robust findings is due to its ability to stimulate an area of the brain with greater spatial focality. However, we addressed this issue in the present study by using HD-tDCS which is far more focal than conventional tDCS (see Fig 1). The mechanisms behind tDCS and TMS also differ; while tDCS is thought to manipulate the membrane potential of neurons, TMS can modulate cortical plasticity and trigger action potentials (Paulus, 2011), which could explain why TMS seems to produce stronger results. However, not all research has been able to replicate these findings. Using a clinical sample, Gay et al. (2016) carried out a multi-session study in which participants underwent 10 rTMS sessions, however no significant effects were found when compared to sham stimulation. Although the effects of TMS seem promising (Lowe et al., 2017), the need for more studies with larger sample sizes, and sufficient power are necessary to better understand these potential effects; the number of studies that have used TMS to investigate its effect within this field is still very small.

While multi-session protocols have produced conflicting results in the TMS literature (e.g. Gay et al., 2016), research has indicated that they may be beneficial in tDCS research. In one study investigating the effect of tDCS on food consumption, there was no effect immediately after stimulation, but there was a significant reduction following eight daily sessions when compared to sham stimulation (Jauch-Chara et al., 2014). This evidence is further supported by a recent meta-analysis that compared the effects of single session tDCS and TMS to multiple sessions, looking at craving and consumption for different substances. Effects did not differ between stimulation type or the substance being investigated, and it was revealed that multi-session protocols were more effective for reducing both craving and consumption, in comparison to single sessions (Song et al., 2019). To our knowledge, only one study thus far has investigated the effects of multiple tDCS sessions on food consumption (Jauch-Chara et al., 2014), and none have looked at food craving. A worthwhile area of investigation could be multiple-session protocols of HD-tDCS.

Much of the research that has demonstrated a reduction in food craving following tDCS has done so in food cravers; either those who self-reported experiencing strong and frequent cravings (Fregni et al., 2008; Goldman et al., 2011; Lapenta et al., 2014), or those identified using a validated measure (Ljubisavljevic et al., 2016). Although we did not specifically recruit food cravers, all participants completed the FCQ-T-r, a questionnaire designed to measure trait craving. In exploratory analyses we included global scores from the FCQ-T-r as a continuous variable to explore whether trait craving acted as a moderator for the effect of HD-tDCS on food craving. Despite sufficient variability in scores across participants (range = 43, min = 16, max = 64), we found no significant effects. Furthermore, a cut off score of 50 has previously been proposed to classify individuals as high food cravers (Meule, 2018). In our sample, almost a quarter of participants met this criterion (23.6%; 13 of 55). Although we

found no evidence to suggest a moderating role of trait craving, in future, researchers may consider recruitment of high trait cravers only.

Previous studies have found that the effects of tDCS on food craving may be dependent on different types of food. While Goldman et al. (2011) and Ljubisavljevic et al. (2016) both found a significant effect of tDCS on craving, they also found that active stimulation decreased craving for sweet foods more substantially than other foods (although Goldman et al., 2011 did also find a significant reduction for savoury foods too). Furthermore, Kekic et al. (2014) found no main effect of tDCS on food craving, however, when foods were split between sweet and savoury, a significant reduction in craving for sweet foods was revealed. Sweet foods are known to produce both stronger and more frequent cravings than savoury foods (Hill, 2007), likely due to the addictive potential of sugar (Avena et al., 2008). Based on this evidence we analysed desire to eat sweet and savoury foods from pre- to post stimulation separately but found no significant difference between active and sham stimulation. This analysis could be insensitive due to participants' personal preferences for the foods used in the study; not accounting for personal preferences could have reduced the potential for observed effects of prefrontal stimulation. For example, Ray et al. (2017) gave participants a food craving task in which they ranked foods based on liking and wanting and the lowest ranked foods were removed to avoid floor effects. Similarly, Burgess et al. (2016) also removed foods that participants did not score highly for liking, stating that craving is unlikely to vary for foods that are not liked. Both studies demonstrated the effects of active stimulation on preferred foods though this was for a decrease in food consumption rather than craving.

