Modulating eating behaviour with transcranial direct current stimulation (tDCS): Towards effective study design, stimulation parameters and participant characteristics

Jordan David Beaumont

Submitted in accordance with the requirements for the

degree of Doctor of Philosophy.

The University of Leeds

Leeds Trinity University

Faculty of Social and Health Sciences

June 2022

The candidate confirms that the work submitted is his own, except where work which has formed part of jointly authored publications has been included. The contribution of the candidate and the other authors to this work has been explicitly indicated below. The candidate confirms that appropriate credit has been given within the thesis where reference has been made to the work of others.

Chapter 3 is based in part on the following jointly-authored publication:

- **Beaumont, J.D.**, Smith, N.C., Starr, D., Davis, D., Dalton, M., Nowicky, A., Russell, M. and Barwood, M.J. 2022. Effective Transcranial Direct Current Stimulation Parameters for the Modulation of Eating Behavior: A Systematic Literature Review and Meta-Analysis. *Psychosomatic Medicine*. **84**(6), pp.646-657. https://doi.org/10.1097/PSY.0000000000001074

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

Chapter 5 is based in part on the following jointly-authored publication:

- **Beaumont, J.D.**, Davis, D., Dalton, M., Nowicky, A., Russell, M. and Barwood, M.J. 2021. The effect of transcranial direct current stimulation

(tDCS) on food craving, reward and appetite in a healthy population. *Appetite*. **157**, p105004. https://doi.org/10.1016/j.appet.2020.105004

Author contributions: **Jordan D. Beaumont**: Conceptualisation, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Writing – review and editing, Visualisation, Project administration. **Danielle Davis**: Conceptualisation, Methodology, Resources, Writing – review and editing, Supervision. **Michelle Dalton**: Conceptualisation, Methodology, Software, Formal analysis, Resources, Data curation, Writing – review and editing. **Alexander Nowicky**: Methodology, Writing – review and editing. **Mark Russell**: Methodology, Writing – review and editing. **Martin J. Barwood**: Conceptualisation, Methodology, Validation, Resources, Writing – original draft, Writing – review and editing, Supervision.

Chapter 6 is based in part on the following jointly-authored publication:

- **Beaumont, J.D.**, Smith, N.C., Starr, D., Davis, D., Dalton, M., Nowicky, A., Russell, M. and Barwood, M.J. 2022. Modulating eating behavior with transcranial direct current stimulation (tDCS): A systematic literature review on the impact of eating behavior traits. *Obesity Reviews*. **23**(2), e13364. https://doi.org/10.1111/obr.13364

  Author contributions: **Jordan D. Beaumont**: Conceptualisation, Methodology, Validation, Investigation, Data curation, Writing – original draft, Writing – review & editing, Visualisation, Project administration. **Natalie C. Smith**: Validation, Data curation. **David Starr**: Validation, Data curation. **Danielle Davis**: Conceptualisation, Writing – review & editing, Supervision.

Michelle Dalton: Conceptualisation, Writing – review & editing, Supervision. **Alexander Nowicky**: Writing – review & editing. **Mark Russell**: Writing – review & editing. **Martin J. Barwood**: Conceptualisation, Methodology, Validation, Writing – review & editing, Supervision.

The candidate confirms that the contributions were primarily intellectual, and he took a principal role in the production and writing of the publications. The co-authors confirm that their contribution was in guiding the research and reviewing drafts of the manuscripts.

Acknowledgements

First, I would like to express my sincere gratitude to my supervisory team; Professor Martin Barwood, Dr Danielle Davis, Dr Michelle Dalton and Professor Mark Russell. You provided unwavering support and guidance throughout my PhD, and the process would not have been possible without your expertise and encouragement. I have been fortunate to have a diverse team of supervisors, and I am thankful to you all for the opportunities and experiences that you have provided throughout my studies.

I would also like to thank Professor Graham Finlayson for opening the doors to the Human Appetite Research Unit (HARU) at the University of Leeds and providing a helping hand when we were struggling to recruit participants. In addition, Dr Beverley O'Hara, Fiona Croden, Dr Kristine Beaulieu, Dominic O'Connor and Dr Pauline Oustric – thank you for your support, and for welcoming me into the HARU family. Also, my thanks to Dr Alexander Nowicky for supporting the research in this thesis and contributing to the publications, and to Dr Jo Corbett for contributing to the protocol development.

To the many faces at Leeds Trinity – Kitty Scott, Rachel Davies, Jess Riman, Dr Nathan Dawkins and Dr Michael Jestico – who supported many of my outlandish requests. I would also like to acknowledge the work of some talented undergraduate students who helped with the brutal onslaught of participant recruitment and made data collection a collaborative and exciting experience. Elizabeth Goodwin, Natalie Smith, Lauren Powell, Lee Newburn, and Liz Senior – thank you! I also thank all of the participants who gave up their time to provide the data on which this thesis is based. Without your help, this work could not have progressed. I must also

acknowledge my fellow PGRs – Naziya O'Reilly, Liz Mistry, Kasi Mistry and Shames Maskeen – who provided an ever-listening ear, sound advice, and an endless stream of caffeine.

I could not write these acknowledgments without thanking my ever-enduring partner. You were always willing to listen to my ramblings, whether they were comprehensible or not, and were a constant anchor for my sanity. Finally, this thesis would not have come to fruition had it not been for the boundless support of my parents; you have always encouraged my academic progression and I am forever grateful for your love and support.

I save my final thanks for the day Danielle stops referring to tDCS as "brain frying", "brain zapping", or similar. Please, stop.

Abstract

Across prior studies using transcranial direct current stimulation (tDCS) to modulate eating behaviour there is heterogeneity in study design, tDCS parameters, and participant characteristics. This variation has led to equivocal findings. The present thesis considered the impact of this variation on eating-related outcomes (subjective appetite, food craving, food reward), and looked to identify the presence of an effect of tDCS with the aim of establishing consistency and replicability in the application of stimulation, with onward use as a modality for modulating eating behaviours and potentially as a tool in weight management.

To consider the impact of heterogeneous stimulation parameters, a systematic literature review and meta-analysis was conducted. This review considered the most comprehensive list of tDCS parameters to date and identified a series of parameters that produce a more consistent reduction across eating-related measures. These parameters were applied in two empirical studies exploring the impact of varying participant characteristics. As part of this, a second systematic review and meta-analysis was conducted. This identified a potential eating behaviour trait-dependent effect where those with traits suggesting susceptibility to overconsumption and weight gain (e.g., binge eating behaviour) appear most responsive to the effects of tDCS.

The empirical studies provided further data on this trait-dependent effect by comparing the effects of tDCS across two populations; “healthy” individuals (i.e., those who do not display susceptibility to overconsumption) and those with binge-type behaviour. No changes across eating-related measures were observed when comparing active versus sham tDCS across both participant populations. This is

largely supported by anecdotal-to-strong evidence in favour of the null hypothesis as indicated by Bayesian analyses.

The novel and original contributions of this thesis include establishing a comprehensive set of tDCS parameters that appear to produce consistent modulation of eating behaviours, and consideration for the eating behaviour trait-dependent effect of tDCS through meta-analytic and empirical data. These findings provide a clear direction for future work exploring the use of tDCS as a modality for the control of eating behaviours, including recommendations for the consistent application of tDCS in this domain.

Publications and Presentations

Publications

Original Articles

- **Beaumont, J.D.**, Davis, D., Dalton, M., Nowicky, A., Russell, M. and Barwood, M.J. 2021. The effect of transcranial direct current stimulation (tDCS) on food craving, reward and appetite in a healthy population. *Appetite*. **157**, p105004. https://doi.org/10.1016/j.appet.2020.105004

Review Articles

- **Beaumont, J.D.**, Smith, N.C., Starr, D., Davis, D., Dalton, M., Nowicky, A., Russell, M. and Barwood, M.J. 2022. Effective Transcranial Direct Current Stimulation Parameters for the Modulation of Eating Behavior: A Systematic Literature Review and Meta-Analysis. *Psychosomatic Medicine*. **84**(6), pp.646-657. https://doi.org/10.1097/PSY.0000000000001074

- **Beaumont, J.D.**, Smith, N.C., Starr, D., Davis, D., Dalton, M., Nowicky, A., Russell, M. and Barwood, M.J. 2022. Modulating eating behavior with transcranial direct current stimulation (tDCS): A systematic literature review on the impact of eating behavior traits. *Obesity Reviews*. **23**(2), e13364. https://doi.org/10.1111/obr.13364

Conference Abstracts

- **Beaumont, J.D.**, Davis, D., Dalton, M., Russell, M., and Barwood, M. 2019. Appeal biases for sweet and fatty foods are robust following a single session of transcranial direct current stimulation (tDCS) in a healthy population. *Obesity Abstracts*, **1**, RFC1.1. DOI: 10.1530/obabs.01.RFC1.1

Presentations

Organised Events

- Transcranial direct current stimulation (tDCS): A demonstration. Leeds Trinity University, October 2018.

Oral Presentations

- "A fear of the unknown": Understanding the perceptions of non-invasive brain stimulation. *Postgraduate Research Conference*, Leeds Trinity University, June 2022.

- Modulating eating behaviour with transcranial direct current stimulation (tDCS). *Faculty of Social and Health Sciences research seminar*, Leeds Trinity University, December 2021.

- The impact of variation in transcranial direct current stimulation (tDCS) parameters and participant characteristics on eating-related outcomes. *Postgraduate Research Conference*, Leeds Trinity University, June 2021.

- Understanding the perceptions of transcranial electrical stimulation (tES). *School of Social and Health Sciences research seminar*, Leeds Trinity University, June 2021.

- Is there a role for transcranial direct current stimulation (tDCS) in appetite control? *Internal Research Conference*, Leeds Trinity University, June 2019.

Invited Talks

- The effects of transcranial direct current stimulation (tDCS) on eating behaviour. *Human Appetite Research Unit laboratory group meeting*, University of Leeds, January 2020.

Poster Presentations with Short Oral Communication

- Modulating eating behaviour with transcranial direct current stimulation (tDCS): A systematic literature review on the impact of eating behaviour traits. *BrainBox Initiative Conference 2021*, BrainBox Initiative, September 2021.

- Appeal biases for sweet and fatty foods are robust following a single session of transcranial direct current stimulation (tDCS) in a healthy population. *UK Congress on Obesity*, University of Leeds, September 2019.

Poster Presentations

- The effects of transcranial direct current stimulation (tDCS) on food craving, food reward, and subjective appetite in those with binge-type eating behaviour. *UK Congress on Obesity*, Lancaster University, September 2022.

- The effects of transcranial direct current stimulation (tDCS) on food craving, food reward, and subjective appetite in those with binge-type eating behaviour. *Postgraduate Research Conference*, Leeds Trinity University, June 2022.

- Understanding the perceptions of transcranial electrical stimulation (tES). *Postgraduate Research Conference*, Leeds Trinity University, June 2021.

- Effective transcranial direct current stimulation (tDCS) parameters for the modulation of eating behaviour: A systematic literature review. *Second International Workshop on Non-Invasive Brain Stimulation (NIBS)*, University of Minnesota, June 2021.

- Transcranial Direct Current Stimulation: A possible intervention for obesity? *Health and Psychology Summit*, Leeds Trinity University, June 2018.

- Transcranial Direct Current Stimulation: A possible intervention for obesity? *Postgraduate Research Mini-Conference*, Leeds Trinity University, June 2018.

Table of Contents

List of Tables

List of Figures

List of Abbreviations

%FM	Percentage of fat mass
α	Cronbach's alpha
η_p^2	Partial eta squared
AEQ	Adverse Events Questionnaire
Af7	Anterior frontal area 7
AIC	Akaike information criteria
ANCOVA	Analysis of covariance
ANOVA	Analysis of variance
AU	Arbitrary unit(s)
BED	Binge eating disorder
BES	Binge Eating Scale
BF_{10}	Bayes factor
BMI	Body mass index
BSSSQ	Brain Stimulation Study Suitability Questionnaire
C	Coulombs
CBIT	Computer-based image task
CBM	Cognitive bias modification
CESD-10	Centre for Epidemiologic Studies Short Depression Scale
CI	Confidence interval(s)
cm	Centimetre(s)
CoEQ	Control of Eating Questionnaire
COMT	Catechol-o-methyl transferase
COVID-19	Coronavirus (SARS-CoV-2)
Cz	Vertex

DLPFC	Dorsolateral prefrontal cortex
EBA	Extrastriate body area
EDNOS	Eating disorders not otherwise specified
EEG	Electroencephalography
F	Female
F3	Frontal area 3
F4	Frontal area 4
F7	Frontal area 7
F8	Frontal area 8
FAB	Fat appeal bias
FCI	Food Craving Inventory
FCQ-S	Food Craving Questionnaire-State
FCQ-T-r	Food Craving Questionnaire-Trait, reduced form
fNIRS	Functional near-infrared spectroscopy
Fp2	Fronto-polar area 2
FWA	Frequency-weighted algorithm
Fz	Frontal zero point
g	Gram(s)
g	Hedges' *g*
GABA	Gamma aminobutyric acid
HFSA	High-fat savoury
HFSW	High-fat sweet
IAT	Implicit association task
ICC	Intra-class correlation coefficient
IFG	Inferior frontal gyrus
kΩ	Kilo-ohms
kcal	Kilocalorie(s)

kg	Kilogram(s)
$kg \cdot m^{-2}$	Kilogram(s) per metre squared
LFPQ	Leeds Food Preference Questionnaire
LFSA	Low-fat savoury
LFSW	Low-fat sweet
LRT	Likelihood ration test
M	Male
m	Metre(s)
mA	Milliampere
$mA \cdot cm^{-2}$	Milliampere per centimetre squared
ml	Millilitre(s)
met	Methionine
min	Minute(s)
mm	Millimetre(s)
MRI	Magnetic resonance imaging
ms	Millisecond(s)
ND	No data available
NIBS	Non-invasive brain stimulation
NHS	National Health Service
NPAR-Q	Neurological Conditions Physical Activity Readiness Questionnaire
NR	Not reported
O2	Occipital area 2
Oz	Occipital zero point
PCC	Pearson's correlation coefficient
PICO	Population, Intervention, Control, Outcome
PFC	Prefrontal cortex
PO2	Parieto-occipital area 2

PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PWS	Prader Willi syndrome
RMR	Resting metabolic rate
RoB	Risk of bias
SD	Standard deviation
SE	Standard error
SPSS	Statistical Package for the Social Sciences
subBED	Subthreshold binge eating disorder
TAB	Taste appeal bias
tDCS	Transcranial direct current stimulation
TFEQ	Three Factor Eating Questionnaire
TFEQ-r18	Three Factor Eating Questionnaire, reduced form
tnM1	Tongue muscle representation of the primary motor cortex
UK	United Kingdom
USA	United States of America
VAS	Visual analogue scale
VNS	Visual numeric scale
X	Cross on visual analogue scale

Glossary of Terms

Active tDCS	A form of tDCS protocol where the current is delivered for several minutes.
Anodal tDCS	Stimulation with the anode (positive charge) electrode placed over the target region.
Anode	Positive charge electrode where the electrical current is emitted from the stimulation device.
Cathodal tDCS	Stimulation with the cathode (negative charge) electrode placed over the target region.
Cathode	Negative charge electrode where the electrical current is returned to the stimulation device.
Cephalic	Electrode montage where both electrodes are placed over the cortex.
Conventional tDCS	Stimulation with two large electrodes (one anode, one cathode).

Current density	The amount of current applied per unit area. Measured as the stimulation strength (milliampere, mA) divided by the electrode size (cm^2).
Current intensity	The steady-state current applied to the anode electrode.
Depolarisation	The increase in neuron cell membrane potential as determined by the cell's threshold voltage.
Electrode	Collective term for the conductive rubber plate, sponge casing and electrolyte (saline, gel or paste).
Explicit liking	Subjective, conscious judgement of the degree of pleasure elicited by food.
Explicit wanting	Subjective, conscious attraction to food triggered by the appearance of food or related cue(s).
Extracephalic	Electrode montage where one electrode is placed away from the cortex.
"Healthy" groups	Individuals who do not present with eating behaviour traits suggesting susceptibility to overconsumption and weight gain. These individuals do not display any medical or behavioural conditions, irrespective of weight status.

Hyperpolarisation	Reduction in neuron cell membrane potential below the normal resting voltage.
Implicit wanting	Automatic, subconscious attraction to food triggered by the appearance of food or related cue(s).
Montage	The placement of electrodes.
Reference electrode	The electrode that is placed over a region of the brain that is not the target of the physiological or behavioural measure.
Sham tDCS	A form of tDCS protocol where the current is ramped down and turned off following several seconds; used as a blinding protocol.
Target electrode	Electrode that is placed over the area of interest, specific for the physiological or behavioural measure of interest.
Trait groups	Individuals who present with eating behaviour traits suggesting susceptibility to overconsumption and weight gain.

Chapter 1 General Introduction

Obesity is a chronic health condition characterised by the accumulation of excess adiposity, which affects around 13% of the worldwide adult population, equating to more than 650 million individuals (World Health Organisation, 2021). It is predicted that this prevalence will rise to around one billion adults by 2030 (Lobstein et al., 2022), with greater prevalence predicted in both the United Kingdom (UK) (35 to 48%) and United States of America (USA) (45 to 52%) (Wang et al., 2011; Ward et al., 2019; Lobstein et al., 2022). The accumulation of excess body fat is driven by a positive energy balance, where energy intake outweighs energy expenditure (Hill, 2006; Hall et al., 2011). Although this is often oversimplified as the result of excess dietary intake and sedentarism, obesity is a multi-faceted condition driven by a complex relationship between behavioural, biological and environmental factors that contribute to energy dysregulation (Hill, 2006; Hruby and Hu, 2015).

The control of energy intake occurs through complex systems that encapsulate the physiological need for energy (homeostatic appetite) and the rewarding components of food (hedonic appetite) (Blundell, 2006; Finlayson and Dalton, 2012b). Although the homeostatic system is an important mediator of food seeking behaviour, through subjective sensations such as hunger and satiety, food and related cues produce a pleasure response that stimulates reward and motivation circuits within the brain that often override homeostatic signals and instead promote overconsumption and weight gain (Alonso-Alonso and Pascual-Leone, 2007; Havermans, 2011; Finlayson and Dalton, 2012b; Boswell and Kober, 2016; Kober and Boswell, 2018). This is especially relevant in the current obesogenic environment where high-calorie, rewarding foods are readily available (Blundell, 2006; Lowe et al., 2019). Poor weight loss outcomes or failure to maintain weight loss can be driven by an individual's inability to resist these highly rewarding foods (Cornier, 2011; Brockmeyer et al., 2017). This is likely due to the physiological and behavioural

adaptions in response to weight loss attempts such as heightened hunger, reduced satiety, and reduced volitional physical activity (Stubbs et al., 2021). This is of particular relevance for those displaying specific eating behaviour traits associated with overconsumption and weight gain, such as binge eating behaviour.

Binge eating is characterised by the uncontrolled consumption of a large quantity of food, with binge eating disorder (BED) recognised as a psychiatric condition (American Psychiatric Association, 2013). While the prevalence of BED is estimated to be between 0.7 and 3.5% (Brownley et al., 2007; Hudson et al., 2007; Kessler et al., 2013), 10 to 20% of the general adult population may experience the emotions, cognitions and behaviours associated with binge eating behaviour (Hudson et al., 2007; Berg et al., 2009; Striegel-Moore et al., 2009). This condition is considered a distinct subtype of obesity (Davis et al., 2009; Davis et al., 2012; Dalton et al., 2013a; Dalton et al., 2013b), and can affect around one quarter of individuals with obesity who are seeking weight loss treatment (Pull, 2004). However, while binge eating severity is positively associated with body mass index (BMI) (Finlayson et al., 2011), and those with BED are more likely to be obese (Villarejo et al., 2012), obesity is not a criterion for binge eating behaviour (Bruce and Wilfley, 1996; Finlayson et al., 2011). Individuals displaying binge eating behaviour, as well as other eating behaviour traits suggesting susceptibility to overconsumption (e.g., emotional eating), appear to have hyper-responsivity to the rewarding aspects of food (Dalton et al., 2013a), which is associated with reduced dietary self-regulation (Munsch et al., 2012).

The prefrontal cortex (PFC) has been implicated in hedonic appetite control through the influence of central brain executive functions, the cognitive processes that allow goal-directed behaviours by inhibiting impulsive actions (Figure 1-1a) (Miller and

Cohen, 2001; Pignatti et al., 2006; Joseph et al., 2011). The dorsolateral PFC (DLPFC) exerts a controlling influence over reward circuits by promoting self-regulation, inhibitory control, and decision-making processes that control appetite through ‘top-down’ regulation of conflicting or maladaptive responses (Miller and Cohen, 2001). Poor appetite control capabilities have been associated with reduced activity in the right DLPFC (Alonso-Alonso and Pascual-Leone, 2007). Individuals displaying binge eating behaviour show hypo-activation of this cortical region (Karhunen et al., 2000; Boeka and Lokken, 2011), and impaired executive functioning (Cserjési et al., 2009; Michaud et al., 2017; Blume et al., 2019). This DLPFC dysregulation has been linked with greater impulsive behaviours, often leading to greater reward response to high-calorie foods and subsequent overconsumption (Figure 1-1b) (Stice et al., 2008; Gluck et al., 2017; Grundeis et al., 2017).

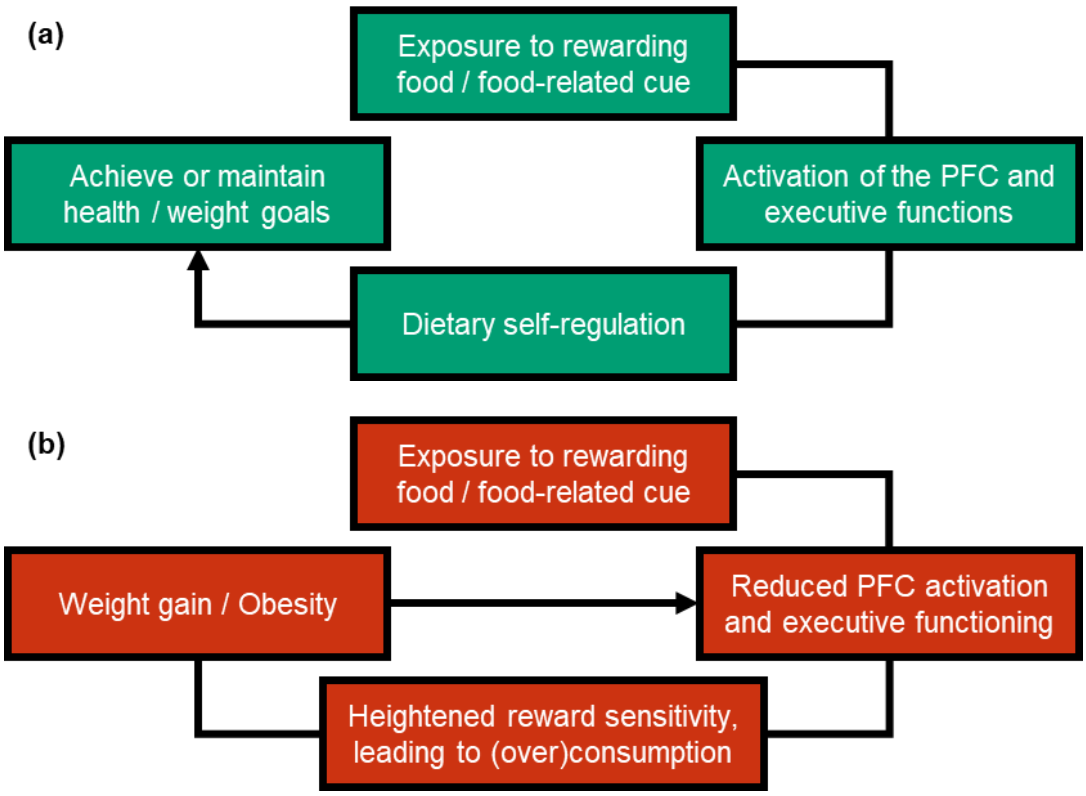


Figure 1-1 Role of the prefrontal cortex (PFC) in weight management. (a) For those with normal prefrontal activity, health goals (e.g., weight maintenance) are achieved through central brain executive functioning. (b) Individuals with hypo-activation of the PFC show reduced executive functioning, and instead experience heightened reward sensitivity, contributing to overconsumption. Over time, this can lead to weight gain and, in turn, further reduction in PFC function (Joseph et al., 2011; Lowe et al., 2019).

By modulating activity within the DLPFC it may be possible to increase executive functioning and improve hedonic appetite control, thereby promoting and maintaining dietary self-regulation and weight loss (Alonso-Alonso and Pascual-Leone, 2007; Lowe et al., 2019). Indeed, greater executive functioning following bariatric surgery is associated with improved weight loss outcomes (Goldman et al., 2013). Such modulation of cortical activity is possible through the use of non-invasive brain stimulation (NIBS) techniques (Thair et al., 2017). Transcranial direct

current stimulation (tDCS) is a form of NIBS, where a constant weak electrical current is emitted from a battery-powered device and applied to the brain through electrodes that are placed on the scalp (Nitsche and Paulus, 2000; Nitsche and Paulus, 2001).

During tDCS, the current is emitted from the stimulation device through an anode (positive charge) electrode and returns to the device through a cathode (negative charge) electrode (Figure 1-2). The effects of tDCS on the underlying cortex are associated with the depolarisation (anodal 'excitatory' tDCS) or hyperpolarisation (cathodal 'inhibitory' tDCS) of neuron cell membranes (Auvichayapat and Auvichayapat, 2011; Bestmann et al., 2015). While the current strength is not sufficient to cause neuronal firing, it can result in the polarity-dependent subthreshold modulation of resting membrane potentials making neuronal firing more likely (Filmer et al., 2014; Jamil and Nitsche, 2017). This process is mediated through neurotransmitters release (e.g., gamma-aminobutyric acid [GABA], glutamate) which increases or decreases the likelihood of spontaneous neuronal firing following anodal and cathodal tDCS, respectively (Filmer et al., 2014).

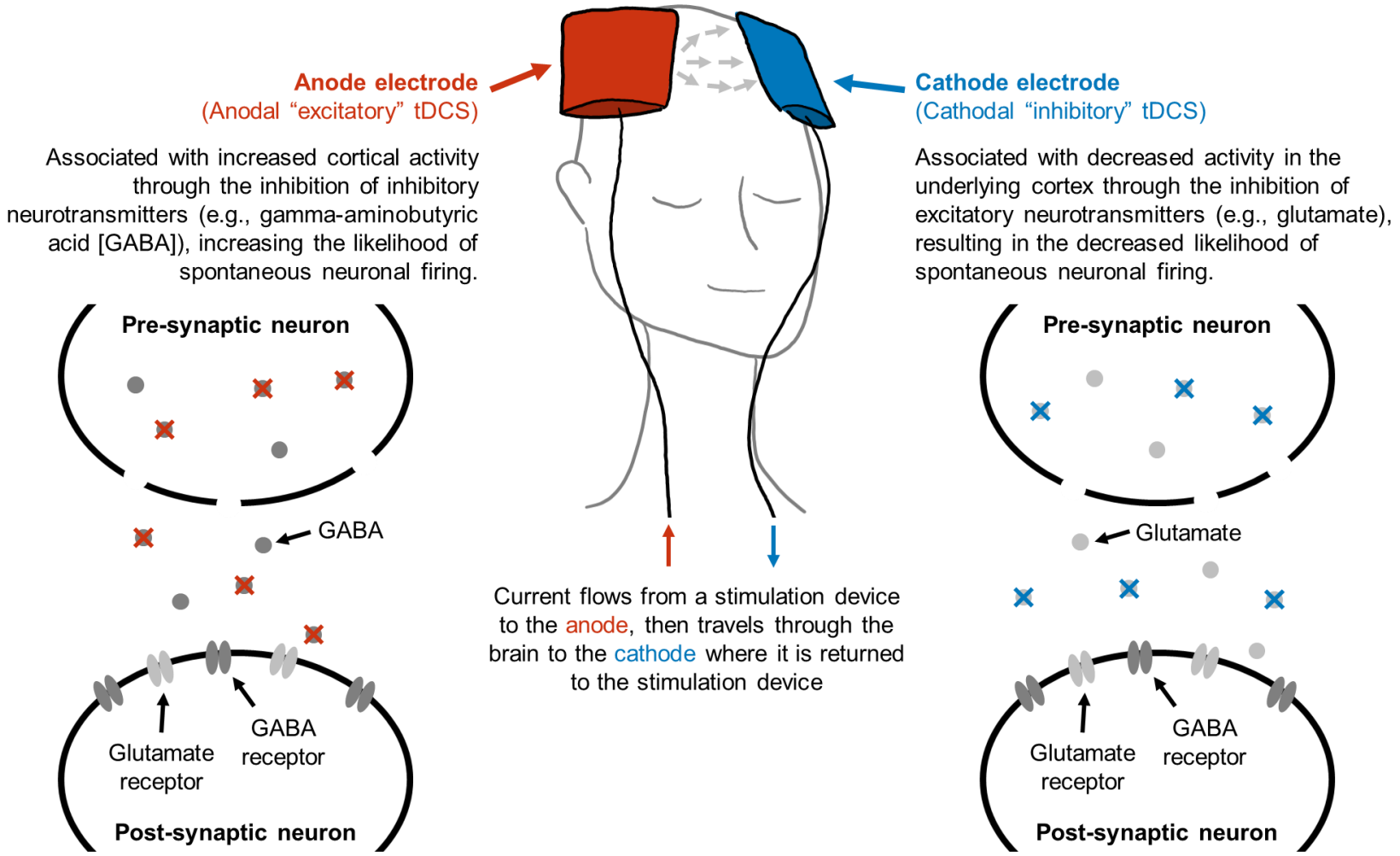


Figure 1-2 The effects of tDCS under the anode and cathode electrodes. Image adapted from Filmer et al. (2014).

This technique is considered safe for adults, children, healthy individuals and patient groups (Matsumoto and Ugawa, 2017), and is becoming a popular method for altering cortical activity as it is simple, scalable and cost-effective (Thair et al., 2017; Hall et al., 2018). There is potential for tDCS to become an alternative or adjunctive treatment modality in obesity, and specifically for improving the control of eating behaviours associated with overconsumption and weight gain (e.g., binge eating). However, current approaches to modulating eating behaviours with tDCS are heterogenous, and as such it is difficult to identify a consistent effect of this technique. Accordingly, this thesis looked to address three areas of heterogeneity – study design, stimulation parameters, and participant characteristics. The empirical studies presented in this thesis further examined the role tDCS plays in altering hedonic appetite control, specifically the rewarding components of food and craving for foods. This work tested the experimental hypothesis that tDCS is able to suppress appetite measures, resulting in a decreased preference and craving for high-calorie foods. It is acknowledged that many factors may influence energy balance – such as individual biology, environment, and societal factors (Butland et al., 2007) – however this programme of work focussed on factors influencing food consumption given that these variables were manipulated in the experiments that follow.

Chapter 2 Aims and Objectives

2.1 General Aims

There is potential for tDCS to become an alternative or adjunctive treatment modality for obesity, particularly for the modulation of eating behaviours associated with overconsumption and weight gain. However, the inconsistency in methodological approaches across eating-related tDCS literature makes it difficult to determine the efficacy of stimulation protocols for improving eating behaviours. The present body of research aimed to identify the efficacy of tDCS as a tool to modulate measures of hedonic appetite.

2.2 Specific Objectives

- Review prior literature to identify the impact of differing study designs and stimulation parameters on eating-related outcome variables.
- Review prior literature to identify the impact of heterogenous participant characteristics on the effects of tDCS on eating-related outcomes.
- Determine the test-retest reliability of common (food craving, subjective appetite) and novel (food reward) measures of hedonic appetite in tDCS research.
- Examine the effects of tDCS on hedonic appetite measures in participants with no apparent susceptibility to overconsumption.
- Examine the effects of tDCS on hedonic appetite measures in those with mild-to-moderate binge eating behaviours who may be susceptible to overconsumption and weight gain.

2.3 Overview of the Thesis

To address the above aims and objectives, two systematic literature reviews and two laboratory-based empirical studies were conducted. The link between these studies is outlined in Figure 2-1.

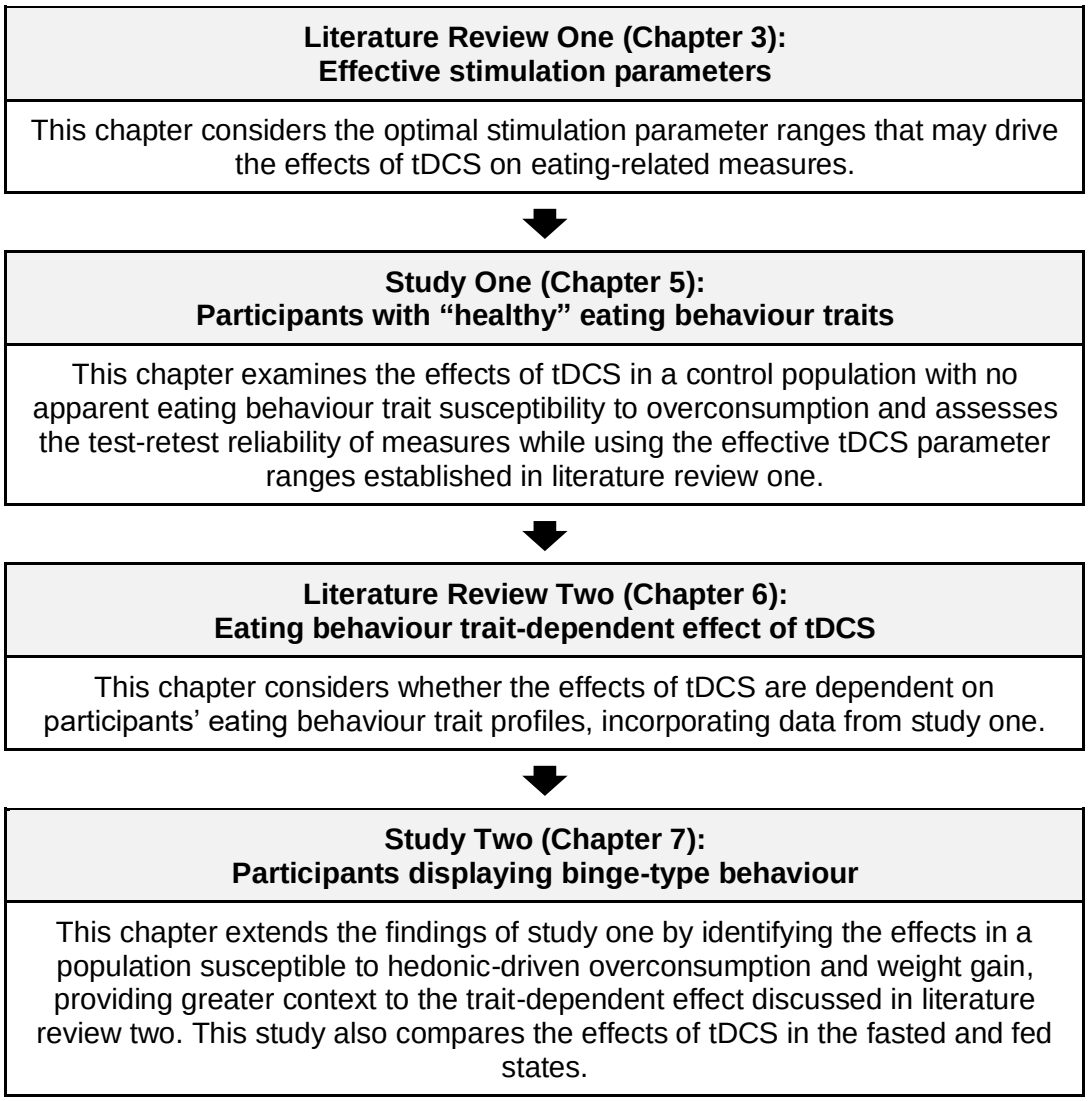


Figure 2-1 Overview and progression of methods.

Chapter 3 Systematic Literature Review One

Effective transcranial direct current stimulation (tDCS) parameters for the modulation of eating behaviour: A systematic literature review and meta-analysis. [1]

Part of this chapter is published as:

Beaumont, J.D., Smith, N.C., Starr, D., Davis, D., Dalton, M., Nowicky, A., Russell, M. and Barwood, M.J. 2022. Effective Transcranial Direct Current Stimulation Parameters for the Modulation of Eating Behavior: A Systematic Literature Review and Meta-Analysis. *Psychosomatic Medicine*. **84**(6), pp.646-657. https://doi.org/10.1097/PSY.0000000000001074

[1] The present review was conducted in parallel to the first study (Chapter 5); this empirical work was incorporated into the published version of this review.

3.1 Chapter Summary

There has been increased interest in the use of tDCS to modulate eating behaviours associated with overconsumption. Despite promising early findings, more recent data shows equivocal effects. This may be due to the variation in applied stimulation parameters (e.g., stimulation intensity, montage) and study design (e.g., within- versus between-participants, blinding protocols). The present chapter looked to systematically review prior literature to establish effective tDCS parameter ranges for the modulation of eating behaviour.

A literature search was conducted across four databases (MEDLINE, PsycINFO, Scopus, Science Direct), which identified 1,134 articles. Studies that used conventional sham-controlled tDCS to modify eating behaviour measures (subjective appetite, food craving, food reward, food consumption) in adult human participants were included in this review. Articles were screened by two independent authors, and study quality was assessed using the Cochrane Collaboration's Risk of Bias tool. A total of 27 eligible studies were identified, including 11 between-participant and 16 within-participant designs. Seven studies showed low risk of bias, with bias arising from issues implementing or reporting blinding protocols in the remaining studies.

Large variation in applied parameters was found, including electrode placement, current intensity and density, participant and researcher blinding protocols, and the use of online or offline tasks. The application of differing parameters appeared to alter the effects of tDCS on eating-related measures, with some parameters resulting in null effects. The absence of tDCS-mediated change in measures of eating behaviour may be driven by variation in applied parameters. Consistent application of parameters which appear effective for modulating eating-related

measures is important for identifying the potential impact of tDCS. Using the findings of this review, a series of parameters are proposed that should be applied in future work; the empirical studies discussed in this thesis comply with these recommendations.

3.2 Introduction

Over the last decade there has been increasing interest in the use of NIBS techniques, particularly tDCS, for modulating eating behaviours associated with overconsumption and weight gain. The ability of tDCS to alter these behaviours, such as food craving and consumption, has been of great interest for researchers due to its potential use in the treatment of obesity (Alonso-Alonso, 2013). Since the first study using tDCS to alter food craving was published over a decade ago (Fregni et al., 2008), the potential for this technique to improve hedonic appetite control has seen an increase in published data. However, despite the promising effects outlined in this early study, more recent data shows equivocal effects (Goldman et al., 2011; Gluck et al., 2015; Georgii et al., 2017; Sedgmond et al., 2019).

Variation in findings may be due to the lack of consistency in study designs (e.g., between- and within-group design), outcome measures and stimulation parameters. The modulatory effects of tDCS are driven largely by the specific stimulation parameters and device set-up (Antal et al., 2017). This includes the electrode montage, current intensity and density, stimulation duration, and number of sessions. Online protocols may also impact the modulatory effects (Tremblay et al., 2014). Despite the evident heterogeneity caused by altering stimulation parameters, these parameters can differ greatly between studies resulting in large variation in data (Fertonani and Miniussi, 2016; Jamil and Nitsche, 2017). This demonstrates the importance of identifying and consistently applying parameters that are known to modulate the outcome measure. This is not a new concept (Filmer et al., 2014; Tremblay et al., 2014; Thair et al., 2017), but has not been discussed in-depth for studies measuring eating-related outcomes.

Understanding the ability of tDCS to modify eating behaviours is particularly difficult with variation in study design, outcome measures and stimulation parameters. If this technique is to be used as an additional or adjunctive treatment modality for weight management and eating disorders, it is important that these inconsistencies are addressed (Krause and Kadosh, 2014). The present chapter builds on recent reviews (Hall et al., 2018; Mostafavi et al., 2018) to provide further detail on the potential impact of different stimulation parameters and widen the discussion to incorporate important parameter considerations, including reference electrode placement, electrode size, current density, blinding efficacy, and the use of offline/online protocols. Specifically, the present review aimed to identify effective tDCS parameter ranges for the modulation of eating behaviour and determine whether null effects are driven by parameters outside of these ranges.

3.3 Method

3.3.1 Search Strategy

An electronic literature search was performed in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Moher et al., 2009) (Appendix 1). The literature search was completed using MEDLINE, PsycINFO and Scopus databases in March 2019, and repeated in July 2020 to include additional articles published during this time. Search terms are displayed in Table 3-1. Due to the limitation on Boolean terms and wildcards (*) in Science Direct, adjusted search terms were used.

Table 3-1 Literature search terms.

Database	Search Terms
MEDLINE PsycINFO Scopus	(“noninvasive brain stimulation” OR “non-invasive brain stimulation” OR “transcranial direct current stimulation” OR “transcranial current stimulation” OR tDCS) AND (appetit* OR food OR “food crav*” OR “food reward” OR “food preference*” OR “food cue” OR “food consumption” OR eat* OR calorie* OR “calorie intake” OR “calorie consumption” OR energy OR “energy intake” OR “energy consumption” OR bing* OR “binge eat*” OR snack*)
Science Direct	(“transcranial direct current stimulation” OR tDCS) AND (“food craving” OR “food reward” OR “food preference” OR “food consumption”)

3.3.2 Inclusion and Exclusion Criteria

Articles were assessed in line with the Population, Intervention, Control and Outcome (PICO) model (Higgins et al., 2020); see Table 3-2. Results were limited to those written in English and published after 1998 to coincide with the development of modern tDCS procedures (Priori et al., 1998; Nitsche and Paulus, 2000). After removing duplicates (n = 248), titles and abstracts were assessed for inclusion. Where elimination based on title and abstract was not possible, full-text articles were retrieved and assessed for inclusion in the final sample. Reviews, abstracts (where full-text articles were unavailable), editorials/commentaries, book chapters, theses, study protocols, case reports and animal studies were not included in the present review (total n = 68). Article selection was performed by two independent authors.

Table 3-2 Participant, Intervention, Control and Outcome (PICO) Criteria.

Population	Adult human participants
Intervention	Conventional tDCS (i.e., one anode, one cathode)
Control	Sham-controlled
Outcome	Eating-related measure (food craving, food consumption, food reward, subjective appetite)

3.3.3 Data Extraction

For each eligible study, the following data were extracted: names of authors; year of publication; participant characteristics; montage and electrode size; current intensity and density; stimulation duration; ramp duration; sham protocol; number of sessions; blinding efficacy; use of online and offline protocols; outcome measures; main findings. Data were extracted as reported in the original article(s).

3.3.4 Study Quality Assessment

Study quality was determined using the Cochrane Collaboration's Risk of Bias (RoB) tool (Sterne et al., 2019). Judgements were made by two independent researchers at the study level, with high agreement between authors (κ = 0.93).

3.3.5 Statistical Analysis

Means, standard deviations (SD) and sample size were extracted for eating-related measures (subjective appetite, food craving, food reward, food consumption). Where standard error (SE) was reported, SD was estimated using the equation: $SD = SE \times \sqrt{n}$ (Higgins et al., 2020). If data were not reported, datasets were requested from corresponding authors. Otherwise, means and SD or SE were extracted from available figures using WebPlotDigitizer (version 4.4) (Rohatgi, 2020), or estimated using the Practical Meta-Analysis Effect Size Calculator (Lipsey

and Wilson, 2000) by entering t or F statistic and sample size. If data or effect sizes were estimated, these were independently validated by two authors. Standardised mean differences were calculated and adjusted using Hedges' *g* due to small sample size (n < 20) across many of the reviewed articles.

Analyses focussed on single session tDCS, to remove the potential cumulative effect of multi-session protocols. Four studies did not measure the effects of single session tDCS and were removed from analyses (Heinitz et al., 2017; Fassini et al., 2019; Amo Usanos et al., 2020; Fassini et al., 2020). Additional studies were removed due to missing data (Montenegro et al., 2012) or due to all participants receiving active tDCS (Ljubisavljevic et al., 2016). To reduce confounding analyses, the expectation effect observed by Ray et al. (2019) was also removed. A total of 21 studies (n = 743 participants) were included in the meta-analysis (Appendix 2). Where possible, separate analyses comparing single versus multi-session tDCS were completed to identify any cumulative effect (additional n = 3 studies, 105 participants). Where effect sizes are based on composite scores (i.e., mean scores across varying levels of a specific parameter) within the same participant group, these were removed from analyses for the specific parameter measure to avoid confounding analyses (Hall and Lowe, 2018; Borenstein et al., 2021).

Differences in comparisons within experiments, journal articles, and research groups can result in dependent effect sizes leading to narrow confidence intervals (CI) and small estimates of SE (Van den Noortgate et al., 2013; Van den Noortgate et al., 2015). Multilevel modelling was completed to account for such dependencies, with separate levels for comparisons within participant samples, experiments within studies, and studies within the same research group. As indicated by Akaike

information criteria (AIC) and likelihood ration test (LRT) results, the addition of each level did not improve model fit (Appendix 3).

Meta-analyses were performed using R (The R Foundation, 2022) with the meta package (Schwarzer et al., 2015). Due to the variability in study design and outcomes, random effects models were used. Effect sizes were interpreted as trivial ($g < 0.20$), small ($g = 0.20$), moderate ($g = 0.50$) or large ($g > 0.80$) (Cohen, 1992). A negative effect size favours active tDCS, indicating that active protocols reduce the outcome measure. In comparison, positive effect sizes would indicate an increase in the measure following active versus sham tDCS, favouring sham tDCS. Effect size heterogeneity was assessed using the I^2 index, and interpreted as might not be important (0 to 40%), may represent moderate heterogeneity (30 to 60%), may represent substantial heterogeneity (50 to 90%), and may represent considerable heterogeneity (75 to 100%) (Deeks et al., 2021). To test for publication bias, Egger's regression was used (Egger et al., 1997). Subgroup analyses were conducted to identify potential moderating effects of tDCS parameters on outcome measures. Individual forest plots for each comparison across eating-related measures are available in Appendix 5. Where a meta-analysis was not possible, a systematic literature review is included.

3.4 Results and Discussion

3.4.1 Study Characteristics

A total of 1,134 articles were identified from database searches. After removing duplicates and assessing eligibility, 27 articles were included in the present review. Figure 3-1 outlines the exclusion process. All reviewed studies used conventional tDCS procedures and were sham-controlled trials, with 11 between-participant and 16 within-participant studies. A total of 975 participants were recruited across the

reviewed studies, ranging from 9 to 172 individuals per study. This included individuals with healthy weight (n = 13 studies, 555 participants), overweight or obese (n = 15 studies, 393 participants). Ljubisavljevic et al. (2016) included those who were healthy weight or overweight (n = 27), but do not provide total n for each weight category.

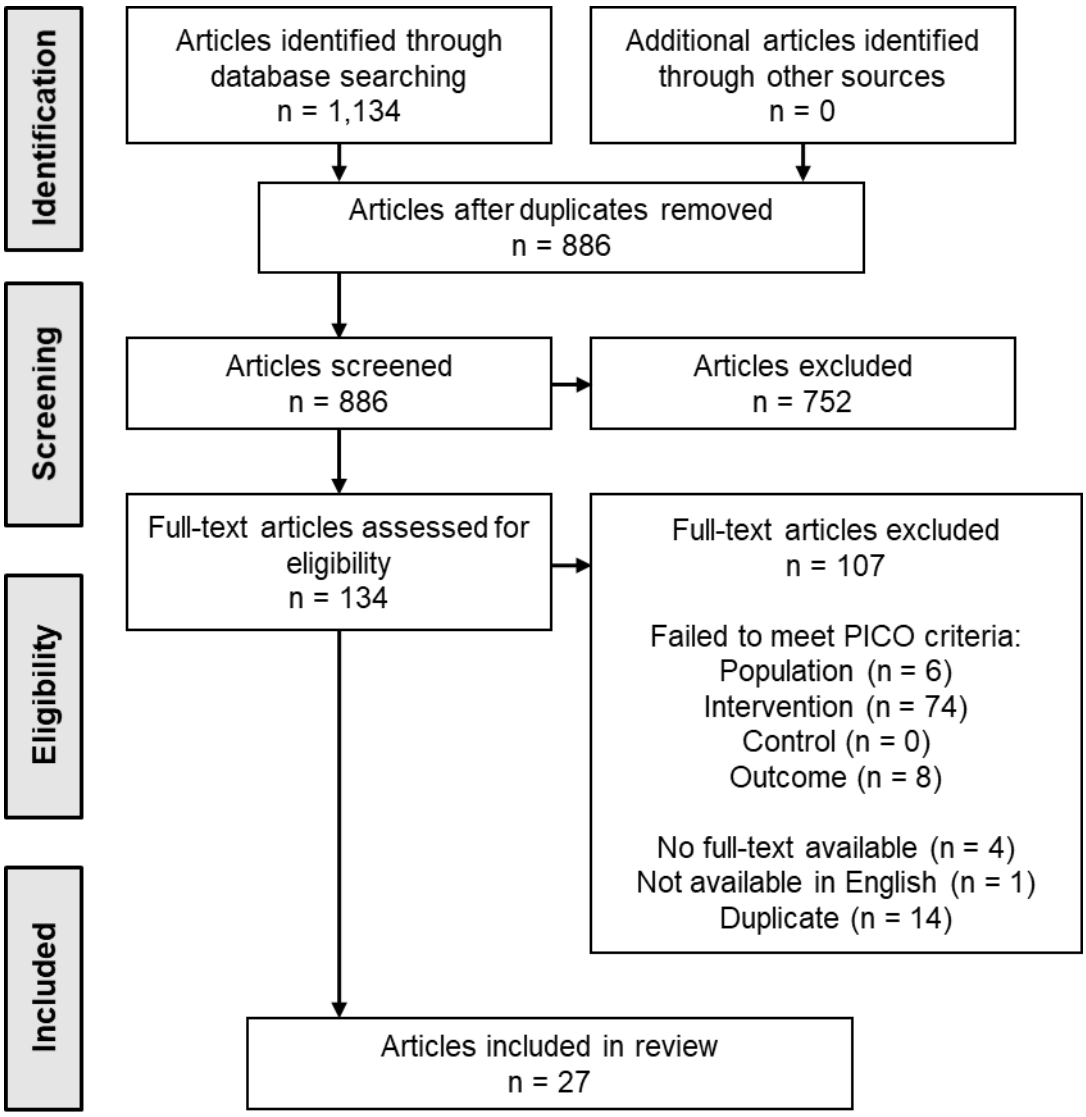


Figure 3-1 PRISMA flow diagram detailing the search and selection process performed to identify studies applying conventional tDCS for the modulation of eating behaviours.

Heterogeneity across studies (I^2 range = 0.0 to 57.4%) largely suggests it might not be important (Table 3-3). Inspection of funnel plots showed good symmetry across measures (Appendix 4). Egger's regression showed little evidence of publication bias for overall analyses ($p > 0.08$).

Table 3-3 Summary of heterogeneity and publication bias data.

Measure	Heterogeneity			Egger's Test		
	I^2 (%)	χ^2	p	β_0	t	p
Hunger	23.6	9.17	0.241	1.191	1.097	0.315
Desire to Eat	33.7	7.54	0.184	−1.377	1.056	0.351
Food Craving	0.0	1.09	0.780	−0.570	0.487	0.674
Explicit Wanting	0.0	4.99	0.662	−1.028	0.558	0.597
Implicit Wanting	57.4	7.04	0.071	−0.570	0.139	0.902
Food Consumption	29.7	15.66	0.154	−1.715	1.932	0.082

3.4.2 Study Quality

The RoB assessment is summarised in Figure 3-2; assessment for individual studies is displayed in Table 3-4. Only 6 of the 27 studies showed low risk of bias across all domains, and therefore an overall low risk of bias. The greatest source of bias across the remaining studies was the blinding protocol (Domain 2); this also affected risk of bias judgement for the measurement of outcome (Domain 4) and selection of reported results (Domain 5). Insufficient detail around the blinding of both participants and researchers was given across some of these studies, particularly the process in which researchers were made blind to the interventions. Most studies (n = 17) maintained a double-blind protocol, either through the use of a pin-protected stimulation device or an independent researcher completing stimulation protocols.

Seven studies used a single-blind design, with a further nine studies providing insufficient detail around blinding protocols.

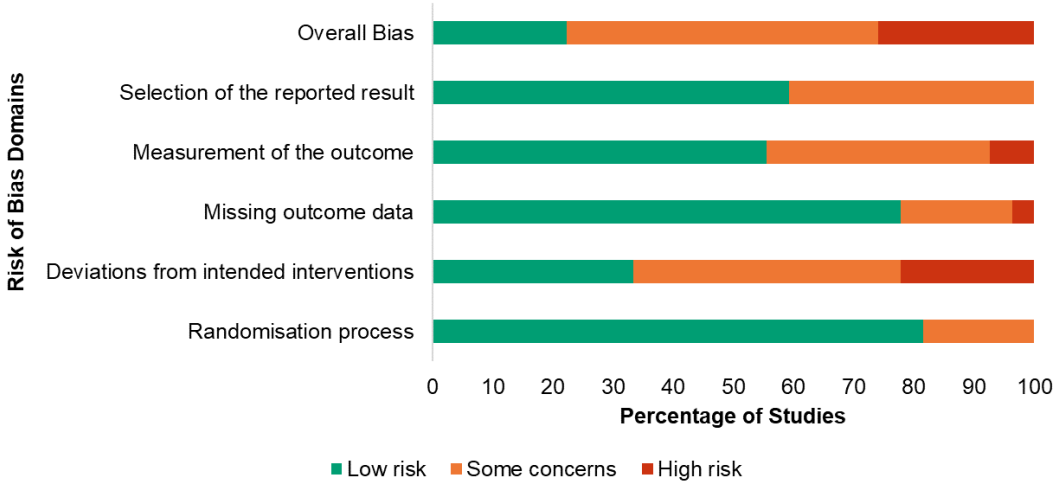


Figure 3-2 Risk of bias across the reviewed studies (n = 27).

Table 3-4 Risk of bias assessment within studies (n = 27).

	D1	D2	D3	D4	D5	Overall
Amo Usanos et al. (2020)	+	+	+	+	+	+
Bravo et al. (2016)	+	!	+	!	!	!
Burgess et al. (2016)	+	!	+	!	!	!
Carvalho et al. (2019)	+	!	+	!	!	!
Chen et al. (2019)	+	!	+	!	!	!
Fassini et al. (2019)	+	+	+	+	+	+
Fassini et al. (2020)	+	+	+	+	+	+
Fregni et al. (2008)	+	!	+	+	+	!
Georgii et al. (2017)	!	!	+	+	+	!
Gluck et al. (2015)	+	-	-	+	!	-
Goldman et al. (2011)	+	!	+	!	!	!
Grundeis et al. (2017)	+	!	+	+	+	!
Heinitz et al. (2017)	+	!	!	+	+	!
Jauch-Chara et al. (2014)	+	!	+	!	!	!
Kekic et al. (2014)	+	!	!	+	+	!
Kekic et al. (2017)	+	+	+	+	+	+
Lapenta et al. (2014)	+	-	!	+	+	-
Ljubisavljevic et al. (2016)	+	-	!	+	+	-
Marron et al. (2019)	+	-	+	!	!	-
Mattavelli et al. (2019)	!	-	+	-	!	-
Max et al. (2020)	+	+	!	+	+	!
Montenegro et al. (2012)	!	-	+	!	!	-
Ray et al. (2017)	!	+	+	!	+	!
Ray et al. (2019)	+	+	+	-	+	-
Sedgmond et al. (2019)	+	+	+	+	+	+
To et al. (2018)	+	+	+	+	+	+
Vicario et al. (2020)	!	!	+	!	!	!

Judgement key: +, low risk; !, some concerns; -, high risk

D1, domain 1: randomisation process; D2, domain 2: deviations from intended interventions; D3, domain 3: missing outcome data; D4, domain 4: measurement of the outcome; D5, domain 5: selection of the reported results.

It should be noted that Ray et al. (2019) included a source of intended bias around blinding of participants, with the aim of assessing the impact of expecting to received active versus sham tDCS on eating-related measures. Although this study received an overall high risk of bias, the study was high-quality, and this source of bias provides important considerations around the information shared with participants. In the remaining studies, bias arose due to the post-randomisation exclusion of participants (n = 14 studies). Many studies do not provide a sample size calculation, which makes it difficult to identify the impact of these exclusions. The exclusion of participants is particular problematic where this leads to a relatively small sample size, which is an important consideration as this area of research repeatedly uses small sample size without clear justification (Li et al., 2015; Thair et al., 2017; de Graaf and Sack, 2018).

3.4.3 Montage

The most common target location is the right DLPFC (n = 16), with a smaller proportion of studies targeting the left DLPFC (n = 8) (Table 3-6). This cortical region is of interest due to its role in executive functioning, a process associated with the control of reward-driven appetite through the increase in inhibitory control and curbing of impulsive behaviours (Gluck et al., 2017; Dohle et al., 2018). Where the anode was placed over the right DLPFC and cathode over the left DLPFC, a reduction across measures was seen (g = −0.39 to 0.01) (Table 3-5). Less consistent patterns were found when both anode and cathode electrodes are placed over alternative cortical regions, although effect sizes are often based only on single studies. The DLPFC is of particular interest as reduced activity of this region is associated with poor control of dietary behaviours and obesity (Karhunen et al., 2000; Alonso-Alonso and Pascual-Leone, 2007; Boeka and Lokken, 2011). The consistent negative effect sizes across eating-related measures when targeting the

right DLPFC may lend support for the right brain hypothesis of obesity whereby reduction of activity within the right DLPFC facilitates obesogenic behaviours through poor executive control of appetite (Alonso-Alonso and Pascual-Leone, 2007).

Table 3-5 Summary of meta-data for montage.

Montage	Outcome Measure	*g*	95% CI	Interpretation
F4/F3	Food Consumption	0.01	−0.30, 0.32	Trivial
	Explicit Wanting	−0.03	−0.27, 0.20	Trivial
	Implicit Wanting [a]	−0.09	−1.01, 0.83	Trivial
	Food Craving	−0.15	−0.47, 0.17	Trivial
	Desire to Eat	−0.39	−8.11, 7.33	Small
	Hunger [a]	−0.17	−0.46, 0.12	Trivial
F4/Left supraorbital	Food Consumption [a]	−0.13	−0.87, 0.61	Trivial
	Hunger	0.20	−3.37, 3.77	Small
F4/Left deltoid	Explicit Wanting [a]	0.01	−0.52, 0.54	Trivial
F4-F8/F3-F7	Food Consumption [a]	0.60	0.01, 1.19	Moderate
F4-F8/Left cheek	Food Craving [a]	0.00	−0.51, 0.51	Trivial
	Desire to Eat [a]	0.09	−0.44, 0.62	Trivial
	Hunger [a]	0.06	−0.47, 0.59	Trivial
F3/Right cerebellum	Desire to Eat [a]	0.53	−0.29, 1.35	Moderate
	Hunger [a]	0.77	−0.05, 1.59	Moderate

F3, frontal area 3; F4, frontal area 4; F7, frontal area 7; F8, frontal area 8.

[a] *n = 1 study.*

Table 3-6 Comparison of tDCS parameters across studies.

		Montage [a,b]				Stimulation Duration			
	Intervention	Target Electrode	Reference Electrode	Electrode Size (cm^2)	Current Intensity (mA)	Ramp (seconds)	Active (minutes)	Sham (seconds)	Number of Stimulation Sessions
Amo Usanos et al. (2020)	Anodal, Sham	F3	Right supraorbital	25	2.0	30	20	15 at start and end	8
Bravo et al. (2016)	Anodal, Sham	F4	Left supraorbital	35	2.0	15	30	0 (ramp only)	5
Burgess et al. (2016)	Anodal, Sham	F4	F3	Not reported	2.0	Not reported	20	120 at start, 60 at end	1
Carvalho et al. (2019)	Anodal, Cathodal, Sham	F4	F3	35	2.0	15	20	15	1
Chen et al. (2019)	Anodal, Sham	Right IFG (midpoint F4-F8)	Left cheek	25	1.5	30	20	0 (ramp only)	1
Fassini et al. (2019)	Anodal, Sham	F3	Right supraorbital	25	2.0	30	30	30	16
Fassini et al. (2020)	Anodal, Sham	F3	Right supraorbital	25	2.0	30	30	30	16
Fregni et al. (2008)	Anodal, Cathodal, Sham	F3 / F4	F4 / F3	35	2.0	Not reported	20	30	1

Table 3-6 continued

		Montage [a,b]				Stimulation Duration			
	Intervention	Target Electrode	Reference Electrode	Electrode Size (cm^2)	Current Intensity (mA)	Ramp (seconds)	Active (minutes)	Sham (seconds)	Number of Stimulation Sessions
Georgii et al. (2017)	Anodal, Sham	F4	F3	35	1.0	15	20	15	1
Gluck et al. (2015)	Anodal, Cathodal, Sham	F3	Left forearm / Right supraorbital	25	2.0	30	40	15	3
Goldman et al. (2011)	Anodal, Sham	F4	F3	Not reported	2.0	30	20	60	1
Grundeis et al. (2017)	Anodal, Cathodal, Sham	F8	Af7	35	2.0	30	20	0 (ramp only)	1
Heinitz et al. (2017)	Anodal, Sham	F3	Right supraorbital	35	2.0	Not reported	40	10	15
Jauch-Chara et al. (2014)	Anodal, Sham	Right DLPFC	Left supraorbital	35	1.0	8	20	0 (ramp only)	8
Kekic et al. (2014)	Anodal, Sham	F4	F3	25	2.0	10	20	30	1
Kekic et al. (2017)	Anodal, Cathodal, Sham	F4	F3	25	2.0	10	20	30	1

Table 3-6 continued

		Montage [a,b]				Stimulation Duration			
	Intervention	Target Electrode	Reference Electrode	Electrode Size (cm^2)	Current Intensity (mA)	Ramp (seconds)	Active (minutes)	Sham (seconds)	Number of Stimulation Sessions
Lapenta et al. (2014)	Anodal, Sham	F4	F3	35	2.0	15	20	30	1
Ljubisavljevic et al. (2016)	Anodal, Sham	F4	Left forearm	35	2.0	30	20	0 (ramp only)	5
Marron et al. (2019)	Anodal, Sham	F3	Right cerebellum	25	2.0	Not reported	20	Not reported	1
Mattavelli et al. (2019)	Anodal, Sham	Midpoint Fz-F3 / O2-PO8	Contralateral supraorbital	16 / 35 [c]	1.0	10	20	40 at start, 30 at end	1
Max et al. (2020)	Anodal, Sham	F4	Left deltoid muscle	35	1.0 / 2.0	5	20	46	1
Montenegro et al. (2012)	Anodal, Sham	F3	Fp2	35	2.0	Not reported	20	30	1
Ray et al. (2017)	Anodal, Sham	F4	F3	24	2.0	Not reported	20	Not reported	Not reported
Ray et al. (2019)	Anodal, Sham	F4	F3	24	2.0	Not reported	20	60 at start and end	Not reported

Table 3-6 continued

		Montage [a,b]				Stimulation Duration			
	Intervention	Target Electrode	Reference Electrode	Electrode Size (cm^2)	Current Intensity (mA)	Ramp (seconds)	Active (minutes)	Sham (seconds)	Number of Stimulation Sessions
Sedgmond et al. (2019)	Anodal, Sham	F4	F3	35	2.0	10	20	30	1
To et al. (2018)	Anodal, Sham	Right IFG (midpoint F4-F8)	Midpoint F3-F7	25	2.0	30	20	0 (ramp only)	Not reported
Vicario et al. (2020)	Anodal, Cathodal, Sham	Left tnM1	Right mastoid process	35	1.0	30	15	0 (ramp only)	1

Af7, anterior frontal area 7; DLPFC, dorsolateral prefrontal cortex; F3, frontal area 3; F4, frontal area 4; F7, frontal area 7; F8, frontal area 8; Fp2, fronto-polar area 2; Fz, frontal zero point; IFG, inferior frontal gyrus; mA, milliampere; O2, occipital area 2; PO2, parieto-occipital area 2; tnM1, area of primary motor cortex representing the tongue muscle.

[a] *See Figure 3-3.*

[b] *All sham protocols used the same montage as active protocols.*

[c] *Target electrode size / reference electrode size.*

Many studies delivering tDCS across other cortical regions also measured effects when targeting the right DLPFC. Composite scores were calculated for these studies, to retain one effect size per participant group and avoid increasing homogeneity (Borenstein et al., 2021) and as such were removed from analyses. However, the results of these studies provide further support for targeting the right DLPFC. For example, Carvalho et al. (2019) found increased preference for chocolate following anode left/cathode right DLPFC stimulation, when compared with both anode right/cathode left DLPFC and sham protocols. The authors also found craving intensity was reduced to a greater extent by anode right/cathode left montages compared with anode left/cathode right DLPFC stimulation; replicating findings by Fregni et al. (2008).

Further studies targeting the left DLPFC failed to identify a change in measures of subjective appetite, food craving or food consumption (Fassini et al., 2019; Fassini et al., 2020). Additionally, Marron et al. (2019) found increased hunger and desire to eat when applying 2.0 milliampere (mA) for 20 minutes with the anode over the left DLPFC and cathode over the cerebellum. Targeting the left DLPFC appears to have minimal effect on eating-related measures and suggests greater importance for targeting the right versus left DLPFC, providing further support for the right brain hypothesis (Alonso-Alonso and Pascual-Leone, 2007). However, not all studies have found an effect of tDCS when applied to the right DLPFC (see Appendix 5.1). This may be due to the eating behaviour traits of the recruited participants, with these studies recruiting individuals who do not display a susceptibility to overconsumption and are likely able to appropriately inhibit impulsive behaviours through effective executive control. In comparison, an effect is more consistently shown in those with frequent food cravings or binge-type behaviours (Fregni et al., 2008; Goldman et al., 2011; Kekic et al., 2014; Lapenta et al., 2014; Burgess et al.,

2016; Max et al., 2020). This highlights a potential behaviour trait-dependent effect of tDCS (discussed further in Chapter 6).

Novel target locations include the right inferior frontal gyrus (IFG) (To et al., 2018; Chen et al., 2019), medial PFC (Mattavelli et al., 2019), right extrastriate body area (EBA) (Mattavelli et al., 2019), and the primary motor cortex representation of the tongue muscle (tnM1) (Vicario et al., 2020) (Figure 3-3). These regions are additionally associated with consumptive behaviours, however data following the use of these more novel montages show no significant stimulation effects or an increase in measures of food consumption and implicit preference (To et al., 2018; Mattavelli et al., 2019). The IFG and medial PFC are in anatomically close proximity to the DLPFC, and the large electrodes used in these studies are likely to overlap the DLPFC with the current entering or passing through this region as demonstrated in the computational modelling by Truong et al. (2013). However, these alternative montages likely change the current distribution when compared to DLPFC-targeted stimulation (Bikson et al., 2010). The effects of tDCS may be dependent on the current entering the DLPFC, specifically the right hemisphere, and so the small amount of current potentially entering through close proximity with an alternative target region may be insufficient to cause any meaningful modulation. This further suggests the DLPFC is an important focal target for the modulation of eating behaviours.

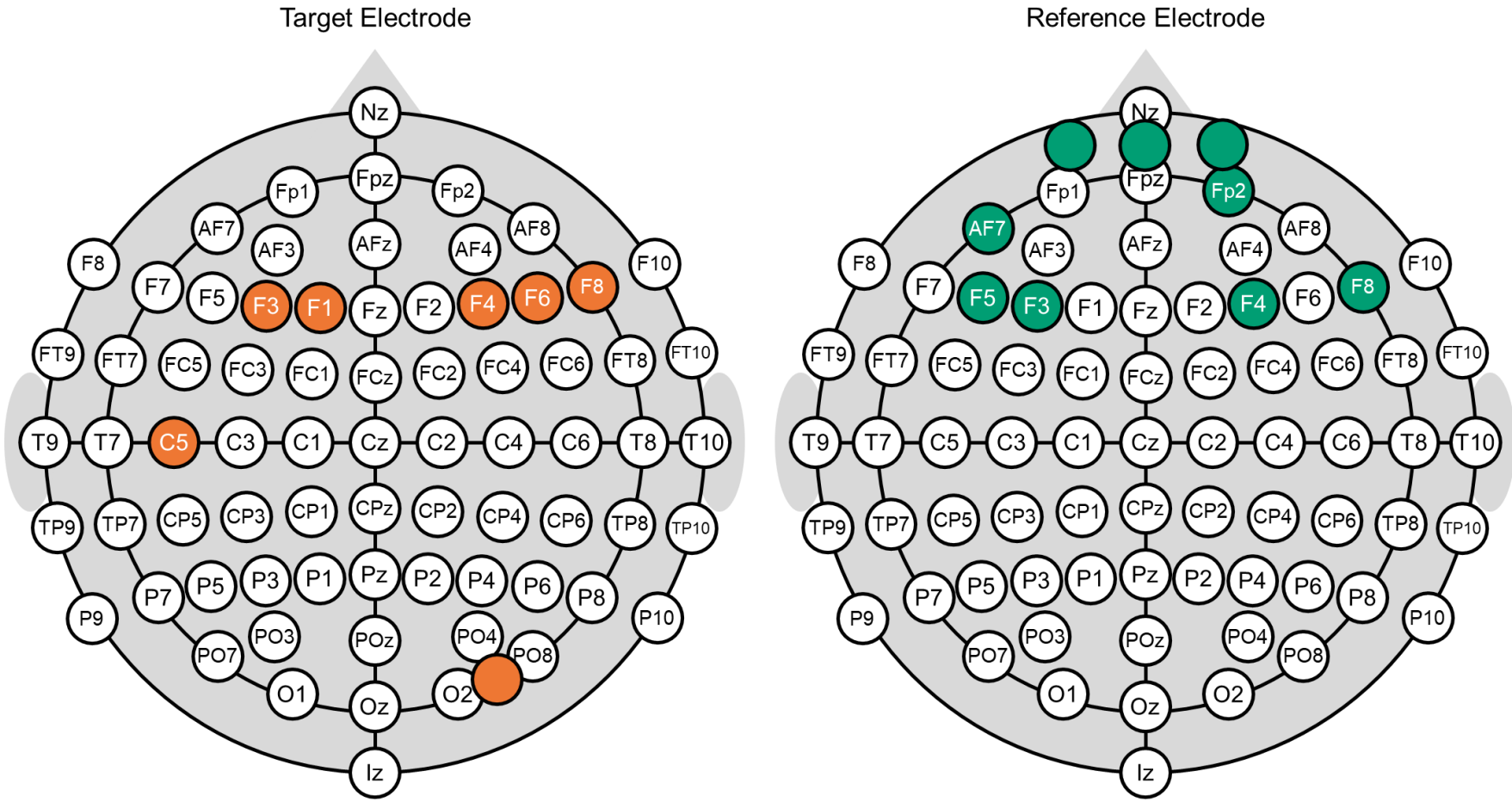


Figure 3-3 A comparison of cephalic montages. Coloured circles represent target (left) or reference (right) electrode locations. Image adapted from Klem et al. (1999).

In addition to variation in target location, researchers opt for different reference electrode locations. Across the included studies, the reference electrode was placed bilaterally to the target electrode (i.e., over the same cortical region, but on the opposite hemisphere; e.g., right and left DLPFC), over the contralateral supraorbital region (i.e., above the eye on the opposite hemisphere; e.g., right DLPFC and left supraorbital region), or over the cerebellum (Figure 3-3). A comparison of the potential effects of different reference electrode positions on eating behaviours has not been conducted, and it is difficult to fully identify any potential impacts.

Moving the reference electrode to alternative locations is likely to alter the current distribution, and may affect the expected tDCS-induced effects (Bikson et al., 2010; Batsikadze et al., 2019). While there are similar changes in eating-related measures when comparing tDCS with the same target location but differing reference electrode positions (e.g., left DLPFC versus left supraorbital region) (Fregni et al., 2008; Goldman et al., 2011; Jauch-Chara et al., 2014; Kekic et al., 2014; Lapenta et al., 2014; Bravo et al., 2016; Burgess et al., 2016), there was variation in effect sizes (Table 3-5). Again, these analyses should be interpreted with caution as the overall effect sizes are often based on single studies and are likely driven by other variables.

As discussed earlier in this thesis, both electrodes exert a physiological effect on the underlying cortex (see Figure 1-2) (Filmer et al., 2014). As such, the reference electrode should not be ignored when considering the impact of stimulation on behaviours as the physiological effect of this electrode on the underlying cortex will likely affect outcome measures (Bikson et al., 2010; Filmer et al., 2014). Therefore, careful consideration of the placement of both electrodes is required, with the reference electrode placed over a region unrelated to the outcome measure (Thair et al., 2017). One way to minimise the physiological impact of the reference

electrode is to place it over an extracephalic region, that is over a region of the body that is not the cortex (Imburgio and Orr, 2018). One study placed the reference electrode over the contralateral cheek (Chen et al., 2019), and three studies placed this electrode on a section of the participant's arm or shoulder (Gluck et al., 2015; Ljubisavljevic et al., 2016; Max et al., 2020). The advantage of these extracephalic montages is that the physiological effects of the reference electrode are minimised (Nitsche and Paulus, 2011; Lowe et al., 2017), however this may be at the expense of altering the direction and distribution of the electric current (Thair et al., 2017; Imburgio and Orr, 2018). Despite these effects, placing the reference electrode over an extracephalic region did not appear to impact the effects of tDCS on behavioural measures as observed when using cephalic montages, with comparable effect sizes following cephalic versus extracephalic montages (Table 3-7).

Table 3-7 Summary of meta-data for cephalic versus extracephalic montages.

Montage Type	Outcome Measure	*g*	95% CI	Interpretation
Cephalic	Food Consumption	0.05	−0.23, 0.33	Trivial
	Explicit Wanting	−0.03	−0.27, 0.20	Trivial
	Food Craving	−0.15	−0.47, 0.17	Trivial
	Desire to Eat	−0.08	−2.04, 1.88	Trivial
	Hunger	0.14	−0.58, 0.86	Trivial
Extracephalic	Explicit Wanting [a]	0.01	−0.52, 0.54	Trivial
	Implicit Wanting [a]	−0.09	−1.02, 0.83	Trivial
	Food Craving [a]	0.00	−0.51, 0.51	Trivial
	Desire to Eat [a]	0.09	−0.44, 0.62	Trivial
	Hunger [a]	0.06	−0.47, 0.59	Trivial

[a] *n = 1 study.*

It is assumed that increasing the distance between electrodes results in a greater amount of the current entering the brain, as opposed to being shunted across the scalp (Bikson et al., 2010). Many studies place the target and reference electrodes relatively close together, such as bilaterally over the DLPFC (Fregni et al., 2008; Goldman et al., 2011). The effect of increasing electrode distance on measures of eating behaviour is not clear. The ability of extracephalic montages to increase the amount of current penetrating deeper brain structures is also unclear (Im et al., 2012; Noetscher et al., 2014), although they do appear able to reduce the amount of current being shunted across the scalp (Miranda et al., 2006; Imburgio and Orr, 2018). If extracephalic montages are able to increase the amount of current reaching deeper brain structures, this may be important for reaching those structures involved in rewarding components of eating behaviour, such as the nucleus accumbens (Pleger, 2018). Further research that includes neuroimaging techniques is needed to support this premise. If an extracephalic montage is used, there should be careful consideration of other parameters; for example, higher current intensities may be required to compensate for the greater distance between electrodes (Moliadze et al., 2010).

3.4.4 Current Intensity and Current Density

The most consistently applied current intensity is 2.0 mA, delivered across 22 of the 27 studies. One study applied 1.5 mA (Chen et al., 2019), and five studies delivered 1.0 mA (Jauch-Chara et al., 2014; Georgii et al., 2017; Mattavelli et al., 2019; Max et al., 2020; Vicario et al., 2020). It has been suggested that 2.0 mA is the minimum intensity required to elicit changes in eating-related measures (Hall and Lowe, 2018; Mostafavi et al., 2018). However, since the publication of these papers, Chen et al. (2019) applied 1.5 mA and found improved reaction times in a stop-signal task. This intensity warrants further investigation, especially in light of the potential issues

surrounding blinding efficacy at higher current intensities (O'Connell et al., 2012) (see section 3.4.6). Unlike the earlier meta-analyses, the present analysis found largely comparable effects of differing current intensities when incorporating more recently published work (Table 3-8).