Food cravings have been linked to calorie intake (Lafay et al., 2000), BMI (Franken & Muris, 2005), the ability to lose weight (Batra et al., 2013) and binge eating (Ng & Davis, 2013). It seems imperative, therefore, that we have a better understanding of the mechanisms involved in food craving and interventions to help reduce them. While there is some evidence that brain stimulation may help to alleviate food cravings, the conflicting evidence suggests that the potential for tDCS, *specifically,* is still preliminary and that other interventions – such as behavioural training – may be worth investigating. In both this study and in Sedgmond et al. (2019) we combined brain stimulation with cognitive control training – specifically Go/No-Go training – on the assumption that the training could augment the effects of stimulation. Similarly, Carvalho et al. (2019) combined tDCS with an approach/avoid task to investigate whether the combination could reduce craving for chocolate, although they also found no significant effect of stimulation. Despite the lack of evidence for an effect of tDCS, in both studies we found evidence that participants learned the association between stopping responses and specific foods. Although this learning did not translate into a reduction in craving, there remains an abundance of evidence suggesting that cognitive training interventions, such as Go/No-Go training, have the potential to not only reduce craving but to also lead to other health-related behaviour changes (see Jones et al., 2018 for a review).

While there are many types of behavioural training tasks being used to retrain attention, and modify automatic associations, the most robust evidence seems to come from studies using response inhibition tasks like the Go/No-Go training that we implemented. For example, several studies have found that pairing foods with response inhibition has led to a reduction in both craving and consumption of those foods (e.g. Camp & Lawrence, 2019; Chen et al., 2019; Houben & Jansen, 2015). Furthermore, this type of training has also been linked to long term effects of continued reduced consumption as well as weight loss (Lawrence,

O'Sullivan, et al., 2015). It is thought that the continual inhibition of a motor response towards specific stimuli leads to a reduction in how much value the individual attributes to the items (Camp & Lawrence, 2019; Chen et al., 2016). As the overvaluation of appetitive foods can lead to excessive consumption (Stice et al., 2008), devaluing these items via response inhibition tasks offers a promising and well supported avenue for further research, especially with regards to the potential long term effects.

In conclusion, the current study failed to replicate previous observations that prefrontal tDCS reduces food cravings, despite using similar tDCS parameters, outcome measures, and improving tDCS methods by being the first such study to assess the effect of HD-tDCS. While tDCS may have the potential to be a useful tool in modifying food related behaviours, the evidence is still conflicting. We had thought that the increased focality of HD-tDCS would increase the likelihood of observing an effect, however, there is a need for more studies comparing these effects to those of conventional stimulation to better understand how important focality is. Alongside this, findings from multi-session protocols indicate that this could be the next step in understanding the benefits of stimulation. There is also still a great deal to be understood regarding how individual differences may affect findings, with factors such as food preferences, trait craving and body weight to be taken into consideration. However, based on findings from using cognitive interventions alone, a worthwhile avenue might be to explore how to make these as impactful as we can. While tDCS is a relatively inexpensive form of stimulation when compared to TMS, cognitive interventions are not only cheaper still, but also more pragmatic. They can be run online and conducted outside of a lab environment, making both long term testing and measurement of effects much easier.

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Figures and Tables

Figure 1. Visualisation of the simulated electrical field strength using SimNIBS (Thielscher et al., 2015). a) A 1.5mA current was simulated using a conventional tDCS montage with 7x5cm (35cm²) electrodes. b) A 1.5mA current was simulated using a 4x1 HD-tDCS montage with 1cm electrodes. These simulations confirm that HD-tDCS should result in a much more focal current.

Figure 2. The results of a Bayes factor design analysis (BFDA) for H_0 and H_1 in a simulated sequential design for the proposed Bayesian paired-sample t-tests for H1a and H1b (informed prior). 10,000 studies were simulated for sample sizes of 40 (n_{min}) , 60, 80 and 100 (n_{max}) , at hypothetical effect sizes of 0, 0.3, 0.4 and 0.5 to highlight the percentage of studies terminating at the correct H_0 or H_1 when the boundary is $BF_{10} \le 1/6$ and ≥ 6 . For H₀,76.2% of studies terminated at the correct boundary at n_{max} and 1.9% at H₁. For an effect size of 0.3 for H₁ at n_{max} ,72.9% of studies terminated at the correct threshold and 3.5% terminated at the H_0 boundary. For an effect size of 0.4, 94% of studies terminated the H_1 boundary and 0.6% at the H_0 boundary. And for an effect size of 0.5, 99.4% of studies terminated at H_1 and 0% at H_0 .