Table 3-8 Summary of meta-data for current intensity.

Current Intensity	Outcome Measure	*g*	95% CI	Interpretation
1.0 mA	Food Consumption	0.04	−1.22, 1.31	Trivial
	Explicit Wanting [a]	0.10	−0.33, 0.53	Trivial
	Implicit Wanting [a]	0.08	−0.39, 0.55	Trivial
	Food Craving [a]	−0.06	−0.49, 0.37	Trivial
	Hunger	−0.08	−5.39, 5.24	Trivial
1.5 mA	Food Craving [a]	0.00	−0.51, 0.51	Trivial
	Desire to Eat [a]	0.09	−0.44, 0.62	Trivial
	Hunger [a]	0.06	−0.47, 0.59	Trivial
2.0 mA	Food Consumption	−0.03	−0.32, 0.26	Trivial
	Explicit Wanting	−0.07	−0.37, 0.22	Trivial
	Implicit Wanting	−0.23	−1.67, 1.21	Trivial
	Food Craving	−0.18	−1.52, 1.15	Trivial
	Desire to Eat	0.05	−0.37, 0.46	Trivial
	Hunger	0.01	−0.39, 0.40	Trivial

mA, milliampere.

[a] *n = 1 study.*

It could be that, rather than current intensity, the effects of tDCS are driven more by the density of applied current (i.e., the amount of current delivered per unit area [$mA \cdot cm^{-2}$]), as low current densities will likely diminish the effect of stimulation on

the underlying cortex (Filmer et al., 2014). The suggested minimum intensity of 2.0 mA equates to a minimum current density between 0.057 and 0.080 $mA \cdot cm^{-2}$, in line with commonly used electrode sizes of 25 and 35 cm^2. Indeed, this appears to be the boundary within which tDCS is able to modulate measures of eating behaviour (Table 3-9). In particular, 0.057 $mA \cdot cm^{-2}$ resulted in a consistent reduction (i.e., favouring active tDCS) across all measures (g = −0.25 to −0.06). As comparable current densities are achieved through varying current intensities and electrode sizes, this may explain why the intensity-dependent effect observed by Mostafavi et al. (2018) was not replicated.

Table 3-9 Summary of meta-data for current density.

Current Density	Outcome Measure	*g*	95% CI	Interpretation
0.029 mA·cm^{-2}	Food Consumption	0.04	−1.22, 1.31	Trivial
	Explicit Wanting	0.10	−0.33, 0.53	Trivial
	Food Craving [a]	−0.06	−0.49, 0.37	Trivial
	Hunger	−0.08	−5.39, 5.24	Trivial
0.057 mA·cm^{-2}	Food Consumption	−0.16	−0.80, 0.48	Trivial
	Explicit Wanting	−0.06	−4.57, 4.45	Trivial
	Implicit Wanting	−0.23	−1.67, 1.21	Small
	Food Craving [a]	−0.14	−0.43, 0.15	Trivial
	Desire to Eat	−0.25	−1.67, 1.17	Small
	Hunger	−0.16	−0.24, −0.09	Trivial
0.060 mA·cm^{-2}	Food Craving [a]	0.00	−0.51, 0.51	Trivial
	Desire to Eat [a]	0.09	−0.44, 0.62	Trivial
	Hunger [a]	0.06	−0.47, 0.59	Trivial
0.062 mA·cm^{-2}	Implicit Wanting [a]	0.08	−0.39, 0.55	Trivial
0.080 mA·cm^{-2}	Food Consumption	0.10	−0.55, 0.75	Trivial
	Explicit Wanting	−0.10	−0.78, 0.58	Trivial
	Food Craving [a]	−0.43	−1.12, 0.26	Trivial
	Desire to Eat	0.19	−2.16, 2.55	Trivial
	Hunger	0.37	−3.05, 3.80	Small
0.083 mA·cm^{-2}	Food Consumption [a]	−0.07	−0.72, 0.58	Trivial
	Explicit Wanting [a]	0.00	−0.65, 0.65	Trivial

mA·cm^{-2}, milliampere per centimetre squared.

[a] *n = 1 study.*

Maintaining a comparable current intensity does not occur in all studies. Four studies applied 1.0 mA using large 35 cm^2 electrodes, resulting in a current density of 0.029

mA·cm^{-2} (Jauch-Chara et al., 2014; Georgii et al., 2017; Max et al., 2020; Vicario et al., 2020). These studies failed to identify an effect of stimulation across measures of hunger and food craving, with the exception of Jauch-Chara et al. (2014) who found reduced food consumption following repeated sessions of active tDCS, potentially due to a cumulative effect (see section 3.4.8). Current densities in line with 2.0 mA protocols can be achieved with 1.0 mA stimulation by reducing the electrode size to between 12.5 and 17.5 cm^2, resulting in current densities between 0.057 and 0.080 mA·cm^{-2}. It should be noted that increasing the current density is unlikely to lead to linear effects on the underlying cortex and outcome measures, but greater current densities may provide more consistent effects (Dedoncker et al., 2016; Imburgio and Orr, 2018). Animal models suggest tissue damage occurs at current densities above 25 mA·cm^{-2} (McCreery et al., 1990); to maintain participant safety, current density should not exceed this threshold (Nitsche et al., 2003).

Reflecting on the issues raised with reference electrode placement (see section 3.4.3), any modulatory effect of the reference electrode may be diminished by using a large electrode size. Electrodes are typically an equal size of 25 or 35 cm^2, but range from 16 to 70 cm^2. When electrodes are equal size there is similar cortical neuromodulation (with opposite polarity) under both electrodes. In comparison, when the size of one electrode is increased, the current density is reduced under that electrode which results in modulation under the smaller electrode area only (Nitsche et al., 2007). One study has used larger reference electrodes (Mattavelli et al., 2019). Although this study did not show improvements in eating-related measures, this again may be driven by methodological issues such as the use of an online task (see section 3.4.7). The use of large reference electrode size in eating behaviour studies, especially with offline protocols, is yet to be fully determined. Large reference electrodes can alter the current distribution and may reduce the

deleterious effects associated with the cathode (Leite et al., 2018). Increasing reference electrode size should be combined with the use of greater distances between electrodes, such as extracephalic montages, to minimise the chance of current shunting across the scalp (Rush and Driscoll, 1968; Miranda et al., 2006).

3.4.5 Stimulation Duration

Stimulation was applied for 15 minutes (n = 1), 20 minutes (n = 21), 30 minutes (n = 3), and 40 minutes (n = 2) across the reviewed studies. Vicario et al. (2020) delivered 15 minutes of 1.0 mA stimulation to the left tnM1, which failed to change subjective hunger scores. All studies that used stimulation durations greater than 20 minutes also used multi-session protocols, where tDCS was delivered over subsequent days (Gluck et al., 2015; Bravo et al., 2016; Heinitz et al., 2017; Fassini et al., 2019; Fassini et al., 2020) (see section 3.4.8). Comparison of effects following single session tDCS as part of these multi-session designs is largely not reported, and so the effects of longer stimulation durations in a single session design cannot be made. Such extended durations should be used with caution, as data from motor cortex stimulation suggests that longer durations may lead to a reversal of the expected effect (Monte-Silva et al., 2013; Hassanzahraee et al., 2020). There are no recorded studies to date that have compared the effects of stimulation duration on eating behaviour outcomes, and further studies utilising shorter (10 to 15 minutes) durations are required as this would reduce the time requirement of participants.

3.4.6 Sham Protocols and Blinding

Commonly applied sham protocols involve the current being ramped up to the desired intensity and then delivered for 0 to 120 seconds before being ramped down (Figure 3-4). To imitate both the incremental and decremental currents integral to

active tDCS protocols, some studies deliver the aforementioned ramping protocol at the start and end of the stimulation period. The common cutaneous sensations associated with delivery of the direct current typically occur at the start of current delivery (i.e., the ramp period) and often habituate within the initial seconds of stimulation (Gandiga et al., 2006). Therefore, sham protocols are considered effective methods of participant blinding as they mimic the initial phase of active tDCS, but are unlikely to result in lasting modulation of the cortex due to the short duration (Gandiga et al., 2006; Brunoni et al., 2011; Nikolin et al., 2018). Although standardised sham protocols are generally assumed to be effective, researchers may struggle to maintain blinding at higher current strengths due to the more pronounced cutaneous sensations (O'Connell et al., 2012).

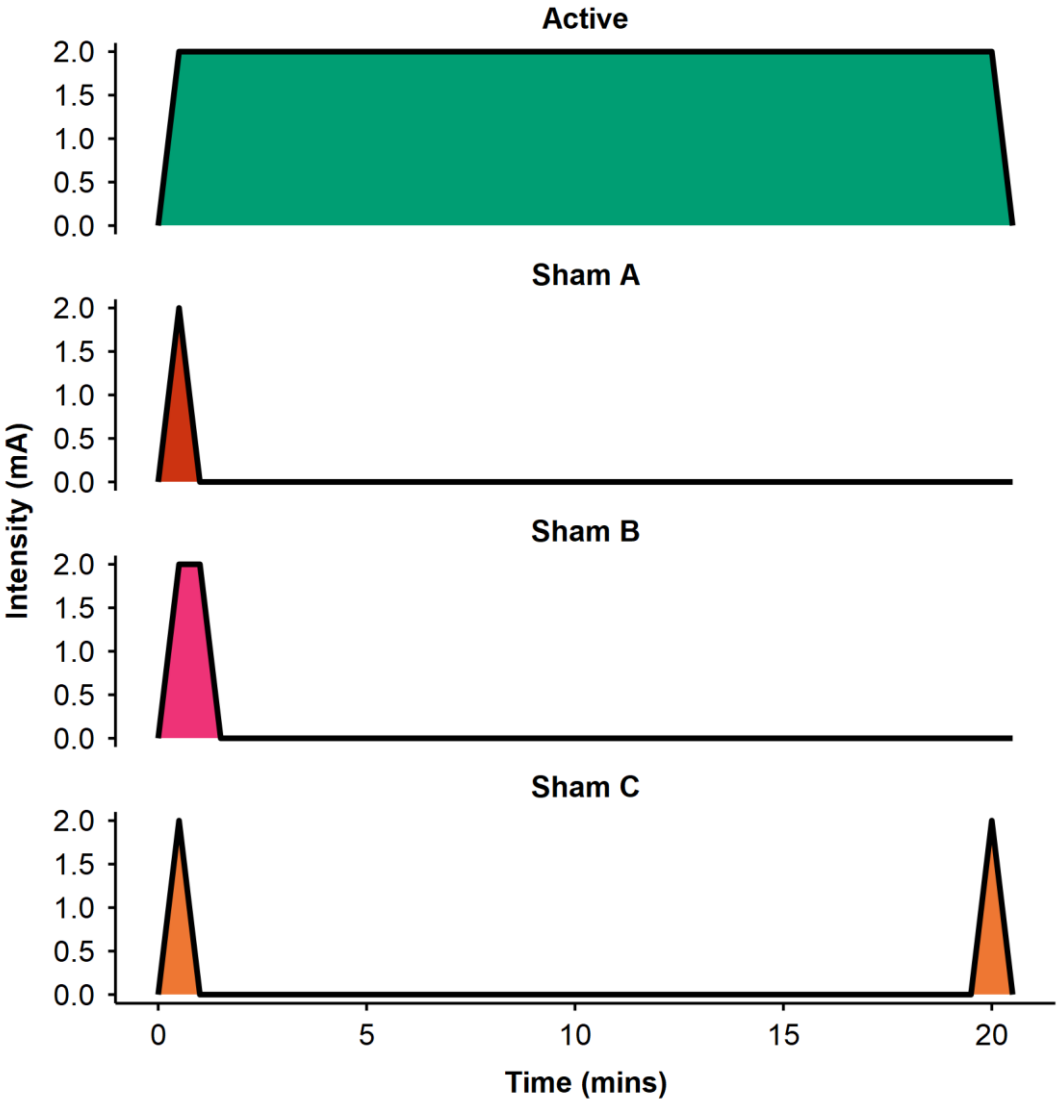


Figure 3-4 A comparison between active and commonly applied sham protocols. Active stimulation involves the current being ramped up to the desired intensity and delivered for several minutes. Three different sham protocols were used: (a) Stimulation is ramped up to the desired intensity and immediately ramped down and turned off; (b) The current is ramped up to the desired intensity, delivered for several seconds and then ramped down and turned off; (c) The current is ramped to the desired intensity and delivered for several seconds before being ramped down and turned off, this is then repeated at the end of the stimulation period.

Only 11 studies included quantitative data on the effectiveness of sham protocols, with participants' ability to correctly guess the condition received ranging from 17 to 97% (Cohen's *d* = 0.33 to 0.58). Of these studies, participants were unable to identify active stimulation above the level of chance across five studies (Gluck et al., 2015; Ljubisavljevic et al., 2016; Georgii et al., 2017; Kekic et al., 2017; Carvalho et al., 2019). Many of these studies utilised 2.0 mA, suggesting that participant blinding can be achieved at higher current strengths. Two further studies report successful participant blinding, but do not provide data to support this (Kekic et al., 2014; Heinitz et al., 2017). The remaining studies reported failure to achieve adequate participant blinding, with correct guesses ranging from 60 to 97% (Goldman et al., 2011; To et al., 2018; Chen et al., 2019; Mattavelli et al., 2019; Sedgmond et al., 2019; Max et al., 2020). Again, these studies oppose the notion that higher current intensities result in poorer participant blinding, as they include 1.0 and 1.5 mA protocols. As such, stimulation intensity itself does not appear to impact participant blinding, and so researchers can be relatively confident that blinding can be achieved using 2.0 mA protocols (Russo et al., 2013).

The greater prevalence of adverse events following active tDCS may reduce the ability to blind participants (Kessler et al., 2012). However, this is of particular debate as not all studies find a difference in adverse events between active and sham conditions (Brunoni et al., 2011). Poor blinding may be driven by visual cues such as erythema (skin redness), which is more common following active stimulation (O'Connell et al., 2012). This visual discrepancy between active and sham protocols easily signifies to the participant and researcher that a difference between conditions exists and potentially which condition the participant has received (O'Connell et al., 2012; Palm et al., 2013). Five studies report either greater erythema following active conditions or similar redness following active and sham protocols (Jauch-Chara et

al., 2014; Gluck et al., 2015; Bravo et al., 2016; Heinitz et al., 2017; Amo Usanos et al., 2020). Two of these studies reported successful participant blinding, while also reporting no difference in skin redness (Gluck et al., 2015; Heinitz et al., 2017), which suggests erythema may indeed be contributing to ineffective participant blinding (O'Connell et al., 2012; Palm et al., 2013).

Participant blinding can be maintained by preventing the participant from observing their skin following stimulation. However, researcher blinding is less straight forward to uphold where visible differences are evident and this may account for some of the variation in data (Horvath, 2015). Careful consideration of stimulation parameters and device set-up should be made to minimise the likelihood of erythema and maintain a double-blind design. Additionally, pre-treatment of the skin with dermatological products may reduce occurrence and severity of redness, but this may not be appropriate for all studies or participant groups (Guarienti et al., 2015). The impact on current resistance by preparing the skin with these products is not well established, and to account for any potential effects all preparatory steps must be recorded (Antal et al., 2017).

Based on the overall correct guess rate (i.e., number of participants able to identify active and sham protocols), there are considerable differences in effect sizes when comparing successful and unsuccessful blinding protocols. Where blinding was upheld, trivial-to-small positive effect sizes were observed (g = 0.06 to 0.31) (Table 3-10). In comparison, studies with unsuccessful tDCS blinding resulted in more consistent negative effect sizes (i.e., favouring an effect of active tDCS), particularly across measures of explicit wanting, food craving and hunger (g = −0.16 to −0.11) (Table 3-10). Fassi and Cohen Kadosh (2021) suggest, rather than focusing on overall correct guess rate, we should instead assess active guess rate (i.e.,

percentage of participants able to correctly guess receiving active protocols). The authors argue that overall correct guess rate can lead to misleading estimate of blinding success (Fassi and Cohen Kadosh, 2020). Across the reviewed literature, overall correct guess rate suggests participant blinding may be upheld (mean 49%, range 17 to 79%) whereas active guess rate demonstrates that participants are consistently able to identify active protocols (mean 73%, range 60 to 85%).

Table 3-10 Summary of meta-data comparing success of blinding protocols.

	Outcome Measure	*g*	95% CI	Interpretation
Blinding upheld	Food Consumption	0.31	−2.82, 3.44	Small
	Explicit Wanting	0.15	−0.07, 0.37	Trivial
	Implicit Wanting [a]	0.28	−0.39, 0.95	Trivial
	Food Craving [a]	0.06	−0.49, 0.37	Trivial
	Desire to Eat [a]	0.09	−0.36, 0.54	Trivial
	Hunger [a]	0.19	−0.26, 0.64	Small
Blinding failure	Food Consumption	0.16	−0.33, 0.65	Trivial
	Explicit Wanting	−0.16	−2.77, 2.46	Trivial
	Implicit Wanting [a]	0.08	−0.39, 0.55	Trivial
	Food Craving	−0.11	−0.88, 0.66	Trivial
	Desire to Eat	0.12	−0.10, 0.34	Trivial
	Hunger	−0.12	−1.36, 1.12	Trivial

[a] *n = 1 study.*

Reflecting on the RoB assessment (see section 3.4.2), the implementation and maintenance of participant and researcher blinding is the main source of bias across many of the reviewed studies. In particular, little detail is given around researcher blinding protocols in several studies. It is likely that poor researcher blinding

contributes to poor participant blinding, as ineffective researcher blinding can lead to several confounding factors such as expectation effects, protocol adjustments or biases in the analysis and reporting of data (Horvath et al., 2014). When comparing the effects of single- and double-blind study designs on tDCS modulation of eating behaviour, variation in effect sizes is evident. In particular, the reduction in food consumption and explicit wanting following tDCS appear to be driven by studies utilising single-blind design (Table 3-11). Discrepancy in effect sizes further emphasises the importance of implementing and maintaining a double-blind study design. Researcher blinding can be achieved through the use of pin-protected devices where the stimulation parameters are pre-set by an independent individual (e.g., see section 4.7.2.5). To control for potential unblinding of researchers it is recommended that the efficacy of researcher blinding is measured.

Table 3-11 Summary of meta-data comparing study blinding protocols.

Blinding Protocol	Outcome Measure	*g*	95% CI	Interpretation
Single-blind	Food Consumption	−0.11	−0.52, 0.30	Trivial
	Explicit Wanting	−0.19	−1.15, 0.76	Trivial
	Implicit Wanting	0.28	−0.39, 0.95	Small
	Food Craving [a]	0.00	−0.51, 0.51	Trivial
	Desire to Eat	0.22	−2.32, 2.76	Small
	Hunger	0.08	−0.52, 0.68	Trivial
Double-blind	Food Consumption	0.01	−0.31, 0.33	Trivial
	Explicit Wanting	0.05	−0.05, 0.16	Trivial
	Implicit Wanting	−0.54	−4.98, 3.90	Small
	Food Craving	−0.15	−0.47, 0.17	Trivial
	Desire to Eat	0.05	−0.68, 0.58	Trivial
	Hunger	−0.08	−0.53, 0.38	Trivial

[a] *n = 1 study.*

Finally, the information provided to participants should also be carefully controlled. Providing information to participants that will lead to an expectation of effect will likely change scores, resulting in an effect that is unrelated to the stimulation technique (Ray et al., 2019). Participants should be given sufficient information to provide informed consent, but this should omit any study hypotheses or expected effects of the study protocol. Answers provided to any participant queries or comments made around the efficacy of tDCS should also be controlled. It should be noted that individuals who have previously undergone or are knowledgeable of tDCS procedures may be more likely to identify active protocols than tDCS-naïve individuals, and so the inclusion of those who have previously undergone stimulation should be avoided to maintain blinding efficacy (Ambrus et al., 2012).

3.4.7 Offline versus Online Protocols

Offline protocols typically involve the participant remaining seated and relaxed with tDCS delivered without distraction. In comparison, online protocols employ specific tasks during the stimulation period, such as cognitive training (Thair et al., 2017). Many of the studies in this review used offline protocols (n = 19). Eight studies applied online tDCS, where participants watched unrelated media (e.g., nature documentary, cartoon) (Gluck et al., 2015; Mattavelli et al., 2019), completed a food-related task (e.g., food choice computer-based task) (Goldman et al., 2011; Georgii et al., 2017; Grundeis et al., 2017; Max et al., 2020), or completed a cognitive task (e.g., approach-avoidance training, Go/No-Go task) (Carvalho et al., 2019; Sedgmond et al., 2019). Variation in effect sizes is evident when comparing offline and online protocols (Table 3-12). Where offline protocols produce a more consistent trivial-to-small negative effect size (g = −0.54 to 0.09), with the exception of hunger measures, there is greater variation in the effects following online protocols (g = −0.16 to 0.15).

Table 3-12 Summary of meta-data comparing offline versus online protocols.

Protocol	Outcome Measure	*g*	95% CI	Interpretation
Offline	Food Consumption	−0.13	−0.63, 0.36	Trivial
	Explicit Wanting	−0.08	−0.46, 0.31	Trivial
	Implicit Wanting	−0.54	−4.98, 3.90	Small
	Food Craving	−0.15	−2.77, 2.46	Trivial
	Desire to Eat	−0.01	−0.52, 0.49	Trivial
	Hunger	0.10	−0.33, 0.52	Trivial
Online	Food Consumption	0.09	−0.06, 0.25	Trivial
	Explicit Wanting	0.02	−0.38, 0.42	Trivial
	Implicit Wanting	0.15	−1.05, 1.34	Trivial
	Food Craving	−0.11	−0.59, 0.36	Trivial
	Desire to Eat [a]	0.13	−0.16, 0.42	Trivial
	Hunger	−0.16	−0.38, 0.06	Trivial

[a] *n = 1 study.*

The effects of tDCS are brain state-dependent and can be shaped by the use of online protocols (Filmer et al., 2014; Krause and Kadosh, 2014). Offline protocols lead to modifications of cortical activity that last beyond the stimulation duration, whereas the use of online tasks leads to modulation of cortical activity related to the specific task (Nitsche and Paulus, 2001; Miniussi et al., 2013). Additionally, the use of an unrelated online task may impact the expected polarity-dependent effects of tDCS (Thair et al., 2017). This may explain the lack of expected effects on eating-related measures across the reviewed studies that use online protocols. Even where a food-based training task is used to modify food choice behaviour, these studies typically measure wider eating-related measures such as food craving and consumption (Georgii et al., 2017; Grundeis et al., 2017). Although food choice is an

important driver of food consumption, food cravings are a more influential predictor of dietary intake and focusing on tasks promoting the regulation of food cravings may provide more fruitful effects (Sun and Kober, 2020).

It is currently unclear which participant populations may benefit from the use of online protocols (Martin et al., 2014; Dedoncker et al., 2016; Hill et al., 2016), and many studies fail to sufficiently justify the use of these protocols. Where tDCS is delivered alongside a cognitive training task there appears to be improved performance relating to the specific task, which highlights the importance of employing an online task that is specific to the outcome measure of interest (Martin et al., 2014; Gill et al., 2015). The impact of online tasks on the direction of stimulation effects and outcome measures warrants careful consideration of their use, but it may prove beneficial to use online protocols to enhance the modulatory effects of tDCS on specific eating-related measures. However, the online tasks performed in the reviewed studies are not always eating behaviour-specific, and typically focus on improving cognitive functions (Carvalho et al., 2019; Sedgmond et al., 2019). This may lead to improvements in the cognitive measure, at the expense of improving eating behaviour scores (Miniussi et al., 2013).

Gluck et al. (2015) performed tDCS while participants watched nature or history documentaries and they were able to show reduced consumption of fats and soda when comparing anodal versus cathodal stimulation. This suggests the use of unrelated media with the aim diverting thoughts away from food may prove a valuable procedure for standardising participants' thoughts during tDCS delivery. Until a clear effect of tDCS on eating behaviours is consistently reported or a clear impact of online protocols on eating-related measures can be identified, online

protocols should be used with caution and a clear justification for their inclusion should be provided.

3.4.8 Number of Stimulation Sessions

A total of nine studies included repeated sessions of active or sham tDCS, ranging from 3 to 16 sessions. These multi-session studies appeared to result in a cumulative effect, with small effect sizes for measures of food craving (g = −0.29; 95% CI = −0.60, 0.03) (Figure 3-5) and food consumption (g = −0.34; 95% CI = −1.03, 0.35) (Figure 3-6), compared to only trivial effect sizes following single session tDCS (g = −0.12 to 0.01). Stimulation was typically applied daily, with four studies initially applying stimulation with a 24-hour interval and increasing this to 48 hours in the second stage of the study (e.g., from inpatient to outpatient treatment) (Heinitz et al., 2017; Fassini et al., 2019; Amo Usanos et al., 2020; Fassini et al., 2020).

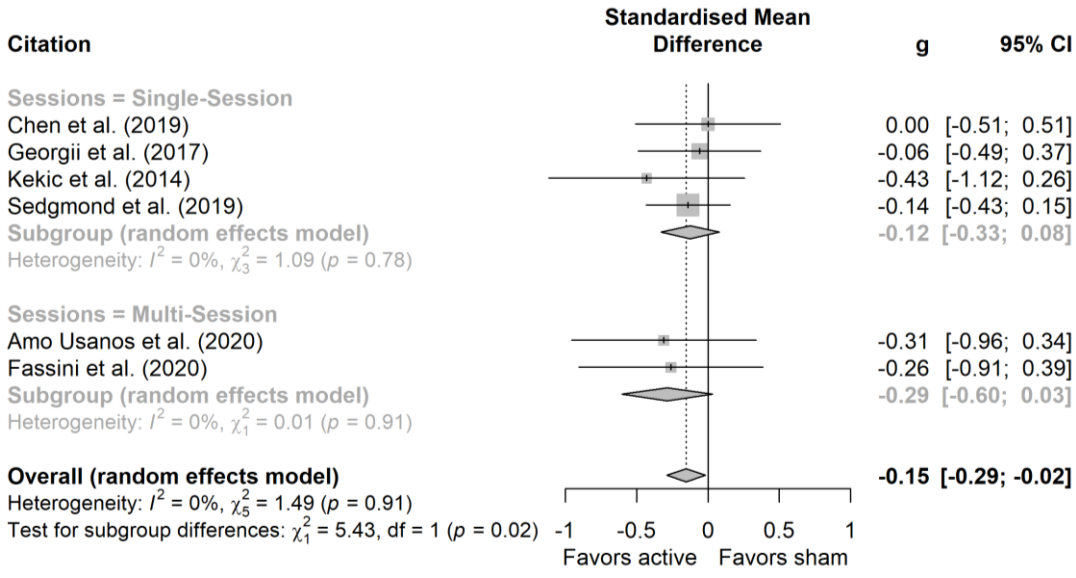


Figure 3-5 Forest plot comparing single- versus multi-session tDCS across food craving scores.

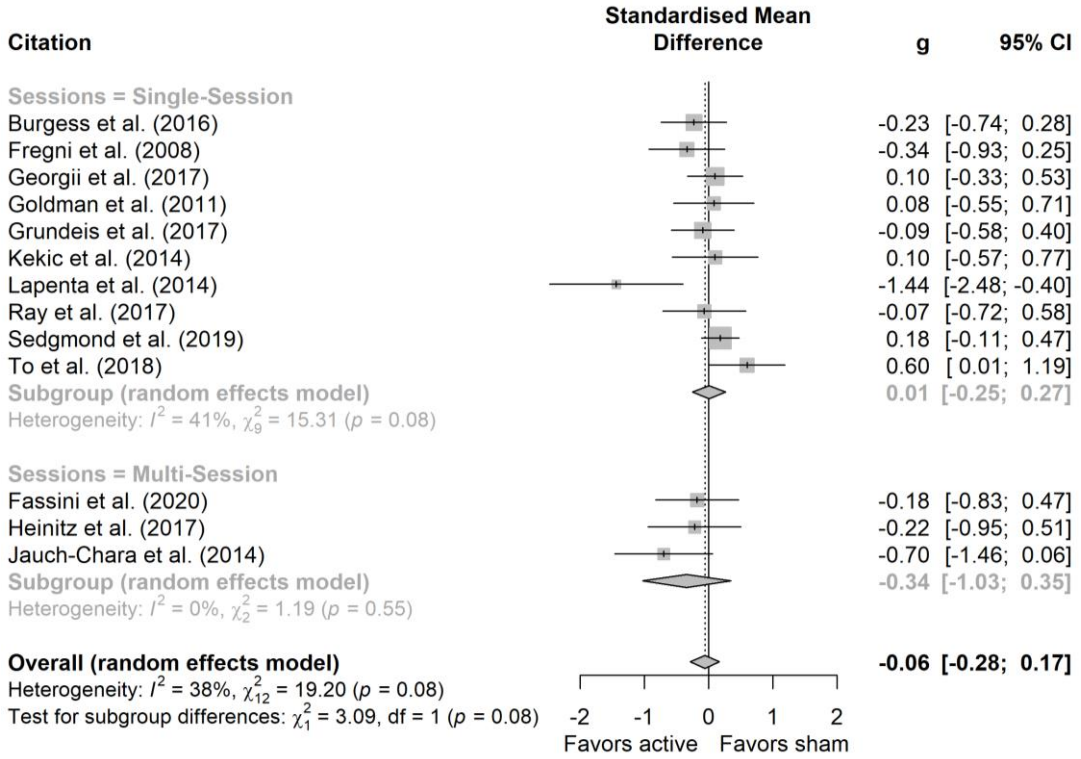


Figure 3-6 Forest plot comparing single- versus multi-session tDCS across measures of food consumption.

Although a 48-hour interval is likely to negate the cumulative effects of stimulation (Alonzo et al., 2012), it is possible that increasing the interval to 48 hours following initial daily stimulation could strengthen the modulatory effects. However, studies that implement this protocol failed to identify any change in subjective appetite or food craving scores (Heinitz et al., 2017; Fassini et al., 2019; Amo Usanos et al., 2020; Fassini et al., 2020), but this may be due to their focus on left DLPFC stimulation or longer stimulation durations. This poses an important consideration for multi-session designs; whether daily sessions of stimulation are required, or if the number of sessions can be reduced later in the study to minimise the time requirements of participants. Again, further data are required to determine the

impact of daily to second-daily stimulation protocols, which should adhere to effective parameters.

Across the reviewed studies, there appears to be the potential for repeated session to negate the deleterious effects when parameters are below the proposed effective range, as discussed in the above sections. For example, Jauch-Chara et al. (2014) used low current intensity (1.0 mA) and density (0.029 $mA \cdot cm^{-2}$), but they were able to demonstrate an ability of anodal tDCS to reduce food consumption and subjective appetite following eight sessions. This suggests that repeated low-level stimulation may lead to a cumulative improvement in eating-related measures, however there is not currently sufficient data to confirm this effect. If low-intensity stimulation is able to modulate eating behaviours across multiple sessions, this may produce a more consistent effect of tDCS than single session stimulation but will require greater resources and commitment from potential participants. Multi-session designs should not come at the cost of appropriate stimulation parameters, and studies using single session stimulation are still important for determining effective parameter ranges and the modulatory effect of tDCS on measures of eating behaviour; they have also demonstrated significant effects on a number of occasions (Fregni et al., 2008; Goldman et al., 2011; Montenegro et al., 2012; Burgess et al., 2016).

3.4.9 Effective tDCS Parameters: A Summary

The present review has considered the impact of a range of stimulation parameters, and what methodological issues may explain the observed inconsistencies in data. Figure 3-7 captures the variation in applied tDCS parameters across the reviewed research. While the meta-analyses were unable to capture all parameter variation, they have identified parameters that appear to modulate eating behaviour. A more

holistic and comprehensive consideration of these parameters is required to identify a consistent effect of tDCS protocols on eating-related measures.

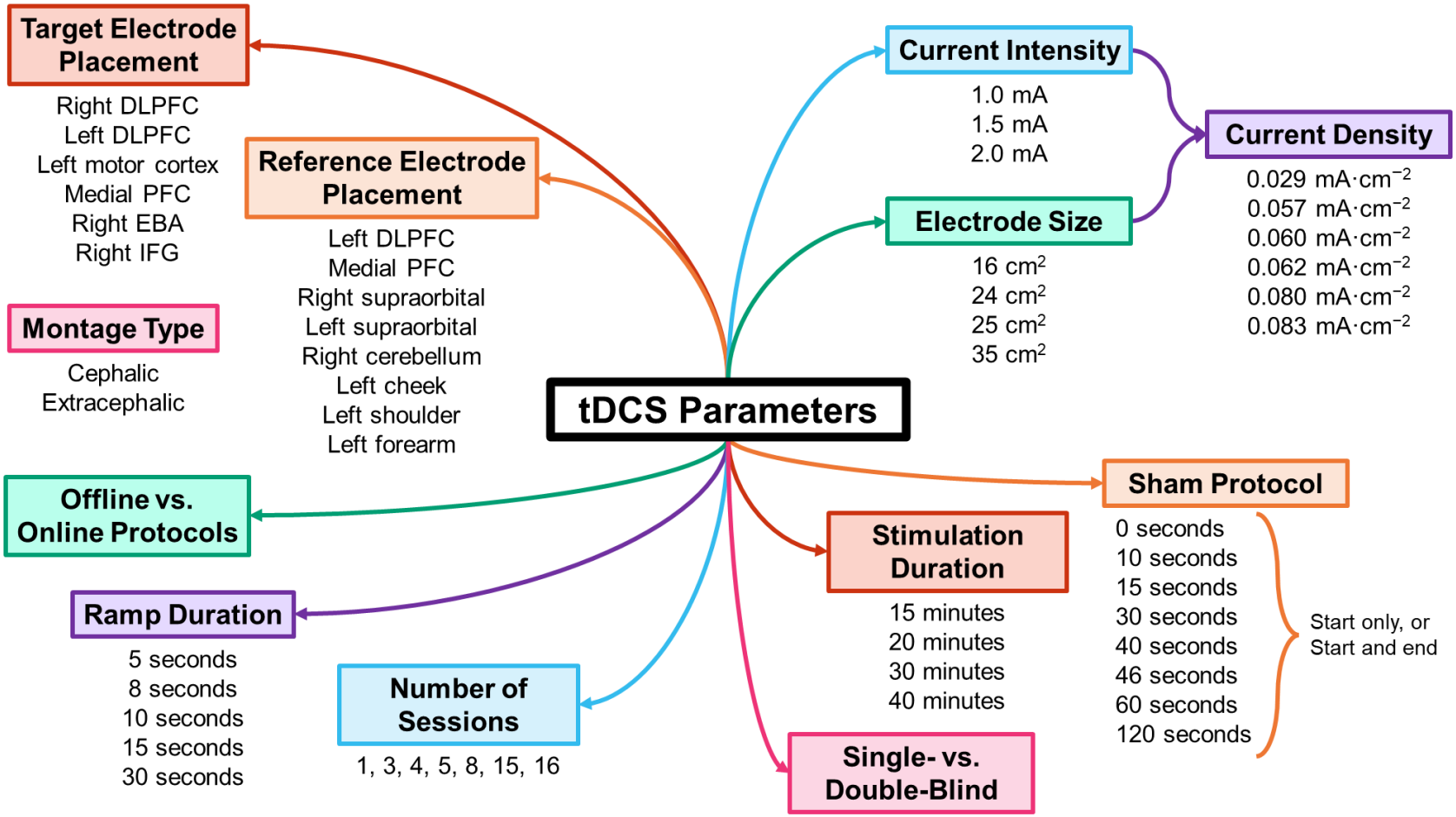


Figure 3-7 Variation in applied tDCS parameters across the reviewed literature.

Table 3-13 outlines the proposed range of tDCS parameters that appear to be most effective for modulating eating behaviours. This is not intended as an absolute recommendation, but as a point of reference and to help further discuss the most effective parameters for eating-related studies. In addition to these, researchers should adhere to a double-blind protocol and due to the inter-individual variation in response to tDCS (Chew et al., 2015; Antal et al., 2017; Jamil and Nitsche, 2017) follow a within-participant (randomised and counterbalanced) design, particularly for single session studies and where this fits the study aims. Studies should also provide sufficient detail on the study design and implemented tDCS parameters so the effects of parameter sets can be fully understood. Protocols using parameters known to affect the outcome, such as online tasks, should be carefully considered with a clear justification for their use.

Table 3-13 Proposed effective tDCS parameters.

Montage	Target:	Right DLPFC
	Reference:	Cortical region away from DLPFC, or extracephalic region
Electrode Size	Target:	≤35 cm^2
	Reference:	Equal or greater than target electrode
Current Intensity	1.5 to 2.0 mA	
Current Density	0.057 to 0.080 $mA \cdot cm^{-2}$	
Stimulation Duration	20 minutes	
Inter-session Interval	Single session:	>48 hours
	Multi-session:	≤24 hours
Offline / Online Protocol	Offline (unrelated media used as an online task may be appropriate for standardising participants' thoughts during stimulation)	

DLPFC, dorsolateral prefrontal cortex; mA, milliampere; $mA \cdot cm^{-2}$, milliampere per centimetre squared.

Further data are required to determine the efficacy of some parameters, such as lower stimulation durations or current intensities of 1.5 mA. Additionally, data are required to confirm some of the assumptions made in the present review, such as the effective current density range. It is not expected that all future studies will adhere to the parameters described in this section, and it is important that further studies test the efficacy of parameters outside these ranges. However, from the data included in this review, these appear to be the most effective parameters for modulating eating-related outcomes. Whilst it is acknowledged that the present review does not extend to the discussion of physiological implications of differing stimulation parameters, this review has been able to describe those parameters that appear effective on a behavioural level. The paucity of research describing the physiological effects of tDCS remains problematic, ensuring it was not possible to

fully discuss these implications in this review. Researchers are encouraged to explore the physiological effects of differing tDCS parameters to highlight the underpinning physiological mechanisms that drive the behavioural effects described here.

3.5 Conclusion

The first study measuring the effects of tDCS on food craving and consumption was published more than a decade ago and understanding of the effects and potential role of this technique for the control of eating behaviours is still at a relatively early stage. Interest in this area has proliferated over recent years, but many studies have employed varying study designs and stimulation parameters which makes it difficult to identify a consistent effect of tDCS. Careful consideration of stimulation parameters is important for all studies. This is not a new concept with many recent reviews highlighting the need for consistent and appropriate parameter use (Filmer et al., 2014; Tremblay et al., 2014; Thair et al., 2017).

The review presented in this chapter has extended the discussion to incorporate a more comprehensive range of parameters and outlines potentially effective ranges for these parameters. It is acknowledged that some of the analyses, conclusions and assumptions are based on a limited number of studies, which reflects the relative novelty of these studies. However, there is good evidence to support these conclusions from wider research, much of which has been cited in this review.

Initial variation in applied parameters is important for identifying the most appropriate parameters to apply. However, consistency in parameter application is required in future work in order to fully understand the impact of tDCS and the efficacy of this technique to modulate the hedonic responses to food. This also highlights the need

for publication of null effects, which can be used to identify those parameters, populations or measures that appear to be outside the modulatory influence of tDCS. It is also recommended that Bayesian statistics be included alongside results, and particularly null findings, to determine the strength of evidence in favour of the null or alternative hypothesis (Quintana and Williams, 2018; Wagenmakers et al., 2018). The aim of this review was to identify effective parameter ranges, with the hope of improving the quality of future studies through the application of appropriate study design and effective stimulation parameters. The empirical studies discussed within this thesis adhered to the recommended parameter ranges discussed in this chapter, with the following chapter considering the specific tDCS parameters applied and other methodological considerations.

Chapter 4 General Method

4.1 Experimental Design

All empirical studies followed a within-participant, double-blind, sham-controlled, crossover design (see Chapter 3). Sample size was determined using G*Power 3.0.10 (Faul et al., 2007), and calculated using mean and SD data from previously published work. Calculations for each study are presented in the relevant following chapters. Participants completed both active and sham tDCS conditions (see section 4.7), in a randomised and counterbalanced order. Randomisation was determined using a permuted block paradigm and performed by an independent researcher using http://www.randomization.com/. Eligible participants were enrolled and assigned sequentially, and researchers involved in data collection or analysis were blind to the treatment allocation until datasets were analysed.

4.2 General Procedures

For studies one (Chapter 5) and two (Chapter 7), participants were required to attend the laboratory on three occasions (Figure 4-1). Following screening (see section 4.4), eligible individuals were invited to an initial baseline visit where anthropometric and body composition measurements were conducted (see section 4.5), and psychometric questionnaires were completed (see section 4.6). Participants were then invited to two test visits. All visits were scheduled with a minimum inter-session interval of 48 hours to prevent any carry-over effects of tDCS (Alonzo et al., 2012), and were scheduled at the same time of day within-participant to reduce the impact of circadian rhythms on stimulation effects and study measures (Krause and Kadosh, 2014; Li et al., 2015).

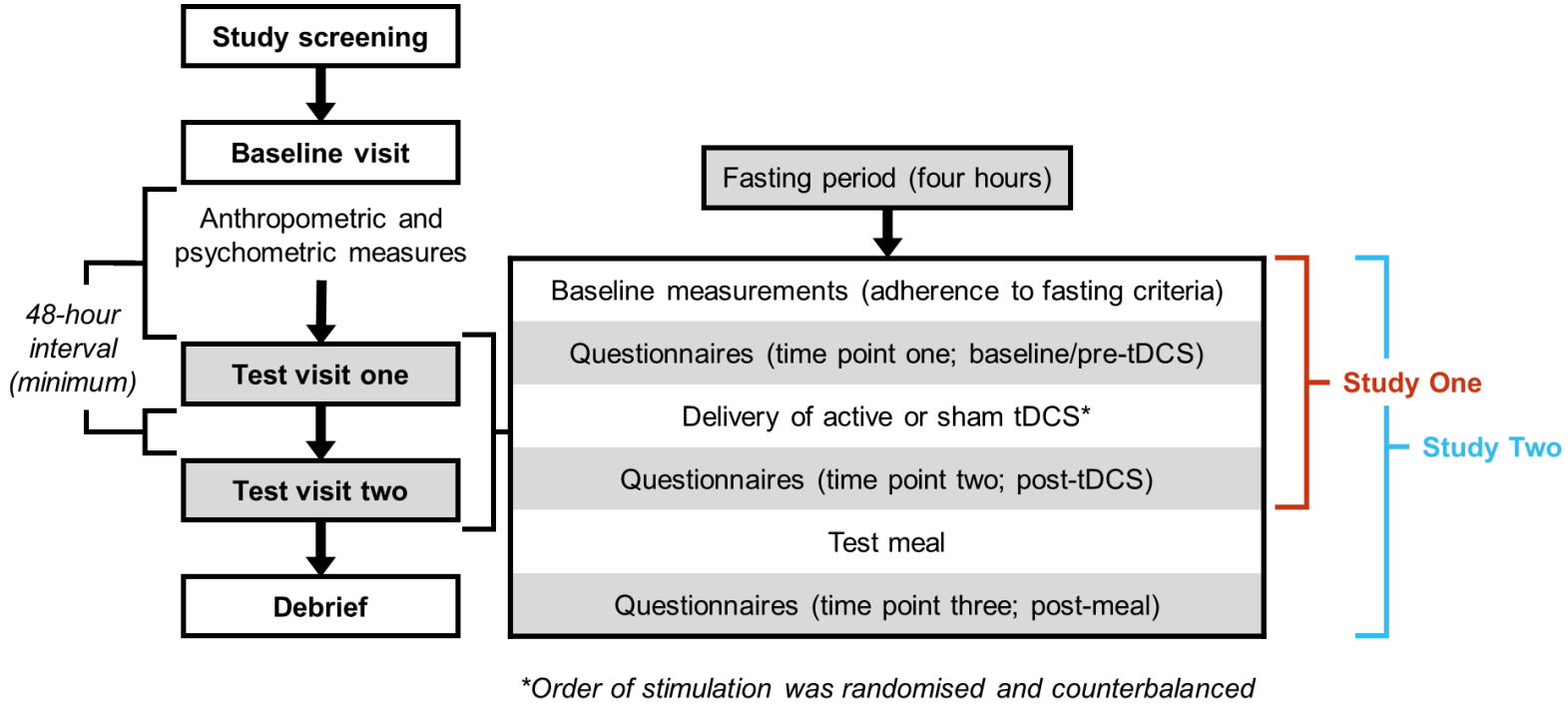


Figure 4-1 Comparison of procedures across empirical studies presented in the thesis. All participants completed screening procedures and attended an initial baseline visit. Studies differ in terms of the subsequent visits, with all studies involving two test visits in which the order of stimulation was randomised and counterbalanced. Coloured sections identify project-specific study design: red, study one (Chapter 5); blue, study two (Chapter 7).

Within each study, test visits were near identical with the exception of the stimulation condition (see section 4.7). Across studies, three measures were conducted; appetite visual analogue scales (VAS) (see section 4.8.1), the Food Craving Questionnaire-State (FCQ-S) (see section 4.8.2), and the Leeds Food Preference Questionnaire (LFPQ) (see section 4.8.3). These questionnaires were completed by each participant pre- and post-tDCS. In study two (Chapter 7), questionnaires were repeated following the consumption of a test meal.

Prior to each test visits, participants were required to fast for a minimum of four hours (Gibbons et al., 2014). During this time, participants were instructed to abstain from the consumption of food or drink, other than water. In addition, participants were asked to abstain from caffeine and alcohol in the 12 and 24 hours prior to each visit, respectively, to minimise the potential impact of these substances on appetitive measures (Yeomans et al., 2003; Caton et al., 2004; Harpaz et al., 2017; Schubert et al., 2017). These substances may also impact cortical activity and alertness which may affect the expected effects of tDCS (Thair et al., 2017). Finally, participants were required to abstain from moderate and vigorous physical activity in the 12 hours before attending the laboratory, again to limit the impact of such behaviours on eating-related measures (Beaulieu et al., 2017; Beaulieu et al., 2018). Adherence to these fasting criteria was self-reported at the start of each visit.

Before commencing any activity, participants were asked to turn off their mobile phones to prevent potential distraction during testing (Buckland and Dalton, 2018). In addition, they were asked to remove any metallic objects from their person as such objects may alter the current direction (Rossi et al., 2009). Personal items were placed away from the testing area at the start of each session to prevent access during testing and minimise any potential distracting effects during food consumption

(Herman et al., 2003; Buckland and Dalton, 2018). Following the completion of all testing requirements, participants were debriefed and informed of the sham protocol (see section 4.7). The study-specific procedures are described in the relevant following chapters.

4.3 Ethical Considerations

Ethical approval for each study was granted by the School of Social and Health Sciences Research Ethics Committee at Leeds Trinity University, in line with guidance set out in the document '*Non-Invasive Brain Stimulation (NIBS) Research Guidelines*' (see section 4.3.1). Additional ethical approval for study two (Chapter 7) was granted by the School of Psychology Research Ethics Committee at the University of Leeds. Prior to enrolment in a study, each participant provided written, informed consent. Participants were informed of study procedures but were not informed of the sham protocol until debrief (see section 4.7.2.5).

Any participant who presented with depressive symptoms or low mood, as indicated by questionnaire responses (see section 4.4.3), were referred to their general practitioner or counselling services at Leeds Trinity University or the University of Leeds. In addition, they were directed to National Health Service (NHS) and university self-help resources and provided with information for Mind and the Samaritans. For those who presented with clinically relevant binge eating symptoms (see section 4.6.1), a similar recommendation was presented with the addition of contact information for Beat eating disorder charity.

At the end of each study participants were provided with a report detailing several anthropometric and body composition measures conducted in the study. Additionally, to thank participants for the time commitment made to study two

(Chapter 7), each participant was given a £50 Amazon voucher, and those studying Psychology received credits for the Research Participation Scheme.

4.3.1 Development of a Standardised NIBS Protocol

Non-invasive brain stimulation techniques are a novel contribution to the research portfolio at Leeds Trinity University, and the present thesis describes their first use at the institution. This section will briefly overview the process undertaken to minimise the risks associated with NIBS and justify the techniques from an ethical perspective. The document '*Non-Invasive Brain Stimulation (NIBS) Research Guidelines*' (Appendix 6) was produced in preparation for research involving NIBS. This document is based on similar guidelines by the University of Edinburgh and Brunel University London, as well as published work on NIBS safety (Nitsche et al., 2008; Rossi et al., 2009; Bikson et al., 2016; Antal et al., 2017).

The NIBS guidelines provide a standardised procedure for researchers to follow, as well as clear and rigorous requirements that research projects must demonstrate. It also provides the requisite information for relevant ethics committees to ensure any proposed project is following safe and ethical practice. The candidate was involved in the creation of this protocol through reviewing and editing drafts and the generation of supporting material. On completion, the document was submitted for review by the highest ethics committee at Leeds Trinity University and was subsequently approved and adopted as a standardised operating procedure by the institution.

The protocol outlines five guidelines and requires explicit information to be provided when applying for ethical approval. These guidelines include: (i) specifying the participants' group; (ii) enhanced screening of all potential participants using

standardised questionnaires, and consideration of potential interacting drugs; (iii) explicit statement of the stimulation parameters; (iv) clear description of all measures taken that may interact with the stimulation protocol or elicit additive effects, and; (v) a clear statement that the guidelines will be adhered. The protocol also outlines additional considerations in light of the potential risk of moderate and serious adverse events. These guidelines and considerations will be discussed in detail in the sections that follow.

Risk assessments specific for tDCS have been written to supplement this protocol, and cover research activities at both Leeds Trinity University and the University of Leeds. These were updated in June 2020 to reflect the additional measures required to adhere with relevant health and safety guidelines in light of the Coronavirus (SARS-CoV-2) (COVID-19) pandemic. The candidate produced these risk assessments in collaboration with laboratory technicians and the supervisory team.

4.3.1.1 Guideline 1: Specifying the Participant Group

Specifying the type of participant to be recruited is important to identify whether institutional ethical approval is appropriate, or in the case of patient populations, if additional NHS ethical approval would be required. Table 4-1 highlights the three categories of participants, which encapsulates healthy adult participants, non-patient special groups, and patient populations. It is important to note that potential participants may be classed as Category A, or healthy adult participants, even when they may be classed as “unhealthy” by other measures (e.g., body mass, psychometric traits). These individuals are not part of special population groups (e.g., children, elderly) nor do they suffer from specific medical conditions that would require enhanced ethical scrutiny. Recruitment of participants falling into Category B or C warrants further considerations for the safety of applied tDCS parameters,

particularly where these individuals use medications that affect the central nervous system (Rossi et al., 2009; McLaren et al., 2018).

Table 4-1 Participant categorisation for studies using NIBS.

Category	Participant Type	Description
A	Healthy adult participants	Members of the general population, aged 18 to 60 years.
B	Non-patient special populations	Non-patient populations who fall into special groups, such as those with severe visual, hearing or perceptual deficits, or those outside the 18-to-60-year age bracket.
C	Patient populations	Individuals who are part of patient groups; the inclusion of this population requires additional NHS ethical approval.

4.3.1.2 Guideline 2: Screening of Potential Participants

All potential participants must be screened using the Brain Stimulation Study Suitability Questionnaire (BSSSQ) (see section 4.4.1) and Neurological Conditions Physical Activity Readiness Questionnaire (NPAR-Q) (see section 4.4.2). These questionnaires identify brain stimulation-specific contraindications, and whether consultation with a medical professional is required before permitting participation. As noted above, the use of medications and recreational drugs should also be considered, due to the potential deleterious effect on stimulation-related adverse events (Rossi et al., 2009; McLaren et al., 2018). Any individual taking antidepressants, antipsychotics, antivirals, antibiotics, anticonvulsants, antimetabolites, antimalarials, immunosuppressants or chemotherapy drugs are to be excluded from participation. Appendix 6.1 contains a comprehensive list of potentially hazardous drugs. As a precautionary measure, any individual wishing to

participate in NIBS studies should not be taking any medications with the exception of anti-allergy and oral contraceptive drugs.

4.3.1.3 Guideline 3: Explicit Statement of Stimulation Parameters

The explicit statement of tDCS parameters allows for estimation of the safety of planned protocols. The safety of tDCS protocols can be determined by calculating the current density and total charge (Nitsche et al., 2003). Current density, in $mA \cdot cm^{-2}$, is the intensity of current (mA) delivered per unit of electrode surface area (cm^2). Total charge density (in coulombs [C] and measured as $C \cdot cm^{-2}$) reflects the current density across the entire stimulation duration. This can be calculated by multiplying the current density ($mA \cdot cm^{-2}$) by stimulation duration (minutes). It is suggested that the current density should not exceed 25 $mA \cdot cm^{-2}$, and the total charge should not exceed 216 $C \cdot cm^{-2}$ (Nitsche et al., 2003). Additional safety guidelines recommend that current intensity should not exceed 4.0 mA and stimulation duration should be no longer than 60 minutes (Nitsche et al., 2003; Nitsche et al., 2008; Antal et al., 2017).

These protocols are considered safe for adults, children, healthy individuals and patient groups (Matsumoto and Ugawa, 2017). In a review of more than 33,200 tDCS sessions, no record of serious adverse events (e.g., seizure), brain damage or detrimental behaviour changes were found as a result of undergoing tDCS within these safety limits (Bikson et al., 2016). To ensure parameters are maintained well within safe limits, the present guideline stipulates that stimulation intensity should not exceed 2.0 mA, electrode size no smaller than 9 cm^2 and stimulation duration no longer than 20 minutes. The HDCstim device (Newronika s.r.l., Milan, Italy) used in the present body of work involves large electrode size (25 to 51 cm^2) with a maximum current intensity of 2.0 mA, resulting in relatively low current densities of

between 0.039 to 0.080 $mA \cdot cm^{-2}$. These parameters are within the acceptable ranges as discussed in Chapter 3.

4.3.1.4 Guideline 4: Description of Additional Measures

A clear description of any additional measures conducted alongside NIBS should be included in applications for ethical approval. This includes all tasks or questionnaires that participants are required to complete before, during or after stimulation (i.e., online or offline tasks), and any likely interaction between these tasks and the stimulation technique. While offline questionnaires and tasks are unlikely to affect current delivery or the expected effects of tDCS, online tasks – particularly cognitive tasks – likely interact with stimulation (Filmer et al., 2014; Krause and Kadosh, 2014). Careful consideration for the effects such activities may have on the expected effects of tDCS is needed (see Chapter 3).

4.3.1.5 Guideline 5: Statement of Adherence to Guidelines

Application for ethical approval must include an explicit statement that the guidelines outlined here will be adhered by all researchers involved in the study. In addition, the identification of researchers that have received relevant NIBS training is required. Such training is important in tDCS research, as delivery of stimulation by untrained individuals – such as those part of the do-it-yourself tDCS community – has been linked with heighted adverse events, particularly moderate and severe sensations (e.g., headaches, metallic taste, skin burns) (Katwala, 2019). Careful consideration for the potential long-lasting effects of tDCS, including risk versus benefit, should be made when identifying tDCS protocols (Wurzman et al., 2016; Antal et al., 2017). Researcher training should be clearly identified through the training checklist (Appendix 6.3).

4.3.1.6 Additional Considerations

Although the risk of a severe adverse event is minimised through the use of standardised screening procedures and rigorous risk assessment, all participants must be informed of potential risks that may occur by participating in a study, including common cutaneous sensations (e.g., itching, tingling). To record all potential adverse events and the severity of these events, participants must remain in the laboratory for a minimum of 45 minutes following the termination of stimulation and complete the Adverse Events Questionnaire (AEQ) (Appendix 6.4) at regular intervals. Two researchers and a qualified (within the last three years) first aider should be available during all experimental visits; these individuals should be named in the ethics applications. In the case of adverse events, relevant procedures are to be followed in line with the type and severity of the event. If a serious adverse event occurs during stimulation, the current is to be immediately ramped down and stimulation is to be terminated. It is important that ramping of the current occurs, as sudden termination of current delivery may heighten the adverse events experienced by the participant (DaSilva et al., 2011). Although there is no known risk of adverse events to the researcher, as pregnancy is a contraindication for participants, any researcher who is pregnant should not deliver NIBS.

4.4 Participant Recruitment and Screening

Participants were recruited from Leeds Trinity University, the University of Leeds, and the surrounding areas through poster, email and social media advertisements. Interested individuals were directed to an initial online screening questionnaire, which assessed their eligibility to participate. All participants were classed as Category A, healthy (i.e., non-patient) adults (see Table 4-1). Individuals were excluded from participation if they presented with a history of: neurological disease or brain disorders; seizures, convulsions, fainting or severe dizziness; head trauma;

stroke, or; operations to the brain, heart or spinal cord. In addition, individuals with implanted devices (e.g., pacemaker) or metallic objects in the body (e.g., shrapnel), or with allergies or skin disease, were excluded from participating in any study. Those who presented with depressive symptoms or low mood were not eligible to participate (see section 4.4.3).

Eligible individuals were 18 to 60 years of age, and were weight stable (i.e., less than ±5% weight change) in the three months prior to each study. Participants were non-smokers and were instructed not to use recreational drugs at the time of data collection. Female participants were not pregnant nor wishing to conceive. Finally, participants' palatability of test meals was assessed for study two (Chapter 7); participants were required to like the test meal to be included in the study (see section 4.9). Study-specific inclusion and exclusion criteria are detailed in the relevant following chapters. History of weight change was self-reported at the start of each study. Adherence to the remaining criteria was assessed using the following standardised questionnaires.

4.4.1 Brain Stimulation Study Suitability Questionnaire

The BSSSQ (University of Edinburgh, 2014) (Appendix 6.2) is a 20-item questionnaire used to assess brain stimulation-specific contraindications. Responding with either yes or no, participants indicated their history of relevant neurological or heart conditions (e.g., epilepsy, convulsions or seizures, stroke), surgical procedures to the central nervous system or spinal cord, and current medication use or pregnancy. A yes response to any question resulted in the participant being screened out of a study, or consultation with a medical professional who has experience of brain stimulation.

4.4.2 Neurological Conditions Physical Activity Readiness Questionnaire

The NPAR-Q (Appendix 6.5), was additionally used to assess contraindications for brain stimulation. It builds on the BSSSQ by including assessment of wider neurological health, collecting data on general illness and disorders affecting the brain, and history of surgery to the brain or heart. This questionnaire comprises of 13 items, requiring a yes or no answer. Individuals were not eligible to participate if they responded with yes to any question.

4.4.3 Centre for Epidemiologic Studies Short Depressions Scale

Depression and low mood are associated with an imbalance in DLPFC activity, and may impact the effects of tDCS on cortical activity and subsequent study measures (Nitsche et al., 2009). To assess for depressive symptoms and low mood, individuals completed the Centre for Epidemiologic Studies Short Depression Scale (CESD-10) (Radloff, 1977; Andresen et al., 1994). The CESD-10 is a 10-item questionnaire where the frequency over which a set of emotions were experienced in the previous seven days is measured using four-point Likert scales. The scales range from "*Rarely or not at all*" to "*All of the time*", and responses are scored from 0 to 3. A combined score of 10 or more highlights clinically relevant depressive symptoms (Andresen et al., 1994), requiring the participant to be screened out a study and directed to the relevant support services. The CESD-10 has both good internal consistency (Cronbach's alpha [α] = 0.86 to 0.89) (Miller et al., 2008; Björgvinsson et al., 2013) and test-retest reliability (intra-class correlation coefficient [ICC] = 0.85) (Miller et al., 2008).

4.5 Anthropometric and Body Composition Measurements

All anthropometric and body composition measures were completed in a private room. Before conducting measurements, participants were instructed to remove

outer layers of clothing, footwear and any objects from their pockets or on their person. Participants' height was measured to the nearest 0.1 cm using the SECA 213 portable stadiometer (SECA Limited, Birmingham, UK). Measures were taken following inhalation where the participant was standing erect with their back to the rule, and their eyeline level with ear canal in the Frankfort horizontal plane.

Body composition and weight were assessed using the Tanita BC-418MA analyser (Tanita Europe B.V., Amsterdam), which was regularly calibrated. Composition was assessed via bioelectrical impedance in the body, using eight electrodes that supplied 0.5 mA current to the hands and feet. An algorithm is used to estimate percentage of fat mass (%FM) from the impedance of current, as well as the age, sex and height of an individual (Tanita, 2018). Weight was measured to the nearest 0.1 kg, and body fat percentage to the nearest 0.1%. The test-retest reliability (coefficient of variation) for the Tanita is 1.4% for %FM (Kelly and Metcalfe, 2012). Participants' BMI ($kg \cdot m^{-2}$) was calculated using the following formula:

$$\frac{Weight\ (kg)}{Height\ (m) \times Height\ (m)} = kg \cdot m^{-2}$$

In study two (Chapter 7), participants' waist and hip circumferences were measured in line with the World Health Organisation standardised procedure (World Health Organisation, 2008). Participants were asked to stand erect, with their feet shoulder-width apart and their weight equally distributed across the feet. Waist circumference was determined by identifying the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, with measurements taken at the end of expiration. Hip circumference was measured at the widest portion of the gluteus muscle. Measures were taken the nearest 0.1 cm, with the measuring tape parallel

to the floor and snug around the body without being taut. All measurements were performed twice; if measurements differed by 2.0 cm or more, they were repeated a third time with the arithmetic mean taken thereafter (World Health Organisation, 2008).

4.6 Psychometric Questionnaires

To determine the eating behaviour traits of participants, and specifically the participants' susceptibility to reward-driven overconsumption, the following validated questionnaires were completed.

4.6.1 Binge Eating Scale

The Binge Eating Scale (BES) (Gormally et al., 1982) measures binge eating severity using 16 sets of statements (Table 4-2), with good internal validity (α = 0.87 to 0.88) (Grupski et al., 2013), and high test-retest reliability (Pearson's correlation coefficient [PCC] = 0.84) (Duarte et al., 2015). Participants selected one statement from each set that best represented their eating behaviour. Each statement was scored from 0 to 2 (for sets of three statements) or 0 to 3 (for sets of four statements), with total scores ranging from 0 to 46. A cut-off of 27 highlights clinically relevant binge eating behaviour (Gormally et al., 1982). In study two (Chapter 7), the BES was used during screening procedures in order to recruit participants with sub-clinical binge eating behaviour; those who scored between 15 and 26 were eligible to participate. This score range highlights mild-to-moderate binge-type behaviour, capturing a habitual pattern of eating that makes an individual susceptible to overconsumption and weight gain, but is not indicative of a clinical disorder (Marcus et al., 1988; Dalton and Finlayson, 2014). For the work presented in this thesis, Cronbach's α was 0.68.

Table 4-2 Example set of statements from the Binge Eating Scale (Gormally et al., 1982).

a.	I eat three meals a day with only an occasional between meal snacks.
b.	I eat 3 meals a day, but I also normally snack between meals.
c.	When I am snacking heavily, I get in the habit of skipping regular meals.
d.	There are regular periods when I seem to be continually eating, with no planned meals.

4.6.2 Three Factor Eating Questionnaire

The Three Factor Eating Questionnaire (TFEQ) (Stunkard and Messick, 1985) is a 51-item questionnaire that measures three aspects of eating behaviour; cognitive restraint (21 items), disinhibition (16 items), and susceptibility to hunger (14 items). Cognitive restraint is the control of food consumption in order to control body weight, disinhibition is the loss of control over eating, and hunger refers to the subjective feelings of hunger and food craving. The TFEQ involves two parts; in the first, participants were required to answer true or false to 36 statements (e.g., "*I often feel so hungry I just have to eat something*"). In the second part, participants rated their agreement with a question (e.g., "*How often are you dieting in a conscious effort to control your weight?*") over a four-point scale. Responses were scored 0 or 1, with total scores ranging from 0 to 21 for cognitive restraint, 0 to 16 for disinhibition, and 0 to 14 for hunger; higher scores indicate greater prevalence of the behaviour type.

The TFEQ has good internal validity ($\alpha = 0.86$) (Stunkard and Messick, 1985) and test-retest reliability (individual factor ICC = 0.75 to 0.90) (Allison et al., 1992; Venti et al., 2010). For the work presented in this thesis, α was 0.84. Cognitive restraint scores are negatively correlated with BES scores, whereas both disinhibition and

hunger are positively correlated with binge eating behaviour (Foster et al., 1998) (see Appendix 7).

A short 18-item form of the TFEQ (TFEQ-r18) (Karlsson et al., 2000) was used in study one (Chapter 5). The TFEQ-r18 measures cognitive restraint (six items), uncontrolled eating (nine items) and emotional eating (three items) aspects of eating behaviour. Uncontrolled eating refers to the difficulty in the regulation of eating and includes items from both disinhibition and hunger factors of the full TFEQ. Emotional eating is the overconsumption of foods as a result of dysphoric mood states, reflecting items included in the TFEQ disinhibition factor. Participants responded to the 18 statements (e.g., "*When I see a real delicacy, I often get so hungry that I have to eat right now*") over a four-point Likert scale, ranging from "*Definitely true*" to "*Definitely false*". Responses were coded 1 to 4, with raw scores ranging from 6 to 24 for cognitive restraint, 9 to 36 for uncontrolled eating, and 3 to 12 for emotional eating. TFEQ-r18 scores were calculated as a percentage of the highest possible raw score for each behaviour subscale.

The construct validity of the TFEQ-r18 in comparison to the TFEQ was evaluated in a large sample (n = 4377) of individuals with obesity (Karlsson et al., 2000). Each scale on the TFEQ-r18 was strongly correlated with the corresponding factor(s) on the TFEQ (Table 4-3). Similar to the TFEQ, the TFEQ-r18 has good internal validity ($\alpha = 0.82$) (Karlsson et al., 2000) with Cronbach's alpha of 0.76 for the work present work.

Table 4-3 Pearson's *r* correlations comparing TFEQ versus TFEQ-r18 factors (Karlsson et al., 2000).

		TFEQ Factors		
		Cognitive Restraint	Disinhibition	Hunger
TFEQ-r18 Factors	Cognitive Restraint	**0.89 ***	−0.25	−0.34
	Uncontrolled Eating	−0.31	**0.77 ***	**0.89 ***
	Emotional Eating	−0.02	**0.69 ***	0.41

TFEQ, Three Factor Eating Questionnaire; TFEQ-r18, Three Factor Eating Questionnaire 18-item form.

** Bold figures highlight correlation between corresponding factors across questionnaires.*

4.6.3 Control of Eating Questionnaire

The Control of Eating Questionnaire (CoEQ) (Dalton et al., 2015) assesses the frequency, intensity and severity of food cravings over 21-items. Participants responded to each question by placing a cross (X) on a 100 mm line, anchored by "*Not at all…*" statements (e.g., "*Not at all hungry*") and "*Extremely…*" statements (e.g., "*Extremely hungry*"). Scores were determined by measuring the position of the X in mm. The CoEQ consists of four factors; craving control (α = 0.88), craving for savoury foods (α = 0.66), craving for sweet foods (α = 0.67), and positive mood (α = 0.74). In the present work, Cronbach's α were 0.89 for craving control, 0.80 for craving for sweet, 0.74 for craving for savoury, and 0.57 for positive mood.

Lower scores for the craving control factor are associated with higher scores for TFEQ disinhibition and hunger, and the BES (Dalton et al., 2015) (Appendix 7). Similarly, lower scores for positive mood are associated with greater scores for

TFEQ disinhibition and the BES. In comparison, higher scores for craving for savoury foods and craving for sweet foods were associated with higher TFEQ disinhibition, hunger and BES scores (Dalton et al., 2015). Two versions of the CoEQ, measuring cravings over the prior 24 hours or 7 days, were used in the present thesis.

4.6.4 Food Craving Questionnaire-Trait

General, habitual food cravings were assessed using the Food Craving Questionnaire-Trait-reduced (FCQ-T-r) (Meule et al., 2014a). 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. Participants rated 15 items (e.g., "*If I eat what I am craving, I often lose control and eat too much*") over a six-point scale, with 1 corresponding to "*Never*" and 6 corresponding to "*Always*". Corresponding numbers were totalled to give a general craving score, with a minimum score of 15 and a maximum of 90. The FCQ-T-r has been shown to have good internal validity ($\alpha = 0.94$) (Meule et al., 2014a) and high test-retest reliability (PCC = 0.74) (Meule et al., 2014b). Cronbach's α for the work presented in this thesis was 0.94. A score of 50 or greater highlights clinically relevant trait food cravings (Meule, 2018b).

4.7 Transcranial Direct Current Stimulation

4.7.1 Stimulation Device

Stimulation was delivered using the HDCstim direct current stimulator (Figure 4-2) (Newronika s.r.l., Milan, Italy), by a trained researcher [2]. Stimulation occured through the delivery of a constant electrical current, emitted from a battery-powered (two 1.5-volt AA batteries) stimulation device. The current travelled between conductive rubber plates housed inside saline-soaked (0.9% sodium chloride) sponge pads and placed on the scalp (Figure 4-3). In this thesis, the term electrode refers to the combination of conductive plate, sponge pad and electrolyte (saline). A constant current was emitted through an anode electrode (positive charge), and returned to the stimulation device through a cathode electrode (negative charge) (Filmer et al., 2014); see Figure 1-2.

[2] The candidate completed the 'Fundamentals and Applications of Transcranial Electrical Stimulation' (December 2017) and 'Advanced Applications of Transcranial Electrical Stimulation' (December 2018) courses provided by BrainBox Initiative (Appendix 11).

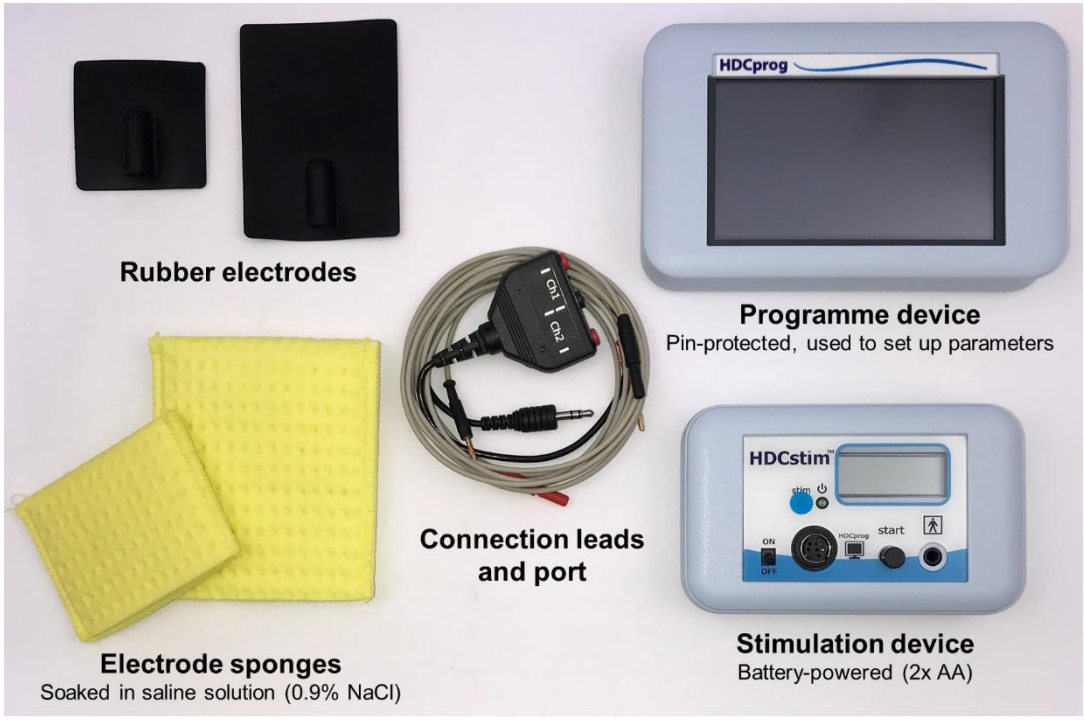


Figure 4-2 HDCstim direct current stimulator.

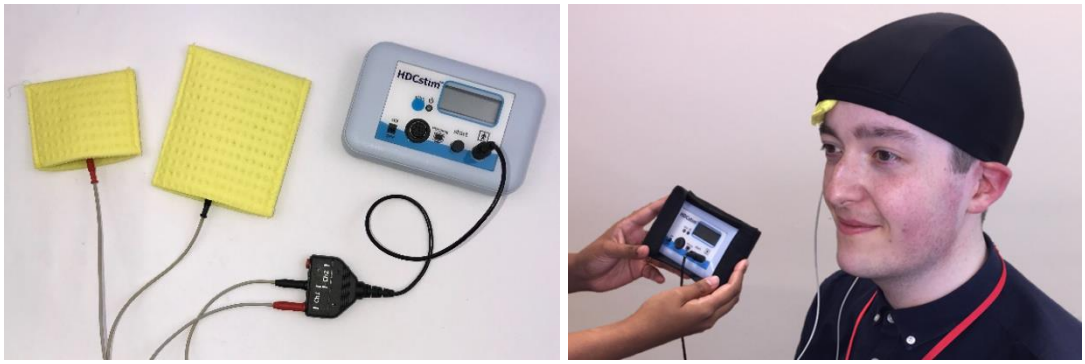


Figure 4-3 Example of HDCstim equipment set-up.

4.7.2 Stimulation Parameters

The following parameters are within the safety limits outlined in the NIBS guidelines (see section 4.3.1), and adhere to the effective ranges as discussed in Chapter 3.

4.7.2.1 Current Intensity, Electrode Size and Current Density

A constant electrical current of 2.0 mA was delivered through electrodes with a surface area of 25 cm^2 (anode) and 51 cm^2 (cathode), culminating in a current density of 0.080 $mA \cdot cm^{-2}$ and 0.039 $mA \cdot cm^{-2}$, respectively. To measure the conductivity of the current, impedance was checked at the start of stimulation and periodically during stimulation. It is recommended that this should remain below five kilo-ohm (kΩ) (DaSilva et al., 2011; Thair et al., 2017). Impedance below this threshold suggests good conductivity and low resistance, and can be achieved by appropriate electrode set-up ensuring good contact between the electrodes and skin (DaSilva et al., 2011; Thair et al., 2017). This is additionally important from a safety perspective as high impendence can result in heightened adverse events (e.g., skin lesions) (Matsumoto and Ugawa, 2017).

4.7.2.2 Electrode Montage

Electrodes were positioned according to the guidelines of the International Standards for Electroencephalography (EEG) 10-20 system (Klem et al., 1999) (Figure 4-4), and held in place with an elasticated cap. The principle of the EEG 10-20 system is that landmarks, and consequently regions of the brain, are identified by establishing total front-to-back and left-to-right distance of the skull. A mid-point (vertex, Cz) is measured as the intersection between the total front-to-back distance from the nasion (intersection of the frontal bone and two nasal bones) to the inion (prominent projections of the occipital bone at the base of the skull), and the left-to-right distance from preauricular points (prominence of the inner side of the external ear). Electrodes are then placed 10% or 20% of the front-to-back or left-to-right distance from the Cz, depending on which anatomical plane that is required.

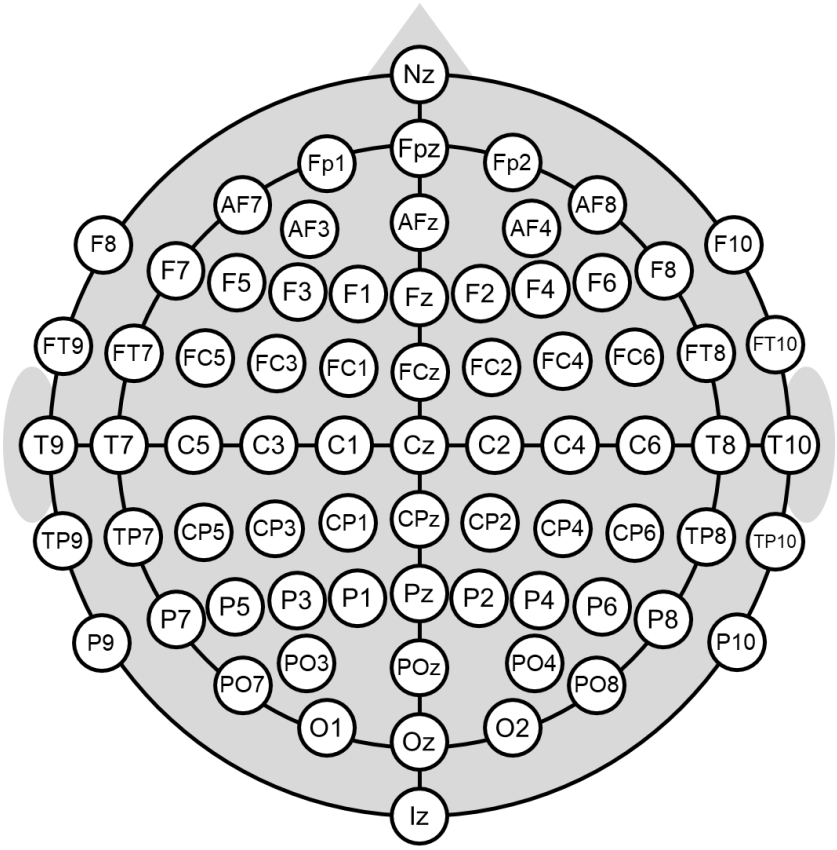


Figure 4-4 Electroencephalography (EEG) 10-20 system. Image adapted from Klem et al. (1999).