Figure 3. The results of a Bayes factor design analysis (BFDA) for H_0 and H_1 in a simulated sequential design for the proposed Bayesian paired-sample t-tests for H2, H3 and H4 (default prior). 10,000 studies were simulated for sample sizes of 40 (n_{min}) , 60, 80 and 100 (n_{max}) , at effect sizes of 0, 0.3, 0.4 and 0.5 to highlight the percentage of studies terminating at the correct H_0 or H_1 when the boundary is $BF_{10} \le 1/6$ and ≥ 6 . For H₀ 80% of studies terminated at the correct boundary at n_{max} and 1.8% at H₁. For an effect size of 0.3 for H₁ at n_{max} 71.8% of studies terminated at the correct threshold and 4.5% terminated at the H_0 boundary. For an effect size of 0.4, 93.5% of studies terminated the H_1 boundary and 0.8% at the H₀ boundary. And for an effect size of 0.5, 99.3% of studies terminated at H₁ and 0.1% at H^0 .

Figure 4. Schematic diagram of the procedure. Participants undertook two sessions in a withinsubjects design. Participants initially completed measures of hunger, mood and craving before receiving either active or sham stimulation, receiving the opposite stimulation condition in their second session. To allow for participants to adjust to the stimulation, participants initially received 5 minutes of stimulation in isolation before beginning the Go/No-Go task. The task and the stimulation then continued for a further 15 minutes. Following the task and stimulation, participants repeated the measures of hunger, mood and craving before completing a speeded version of the Go/No-Go task (full details can be found in the Method section). Note. $VAS =$ visual analogue scale; $PANAS =$ Positive and Negative Affect Schedule; G-FCQ-S = General Food Craving Questionnaire – State Version; HD-tDCS = high definition transcranial direct current stimulation.

Figure 5. Change in desire to eat no-go foods (a) and go foods (b) from pre-to post stimulation as a function of HD-tDCS condition. A positive score indicates increased desire to eat and a negative score indicates decreased desire to eat. No significant difference was found between HD-tDCS conditions.

Figure 6. Change in state craving score from pre-to post stimulation as a function of HD-tDCS condition. A positive score indicates increased craving and a negative score indicates decreased craving. No significant difference was found between stimulation groups.

Table 1. The selection of foods that were presented in the training task and desire to eat measure. Nb.

Images shown are of the products as purchased rather than the stimuli presented in the task.

Healthy Foods Unhealthy Foods Green Grapes Per $100g$: kCals = 66; fat = 0.1g Weight consumed: $\sim 6g(1 \text{ grape})$ Weight provided: ~42g (6 grapes) - green grapes; available at most supermarkets Chocolate Per $100g$: kCals = 535; fat = $30g$ Weight consumed: \sim 2g (1 button) Weight provided: ~15g (6 buttons) - Cadbury giant buttons; available at most supermarkets Carrot Batons Per $100g$: kCals = 43; fat = $0.4g$ Weight consumed: \sim 4g (1 baton) Weight provided: $\sim 31g$ (6 batons) - pre-cut carrot batons; available at most supermarkets Plain crisps Per $100g$: kCals = 544; fat = 33.2g Weight consumed: $\sim 3g(1 \text{ crisp})$ Weight provided: $\sim 20g$ (6 crisps) - Tesco ready salted crisps

Table 2. All planned comparisons. For H1a, H1b and H3a, a mean difference score for desire to eat will be calculated across go and no-go foods, separately.

Gender (% female)	76.36%					
Age	22.25(0.76)					
BMI	23.34(0.43)					
	Active	Sham	$t =$	$p=$	$dz=$	B_{JZS}
Hunger (baseline)	5.27(0.27)	5.76(0.24)	1.81	0.08	0.24	0.68
Fullness (baseline)	2.87(0.29)	2.74(0.25)	0.6	0.55	0.08	0.17
Desire to eat (baseline)	5.65(0.33)	6.09(0.28)	1.31	0.2	0.18	0.33
State craving (baseline)	47.66(1.13)	48.16(1.15)	0.46	0.65	0.06	0.16
Positive affect (baseline)	28.13(0.8)	27.36(0.96)	1.01	0.32	0.14	0.24
Negative affect (baseline)	12(0.36)	11.86(0.32)	0.36	0.72	0.05	0.16
Nausea (baseline)	1.09(0.06)	1.04(0.03)	0.9	0.37	0.12	0.22
Discomfort/pain (baseline)	1.24(0.06)	1.13(0.05)	1.77	0.08	0.24	0.63

Table 3. Group characteristics and within-subject significant tests (SE within parentheses).

Table 4. Outcomes of the primary hypothesis tests. In all cases, the evidence favoured the null hypothesis (H0) over the corresponding alternative hypothesis.