The right DLPFC was targeted by placing the anode electrode over the right frontal area (F4) (Figure 4-5). This area is located 20% left-to-right distance from the frontal zero point (Fz), which is located 20% front-to-back distance from the Cz. Individuals with obesity or those displaying binge-type behaviour appear to have hypoactivation of the right DLPFC (Karhunen et al., 2000; Wang et al., 2004; Boeka and Lokken, 2011), and stimulation over this hemisphere appears more effective for reducing eating-related measures when compared with left hemispheric stimulation (see Chapter 3). The cathode was placed over the occipital lobe (occipital zero-point, Oz), located on the rear side of the skull, 40% front-to-back distance from the Cz. The Oz is not associated with any measure conducted during the research described in this

thesis (Galetta, 2017), and so the inhibition of activity associated with the cathode is unlikely to have an impact on the results.

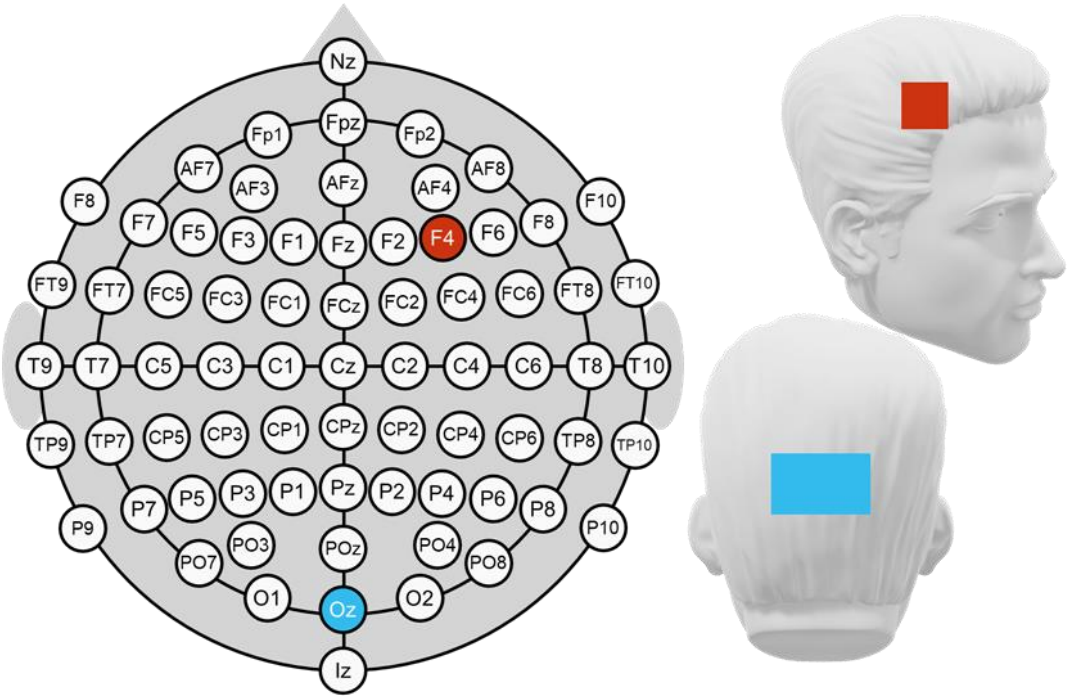


Figure 4-5 Montage targeting the right DLPFC. Coloured landmarks represent target regions: red, frontal area 4 (F4); blue, occipital zero point (Oz).

4.7.2.3 Stimulation Duration

Active tDCS was delivered for 20 minutes, with total charge not exceeding 1.6 $C \cdot cm^{-2}$. Sham tDCS was delivered for 36 seconds (3% duration of active tDCS) (see section 4.7.2.5). A 30-second ramping phase prior and following both stimulation protocols was used (Figure 4-6), as immediate stimulation at the desired intensity is associated with heightened and uncomfortable sensations (DaSilva et al., 2011).

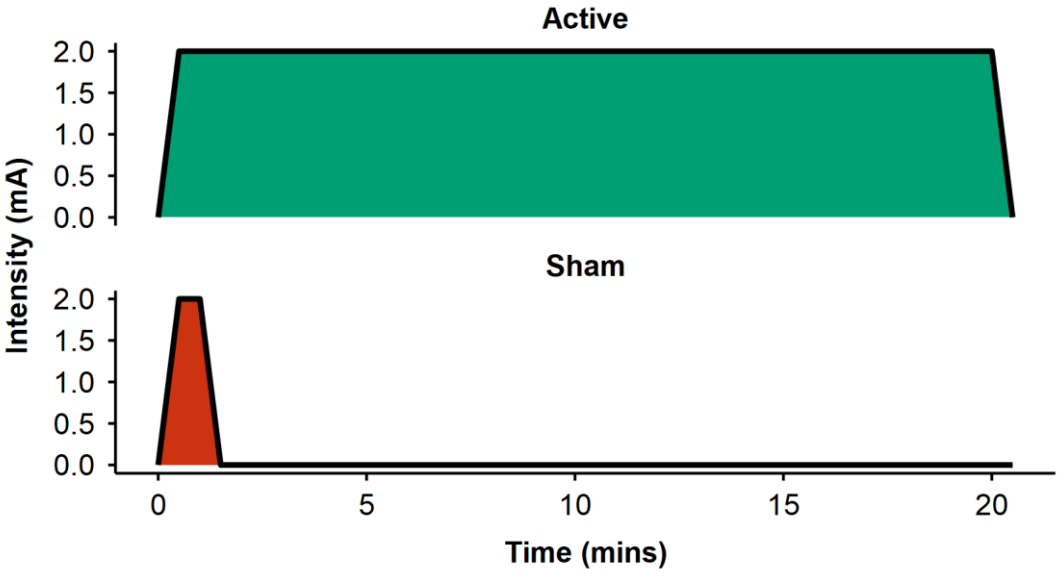


Figure 4-6 Active and sham tDCS protocols. The current is ramped up over 30 seconds, where it is then delivered at 2.0 milliampere (mA) for 20 minutes under active and 36 seconds under sham conditions. The current is then ramped down over 30 seconds.

4.7.2.4 Offline Protocol

Differences in the level of attention and cognition during tDCS can result in variation of effects (Fricke et al., 2010), which appears to affect the role tDCS has in modulating eating behaviours (Chapter 3). To reduce the potential impact of this, stimulation was delivered in a quiet room, where the participant was instructed to remain seated, relaxed and awake, keeping their attention at the same level and not to think of anything of major personal importance (Gálvez et al., 2013).

4.7.2.5 Treatment Blinding

Due to the common mild and transient cutaneous sensations (e.g., itching, tingling, burning sensation) often felt by participants (Poreisz et al., 2007; Matsumoto and Ugawa, 2017), a sham protocol was used to account for potential conscious or subconscious bias. This involved the same set-up as active stimulation, but the

current was delivered only over 36-seconds rather than the 20 minutes for active protocols (Figure 4-6). Such blinding protocols elicit similar cutaneous sensations compared with active tDCS, but have limited neuromodulatory effects (Gandiga et al., 2006; Brunoni et al., 2011; Nikolin et al., 2018). To compare the sensations experienced following active and sham procedures, participants completed the AEQ immediately after the termination of tDCS and at regular intervals for up to 45 minutes post-tDCS. The AEQ measured both the incidence and severity of any adverse events. To maintain researcher blinding, all tDCS parameters were pre-set by an independent researcher using the separate programme device (see Figure 4-2). This device was pin-protected, which allowed blinding of the researcher delivering tDCS who was only provided with the stimulation device and was unable to view the specific parameters.

At the end of each study, participants were debriefed and informed of the sham protocol. They were asked whether they could differentiate between active and sham conditions, and to identify which session they believe active tDCS was delivered (Appendix 12). This provided an insight on the validity and efficacy of study blinding but did not take into account whether the perceived difference was based on objective differences between the sessions or purely based on chance. With the aim of differentiating between these factors, and in line with Santos et al. (2018), assessment of the confidence a participant placed in their choice was added in study two (Chapter 7). This was measured via a 10-point Likert scale ranging from "*Not at all confident*" to "*Very confident*". To additionally determine the efficacy of double-blind protocols, experimenter blinding was also measured in study two. To minimise the impact of expectation effect, all participants were naïve to tDCS protocols.

4.8 Study Questionnaires

4.8.1 Appetite Visual Analogue Scales

The subjective ratings of appetite were measured across four 100 mm VAS (Blundell et al., 2010). Hunger ("*How hungry do you feel right now?*") and fullness ("*How full do you feel right now?*") measures were anchored by "*Not at all*" and "*Extremely*". Prospective consumption ("*How much food could you eat right now?*") was anchored by "*Not at all*" and "*A very large amount*", and the desire to eat ("*How strong is your desire to eat right now?*") by "*Not very strong*" and "*Very strong*". Participants rated each sensation by placing a X over the 100 mm line, and scores were calculated by determining the position of the X in mm. VAS are considered reliable and valid measures of subjective appetite, are sensitive to experimental manipulation, have good test-retest reliability, are easy to understand and complete, and scores can be compared across different populations (see Beechy et al. (2012) for review).

4.8.2 Food Craving Questionnaire-State

In-the-moment craving for food was assessed using the FCQ-S (Cepeda-Benito et al., 2000). Food cravings, the desire to eat, and emotional responses to food and consumption were assessed over 15 statements (e.g., "*I have an intense desire to eat one or more specific foods*"). Participants rated their agreement with each statement on a five-point scale, where 1 corresponds with "*Strongly disagree*" and 5 corresponds with "*Strongly agree*". Corresponding scores were totalled, with a minimum score of 15 and a maximum of 75. The yielding score was used to quantify in-the-moment craving. The FCQ-S has been shown to be responsive to experimental manipulation (Cepeda-Benito et al., 2000; Meule et al., 2014b), and is widely used in tDCS research.

4.8.3 Leeds Food Preference Questionnaire

The LFPQ (Finlayson et al., 2007; Dalton and Finlayson, 2014) is a validated computer-based assessment of the hedonic preference for food, measuring implicit wanting and explicit liking and wanting as components of reward. Using a standardised set of 16 food images (Figure 4-7), these components were assessed according to the fat content and taste of food items. Images depicted ready-to-eat foods that are common in the diet and were categorised as either sweet or savoury with a high (more than 40% energy) or low (less than 20% energy) fat content. The images were split into four categories; high-fat sweet (HFSW), low-fat sweet (LFSW), high-fat savoury (HFSA), and low-fat savoury (LFSA). Food items are similar in protein content, palatability and familiarity. During screening procedures, participants' acceptance of the food items were assessed to improve the internal validity of the LFPQ (Oustric et al., 2020). Any foods that were disliked or not consumed as part of the participants' normal diet were substituted from a database of additional images (Appendix 13) with similar nutritional and sensory properties (Oustric et al., 2020); see Appendix 14 for a list of image substitutions made in the present body of work.

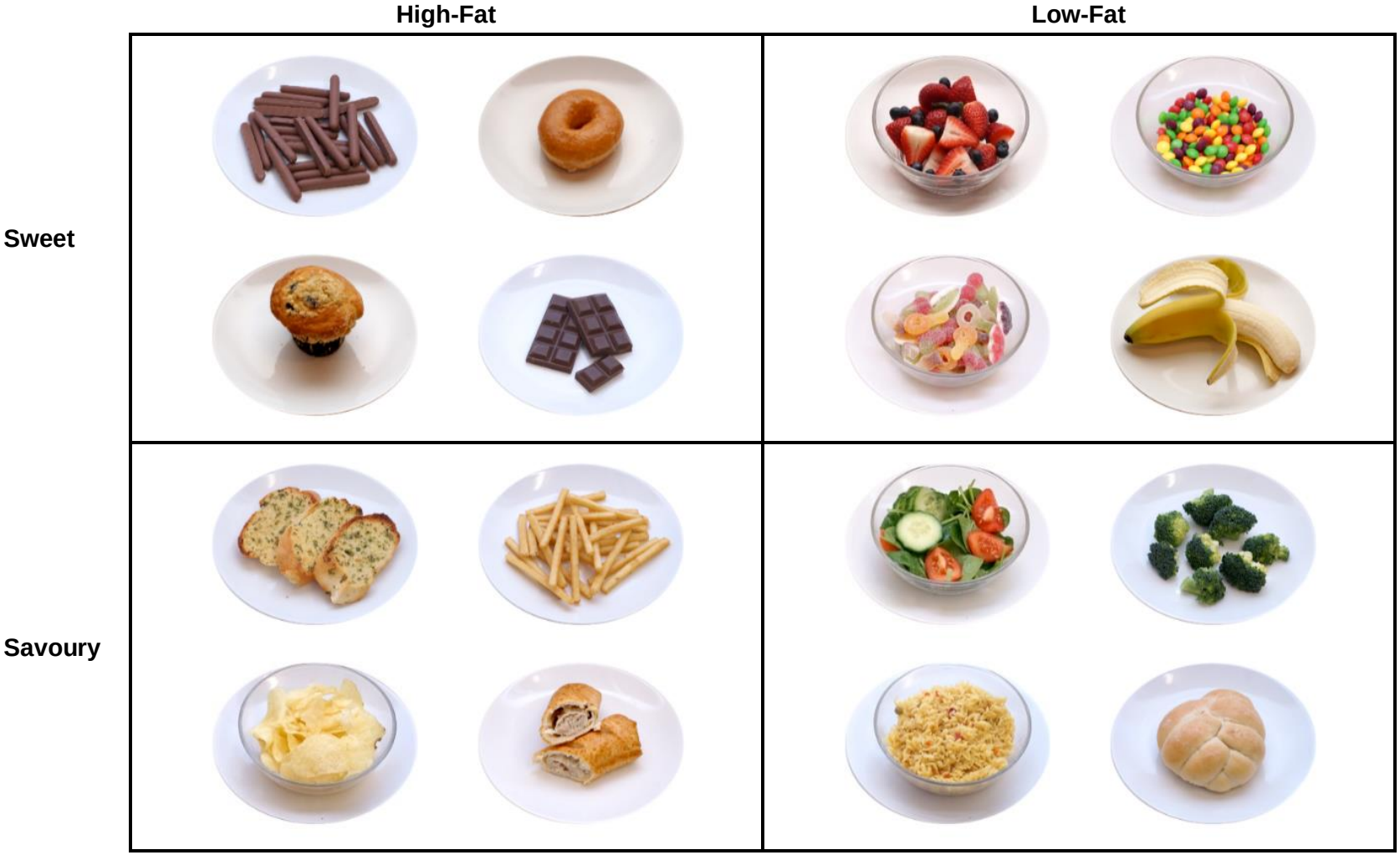


Figure 4-7 Standardised images for the LFPQ (Dalton and Finlayson, 2014).

Participants were required to complete two tasks, where each image was displayed individually (single-food task, see section 4.8.3.2) or in pairs (paired-food task, see section 4.8.3.1). These tasks were completed in a randomised order, and collectively lasted approximately six to eight minutes (Oustric et al., 2020). Practice trials were completed at the start of the LFPQ to familiarise participants; data from the practice trials were not included in the final dataset (Dalton and Finlayson, 2014; Oustric et al., 2020). During the LFPQ, participants were left to complete both tasks in a quiet environment for 10 minutes. The LFPQ is sensitive to individual eating behaviour traits (Finlayson et al., 2011; Dalton et al., 2013a; Dalton et al., 2013b), and is a good predictor of in-laboratory and real-world food choice and intake (Griffioen-Roose et al., 2011; French et al., 2014).

4.8.3.1 Implicit Wanting

Implicit wanting is the automatic, unconscious attraction to a food item that is triggered by the perception of the food or related cue in the environment (Dalton and Finlayson, 2014). Implicit wanting was assessed using a forced-choice task (Figure 4-8). In response to the question "*Which food do you most want to eat now?*", participants were required to choose the food they most want to consume "right now" between two food images displayed on the computer screen. Images from each food category (HFSW, LFSW, HFSA, LFSA) were compared with all other food types over 96 randomised trials. Participants were given the opportunity to have a break from the task after every 32 trials. To improve compliance, between each trial participants were presented with a white screen displaying a central fixation cross for 500 milliseconds (Oustric et al., 2020).

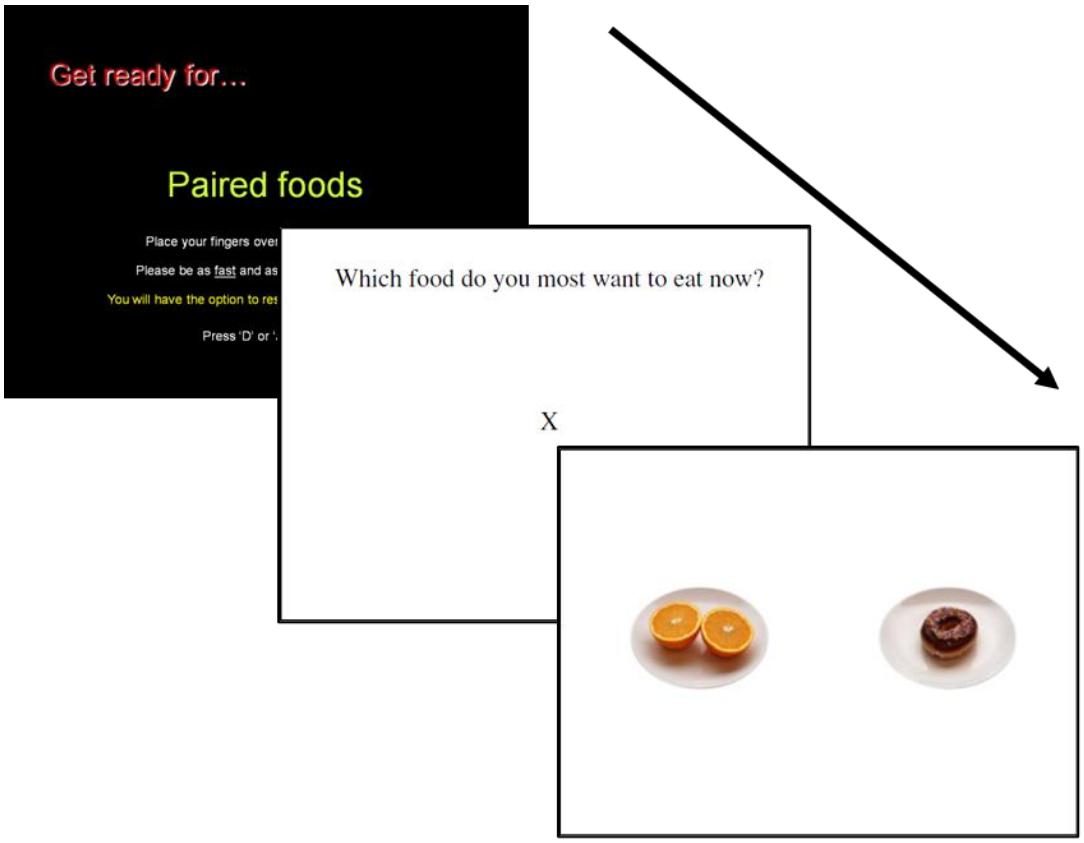


Figure 4-8 Measure of implicit wanting in the LFPQ. Image adapted from Dalton and Finlayson (2014).

Mean response times were used as a quantifiable measure of implicit wanting, with a quicker response highlighting greater preference for a particular food type. Responses were scored using a frequency-weighted algorithm (FWA) accounted for the selection and non-selection of a food item. Scores typically range from −100 to 100, with a positive score indicating a greater preference for the food category, and a negative score indicating a less preferred category, relative to all other food categories.

4.8.3.2 Explicit Liking and Wanting

Explicit liking is the subjective, conscious judgement of the degree of pleasure a food item would provide, whereas explicit wanting is the subjective, conscious

perception of the food or related cue in the environment (Dalton and Finlayson, 2014). Participants were presented with an individual food item and asked "*How pleasant would it be to taste some of this food now?*" to measure explicit liking, or "*How much do you want some of this food now?*" to measure explicit wanting. Responses were recorded using a 100-unit VAS (Figure 4-9). Each question was presented in a different font colour to enable participants to discriminate between the two different questions. Images were presented in a randomised order, and the order of question was counterbalanced (Oustric et al., 2020). At the start of each question the mouse cursor was re-centred, and in the middle of the task participants were given the opportunity to have a break. Both explicit liking and wanting were scored by food category, ranging from 0 to 100, as an average of individual food item rating scores.

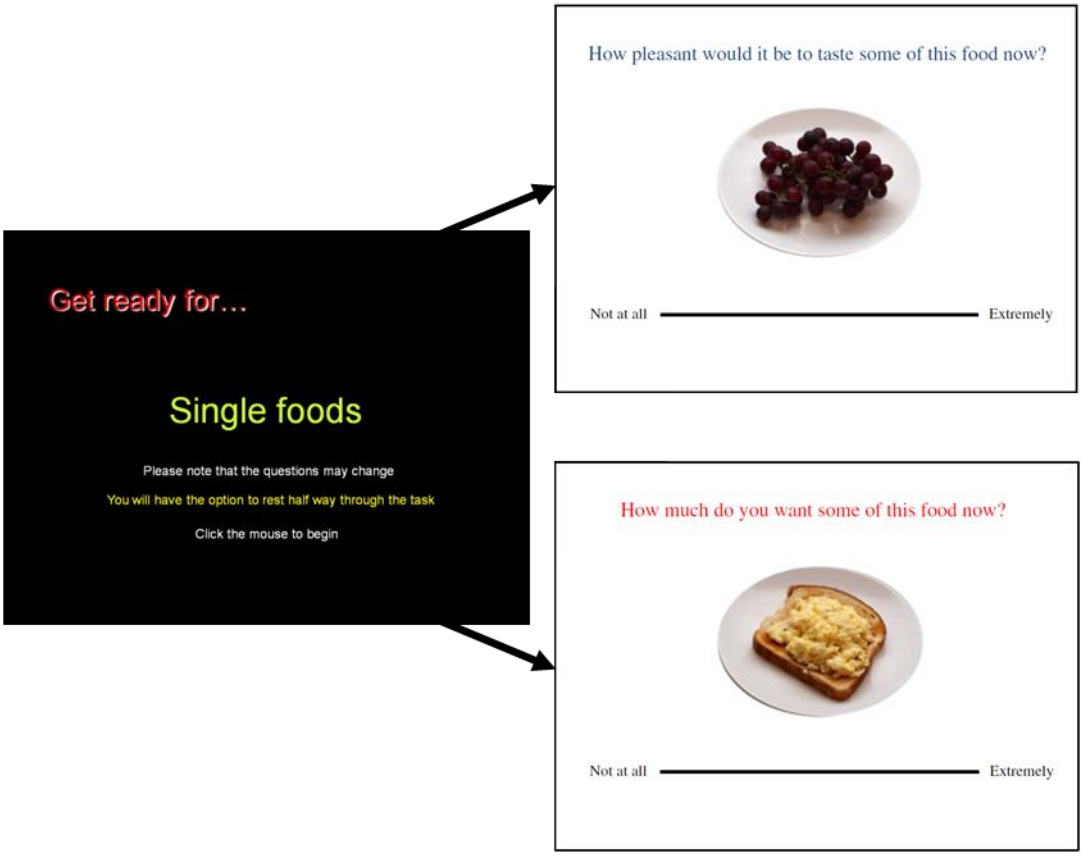


Figure 4-9 Measures of explicit liking and wanting in the LFPQ. Image adapted from Dalton and Finlayson (2014).

4.8.3.3 Appeal Bias Scores

Fat appeal bias (FAB) and taste appeal bias (TAB) were calculated by subtracting low-fat scores from high-fat scores, or savoury scores from sweet scores, respectively. A positive score highlights a bias towards high-fat or sweet foods, and a negative score highlights the preference for low-fat or savoury foods. Appeal bias scores were calculated for implicit wanting, explicit liking and explicit wanting.

4.9 Test Meal

A fixed-energy meal was provided to participants in study two (Chapter 7). This meal was a cheese sandwich comprising of white bread, medium grated cheddar cheese, and sunflower spread (ASDA, UK). This test meal was chosen as it is an appropriate

meal for the time of day tested (i.e., lunch), and easily allowed manipulation of calorie content to meet individual requirements (see below). The use of a fixed-energy meal also allowed the transition from the fasted to fed state, and so the assessment of tDCS effects on eating behaviour under both of these conditions. Participants' liking for the meal was assessed during study screening using a seven-point Likert scale, ranging from "*Dislike extremely*" to "*Like extremely*". A score of 4 or more, indicating a liking for the meal, was required for participants to be eligible for participation. Food allergies and intolerances were also measured during screening, and individuals were not permitted to participate if they presented with an allergy or intolerance to any foodstuff.

The nutritional composition of each component is displayed in Table 4-4; the weight of each component was altered so the sandwich would provide sufficient energy to meet 30% resting metabolic rate (RMR) for each participant (Buckland and Dalton, 2018). The RMR was estimated using the Mifflin-St Joer equation (Mifflin et al., 1990):

$$(9.99 \times weight\ [kg]) \times (6.25 \times height\ [cm]) - (4.92 \times age\ [years]) - 161$$

This equation is suitable for individuals with healthy weight or obesity due to a high accuracy and small error ranges in both populations (Frankenfield et al., 2005).

Table 4-4 Nutritional composition for individual components of the test meal [a].

	Energy (kcal / 100 g)	Carbohydrate (g / 100 g)	Protein (g / 100 g)	Fat (g / 100 g)
White bread	239	46.0	8.1	2.2
Medium cheddar cheese	416	0.5	25.0	35.0
Sunflower spread	422	4.2	0.5	45.0

[a] *Composition determined using manufacturer's information.*

The use of laboratory-based measures of food intake allow for control of the environment in which a participant consumes food, isolating the participant from confounding factors (Best et al., 2018). However, the presence of others and of distractions such as mobile phones can influence the consumptive behaviour of an individual (Herman et al., 2003; Buckland and Dalton, 2018). Participants were required to turn off their mobile phone and place this with their belongings away from the testing area at the beginning of each visit. Participants were instructed to consume the entire sandwich and were left to consume alone for 10 minutes in a quiet environment.

Test meals were presented in the same manner within-participant, i.e., environment and utensils were identical across sessions, but different laboratory spaces were used between-participants to accommodate multi-site data collection. The sandwich was presented on a plain white plate. One litre of water was provided for the participant to consume as desired, presented in a clear glassware, and was measured following consumption. Immediately following the test meal, participants were given a copy of the appetite VAS (see section 4.8), with an additional question to assess participants' liking of the cheese sandwich ("*How pleasant did you find the meal?*").

4.10 Statistical Analyses

Data were analysed using R (The R Foundation, 2022), Statistical Package for the Social Sciences (SPSS) versions 21, 26 and 27 (IBM, New York, USA), and JASP versions 0.13.1 and 0.16.2.0 (University of Amsterdam, Amsterdam, The Netherlands). All questionnaires and scales were scored in line with the questionnaire guidance notes, and the normality of data were assessed using Shapiro-Wilk test. Bayes factors (BF_{10}) were computed using JASP software and were used to interpret findings and assess the strength of evidence. The classification scheme by Lee and Wagenmakers (2013) was used to interpret Bayes factor (Table 4-5). Figures were created in Excel, using the Chart function by transferring relevant statistics from SPSS, and in JASP and RStudio (version 1.4.1717) (RStudio Team, 2022). Statistical procedures for each study are described in further detail in the following chapters.

Table 4-5 Classification scheme for Bayes factors (Lee and Wagenmakers, 2013).

Bayes factor (BF_{10})	Classification
>100	Extreme evidence in favour of the experimental hypothesis
30 – 100	Very strong evidence in favour of the experimental hypothesis
10 – 30	Strong evidence in favour of the experimental hypothesis
3 – 10	Moderate evidence in favour of the experimental hypothesis
1 – 3	Anecdotal evidence in favour of the experimental hypothesis
1	No evidence
1 – 0.33	Anecdotal evidence in favour of the null hypothesis
0.33 – 0.10	Moderate evidence in favour of the null hypothesis
0.10 – 0.03	Strong evidence in favour of the null hypothesis
0.03 – 0.01	Very strong evidence in favour of the null hypothesis
<0.01	Extreme evidence in favour of the null hypothesis

Chapter 5 Study One

The effects of transcranial direct current stimulation (tDCS) on food craving, reward and appetite in a healthy population. [3]

Part of this chapter is published as:

Beaumont, J.D., Davis, D., Dalton, M., Nowicky, A., Russell, M. and Barwood, M.J. 2021. The effect of transcranial direct current stimulation (tDCS) on food craving, reward and appetite in a healthy population. *Appetite*. **157**, p105004. https://doi.org/10.1016/j.appet.2020.105004

Beaumont, J.D., Davis, D., Dalton, M., Russell, M. and Barwood, M. 2019. Appeal biases for sweet and fatty foods are robust following a single session of transcranial direct current stimulation (tDCS) in a healthy weight population. *Obesity Abstracts*. **1**. https://doi.org/10.1530/obabs.01.RFC1.1

[3] The present study was conducted in parallel to the review chapters (Chapter 3 and Chapter 6); this empirical work was incorporated into the published versions of these reviews.

5.1 Chapter Summary

This chapter examines the effects of tDCS on food reward, craving and subjective appetite in a healthy weight cohort who display low susceptibility to overconsumption and weight gain. To fully determine the impact of tDCS on eating-related measures, it is important to examine the impact within a “healthy” population who do not display trait susceptibilities to overconsumption. This has not been well controlled in prior studies. This study also looked to establish the test-retest reliability of measures for onward use in this programme of work and is amongst the first to explore both explicit and implicit components of reward for different food categories following tDCS.

Twenty-one healthy weight individuals completed two sessions involving double-blind, randomised and counterbalanced anodal or sham tDCS over the right DLPFC, at 2.0 mA for 20 minutes. Applied parameters were in line with the recommendations made in Chapter 3. Study measures included appetite VAS, FCQ-S and LFPQ, with participants’ eating behaviour traits assessed using the TFEQ-r18, CoEQ and FCQ-T-r. Participants displayed “healthy” eating behaviour traits, with low trait craving, good craving control, and low uncontrolled eating and emotional eating behaviour. Test-retest analysis of baseline study measures indicated moderate-to-good reliability (r = 0.536 to 0.955), which was highest for implicit wanting and FAB scores suggesting these are robust targets for future research.

Results indicated that stimulation did not alter food craving ($p = 0.797$, $BF_{10} = 0.284$), reward ($p = 0.057$ to 0.782, $BF_{10} = 0.030$ to 0.313) or subjective appetite ($p = 0.092$ to 0.574, $BF_{10} = 0.264$ to 0.858) in healthy weight participants with no apparent eating behaviour trait susceptibilities to overconsumption. This is supported by anecdotal-to-moderate evidence in favour of the null hypothesis as indicated by

Bayes factors, and suggests that applying anodal tDCS over the DLPFC does not change food reward response in healthy controls. The following chapters in this thesis will further explore this potential eating behaviour trait-dependent effect of tDCS, with the next empirical study focussing on those susceptible to overconsumption, who display binge-type behaviour.

5.2 Introduction

When using tDCS to induce hyper-activation of the right DLPFC, early studies identified an ability of stimulation to reduce state food craving scores. The first study to identify the impact of tDCS on hedonic appetite measures compared anodal stimulation to the left and right DLPFC in 21 healthy weight individuals with frequent food cravings, defined as experiencing three or more strong urges to consume high-calorie foods per day (Fregni et al., 2008). When applying 2.0 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).

Although significant effects of tDCS on food craving have been identified in these early studies, this has not been consistently shown in later work (Georgii et al., 2017; Sedgmond et al., 2019). Across studies there is large variation in state food craving scores, ranging from 0.4% to 41.7% following the active condition (Fregni et al., 2008; Goldman et al., 2011; Kekic et al., 2014; Ljubisavljevic et al., 2016), which may be due to the poor reliability of these measures. Publications aimed at developing the FCQ-S suggest low-to-moderate reliability (r = 0.39 to 0.56) (Cepeda-Benito et al., 2000; Meule et al., 2014b). Measures of food consumption have also been utilised, primarily using *ad libitum* buffets of highly palatable foods (Gluck et al., 2015; Burgess et al., 2016; Georgii et al., 2017; Ray et al., 2017; Sedgmond et al., 2019), again with equivocal findings.

As the rewarding components of food can dysregulate energy balance in favour of overconsumption (Boswell and Kober, 2016; Kober and Boswell, 2018), it is important to look beyond the measures of food craving and consumption. Other

targets are required to validate tDCS as an intervention to alter eating behaviour, and it is important to consider the role of tDCS in modulating food reward. Prior work has assessed the effects of tDCS on explicit reward for foods differing in carbohydrate content (Burgess et al., 2016; Georgii et al., 2017; Ray et al., 2017; Carvalho et al., 2019), but no study has reported the impact of tDCS on both implicit and explicit components of reward across different food categories. Although foods high in sugar are commonly craved, energy density appears to be a more important driving factor for food reward rather than contribution of a single macronutrient (Gilhooly et al., 2007). As such, it is important to consider the impact of tDCS across different food categories.

As highlighted in Chapter 3, and will be further discussed in the chapters that follow, equivocal findings may be due to the inconsistent application of stimulation parameters, inadequate experimental blinding, and large variation in participant characteristics and experimental measures. Greater control of these factors is required to determine the efficacy of tDCS for modulating eating behaviour. This includes addressing heterogeneity in sample characteristics, such as eating behaviour traits, that may affect cortical activity and subsequent susceptibility to reward-driven appetite and overconsumption (Karhunen et al., 2000; Boeka and Lokken, 2011). To date, a lack of sufficient control for “healthy” populations has led to null or conflicting effects. It is logical to assume that these “healthy” participants will possess sufficient executive functioning capabilities to allow successful control of eating behaviours (Cserjési et al., 2009; Michaud et al., 2017; Blume et al., 2019). As such, it is of debate whether we should expect to see a change in eating behaviour following tDCS in these individuals (see Chapter 6 for further discussion).

The present study expanded the assessment of tDCS effects to include a measure of implicit and explicit reward, using a validated computer-based assessment; the LFPQ (Dalton and Finlayson, 2014). This task considers the liking and wanting for different food categories, varying in energy density and taste (Oustric et al., 2020). This study also looked to recruit “healthy” participants, who were healthy weight and displayed low susceptibility to reward-driven consumption.

5.3 Aims and Hypotheses

The aim of this study was to identify the effects of tDCS on commonly used measures of eating behaviour (food craving, subjective appetite) and a novel measure (implicit and explicit food reward) in a healthy weight cohort. This study also looked to identify the test-retest reliability of these measures to determine the viability of their use in this programme of research and for the wider benefit of the research community. Based on the findings from prior work using healthy weight individuals (Fregni et al., 2008; Goldman et al., 2011; Kekic et al., 2014; Ljubisavljevic et al., 2016), it was hypothesised that active tDCS to the right DLPFC would reduce state food craving and participants’ preference for and perceived rewarding value of high calorie foods.

5.4 Method

5.4.1 Participant Recruitment

Sample size was determined using G*Power with a target effect size f of 0.33, α error probability of 0.05, one group with two measurements, a correlation among repeated measures equal to 0.5, and non-sphericity correlation Є of 1. A minimum sample size of 21, with actual power of 0.82, was required to minimise the risk of type II error based on mean percentage difference from baseline in food craving scores following single session tDCS (mean difference between conditions −22.2 ±

33.7%) (Fregni et al., 2008; Goldman et al., 2011; Kekic et al., 2014; Ljubisavljevic et al., 2016). A total of 52 individuals were screened using an online questionnaire, with 31 of these excluded from participation (Figure 5-1).

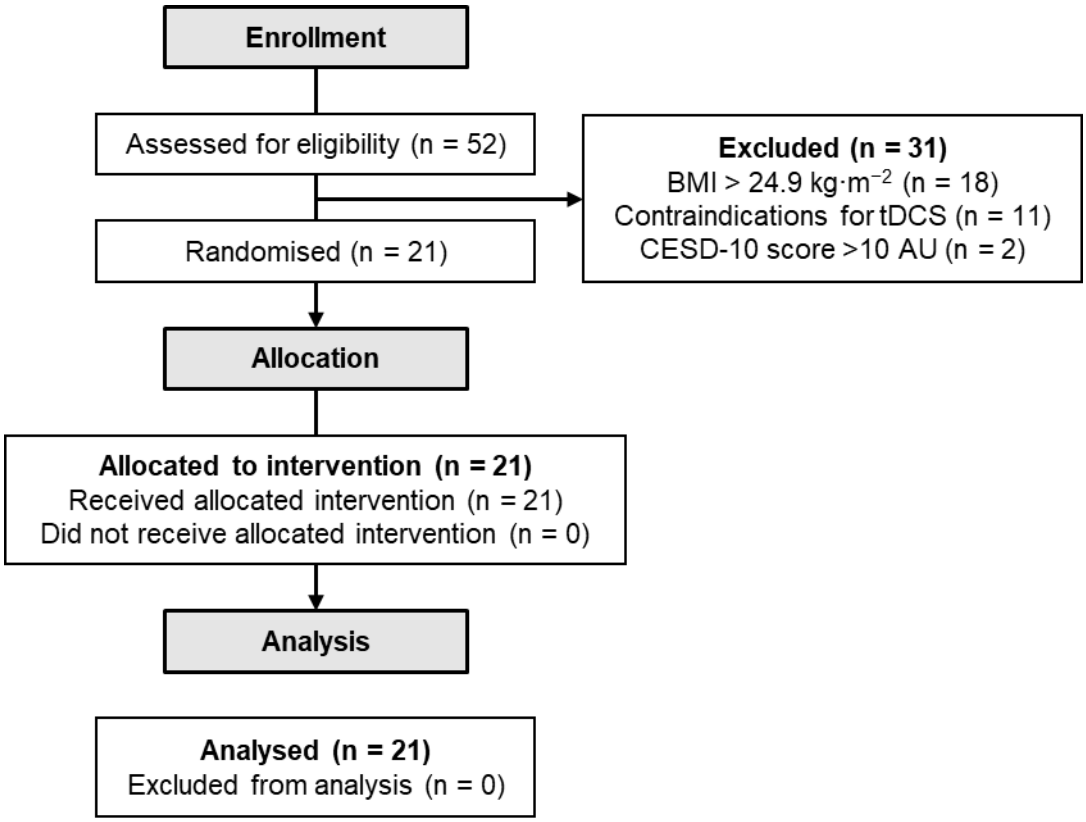


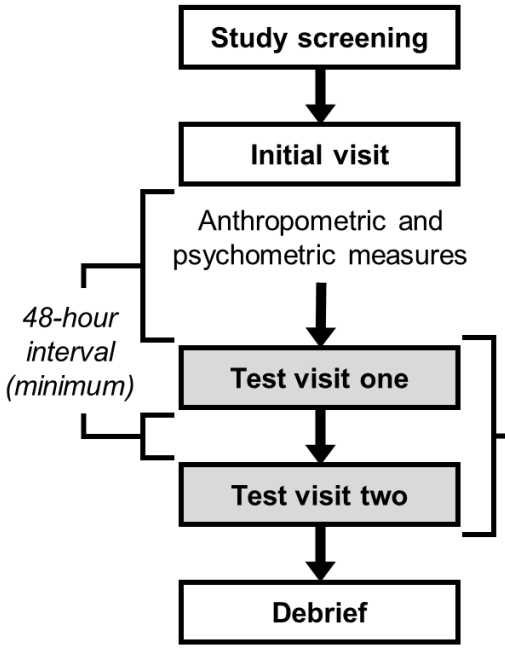
Figure 5-1 CONSORT diagram for recruitment of participants to study one.

Twenty-one participants were recruited via email and poster advertisements, and classed as 'healthy adult participants' (Category A; see Table 4-1). Eligible participants were male or female, between 18 and 60 years of age and presented with a healthy BMI between 18.5 and 24.9 $kg \cdot m^{-2}$. All participants were naïve to tDCS procedures and met the inclusion criteria discussed in section 4.4; they were free of brain stimulation-specific contraindications, non-smokers, not pregnant nor wishing to conceive, not on any medications (excluding anti-allergy medications and oral contraceptives) and did not present with low mood or depressive symptoms.

5.4.2 Procedure

The study utilised a double-blind, within-participant, repeated measures design. Following initial online screening procedures (see section 4.4), participants attended the laboratory on three occasions. Prior to these visits, all participants were required to fast for a minimum of four hours, 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 these fasting criteria was self-reported at the start of each visit. During the initial visit, participants' eating behaviour traits were assessed using the TFEQ-r18, CoEQ and FCQ-T-r. Height, weight and body composition measures were then completed (see section 4.5).

Visits two and three were experimental trials that lasted approximately 90 minutes and were scheduled at least 48 hours apart (mean 120 ± 108 hours) (Figure 5-2). Sessions were scheduled at the same time of day within-participant, occurring between 09:00 and 15:00. After determining the adherence to fasting criteria, participants were required to complete baseline (pre-tDCS) assessment of the appetite VAS, FCQ-S and LFPQ. Participants then underwent preparatory tDCS procedures, where the anodal electrode was placed over F4 to target the right DLPFC (see Figure 4-5). Following 20 minutes of tDCS, participants were then required to complete the AEQ and repeat baseline questionnaire (post-tDCS). The AEQ was repeated at regular intervals for a minimum of 45 minutes. Visits two and three were identical, apart from the stimulation condition. At the end of visit three, participants were debriefed. They were informed of the sham stimulation condition, were asked whether they were able to differentiate between the active and sham conditions, and in which visit they believe active tDCS was delivered (Appendix 12).



Time (min)	Task
0	Baseline questionnaire (adherence to fasting criteria)
2	Questionnaires (pre-tDCS): Appetite VAS → LFPQ → FCQ-S
17	tDCS preparatory procedures
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 5-2 Study one procedure outline. FCQ-S, Food Craving Questionnaire-State; LFPQ, Leeds Food Preference Questionnaire; min, minute; tDCS, transcranial direct current stimulation; VAS, visual analogue scale.

5.4.3 Data Analysis

Mean and SD were calculated at each time point (i.e., pre- and post-tDCS) under both active and sham conditions. Pearson's *r* correlations were used to determine the test re-test reliability of baseline measures. To examine the effects of tDCS on FCQ-S and LFPQ scores (i.e., food craving and food preference), data were analysed using two (condition; active or sham) by two (time point; pre- or post-stimulation) repeated-measures analysis of variance (ANOVA). Post-hoc significant effects were determined using pair-wise comparisons with Bonferroni corrections. Despite the standardisation of fasting protocols, appetite VAS scores differed significantly at baseline (see section 5.5.3). To control for these differences, scores were transformed to difference from baseline and analysed using paired-samples t-tests. Analysis of covariance (ANCOVA) were performed to control for the difference in baseline hunger when analysing FCQ-S and LFPQ scores. To compare differences in adverse events, data were compared using paired-samples t-tests.

Statistical analyses were performed using SPSS versions 21 and 26 (IBM, New York, USA). Data are presented as mean ± SD, to an alpha level of 0.05. Bayes factors were computed using JASP version 0.13.1 (University of Amsterdam, Amsterdam, The Netherlands) to interpret null findings and assess the strength of evidence in support of the experimental or null hypothesis. The classification scheme by Lee and Wagenmakers (2013) (Table 4-5) was used to interpret BF_{10}.

5.5 Results

5.5.1 Participant Characteristics

Participant characteristics are displayed in Table 5-1. Participants displayed "healthy" eating behaviour trait profiles; scores for the FCQ-T-r were below the 50-

point cut-off for clinically relevant trait craving, and CoEQ and TFEQ-r18 scores were comparable to healthy weight individuals in other studies.

Table 5-1 Participant anthropometric and psychometric characteristics (mean ± SD).

	All (n = 21)	Female (n = 11)	Male (n = 10)
Age (years)	24 ± 7	25 ± 9	23 ± 4
Height (cm)	172 ± 9	165 ± 6 *	179 ± 6 *
Weight (kg)	67.9 ± 11.0	60.1 ± 7.4 *	76.5 ± 7.1 *
BMI ($kg \cdot m^{-2}$)	22.8 ± 2.3	22.0 ± 2.1	23.8 ± 2.2
Body fat (kg)	14.7 ± 4.8	16.3 ± 4.3	12.9 ± 4.9
Body fat (%)	21.9 ± 7.1	26.8 ± 4.3 *	16.6 ± 5.5 *
CESD-10 (AU)	5 ± 3	5 ± 3	5 ± 4
FCQ-T-r (AU)	35 ± 9	36 ± 8	34 ± 10
TFEQ-r18 Cognitive Restraint (AU)	40 ± 20	40 ± 20	39 ± 22
TFEQ-r18 Uncontrolled Eating (AU)	33 ± 14	33 ± 11	34 ± 18
TFEQ-r18 Emotional Eating (AU)	22 ± 22	24 ± 24	20 ± 23
CoEQ Craving Control (mm)	65 ± 18	66 ± 18	68 ± 18
CoEQ Craving for Sweet Foods (mm)	29 ± 18	30 ± 16	28 ± 21
CoEQ Craving for Savoury Foods (mm)	51 ± 23	54 ± 19	46 ± 26
CoEQ Positive Mood (mm)	52 ± 14	51 ± 16	54 ± 13

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

** $p < 0.001$ for comparison between males and females.*

5.5.2 Test-Retest Analysis

Variables across the FCQ-S, LFPQ and appetite VAS were significantly correlated when analysing baseline assessment during test visits, with the exception of desire to eat ($r = 0.382$, $p = 0.088$). Across measurement instruments, 12 of the 23 variables measured displayed a strong correlation ($r > 0.71$), with LFPQ implicit wanting ($r = 0.72$ to 0.89) and FAB ($r = 0.68$ to 0.89) appearing most consistent (Table 5-2). In contrast, FCQ-S and appetite VAS measures only indicated moderate reliability ($r = 0.38$ to 0.84).

Table 5-2 Correlations between baseline (pre-tDCS) measures (n = 21).

			r	p
FCQ-S			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

FCQ-S, Food Craving Questionnaire-State; 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.

5.5.3 Appetite Visual Analogue Scales

Across all appetite VAS measures, baseline scores were significantly different when comparing active and sham sessions. Mean baseline hunger scores were significantly higher in the active session (63.1 ± 21.4 mm) compared with the sham session (51.9 ± 25.8 mm) ($t_{(20)}$ = 2.567, p = 0.018). In comparison, baseline fullness scores were significantly lower in the active (19.0 ± 15.3 mm) versus sham session (28.8 ± 17.8 mm) ($t_{(20)}$ = 2.925, p = 0.008). Similar to hunger, prospective consumption (active 62.5 ± 22.9 mm, sham 53.8 ± 20.2 mm; $t_{(20)}$ = 3.196, p = 0.005), and desire to eat (active 65.3 ± 17.4 mm, sham 60.1 ± 18.8 mm; $t_{(20)}$ = 2.756, p = 0.012) scores were greater at baseline in the active versus sham session.

When transformed to difference from baseline, no significant change in scores were identified for 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 active versus sham tDCS conditions (Figure 5-3). Bayes factors show moderate evidence in favour of the null hypothesis over the experimental hypothesis for hunger and fullness, whereas prospective consumption and desire to eat were only supported by anecdotal evidence in favour of the null hypothesis.

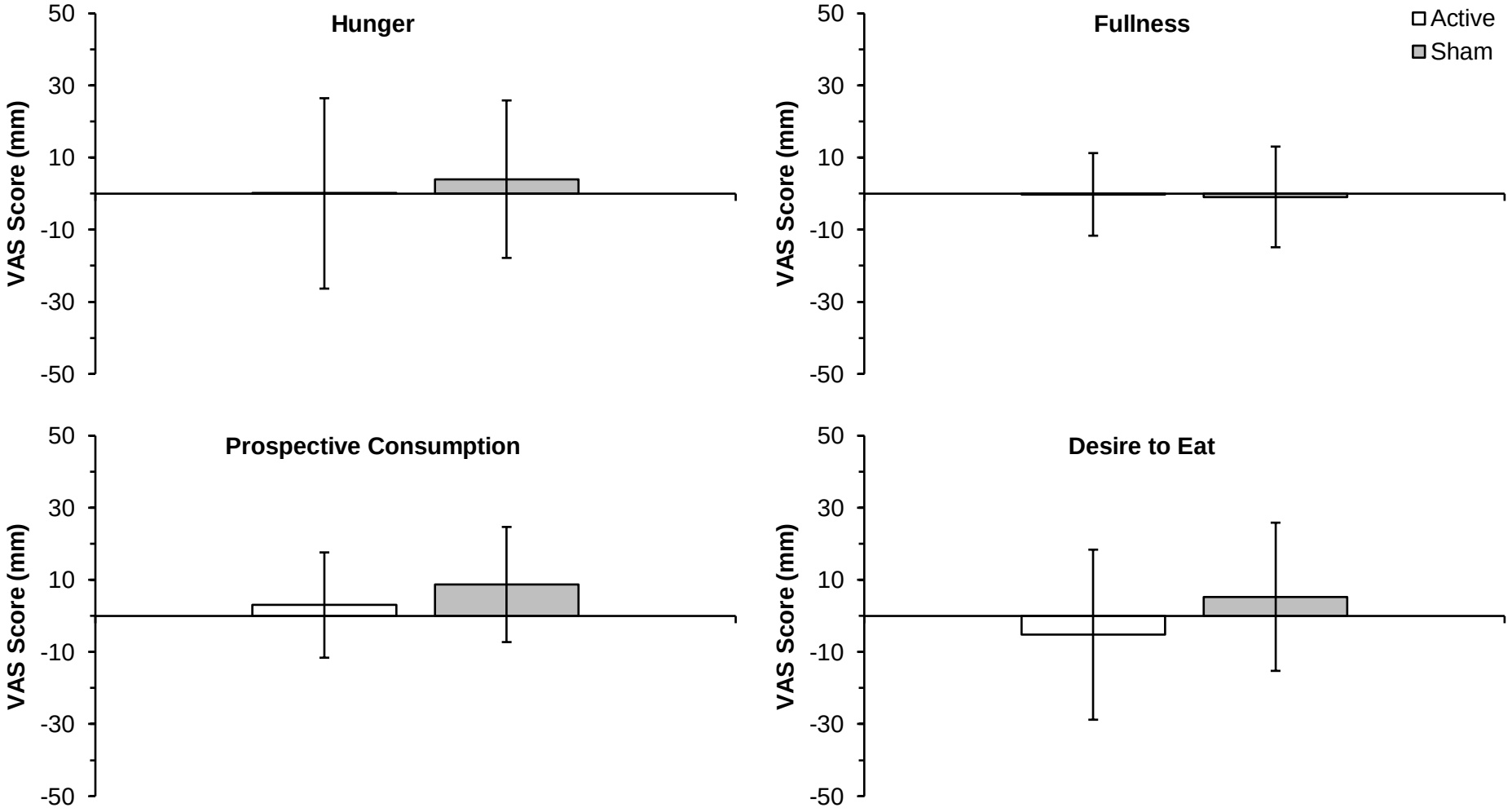


Figure 5-3 Absolute difference from baseline scores for subjective appetite measures (n = 21).

5.5.4 Food Craving Questionnaire-State

There were no significant differences in craving from pre- to post-stimulation under active (pre-tDCS 47.2 ± 9.9 arbitrary units [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) ($F_{(1, 19)} = 0.069$, $p = 0.797$) (Figure 5-4). This is supported by moderate evidence in support of the null hypothesis over the experimental hypothesis ($BF_{10} = 0.284$), and this effect remained non-significant when controlling for baseline hunger ($F_{(1, 38)} = 0.037$, $p = 0.849$).

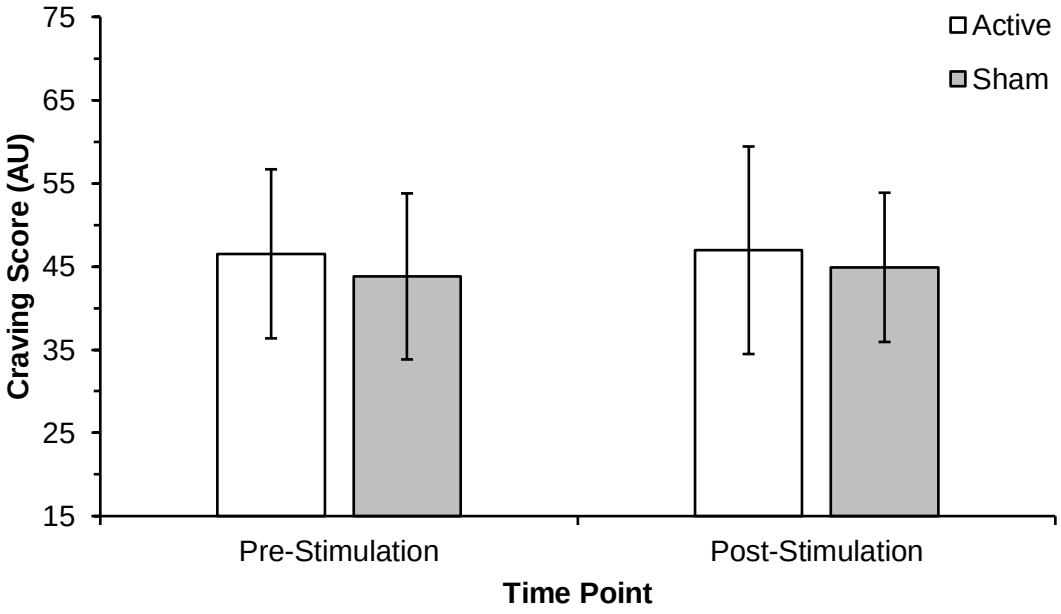


Figure 5-4 Pre- and post-tDCS FCQ-S scores (mean ± SD) (n = 21).

5.5.5 Leeds Food Preference Questionnaire

Implicit and explicit food reward was not significantly different across HFSA, LFSA, HFSW and LFSW food categories, when comparing stimulation condition by time point interactions ($p > 0.05$) (Table 5-3). This is supported by moderate-to-strong evidence in favour of the null hypothesis over the experimental hypothesis ($BF_{10} = 0.041$ to 0.168), and the interactions remained non-significant when controlling for

baseline hunger (p's > 0.10). In addition, tDCS did not significantly change implicit or explicit TAB, with non-significant condition by 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).

Table 5-3 Pre- and post-stimulation LFPQ scores (mean ± SD) (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

*AU, arbitrary unit; HFSA, high-fat savoury; LFSA, low-fat savoury; HFSW, high-fat sweet; LFSW, low-fat sweet; FAB, fat appeal bias; TAB, taste appeal bias. * $p < 0.05$.*

Similar to TAB, there were no significant condition by time point interactions for FAB explicit wanting ($F_{(1, 18)}$ = 0.136, p = 0.716, BF_{10} = 0.183) or implicit wanting ($F_{(1, 17)}$ = 0.646, p = 0.433, BF_{10} = 0.111). However, there was a significant time point ($F_{(1, 18)}$ = 6.785, p = 0.018) and condition by 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 conditions, with a greater increase following active tDCS (Table 5-3). When controlling for baseline hunger, this interaction was no longer significant ($F_{(1, 36)}$ = 2.944, p = 0.095), which is supported by moderate evidence in favour of the null hypothesis (BF_{10} = 0.313).

5.5.6 Response to tDCS

The successful delivery of electric current occurred across all 42 stimulation events, with mean impendence levels of 8 ± 4 kΩ at the start of stimulation. This reduced to 3 ± 2 kΩ within the initial minutes of current delivery. Participants tolerated stimulation well, with only minor adverse events experienced during tDCS. The most common events were cutaneous sensations, such as tingling, itching and a burning sensation, as well as sleepiness (Table 5-4). Only tingling ($t_{(20)}$ = 2.646, p = 0.016, BF_{10} = 3.507), itching ($t_{(20)}$ = 2.500, p = 0.021, BF_{10} = 2.711) and sleepiness ($t_{(20)}$ = 2.500, p = 0.021, BF_{10} = 2.711) were reported by significantly more participants following active tDCS, when compared with sham stimulation. No other sensations were significantly different between conditions, and only the severity score for tingling was significantly different between stimulation conditions ($t_{(20)}$ = 2.257, p = 0.035, BF_{10} = 1.797) (Table 5-5). Despite experiencing more minor adverse events, participants were unable to identify which visit involved active tDCS above the level of chance; only 8 out of 21 (38%) participants were able to successfully distinguish between conditions.

Table 5-4 Frequency of adverse events immediately post-stimulation (n = 21).

Sensation	Active tDCS	Sham tDCS	p	BF_{10}
Headache	7 (33%)	4 (19%)	0.186	0.514
Neck pain	0 (0%)	0 (0%)	-	-
Scalp pain	3 (14%)	1 (5%)	0.329	0.354
Tingling	14 (67%)	7 (33%)	0.016	3.507
Itching	11 (52%)	6 (29%)	0.021	2.711
Burning sensation	9 (43%)	2 (10%)	0.267	0.404
Skin redness	5 (24%)	2 (10%)	0.186	0.514
Sleepiness	12 (57%)	7 (33%)	0.021	2.711
Trouble concentrating	5 (24%)	3 (14%)	0.329	0.354
Acute mood change	2 (10%)	2 (10%)	1.000	0.228
Other	0 (0%)	0 (0%)	-	-

Table 5-5 Severity scores for adverse events experienced immediately post-tDCS (mean ± SD) [a].

Sensation	Active tDCS	Sham tDCS	p	BF_{10}
Headache	1.0 ± 0.0	1.2 ± 0.4	0.493	0.283
Scalp pain	1.0 ± 0.0	1.0 ± 0.0	0.329	0.354
Tingling	1.4 ± 0.5	1.6 ± 0.7	0.035	1.797
Itching	1.4 ± 0.5	1.7 ± 0.7	0.135	0.645
Burning sensation	1.2 ± 0.4	1.5 ± 0.5	0.605	0.258
Skin redness	1.2 ± 0.4	1.0 ± 0.0	0.162	0.565
Sleepiness	1.4 ± 0.6	1.3 ± 0.5	0.057	1.231
Trouble concentrating	1.2 ± 0.4	1.7 ± 0.5	0.748	0.239
Acute mood change	1.0 ± 0.0	1.5 ± 0.5	0.576	0.268

[a] *Scored on a four-point scale; 0 = not present, 1 = mild, 2 = moderate, 3 = severe.*

5.6 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. This study also sought to examine the reliability of measures prior to tDCS with a view to establishing the viability of their future use in this programme of research and for wider reporting to the research community. When preparatory procedures prior to tDCS were standardised, strong relationships between key variables were found indicating good reliability, particularly for implicit wanting and FAB. Collectively these 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; Goldman et al., 2011; Georgii et al., 2017; Sedgmond et al., 2019). Many of these studies have recruited

“healthy” individuals, but the effects of tDCS appear to be related to participants’ eating behaviour trait profiles (Burgess et al., 2016; Ray et al., 2017). That is, those who present with eating behaviour traits associated with overconsumption and weight gain (e.g., binge eating, frequent food craving), appear responsive to tDCS. However, large heterogeneity in sample characteristics and screening procedures means it is difficult to fully determine the impact of tDCS in “healthy” individuals. As such, the present study looked to establish the effects of tDCS across eating-related measures in a control sample of healthy weight individuals who presented with eating behaviour trait profiles suggesting low susceptibility to overconsumption. Data from the present study suggest that these “healthy” individuals are indeed unresponsive to the effects of tDCS, which was verified by the Bayesian analyses. The present study is favourable by comparison in sample size, study design (i.e., sham-controlled and double-blind) and stimulation parameters (Fregni et al., 2008; Goldman et al., 2011; Burgess et al., 2016; Ray et al., 2017).

Recently published meta-analyses have cast doubt in the ability of tDCS to alter measures of food craving (Lowe et al., 2017; Hall and Lowe, 2018), which may be due to the poor test-retest reliability of food craving measures (Cepeda-Benito et al., 2000; Meule et al., 2014b). This is in agreement with data from the present study which highlighted only moderate reliability (r = 0.55) of baseline FCQ-S scores, for example. In comparison, strong relationships between baseline measures of implicit and explicit reward were reported in the present study. In developing the LFPQ, Dalton and Finlayson (2014) reported a reliability coefficient of 0.6 to 0.7 for implicit wanting and 0.8 to 0.9 for explicit liking measures, which is supported by moderate-to-strong reliability (r = 0.54 to 0.89) shown in the present study. These variables may prove to be sensitive targets for detecting significant effects in future eating behaviour-focussed tDCS research. The LFPQ has been utilised in several settings,

and is considered a sensitive measure for individual eating behaviour traits (Finlayson et al., 2011; Dalton et al., 2013a; Dalton et al., 2013b), and a good predictor of in-laboratory and real-world food choice and consumption (Griffioen-Roose et al., 2011; French et al., 2014). The present study was 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) . This is supported by the Bayesian statistics, suggesting moderate evidence in favour of the null hypothesis. In addition, healthy individuals are unlikely to have altered prefrontal activity as observed in individuals with obesity and those with binge eating profiles, which are associated with alteration in reward response (Balodis et al., 2015; Lowe et al., 2019). Therefore, these 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). 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 (Finlayson et al., 2008; Mehta et al., 2012; Cameron et al., 2014).

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. These were carefully

measured and considered in the present study. Two previous studies have directly linked tDCS effects as occurring in those with abnormal eating behaviours (Burgess et al., 2016; Ray et al., 2017). When comparing further studies that utilise similar tDCS parameters (i.e., 2.0 mA for 20 minutes over the right DLPFC), a trait-dependent effect is evident, whereby those who present with eating behaviour traits associated with overconsumption appeared responsive to tDCS modulation. For example, studies that recruited participants with frequent food cravings, irrespective of weight status, show a more 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). This trait-dependent effect is further explored in the following chapters.

Hypoactivation of the DLPFC is assumed to occur in populations with obesity or BED and is linked with poor appetite control (Karhunen et al., 2000; Stice et al., 2008; Boeka and Lokken, 2011). The present study provides further support for the association between healthy eating behaviours and normative cortical activity within the DLPFC, where the present data suggests 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. It is possible that inducing hyper-activity in this cortical region may have a ceiling effect beyond which no further improvement is seen (Furuya et al., 2014; da Silva Machado et al., 2021). This may account for the null effects 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 the 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 et al., 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; prior studies that have recruited both male and female participants, with a similar overall sample size as the present study, have shown an experimental effect (Goldman et al., 2011; Montenegro et al., 2012; Gluck et al., 2015; Burgess et al., 2016; Ljubisavljevic et al., 2016; Heinitz et al., 2017; Max et al., 2020). Additionally, data from the present study shows comparable eating behaviour trait profiles across male and female participants (Table 5-1). Given the novelty of using the LFPQ it was important to consider the wider effects of tDCS on this variable before focussing on a specific sex. Additionally, the original hypotheses did not consider the impact of eating behaviour traits and as such these were not controlled for during screening but were considered at the point of analysis. 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. The participants' eating behaviour traits were largely in line with healthy individuals from other studies (Fleurbaix Laventie Ville Sante Study Group, 2004; Anglé et al., 2009; De Lauzon-Guillain et al., 2009; Wardle et al., 2018).

The present study is potentially limited in terms of montage. Prior studies have induced hyperactivity in the DLPFC through bilateral and unilateral stimulation of the cortex (see section 3.4.3). Although these montages have been shown to reduce measures of hedonic appetite, as indicated by the meta-data presented in Chapter 3, the efficacy of such electrode placement has been debated due to the

simultaneous effects of anodal and cathodal stimulation on the same cortical region (i.e., simultaneous excitation and inhibition of the DLPFC) (Bestmann et al., 2015). The inhibitory effects associated with cathodal stimulation during traditional montages may 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 (Vitor-Costa et al., 2015; Marron et al., 2019). The ability of this montage to induce hyperactivity in the DLPFC has been confirmed in several recent computational models (Zheng et al., 2016; Zheng et al., 2017; Marron et al., 2019). Moreover, it was verified that the electric current was delivered in a consistent manner across all 42 stimulation sessions by checking impedance (mean impedance at start of delivery: 8 ± 4 kΩ).

Finally, the efficacy 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). Although participant blinding was assessed, the present study did not overtly assess experimenter blinding as it was assumed from the use of a pin-protected device. Where a double-blind protocol is maintained through a pin-protected device, the experimenter is only able to differentiate between stimulation

conditions by significant differences in visual cues such as skin redness (Palm et al., 2013). In the present study, no significant difference in skin redness was identified between stimulation conditions, and so it can be assumed that experimenter blinding was maintained due to a lack of visual differences between active and sham protocols. Nevertheless, experimenter blinding will be incorporated into the next empirical study in this thesis.

5.7 Conclusion

The present study is the first to report the effects of tDCS on components of food reward in a sample of healthy individuals with no susceptibility to overconsumption. Prior to examining these effects, an indication of data reliability was established and revealed some plausible targets for future effects through tDCS exposure, which will be explored in the next empirical study within this thesis (Chapter 7). Data indicated no significant effects of tDCS on test variables in the present sample, which is supported by Bayesian statistics. This suggests a behaviour trait-dependent effect of tDCS on eating behaviour measures, which will be explored in the following chapter.

Chapter 6 Systematic Literature Review Two

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

Part of this chapter is published as:

Beaumont, J.D., Smith, N.C., Starr, D., Davis, D., Dalton, M., Nowicky, A., Russell, M. and Barwood, M.J. 2022. Modulating eating behavior with transcranial direct current stimulation (tDCS): A systematic literature review on the impact of eating behavior traits. *Obesity Reviews*. **23**(2), e13364. https://doi.org/10.1111/obr.13364

6.1 Chapter Summary

Transcranial direct current stimulation (tDCS) is becoming an increasingly popular technique for altering eating behaviours. In addition to the variation in stimulation parameters and study design, as discussed in Chapter 3, studies recruit participant populations with heterogenous eating behaviour trait characteristics. Recent research suggests a possible eating behaviour trait-dependent effect of tDCS. However, many studies recruit “healthy” individuals who do not present with eating behaviour traits suggesting susceptibility to overconsumption, as shown in Chapter 5. This chapter will considered the effects of tDCS across eating-related measures and explored whether a trait-dependent effect of tDCS is evident across the literature.

In line with Chapter 3, an electronic literature search of four databases (MEDLINE, PsycINFO, Scopus and Science Direct) was conducted and identified 28 articles using sham-controlled tDCS to modify eating-related measures. Random effects meta-analyses were performed, with subgroup analyses to identify differences between “healthy” and trait groups. Trivial overall effects (g = −0.12 to 0.09) of active versus sham tDCS were found. Subgroup analyses showed a more consistent effect for trait groups, with small-to-large effect size (g = −1.03 to 0.60), suggesting tDCS is dependent on participants’ eating behaviour traits. Larger effect sizes were found for those displaying traits associated with study outcomes (e.g., heightened food cravings). “Healthy” individuals appear to be unresponsive to stimulation, but further evidence is required as studies typically do not measure eating behaviour traits in these populations.

Based on this meta-data, future work should recruit those with eating behaviour trait susceptibilities to overconsumption, focussing on those who present with traits

associated with the outcome of interest. The study discussed in the following chapter will further explore this eating behaviour trait-dependent effect of tDCS.

6.2 Introduction

The control of hedonic-driven eating behaviours involve central brain executive functions, such as inhibitory control, which are strongly associated with activity within the DLPFC and allow goal-directed behaviours through the inhibition of impulsive actions (see Figure 1-1) (Miller and Cohen, 2001; Pignatti et al., 2006; Joseph et al., 2011). Individuals displaying eating behaviour traits such as binge eating behaviour appear to have hypo-activation of the DLPFC (Karhunen et al., 2000; Boeka and Lokken, 2011), and show impaired executive functioning (Cserjési et al., 2009; Michaud et al., 2017; Blume et al., 2019). This dysregulation of the DLPFC has been linked with greater impulsive behaviours, often leading to overconsumption of energy-dense foods (Stice et al., 2008; Gluck et al., 2017; Grundeis et al., 2017). Of note, those with greater executive functioning following bariatric surgery show improved weight loss outcomes (Goldman et al., 2013). By modulating activity within cortical regions associated with executive functioning, it may be possible to improve hedonic appetite control through the inhibition of the rewarding valuation of foods, which may be beneficial for weight management (Alonso-Alonso and Pascual-Leone, 2007). Such modulation is possible through tDCS (Thair et al., 2017).

The ability of tDCS to alter eating behaviours, such as food craving and consumption, has been of great interest for researchers due to its potential use in the treatment of obesity (Alonso-Alonso, 2013), amongst other conditions such as eating disorders and addiction-related conditions (Filmer et al., 2014; Lefaucheur, 2016). Despite promising effects for eating-related measures outlined in early studies (Fregni et al., 2008; Goldman et al., 2011), more recent data shows equivocal effects (Gluck et al., 2015; Georgii et al., 2017; Sedgmond et al., 2019), including the data presented in Chapter 5. As discussed in Chapter 3, there is variation in study design, stimulation parameters and participant characteristics

across tDCS research. If tDCS is to be used as an additional or adjunctive treatment modality for weight management or eating disorders, it is important that inconsistencies are addressed (Krause and Kadosh, 2014).

Participants recruited to tDCS research include those who are healthy weight (Georgii et al., 2017; Carvalho et al., 2019), and individuals with overweight or obesity (Gluck et al., 2015; Grundeis et al., 2017). In addition, the eating behaviour traits of these participants also appear to differ across studies. For instance, two recent studies compared the effects of tDCS on food craving and consumption in participants with and without binge eating symptomatology and only found an effect of tDCS in those displaying binge-type behaviours (Burgess et al., 2016; Ray et al., 2017). Recent data shows improved task performance (e.g., verbal learning, working memory) following tDCS only in low-cognitive groups (Berryhill and Jones, 2012; Learmonth et al., 2015; Perceval et al., 2020). As such, only those with impaired DLPFC activity and poor executive control may benefit from tDCS modulation. Together, this suggests a trait-dependent effect of tDCS, but further data are required to support this assumption. This chapter considered the effects of tDCS across measures of eating behaviour and discussed the impact of behavioural traits on these measures.

6.3 Methods

This review was conducted as described in Chapter 3. In brief, the literature review was performed in line with PRISMA (Appendix 8), with a literature search conducted across MEDLINE, PsycINFO, Scopus and Science Direct databases in March 2019, and repeated in July 2020. Search terms are displayed in Table 3-1. Articles were included if they were peer-reviewed intervention studies that recruited adult human participants *(population)*, applying conventional (i.e., one anode and one cathode)

tDCS procedures *(intervention)* using a sham-controlled design *(control)* to determine the effects on hedonic-related eating behaviours (subjective appetite, food craving, consumption or reward) *(outcome)* (see Table 3-2). Results were limited to those written in English and published after 1998 to coincide with the development of modern tDCS procedures (Priori et al., 1998; Nitsche and Paulus, 2000). The data extraction and study quality assessment processes are outlined in section 3.3.

6.3.1 Statistical Analysis

Effect size calculations and multilevel modelling processes are outlined in section 3.3.5. Only data following single session active and sham tDCS were included in the present review to provide comparison across studies. Four studies did not measure the effects of single session tDCS (Heinitz et al., 2017; Fassini et al., 2019; Amo Usanos et al., 2020; Fassini et al., 2020); these were excluded from the analysis. The study by Ljubisavljevic et al. (2016) was excluded as all participants received active tDCS for the first stimulation session. A further study was removed due to missing data (Montenegro et al., 2012). A total of 22 studies (total n = 817 participants; “healthy” group n = 490, trait group n = 327) were included in the meta-analysis (Appendix 9). Meta-analyses were performed and interpreted, as outlined in section 3.3.5. Where meta-analysis was not possible, a systematic review of the literature is included.

6.4 Results and Discussion

6.4.1 Study Characteristics

The literature search identified 1,135 records, with 28 of these included in the present review after removing duplicates and assessing eligibility (Figure 6-1). In line with the PICO model, all included studies used conventional sham-controlled

tDCS procedures (i.e., one anode, one cathode), with 11 between-participant and 17 within-participant designs (Table 6-1). Eight studies involved repeated sessions of tDCS. Across the reviewed studies, a total of 996 participants were recruited, which ranged from 9 to 172 individuals per study. This included individuals with healthy weight (n = 14 studies, 576 participants), overweight or obesity (n = 15 studies, 393 participants). One study included those with healthy weight and overweight (n = 27), but the authors did not provide a breakdown for each weight category (Ljubisavljevic et al., 2016).

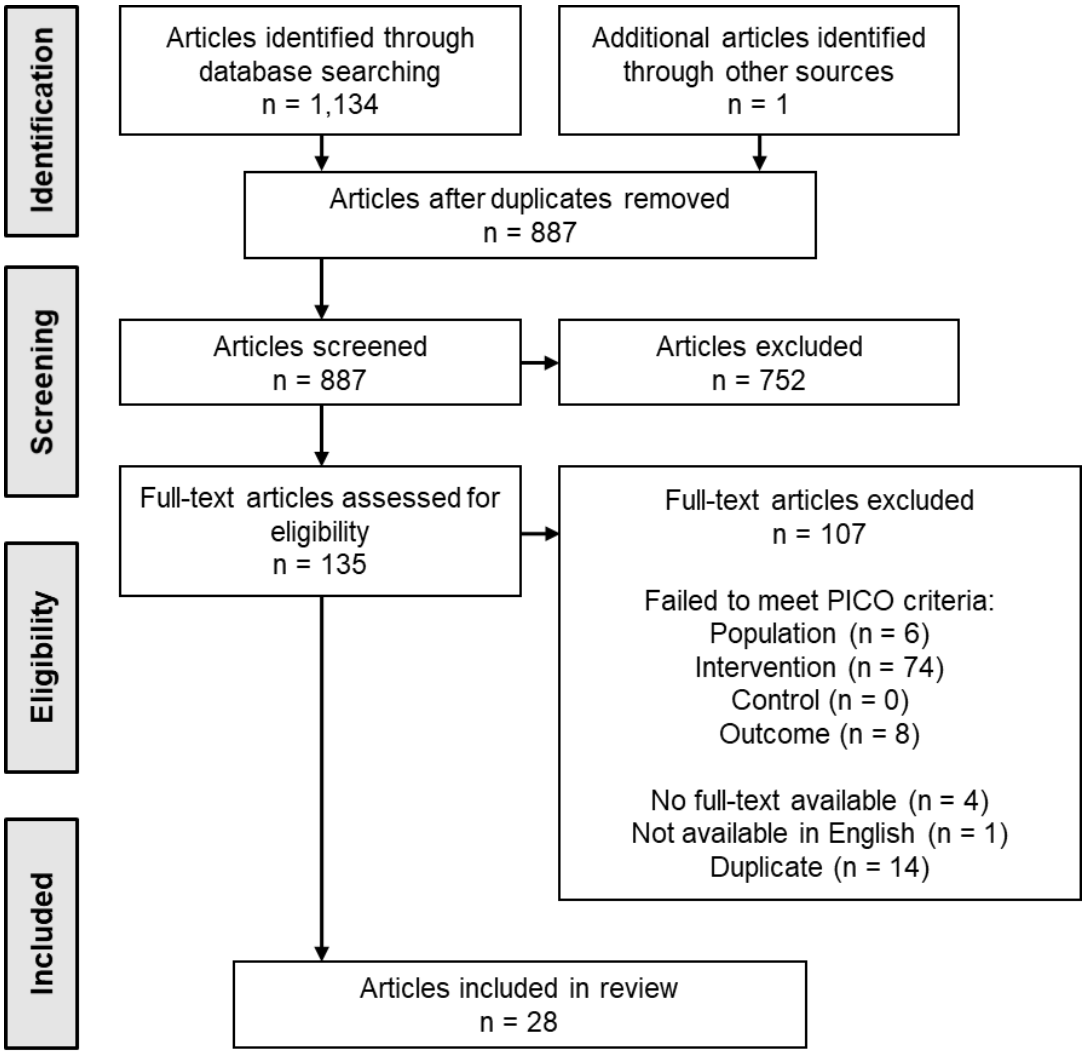


Figure 6-1 PRISMA flow diagram detailing the search and selection process performed to identify studies applying conventional tDCS for the modulation of eating behaviours.

Table 6-1 Summary of participant characteristics and study design.

	n (M/F)	Participant Characteristics	Age (years)	BMI ($kg \cdot cm^{-2}$)	Design	Randomised / Counterbalanced	Blinding	Stimulation Parameters
Amo Usanos et al. (2020)	38 (0/38)	“Healthy”, overweight/obese	52.5 ± 8.0	32.4 ± 4.3	Between	Yes / NR	Double	Anodal or sham over left DLPFC; 8x 2.0 mA for 20 min
Beaumont et al. (2021)	21 (10/11)	“Healthy”, healthy weight	24.0 ± 7.0	22.8 ± 2.3	Within	Yes / Yes	Double	Anodal or sham over right DLPFC, 2.0 mA for 20 min
Bravo et al. (2016)	31 (NR)	Healthy weight, obese or PWS	35.7 ± 11.0	29.1 ± 5.5	Between	Yes / Yes	Single	Anodal or sham over right DLPFC; 5x 2.0 mA for 30 min
Burgess et al. (2016)	30 (10/20)	Obese with BED or subBED [a]	NR	36.1 ± 6.1	Within	NR / NR	Single	Anodal and sham over right DLPFC; 2.0 mA for 20 min
Carvalho et al. (2019)	51 (13/38)	“Healthy”, healthy weight	22.1 ± 3.4	22.0 ± 2.8	Between	Yes / NR	Single	Anodal, cathodal or sham over right DLPFC; 2.0 mA for 20 min
Chen et al. (2019)	57 (0/57)	Disinhibited restrained eaters	20.7 ± 1.7	21.6 ± 2.5	Between	Yes / NR	Single	Anodal or sham over right IFG; 1.5 mA for 20 min
Fassini et al. (2019)	38 (0/38)	Obese with COMT Val158Met polymorphism	31.6 ± 11.7	33.1 ± 2.5	Between	Yes / NR	Double	Anodal or sham over left DLPFC; 16x 2.0 mA for 30 min
Fassini et al. (2020)	38 (0/38)	Obese with COMT Val158Met polymorphism	31.4 ± 6.8	33.1 ± 1.9	Between	Yes / NR	Double	Anodal or sham over left DLPFC; 16x 2.0 mA for 30 min

Table 6-1 continued

	n (M/F)	Participant Characteristics	Age (years)	BMI ($kg \cdot cm^{-2}$)	Design	Randomised / Counterbalanced	Blinding	Stimulation Parameters
Fregni et al. (2008)	23 (2/21)	Food cravers [b]	23.7 ± 7.1	NR	Within	Yes / Yes	Double	Anodal, cathodal and sham over right DLPFC; 2.0 mA for 20 min
Georgii et al. (2017)	42 (0/42)	"Healthy", healthy weight	22.0 ± 4.3	22.6 ± 3.1	Within	NR / NR	Double	Anodal and sham over right DLPFC; 1.0 mA for 20 min
Gluck et al. (2015)	9 (3/6)	"Healthy", obese	42.0 ± 8.0	38.0 ± 7.0	Between	Yes / NR	Double	Anodal, cathodal or sham over left DLPFC; 3x 2.0 mA for 40 min
Goldman et al. (2011)	19 (6/13)	Overweight or obese food cravers	32.5 ± 10.9	27.3 ± 6.2	Within	Yes / NR	Single	Anodal and sham over right DLPFC; 2.0 mA for 20 min
Grundeis et al. (2017)	32 (0/32)	"Healthy", obese	28.8 ± 6.0	36.5 ± 4.1	Within	Yes / NR	Double	Anodal, cathodal and sham over left DLPFC; 2.0 mA for 20 min
Heinitz et al. (2017)	29 (12/17)	"Healthy", obese	35.6 ± 9.1	38.9 ± 6.7	Between	Yes / NR	Double	Anodal or sham over left DLPFC; 15x 2.0 mA for 40 min
Jauch-Chara et al. (2014)	14 (14/0)	"Healthy", healthy weight	24.8 ± 2.2	22.7 ± 1.3	Within	Yes / Yes	Single	Anodal and sham over right DLPFC; 8x 1.0 mA for 20 min
Kekic et al. (2014)	17 (0/17)	Food cravers	26.4 ± 8.3	23.8 ± 2.6	Within	Yes / Yes	Double	Anodal and sham over right DLPFC; 2.0 mA for 20 min

Table 6-1 continued

	n (M/F)	Participant Characteristics	Age (years)	BMI ($kg \cdot cm^{-2}$)	Design	Randomised / Counterbalanced	Blinding	Stimulation Parameters
Kekic et al. (2017)	39 (2/37)	Bulimia nervosa	25.9 ± 6.6	21.7 ± 3.2	Within	Yes / Yes	Double	Anodal, cathodal and sham over right DLPFC; 2.0 mA for 20 min
Lapenta et al. (2014)	9 (9/0)	Food cravers	23.4 ± 2.0	21.9 ± 1.6	Within	Yes / Yes	Double	Anodal and sham over right DLPFC; 2.0 mA for 20 min
Ljubisavljevic et al. (2016)	27 (19/9)	“Healthy”, healthy weight/overweight	21.3 ± 2.0	25.6 ± 4.4	Between	Yes / NR	Double	Anodal or sham over right DLPFC; 5x 2.0 mA for 20 min
Marron et al. (2019)	12 (3/9)	“Healthy”, overweight/obese	41.6 ± 4.8	32.7 ± 1.9	Within	Yes / Yes	Single	Anodal and sham over left DLPFC; 2.0 mA for 20 min
Mattavelli et al. (2019)	72 (0/72)	With or without eating disorders	24.8 ± 5.8	19.5 ± 2.2	Within	NR / NR	Not reported	Anodal and sham over medial PFC or right EBA; 1.0 mA for 20 min
Max et al. (2020)	27 (4/23)	Overweight or obese with BED	38.2 ± 14.3	33.0 ± 10.3	Within	Yes / Yes	Double	Anodal and sham over right DLPFC; 1.0 / 2.0 mA for 20 min
Montenegro et al. (2012)	9 (5/4)	“Healthy”, overweight	24 (20 to 32)	28.2 (25.2 to 43.5)	Within	Yes / Yes	Single	Anodal and sham over left DLPFC; 2.0 mA for 20 min
Ray et al. (2017)	18 (8/10)	“Healthy”, obese	22.7 ± 7.9	37.4 ± 9.1	Within	NR / NR	Double	Anodal and sham over right DLPFC; 2.0 mA for 20 min
Ray et al. (2019)	74 (30/44)	“Healthy”, overweight/obese	19.9 ± 3.4	31.8 ± 5.5	Between	Yes / NR	Double	Anodal or sham over right DLPFC; 2.0 mA for 20 min

Table 6-1 continued

	n (M/F)	Participant Characteristics	Age (years)	BMI ($kg \cdot cm^{-2}$)	Design	Randomised / Counterbalanced	Blinding	Stimulation Parameters
Sedgmond et al. (2019)	172 (38/134)	"Healthy", healthy weight	20.8 ± 3.4	22.9 ± 5.3	Between	Yes / NR	Double	Anodal or sham over right DLPFC; 2.0 mA for 20 min
To et al. (2018)	24 (0/24)	Restrained eaters	24.7 ± 4.2	24.3 ± 4.3	Within	Yes / Yes	Double	Anodal and sham over right IFG; 2.0 mA for 20 min
Vicario et al. (2020)	24 (9/15)	"Healthy", healthy weight	29.0 ± 5.6	24.1 ± 3.5	Within	Yes / Yes	Single	Anodal, cathodal and sham over left tnM1; 1.0 mA for 15 min

BED, Binge Eating Disorder; BMI, body mass index; COMT, catechol-o-methyl transferase; DLPFC, dorsolateral prefrontal cortex; EBA, extrastriate body area; F, female; IFG, inferior frontal gyrus; M, male; mA, milliampere; min, minute; NR, not reported; PFC, prefrontal cortex; PWS, Prader-Willi Syndrome; subBED, subthreshold Binge Eating Disorder; tnM1, area of primary motor cortex representing the tongue muscle.

[a] *Defined as meeting all diagnostic criteria for BED, except for binge frequency per week (Burgess et al., 2016).*

[b] *Defined as three or more times per day (Fregni et al., 2008).*

Many studies recruited participants described as “healthy” (n = 593) (Table 6-1). The consensus definition of “healthy” related to a lack of medical or behavioural conditions, and was irrespective of weight status (Gluck et al., 2015; Grundeis et al., 2017; Amo Usanos et al., 2020). It should be noted that four of these studies did not measure participants’ wider eating behaviour traits, but reported that participants were “healthy” regardless of weight status (Gluck et al., 2015; Ljubisavljevic et al., 2016; Ray et al., 2019; Vicario et al., 2020). Thirteen studies recruited participants (n = 403) with differing eating behaviour traits or medical conditions, including PWS (Bravo et al., 2016), COMT Val158Met polymorphism (Fassini et al., 2019; Fassini et al., 2020), frequent food cravings (Fregni et al., 2008; Goldman et al., 2011; Kekic et al., 2014; Lapenta et al., 2014), restrained eating (To et al., 2018; Chen et al., 2019), BED (Burgess et al., 2016; Max et al., 2020), and anorexia or bulimia nervosa (Kekic et al., 2017; Mattavelli et al., 2019).

Heterogeneity across studies (I^2 range = 0.0 to 48.4%) largely suggests it might not be important (Table 6-2). However, potential moderate to substantial heterogeneity is evident for some measures, particularly in trait subgroup analyses. Inspection of funnel plots showed good symmetry across measures (Appendix 10). Egger’s regression showed little evidence of publication bias for overall analyses ($p > 0.07$). Study quality assessment is discussed in section 6.4.2, and a summary of the key measures and outcomes is presented in Table 6-3.

Table 6-2 Summary of heterogeneity and publication bias data.

Measure	Heterogeneity			Egger's Test		
	I^2 (%)	χ^2	p	β_0	t	p
Hunger	32.0%	13.24	0.152	0.908	0.872	0.408
Fullness	18.2%	3.67	0.300	0.773	0.427	0.711
Desire to Eat	21.4%	7.64	0.266	−1.357	1.158	0.299
Prospective Consumption	0.0%	0.00	0.985	−0.100	-	-
Food Craving	0.0%	2.54	0.638	0.417	0.306	0.780
Explicit Liking	0.0%	0.07	0.965	−0.700	1.258	0.427
Explicit Wanting (with expectation effect)	27.3%	13.75	0.185	0.004	0.002	0.998
Explicit Wanting (without expectation effect)	0.0%	5.28	0.809	−1.144	0.794	0.450
Implicit Wanting	48.4%	9.70	0.084	−0.844	0.290	0.786
Food Consumption (with expectation effect)	45.0%	23.63	0.035	−1.581	1.460	0.170
Food Consumption (without expectation effect)	24.2%	15.83	0.199	−1.720	1.996	0.071

Table 6-3 Overview of appetite-related measures and main results.

	Subjective Appetite	Food Craving	Food Reward	Food Consumption	Main Results
Amo Usanos et al. (2020)	VAS	FCQ-S	-	-	No change in measures of subjective appetite ($p > 0.062$) or food craving ($p = 0.3$).
Beaumont et al. (2021)	VAS	FCQ-S	LFPQ	-	No change in measures of subjective appetite ($t_{(20)} \geq 0.146$, $p \geq 0.092$, $BF_{10} = 0.230 – 0.858$), food craving ($F_{(1, 19)} = 0.069$, $p = 0.797$, $BF_{10} = 0.284$) or food reward ($p \geq 0.05$, $BF_{10} = 0.041 – 0.168$).
Bravo et al. (2016)	VNS [a]	-	-	-	Hunger scores were lower in the anodal (4.1 ± 2.1 AU) versus sham tDCS (8.3 ± 2.5 AU) group at follow-up day 10 in participants with PWS ($p < 0.05$). No difference in hunger scores in participants with healthy weight or obesity.
Burgess et al. (2016)	-	-	CBIT [b]	*Ad libitum* buffet	Reduced craving for desserts ($F_{(1, 28)} = 4.99$, $p = 0.03$), savoury proteins ($F_{(1, 28)} = 7.34$, $p = 0.01$) and all-food categories ($F_{(1, 28)} = 6.03$, $p = 0.02$) following anodal versus sham tDCS. This effect was more pronounced in males versus females for desserts ($F_{(1, 28)} = 4.99$, $p = 0.03$) and all-food categories ($F_{(1, 28)} = 4.09$, $p = 0.049$). 11% reduction in food consumption following active (614.50 ± 55.5 kcal) versus sham tDCS (689.54 ± 60.8 kcal) ($F_{(1, 29)} = 4.35$, $p = 0.046$). This effect was more pronounced for preferred versus less-preferred foods ($F_{(1, 29)} = 5.35$, $p = 0.03$).

Table 6-3 continued

	Subjective Appetite	Food Craving	Food Reward	Food Consumption	Main Results
Carvalho et al. (2019)	-	-	VAS, IAT	-	Anodal tDCS combined with CBM training reduced implicit wanting for chocolate versus fast food (−0.101 AU, SE 0.123 AU) when compared with cathodal tDCS (0.285 AU, SE 0.130 AU) ($p = 0.009$). Cathodal tDCS combined with CBM training increased explicit wanting for chocolate (1.824 AU, SE 0.472 AU) when compared with anodal tDCS (0.563 AU, SE 0.387 AU ($p = 0.023$).
Chen et al. (2019)	VAS	FCQ-S	-	-	No change in hunger ($F_{(1, 55)} = 0.061$, $p = 0.805$), desire to eat ($F_{(1, 55)} = 0.106$, $p = 0.746$) or food craving scores ($F_{(1, 55)} = 0.0001$, $p = 0.98$).
Fassini et al. (2019)	VAS	-	-	-	No overall difference in appetite scores when comparing active versus sham tDCS ($p > 0.05$). Met carriers had reduced appetite following active versus sham tDCS ($p \leq 0.031$), with no difference in scores for met non-carriers.
Fassini et al. (2020)	VAS	FCQ-S	-	Food recall	No change in scores for subjective appetite or food craving ($p > 0.05$). No change in food consumption ($p > 0.05$).
Fregni et al. (2008)	VNS [b]	-	Eye tracking	*Ad libitum* buffet	17.9% reduction in craving score following anodal tDCS ($F_{(2, 62)} = 7.1$, $p = 0.0017$). Reduced food consumption following both anodal and cathodal tDCS ($F_{(2, 39)} = 4.94$, $p = 0.012$). 12.4% decreased in fixation on food following anodal tDCS ($F_{(1, 29)} = 5.12$, $p = 0.0313$).

Table 6-3 continued

	Subjective Appetite	Food Craving	Food Reward	Food Consumption	Main Results
Georgii et al. (2017)	VAS	FCQ-S	CBIT	*Ad libitum* buffet	No change in food craving scores or interaction with impulsivity ($F \leq 1.194$, $p \geq 0.281$). No effect of stimulation or impulsivity on food choice ($F \leq 2.79$, $p \geq 0.103$). No overall difference in food consumption ($F_{(1, 50)} = 0.102$, $p = 0.751$). Higher impulsivity scores were associated with greater food consumption ($r(42) = 0.413$, $p = 0.007$).
Gluck et al. (2015)	-	-	-	Vending machine	Reduced consumption of fat ($\Delta = -337 \pm 234$ kcals/day, $p = 0.03$) and soda ($\Delta = -66 \pm 42$ kcals/day, $p = 0.02$) following anodal versus cathodal tDCS.
Goldman et al. (2011)	-	-	CBIT [b]	*Ad libitum* buffet	Reduced food craving following anodal ($-26.81 \pm 26.11\%$) versus sham tDCS ($-8.98 \pm 41.87\%$) ($t_{(18)} = -2.28$, $p = 0.035$), particularly for sweet foods ($t_{(18)} = -2.34$, $p = 0.031$). Reduced inability to resist foods following anodal (-30.36 ± 30.82) versus sham tDCS (-13.38 ± 39.52) ($t_{(18)} = -2.28$, $p = 0.035$), particularly for sweet foods ($t_{(18)} = -2.42$, $p = 0.026$). No difference in amount of food consumed.
Grundeis et al. (2017)	VAS	-	CBIT	*Ad libitum* buffet	No change in measures of hunger ($F_{(2, 48)} = 0.246$, $p = 0.78$), fullness ($F_{(2, 48)} = 1.291$, $p = 0.28$) or consumption ($F_{(2, 48)} = 0.16$, $p = 0.853$).
Heinitz et al. (2017)	VAS	-	-	Vending machine	General *ad libitum* and daily intake did not differ between conditions ($p > 0.3$). Reduced consumption of candy following anodal versus sham tDCS ($p = 0.01$). No change in subjective appetite scores during in-patient treatment ($p \geq 0.05$). For out-patient treatment, hunger ($p = 0.01$) and urge to eat ($p = 0.05$) were reduced following anodal versus sham tDCS, when adjusted for age and sex.

Table 6-3 continued

	Subjective Appetite	Food Craving	Food Reward	Food Consumption	Main Results
Jauch-Chara et al. (2014)	VAS	-	-	*Ad libitum* buffet	14.2% reduction in food consumption following 8 sessions of anodal versus sham tDCS ($p = 0.016$). Effect associated with reduced carbohydrate intake ($p = 0.001$). No change in hunger scores following 8 days of tDCS ($p = 0.165$). Scores for non-specific appetite ($p = 0.016$), appetite for savoury foods ($p = 0.006$) and appetite for sweet foods ($p = 0.033$) were reduced following 8 days of anodal versus sham tDCS.
Kekic et al. (2014)		FCQ-S	CBIT	*Ad libitum* buffet	Sham tDCS reduced food craving scores (−11.32 ± 21.12%) more than anodal tDCS (−1.94 ± 21.36%) ($F_{(1, 16)} = 5.02$, $p < 0.05$). Craving for sweet foods were reduced more by anodal (−13.31 ± 34.73%) versus sham tDCS (−6.06 ± 29.86%) ($F_{(1, 16)} = 4.56$, $p < 0.05$). No change in craving for savoury foods ($F_{(1, 16)} = 2.20$, $p > 0.05$). Those with greater intertemporal decision-making abilities at baseline appeared to be more susceptible to the effects. No effect on food consumption ($p > 0.30$).
Kekic et al. (2017)	VAS	-	CBIT	-	Urge to binge eat was reduced following anodal ($Z = −2.42$, $p = 0.016$, $r = −0.27$) and cathodal ($Z = −2.52$, $p = 0.012$, $r = −0.28$) tDCS. No change in liking and wanting scores ($p \geq 0.1$).
Lapenta et al. (2014)	VAS [b]	-	Eye tracking	*Ad libitum* buffet	Active tDCS reduced in food craving scores when compared to sham ($F_{(4, 34)} = 3.0$, $p = 0.03$). Ingested calories were lower following anodal versus sham ($F_{(1, 8)} = 8.4$, $p = 0.02$). No effect of stimulation on eye tracking ($F_{(1, 8)} = 1.7$, $p = 0.2$).

Table 6-3 continued

	Subjective Appetite	Food Craving	Food Reward	Food Consumption	Main Results
Ljubisavljevic et al. (2016)	-	FCQ-S, FCI	CBIT	-	Food craving intensity was reduced following a single session of tDCS in both active and sham groups, but both groups received active tDCS in the first session. Craving intensity reduced further following 5 days of active tDCS and remained reduced at day 30 ($F_{(2, 24)} = 4.4284$, $p < 0.023$). Craving intensity did not change in the sham group. Craving was reduced for fast-food ($F_{(2, 24)} = 11.327$, $p < 0.001$), sweets ($F_{(2, 24)} = 3.551$, $p < 0.044$) and fat groups ($F_{(2, 24)} = 7.844$, $p < 0.002$).
Marron et al. (2019)	VAS	-	-	-	Increase in subjective hunger scores following active ($t_{(11)} = 2.75$, $p = 0.019$) versus sham tDCS ($t_{(11)} = 1.019$, $p = 0.299$).
Mattavelli et al. (2019)	-	-	IAT	-	Those with eating disorders assigned lower value to tasty food images and higher value to body weight images for both underweight and overweight. No effect of active tDCS on implicit attitudes towards food ($p = 0.35$).
Max et al. (2020)	VAS	-	Anti-saccade task	-	Active tDCS at 1.0 mA led to slower latencies of correct anti-saccades when compared to sham tDCS ($\beta = -10.7$ ms, SE = 2.27, $p < 0.001$). Active tDCS at 2.0 mA led to faster latencies of correct anti-saccades when compared to sham tDCS (β 11.29 ms, SE 2.77, $p < 0.001$). Binge eating episodes were reduced following 2.0 mA active versus sham tDCS ($\beta = 2.46$, SE = 0.69, $p = 0.009$).
Montenegro et al. (2012)	VAS	-	-	-	Decrease in desire to eat following anodal tDCS ($p = 0.05$), with cumulative effects following isocaloric exercise bout ($p = 0.04$).

Table 6-3 continued

	Subjective Appetite	Food Craving	Food Reward	Food Consumption	Main Results
Ray et al. (2017)	-	-	CBIT	*Ad libitum* buffet	No main effect of stimulation on food craving scores ($p \geq 0.05$). In females, reduction in food craving following active tDCS was shown when attentional impulsivity [c] was included as a covariate, specifically for sweets ($F_{(1, 8)} = 5.4$, $p = 0.049$), fatty proteins ($F_{(1, 8)} = 6.0$, $p = 0.04$) and mixed food ($F_{(1, 8)} = 6.4$, $p = 0.035$) categories. No main effect of stimulation on food consumption ($p \geq 0.05$). In males, a 13.3% reduction in calories from preferred foods following active tDCS was shown when intent to restrict scores were included as a covariate ($F_{(1, 6)} = 10.2$, $p = 0.019$). A similar effect was shown when non-planning impulsiveness [d] was included as a covariate ($F_{(1, 6)} = 14.3$, $p = 0.009$).
Ray et al. (2019)	-	-	CBIT	*Ad libitum* buffet	There was no main effect of tDCS on craving ($F_{(1, 69)} = 0.08$, $p = 0.776$). Expectation of receiving active versus sham tDCS reduced the craving for sweet ($F_{(1, 69)} = 9.914$, $p = 0.002$), carbohydrate ($F_{(1, 69)} = 9.893$, $p = 0.002$) and all-food ($F_{(1, 69)} = 10.012$, $p = 0.002$) categories, irrespective of whether participants actually received active or sham tDCS. No main effect of tDCS on food consumption ($F_{(1, 69)} = 0.006$, $p = 0.936$). Expectation of receiving active versus sham tDCS led to a 37.4% reduction in food consumption ($F_{(1, 69)} = 8.425$, $p = 0.005$), irrespective of whether participants actually received active or sham tDCS.
Sedgmond et al. (2019)	VAS	FCQ-S	-	*Ad libitum* buffet	No main change in food consumption ($F_{(1, 170)} = 1.54$, $p = 0.217$, $BF_{10} = 0.19$). 22% increase in healthy food consumption following active (134.07, SE 8.15) versus sham tDCS (109.98, SE 6.7) ($F_{(1, 170)} = 7.08$, $p = 0.009$). This effect was related to familiar foods ($p = 0.008$); No change in food craving scores ($F_{(1, 170)} = 0.66$, $p = 0.420$).

Table 6-3 continued

	Subjective Appetite	Food Craving	Food Reward	Food Consumption	Main Results
To et al. (2018)	-	-	-	*Ad libitum* buffet	Chocolate consumption was greater following anodal (42.7 g, SE 3.4 g) versus sham tDCS (32.7 g, SE 3.3 g) (β = 10.0, 95% CI 2.9, 17.1, p = 0.006).
Vicario et al. (2020)	VAS	-	-	-	Hunger increased following all stimulation conditions, but increase was smaller following cathodal (11.75 ± 3.85%) versus sham tDCS (30.85 ± 6.94%) (p = 0.047). No difference in hunger scores when comparing anodal versus cathodal or anodal versus sham tDCS (p = 0.277 and 0.651, respectively).

AU, arbitrary unit; BF_{10}, Bayes factor; CBIT, computer-based image task; CBM, cognitive bias modification; CI, confidence interval; FCI, Food Craving Inventory; FCQ-S, Food Craving Questionnaire-State; IAT, implicit association task; kcal, kilocalories; ms, milliseconds; PWS, Prader Willi Syndrome; SE, standard error; tDCS, transcranial direct current stimulation; VAS, visual analogue scale; VNS, visual numeric scale.

NB: Data are reported as described in the original article.

[a] *Authors use a 10-point VNS to measure subjective hunger, which they use as a proxy for food craving.*

[b] *Measure of desire to eat was used as a proxy for food craving.*

[c] *Defined as the inability to concentrate or focus attention.*

[d] *Defined as the lack of future planning and forethought.*

6.4.2 Study Quality

Similar to the RoB assessment presented in Chapter 3, only seven of the 28 studies showed low risk of bias across all domains and therefore overall low risk of bias (Figure 6-2, Table 6-4). The main sources of bias were issues with blinding protocol (Domain 2), measurement of outcome (Domain 4), and selection of reported results (Domain 5). In line with the prior RoB outcome (see section 3.4.2), there is insufficient information provided in published articles around participant and researcher blinding protocols. For further consideration of study quality, see section 3.4.2.

Figure 6-2 Risk of bias across the reviewed studies (n = 28).

Table 6-4 Risk of bias assessment within studies (n = 28).

	D1	D2	D3	D4	D5	Overall
Amo Usanos et al. (2020)	+	+	+	+	+	+
Beaumont et al. (2021)	+	+	+	+	+	+
Bravo et al. (2016)	+	!	+	!	!	!
Burgess et al. (2016)	+	!	+	!	!	!
Carvalho et al. (2019)	+	!	+	!	!	!
Chen et al. (2019)	+	!	+	!	!	!
Fassini et al. (2019)	+	+	+	+	+	+
Fassini et al. (2020)	+	+	+	+	+	+
Fregni et al. (2008)	+	!	+	+	+	!
Georgii et al. (2017)	!	!	+	+	+	!
Gluck et al. (2015)	+	-	-	+	!	-
Goldman et al. (2011)	+	!	+	!	!	!
Grundeis et al. (2017)	+	!	+	+	+	!
Heinitz et al. (2017)	+	!	!	+	+	!
Jauch-Chara et al. (2014)	+	!	+	!	!	!
Kekic et al. (2014)	+	!	!	+	+	!
Kekic et al. (2017)	+	+	+	+	+	+
Lapenta et al. (2014)	+	-	!	+	+	-
Ljubisavljevic et al. (2016)	+	-	!	+	+	-
Marron et al. (2019)	+	-	+	!	!	-
Mattavelli et al. (2019)	!	-	+	-	!	-
Max et al. (2020)	+	+	!	+	+	!
Montenegro et al. (2012)	!	-	+	!	!	-
Ray et al. (2017)	!	+	+	!	+	!
Ray et al. (2019)	+	+	+	-	+	-
Sedgmond et al. (2019)	+	+	+	+	+	+
To et al. (2018)	+	+	+	+	+	+
Vicario et al. (2020)	!	!	+	!	!	!

Judgement key: +, low risk; !, some concerns; -, high risk

D1, domain 1: randomisation process; D2, domain 2: deviations from intended interventions; D3, domain 3: missing outcome data; D4, domain 4: measurement of the outcome; D5, domain 5: selection of the reported results

6.4.3 Subjective Appetite

The subjective rating of hunger, fullness, desire to eat and prospective consumption are the most consistently measured variables in the reviewed research, particularly the rating of hunger, and are assessed across 18 of the 28 studies (Table 6-3). There was an overall lack of tDCS-related effect shown for measures of appetite across the reviewed studies (g = −0.12 to 0.09) (Table 6-5). This trivial effect size was also seen for "healthy" groups (g = 0.06 to 0.15) (Figure 6-3 and Figure 6-4), where a lack of change in scores, or increase in measures of hunger, is often shown (Table 6-3).

Table 6-5 Summary of meta-data for subjective appetite measures.

Measure	*g*	95% CI	Interpretation
Hunger	0.03	−0.23, 0.29	Trivial
Healthy	0.06	−0.32, 0.44	Trivial
Trait	0.08	−0.72, 0.88	Trivial
Prader Willi syndrome [b]	−1.03	−2.50, 0.43	Large
Disinhibited / Restrained eating [b]	0.06	−0.45, 0.58	Trivial
Bulimia Nervosa [b]	0.19	−0.25, 0.64	Trivial
Fullness [a]	−0.12	−0.52, 0.29	Trivial
Desire to Eat	0.05	−0.22, 0.31	Trivial
Healthy	0.15	−0.24, 0.54	Trivial
Trait	−0.08	−0.69, 0.52	Trivial
Disinhibited / Restrained eating [b]	0.09	−0.43, 0.60	Trivial
Frequent food cravings	−0.43	−1.11, 0.25	Small
Bulimia Nervosa [b]	0.09	−0.36, 0.53	Trivial
Prospective Consumption [a]	0.09	0.03, 0.15	Trivial

[a] *Includes healthy participants only.*

[b] *n = 1 study.*

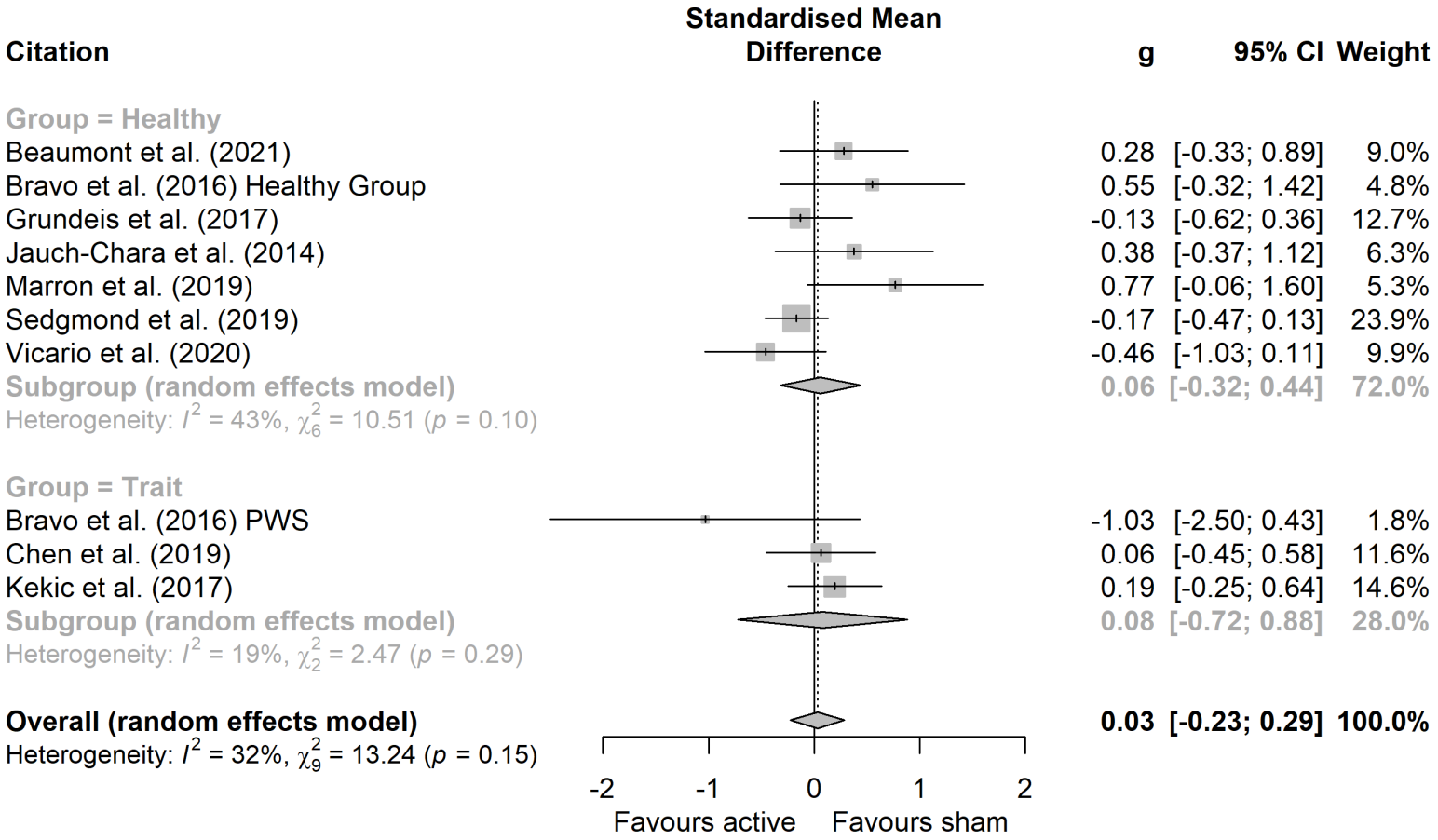


Figure 6-3 Forest plot showing overall and subgroup effect sizes for hunger scores.

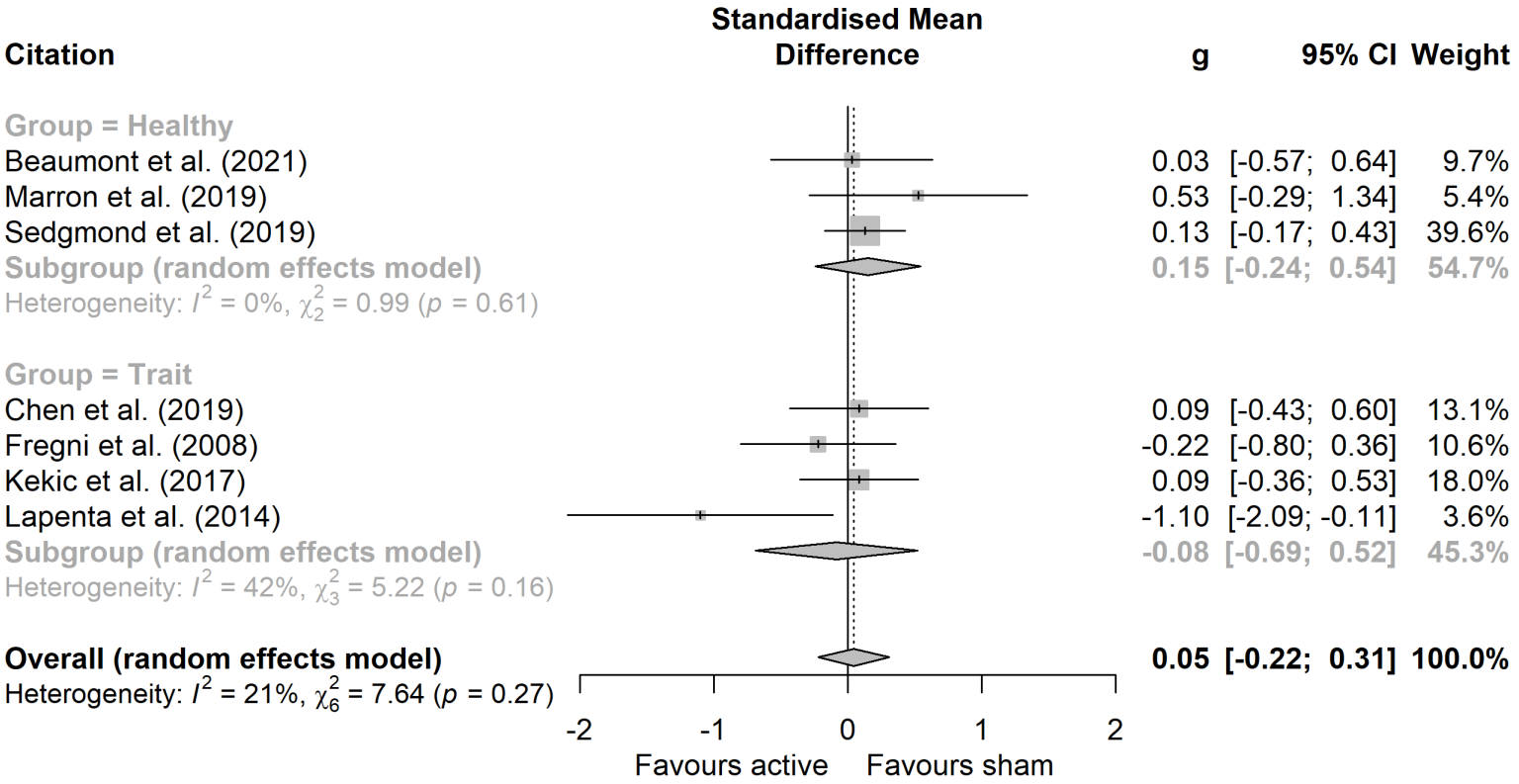


Figure 6-4 Forest plot showing overall and subgroup effect sizes for desire to eat scores.

Although Heinitz et al. (2017) found no difference in subjective appetite scores when delivering daily inpatient tDCS, they did observe reductions in hunger and the urge to eat following outpatient treatment and after adjusting for age and sex. This suggests that long stimulation duration (40 minutes) and repetition (15 sessions) may affect the subjective appetite sensations of individuals with obesity. A similar effect was shown in participants who were overweight, with reduced desire to eat following single session active versus sham tDCS, which was further reduced following isocaloric exercise (Montenegro et al., 2012). Although these studies include participants either considered or assumed to be “healthy”, neither fully measure or report the participants’ behaviour traits, and so it is difficult to identify what impact these traits may have on the change in subjective appetite scores.

When comparing these effects to those studies using populations with specific behavioural traits or conditions relating to a heightened hedonic response to food, an overall trivial effect size was seen (g = −0.08 to 0.08) (Figure 6-3 and Figure 6-4). However, greater effects were observed when considering those displaying specific traits associated with the subjective appetite measure. For example, in individuals with PWS who experience hyperphagia (Bravo et al., 2016), and appear to have hypoactivation of the DLPFC in response to food stimuli (Holsen et al., 2012), a large effect size was seen for hunger scores (g = −1.03; 95% CI = −2.50, 0.43) (Table 6-5). Additionally, the desire to eat was reduced in those who display frequent food cravings (g = −0.43; 95% CI = −1.11, 0.25). A similar comparison between “healthy” and trait populations cannot be made for fullness or prospective consumption scores, as all studies included in the analyses recruited “healthy” individuals.

There appeared to be an influence of COMT Val158Met polymorphism, whereby those who are carriers of the methionine (met) allele showed reduced appetite

following 16 sessions of active tDCS compared to no change in scores for non-carriers (Fassini et al., 2019). The COMT enzyme is important for dopaminergic neurotransmission (Tunbridge et al., 2007), and absence of the met allele is associated with reduced dopamine degradation which can increase the sensitivity to rewarding cues (Dreher et al., 2009). This altered dopamine transmission impacts activity within the DLPFC and executive functioning capabilities (Pomarol-Clotet et al., 2010; Ceaser et al., 2013). The findings by Fassini et al. (2019) suggest that absence of the met allele can inhibit the modulatory influence of tDCS. Indeed, COMT Val158Met polymorphism has previously been shown to impact the effects of stimulation (Wiegand et al., 2016). However, when Fassini et al. repeated their study in a further cohort of met carrier and non-carriers, they did not find a difference in subjective appetite scores (Fassini et al., 2020). Further data are required to fully understand the influence of COMT Val158Met polymorphism on the modulation of eating behaviour by tDCS.

Across studies, the fasting period and baseline subjective appetite levels were not well controlled. Fasting duration ranged from two to seven hours, with seven studies either not measuring/reporting fasting duration or not asking participants to fast (Montenegro et al., 2011; Kekic et al., 2014; Bravo et al., 2016; Heinitz et al., 2017; Kekic et al., 2017; Ray et al., 2017; Ray et al., 2019). Longer fasting periods can lead to heightened appetite and greater hedonic response to foods and related cues (Castellanos et al., 2009; Goldstone et al., 2009). No study has assessed the effects of differing fasting durations on eating-related outcome measures following tDCS, but the impact of these uncontrolled fasting periods cannot be excluded. It may be that the equivocal effects following tDCS are driven by greater baseline appetite levels, but only two papers included subjective appetite scores as covariates in statistical analyses (Ray et al., 2017; Beaumont et al., 2021). To identify a more

consistent effect of tDCS on subjective appetite and other eating-related behaviours, greater control of fasting duration and baseline appetite is required (Gibbons et al., 2014).

Across the reviewed studies, the effects of tDCS on measures of subjective appetite are not consistent, although the present meta-analysis shows a more promising effect in some populations. This may be due to these individuals experiencing abnormal levels of appetitive sensations or being unable to appropriately respond to these sensations (Rolls et al., 1992; Kissileff et al., 1996; Butler and Thompson, 2000; Wallace et al., 2015), with tDCS stabilising the response. It should also be noted that these subjective sensations, particularly hunger, are largely under homeostatic control (Blundell, 2006), and may be outside the modulatory influence of tDCS (Keller, 2017). Instead, other behaviours may be more important variables, particularly where these behaviours are related to the hedonic response to foods and require executive control mediated by the PFC. These potentially more malleable behaviours include food craving, food reward, and food consumption and will be discussed in the following sections.

6.4.4 Food Craving

This section will focus specifically on the measure of in-the-moment food craving as assessed via the FCQ-S (Cepeda-Benito et al., 2000). Food craving was measured in seven of the reviewed studies (Table 6-3). An additional six studies measured food craving as a proxy of explicit wanting (Fregni et al., 2008; Goldman et al., 2011; Lapenta et al., 2014; Burgess et al., 2016; Ray et al., 2017; Ray et al., 2019); these studies will be discussed in the following section.

As with subjective appetite, there is a lack of a consistent overall effect of stimulation on measures of food craving across studies (*g* = −0.08; 95% CI −0.28, 0.12) (Figure 6-5). Where these studies recruited those participants considered “healthy,” no change in food craving scores was observed when comparing anodal versus sham tDCS (*g* = −0.06; 95% CI = −0.29, 0.17). Of interest, although Ljubisavljevic et al. (2016) recruited “healthy” individuals they demonstrated that repeated sessions of tDCS were able to reduce food craving scores, and particularly the craving for fast-food, sweet and high-fat food groups. This may highlight a beneficial impact of multi-session designs on eating behaviour measures, which was also demonstrated for subjective appetite (Heinitz et al., 2017) (see section 6.4.3). Again, the authors did not fully describe the behavioural traits of their participants, and so the impact of these traits cannot be fully identified.

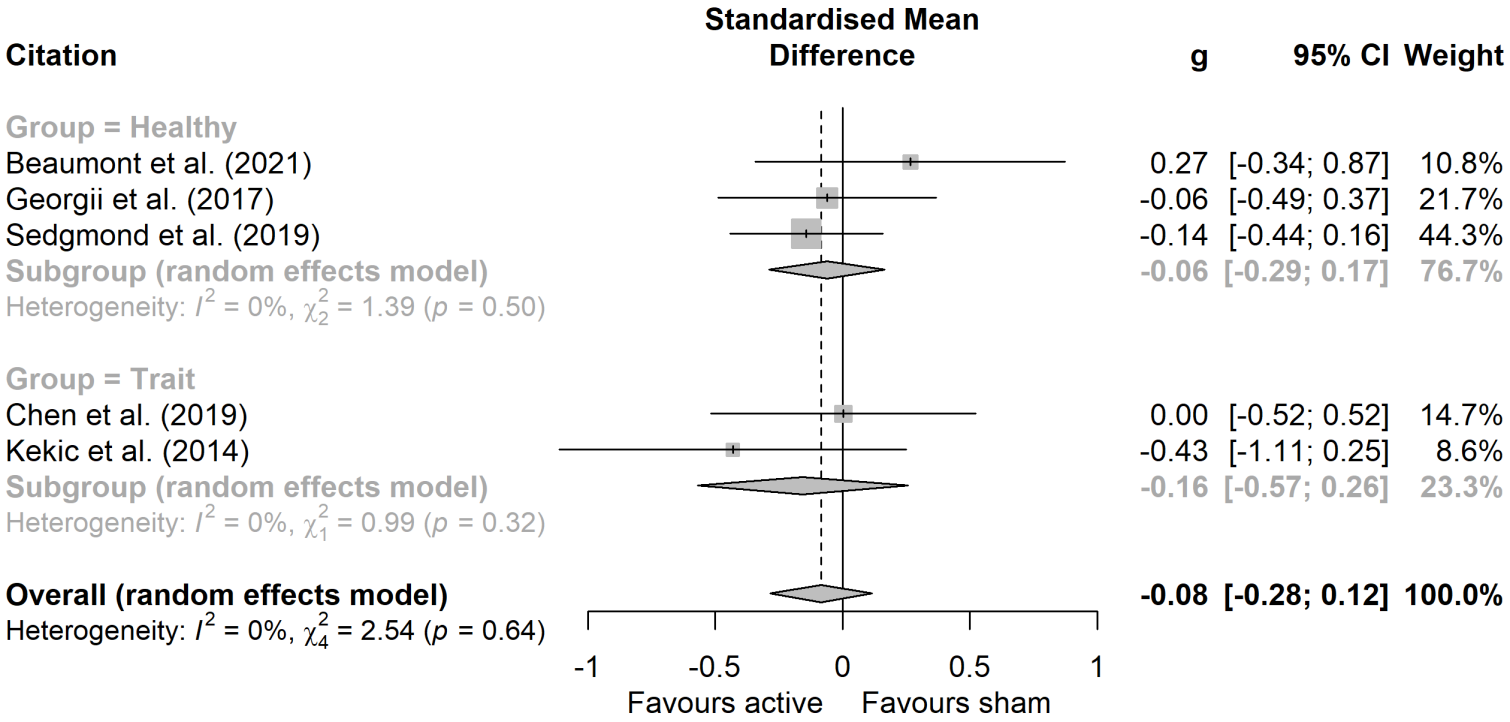


Figure 6-5 Forest plot showing overall and subgroup effect sizes for food craving (FCQ-S) scores.

The overall effect for trait groups shows only a trivial effect size (*g* = −0.16; 95% CI = −0.57, 0.26) (Figure 6-5). Of note, a small negative effect size was observed for those displaying frequent food cravings (*g* = −0.43; 95% CI = −1.11, 0.25), suggesting active protocols produce a more prominent reduction in food craving measures within this population (Table 6-6). This effect was not extended to those with disinhibited and restrained eating behaviour (*g* = 0.00; 95% CI = −0.52, 0.52). Finally, COMT Val158Met polymorphism did not appear to influence the effects of repeated-session tDCS on food craving scores, with no change in scores for met carriers and non-carriers when comparing active versus sham tDCS (Fassini et al., 2020).

Table 6-6 Summary of meta-data for food craving measures.

Measure	*g*	95% CI	Interpretation
Overall	−0.08	−0.31, 0.14	Trivial
Healthy	−0.06	−0.48, 0.35	Trivial
Trait	−0.16	−0.57, 0.26	Trivial
Disinhibited / Restrained eating [a]	0.00	−0.52, 0.52	Trivial
Frequent food cravings [a]	−0.43	−1.11, 0.25	Small

[a] *n = 1 study.*

A large proportion (62.5%) of studies recruited “healthy” individuals, with only single studies recruiting those experiencing frequent food cravings (Kekic et al., 2014), disinhibited restrained eaters (Chen et al., 2019), or those with COMT Val158Met polymorphism (Fassini et al., 2020). Across populations there are equivocal findings, with a more consistent effect in those experiencing frequent food cravings. When considering explicit wanting, which incorporates the sensation of food craving (Finlayson and Dalton, 2012b), the reduction in craving score in those who

experience frequent food cravings is consistently shown (*g* = −0.45; 95% CI = −1.03, 0.11) (see section 6.4.5).

This highlights the importance of recruiting participants who show specific behavioural trait susceptibility to the particular behavioural outcome of interest. For example, recruiting those who experience heightened food cravings when the study aims to reduce food cravings intensity. The lack of effect in "healthy" populations should not be surprising as these individuals are likely to experience infrequent food cravings, and when they do experience a craving they are likely able to sufficiently control their response to these (Joseph et al., 2011; Lowe et al., 2019).

6.4.5 Food Reward

Food reward can be measured as "liking" (perceived impact of a food or related cue on subject affect or pleasure) and "wanting" (subjective motivation that encompasses the desire, craving or awareness of the 'lack of something desirable') responses to food (Finlayson and Dalton, 2012b). Where liking operates on an explicit level (i.e., conscious, introspective), wanting can be expressed on both explicit and implicit (i.e., subconscious, automatic) levels (Finlayson and Dalton, 2012b; Dalton and Finlayson, 2014). These reward measures are important in the control of eating behaviour, as the presence of food cues or consumption of food results in a pleasure response that stimulates reward and motivation circuits within the brain that can override physiological need and promote overconsumption (Alonso-Alonso and Pascual-Leone, 2007; Havermans, 2011; Finlayson and Dalton, 2012b; Boswell and Kober, 2016; Kober and Boswell, 2018).

Across the reviewed studies, food reward was typically measured using a computer-based image task (CBIT), where participants were shown food images and asked to

respond to questions across VAS (e.g., "*Which food do you most want to eat now?*"). Fourteen studies measured food reward, mainly through measures of explicit wanting (Table 6-3). It should be noted that many of these tasks are not validated measures but are often created ad-hoc in response to study needs.

The overall effect of active versus sham tDCS on measures of explicit wanting (g = −0.10; 95% CI = −0.31, 0.11), explicit liking (g = 0.08; 95% CI = −0.05, 0.21), and implicit wanting (g = −0.06; 95% CI = −0.50, 0.37) show only trivial effect sizes (Table 6-7). These effect sizes are mirrored in "healthy" participant populations (g = 0.00 to 0.09). Although no effect of tDCS was found, Ray et al. (2019) did show that the expectation of receiving active tDCS led to reduced explicit wanting for foods. When this effect was removed from analyses, the effect size for overall (g = −0.01; 95% CI = −0.16, 0.14) and "healthy" groups (g = 0.09; 95% CI = −0.04, 0.22) increased, although remained trivial (Figure 6-6, Figure 6-7 and Figure 6-8). This emphasises the importance of controlled study designs and limiting the information shared with participants, with the aim of reducing the bias that expectation may have on the dataset.

Table 6-7 Summary of meta-data for food reward measures.

Measure	*g*	95% CI	Interpretation
Explicit Wanting			
With expectation effect	−0.10	−0.31, 0.11	Trivial
Without expectation effect	−0.01	−0.16, 0.14	Trivial
Healthy			
With expectation effect	−0.07	−0.46, 0.33	Trivial
Without expectation effect	0.09	−0.04, 0.22	Trivial
Trait	−0.12	−0.42, 0.19	Trivial
Binge eating	−0.19	−0.57, 0.19	Trivial
Frequent food craving	−0.45	−1.03, 0.11	Small
Bulimia Nervosa	0.13	−0.31, 0.58	Trivial
Explicit Liking	0.08	−0.05, 0.21	Trivial
Healthy	0.05	−0.53, 0.62	Trivial
Trait [a,b]	0.10	−0.34, 0.55	Trivial
Implicit Wanting	−0.06	−0.50, 0.37	Trivial
Healthy	0.00	−0.52, 0.53	Trivial
Trait	−0.19	−1.66, 1.29	Trivial
Frequent food craving	−0.54	−1.23, 0.15	Moderate
Anorexia, Bulimia or EDNOS [b]	0.31	−0.15, 0.78	Small

EDNOS, Eating disorders not otherwise specified.

[a] *Includes those with Bulimia Nervosa only.*

[b] *n = 1 study.*

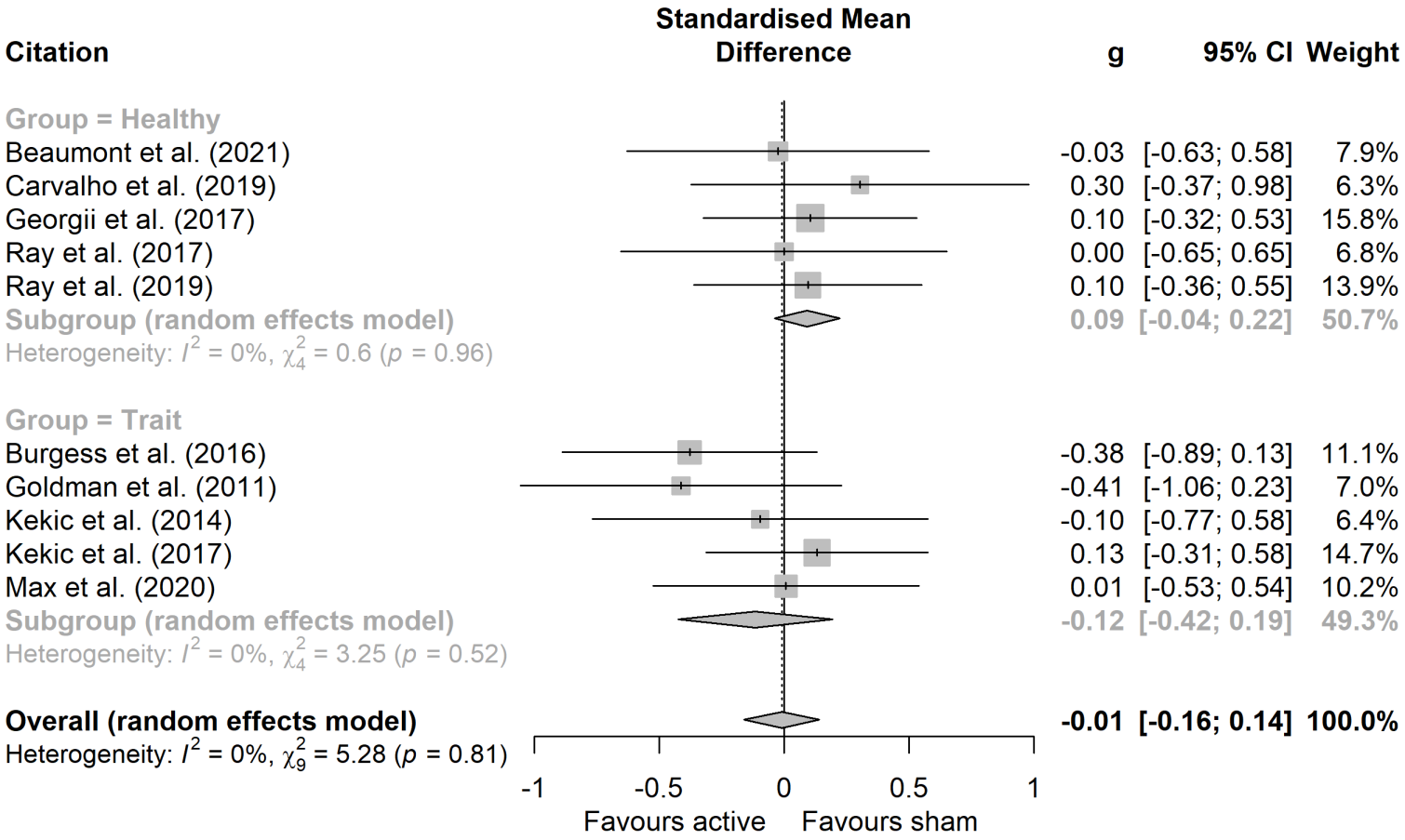


Figure 6-6 Forest plot showing overall and subgroup effect sizes for explicit wanting measures.

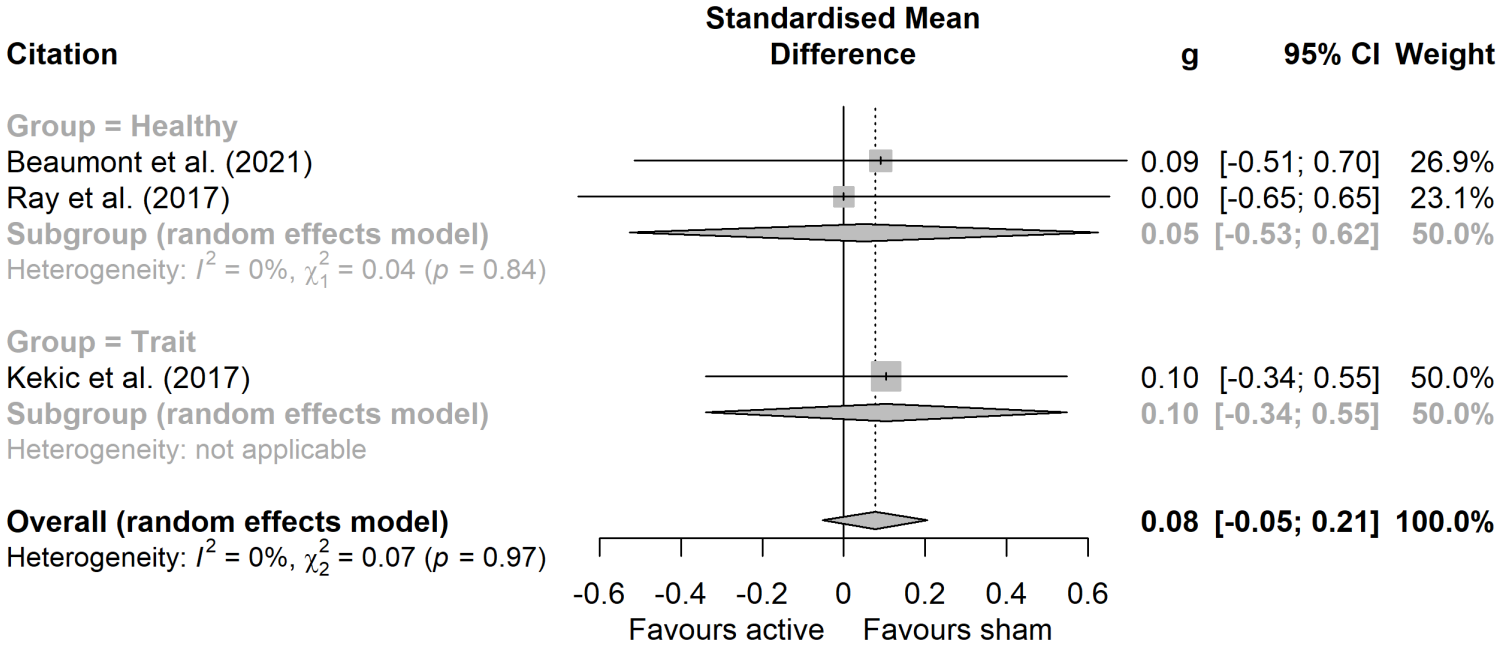


Figure 6-7 Forest plot showing overall and subgroup effect sizes for explicit liking measures.

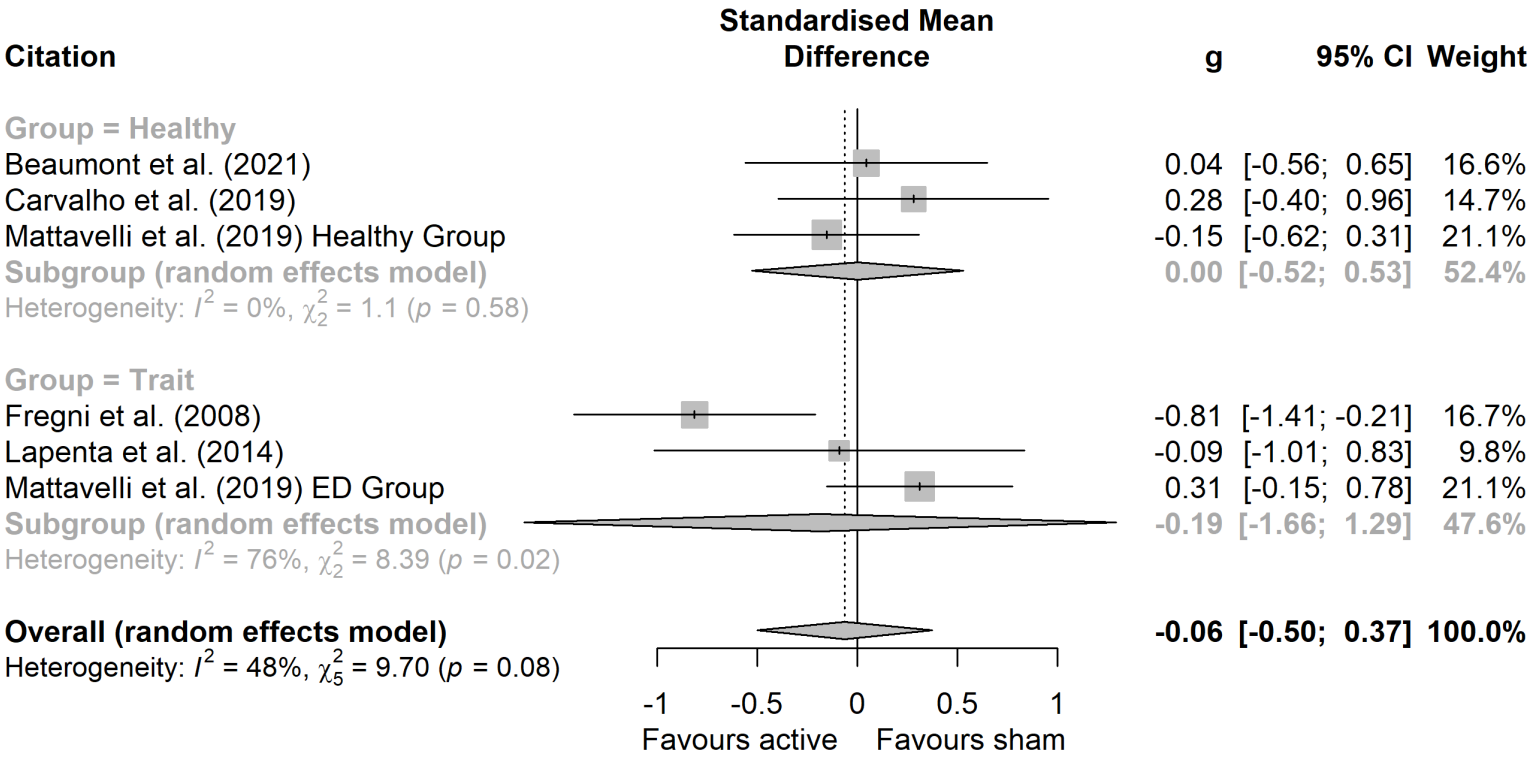


Figure 6-8 Forest plot showing overall and subgroup effect sizes for implicit wanting measures.

A more consistent pattern of effects on food reward measures appeared for trait groups. A small effect size was seen for both explicit (g = −0.12; 95% CI = −0.42, 0.19) and implicit wanting (g = −0.19; 95% CI = −1.66, 1.29) (Figure 6-6 and Figure 6-7). These effects were driven by individuals with binge eating or frequent food craving trait characteristics (Table 6-7), again who appear to have altered activity within the DLPFC (Karhunen et al., 2000; Boeka and Lokken, 2011). Burgess et al. (2016) showed reduced craving (explicit wanting) scores for desserts, savoury proteins and all-food categories in those with BED. In addition, Goldman et al. (2011) found reduced explicit liking and wanting, particularly for sweet foods, and highlighted an improved ability to resist foods in participants with frequent food cravings. Of note, there does not appear to be an effect of active tDCS in a heterogeneous sample of individuals with anorexia, bulimia or eating disorders not otherwise specified (EDNOS), with only a small positive effect size (Table 6-7).

Here studies that measure eye tracking are also included (Fregni et al., 2008; Lapenta et al., 2014; Max et al., 2020), as this can be used as a measure of reward sensitivity (Castellanos et al., 2009; Schag et al., 2013). Two studies tracked participants' eye movement while they were presented with a series of food and non-food images on a computer screen, and recruited those with frequent food cravings (Fregni et al., 2008; Lapenta et al., 2014). Although both studies showed reduced food craving intensity (g = −0.54; 95% CI = −1.23, 0.15) (Table 6-7), the significant reduction in fixation on food by Fregni et al. (2008) was not replicated by Lapenta et al. (2014). An additional study used an anti-saccade task, where participants were sat in front of a computer screen displaying a central cross; a food image was displayed on either the left or right side of the screen, and participants were required to look in the opposite direction as fast as possible (Max et al., 2020). The authors found a current intensity-dependent effect, where faster latency of anti-saccades

were shown following 2.0 mA, but not 1.0 mA, tDCS in participants with BED. This likely reflects low current density under 1.0 mA protocols (see section 3.4.4).

Although there appears to be a more consistent effect of tDCS on food reward, when compared to craving and subjective appetite, there are only a limited number of studies confirming these effects. A greater number of studies incorporating reward-based measures is needed, and these studies should focus on recruiting participants with deficits in the control of this reward, as these individuals are likely to be responsive to the modulatory effects of stimulation (Alonso-Alonso and Pascual-Leone, 2007). In addition, studies should focus on a more comprehensive measure of explicit and implicit components of reward and use validated measures such as the LFPQ.

6.4.6 Food Consumption

Total food consumption, often reported as caloric intake, was measured across 15 studies. Intake was primarily assessed through *ad libitum* buffets, with some studies using a vending machine paradigm (Gluck et al., 2015; Heinitz et al., 2017) or food recall (Fassini et al., 2020). The *ad libitum* buffets vary in quality, with many studies only providing participants with energy-dense, high-sugar and high-fat foods (e.g., chocolate, potato chips, cookies) (Fregni et al., 2008; Goldman et al., 2011; Kekic et al., 2014; Lapenta et al., 2014; Burgess et al., 2016; Ray et al., 2017; To et al., 2018; Ray et al., 2019). Although this type of buffet can be used to measure the amount of food consumed, it ignores the more qualitative nutrient and sensory aspects of food choice (Buckland and Dalton, 2018).

Studies that use highly palatable foods typically only provide three to four different food options, with only two studies providing a greater variety of 9 to 11 options

(Fregni et al., 2008; Lapenta et al., 2014). In addition, only a small number of studies included a greater selection of foods, incorporating healthier items (e.g., fruits, vegetables) with the more energy-dense foods (e.g., chocolate, potato chips), and providing 8 to 29 options (Jauch-Chara et al., 2014; Georgii et al., 2017; Grundeis et al., 2017; Sedgmond et al., 2019). It should be noted that providing a large variety of foods can lead to overconsumption through delayed satiation (Hetherington et al., 2006; Embling et al., 2021), as such the number of food options should be carefully considered. As well as providing a greater variety of foods, it is important to consider the liking for each food made available as this will likely drive the amount of the food consumed (Blundell et al., 2010; Buckland and Dalton, 2018). A limitation of many of the studies included in this review is that they do not measure or report participants' liking of the test foods.

In line with previous measures, there was a lack of overall effect of active versus sham tDCS on food consumption measures (g = −0.09; 95% CI = −0.31, 0.14), with a similar trivial effect in the "healthy" group (g = −0.08; 95% CI = −0.32, 0.16) (Table 6-8). As with explicit wanting, the expectation effect observed by Ray et al. (2019) led to greater effect sizes in favour of active tDCS. When this was removed from analyses, the effect in favour of active tDCS was reduced for both the overall (g = 0.01; 95% CI = −0.18, 0.20) and "healthy" groups (g = 0.05; 95% CI = −0.07, 0.17) (Figure 6-9). In comparison, a greater effect of active versus sham tDCS was seen in trait groups (g = −0.12; 95% CI = −0.76, 0.51), driven particularly by participants displaying frequent food cravings (g = −0.30; 95% CI = −1.32, 0.72) and binge eating traits (g = −0.23; 95% CI = −0.74, 0.28) (Table 6-8).

Table 6-8 Summary of meta-data for food consumption measures.

Measure	*g*	95% CI	Interpretation
Overall			
With expectation effect	−0.09	−0.31, 0.14	Trivial
Without expectation effect	0.01	−0.18, 0.20	Trivial
Healthy			
With expectation effect	−0.08	−0.32, 0.16	Trivial
Without expectation effect	0.05	−0.07, 0.17	Trivial
Trait	−0.12	−0.76, 0.51	Trivial
Binge eating [a]	−0.23	−0.74, 0.28	Small
Frequent food cravings	−0.30	−1.32, 0.72	Small
Restrained eating [a]	0.60	0.02, 1.18	Moderate

[a] *n = 1 study.*

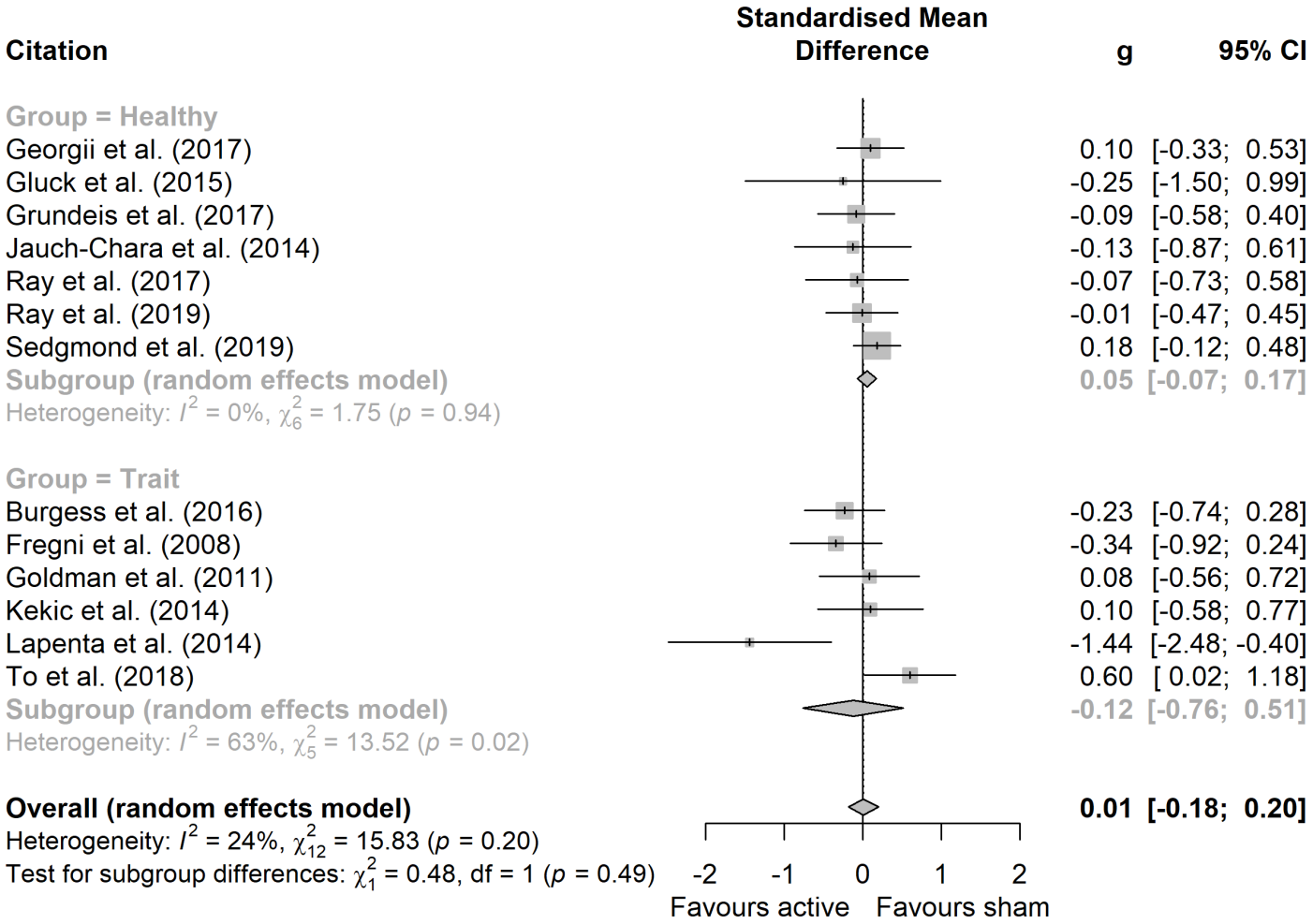


Figure 6-9 Forest plot showing overall and subgroup effect sizes for food consumption measures.

Although two studies found reduced *ad libitum* consumption when comparing active to sham tDCS in those who experience frequent food cravings (Fregni et al., 2008; Lapenta et al., 2014), this effect was not shown across further studies recruiting similar populations (Goldman et al., 2011; Kekic et al., 2014), with an increase in chocolate consumption in a cohort with specific cravings for chocolate (To et al., 2018). It is important to note that food craving is not correlated with food consumption (Burgess et al., 2016). However, where specific behavioural traits are evident (e.g., binge-type behaviour), heightened food cravings can lead to greater food intake (Ng and Davis, 2013). Therefore, it is possible that other eating behaviour traits are also influencing this discrepancy in effects.

Burgess et al. (2016) recruited participants with BED or subthreshold BED (i.e., meet all BED criteria with the exception of binge eating frequency), and found an 11% reduction in food consumption. However, when the authors replicated their study in participants with frank (non-binge eating) obesity, they did not find a main effect of active versus sham tDCS on food consumption (Ray et al., 2017). Only when specific behaviour traits were included as covariates in statistical analyses did an effect appear; males with intent to restrict or non-planning impulsiveness traits had a 13% reduction in the consumption of preferred foods. The studies that recruited participants experiencing frequent food cravings did not measure wider eating behaviour traits, and so a definitive effect of these wider traits on food consumption is not clear.

This effect on preferred versus less-preferred foods has been demonstrated across several studies (Burgess et al., 2016; Ray et al., 2017; Ray et al., 2019). Sedgmond et al. (2019) also found that the consumption of familiar healthier foods (carrots, grapes, rice cakes, breadsticks) was greater following active tDCS in a “healthy”

cohort. This again demonstrates the need for providing wider food options as part of an *ad libitum* buffet to account for differences in individual taste, preference and familiarity (Blundell et al., 2010; Buckland and Dalton, 2018). It is particularly difficult to determine the impact of behaviour traits on tDCS-mediated changes in food consumption across different food groups, as the studies that include a more varied buffet only recruit those participants deemed “healthy” (i.e., do not report a susceptibility to overconsumption). Future studies should identify the effects of a varied *ad libitum* buffet in a population susceptible to overconsumption, to determine whether the effects of tDCS on consumptive behaviours are specific to highly palatable foods or can modulate the consumption of wider food groups.

The vending machine paradigm involved unrestricted and *ad libitum* access to an automated vending machine for 23.5 hours per day as part of an inpatient facility (Gluck et al., 2015; Heinitz et al., 2017). The vending machines were filled with 40 foods that were pre-selected by each participant as the most preferred items from a larger group of foods. Participants were also given access to soda, juice, milk and condiments in addition to the pre-selected foods, and any food not consumed by the participant was recorded. This method of measuring food consumption is considered accurate, particularly in comparison to self-reported measures such as a food diary, with an ICC of 0.84 to 0.90 (Venti et al., 2010). In this vending machine paradigm, Gluck et al. (2015) and Heinitz et al. (2017) were able to demonstrate reduced food consumption when comparing active versus sham tDCS. However, this was only for particular food groups, being candy (Heinitz et al., 2017) or fat and soda (Gluck et al., 2015), and there was no repetition of effect for these specific food groups across the studies. Although both studies report successful blinding, 75% of those in the active group were able to correctly identify the condition they received (Gluck et al., 2015) and the effect of this bias on food consumption cannot be ruled out. This is an

important consideration, as Ray et al. (2019) found that the expectation of receiving active tDCS resulted in a 37.4% reduction in consumption, regardless of which condition the participants actually received.

Finally, Fassini et al. (2020) measured food consumption via recall. To increase the validity of this measure, the authors asked participants to complete a photo record book. The study did not find any difference in food consumption between stimulation groups. This may be due to the issues with accuracy and bias during food recall if not conducted in a standardised manner (Moshfegh et al., 2008), but may also be due to an inability of tDCS to modulate food consumption beyond the testing period. This technique has been shown to alter cortical activity for up to 90 minutes post-stimulation (Nitsche and Paulus, 2001), with the consumption of foods that were recalled likely being outside of this window.

The impact of tDCS on food consumption is less clear than other measures discussed in this chapter, and the efficacy of tDCS to reduce food consumption has previously been questioned (Heinitz et al., 2017; Lowe et al., 2017). Although there is some evidence to suggest tDCS can modulate energy intake for specific food groups, the method of measuring food consumption and other methodological considerations (e.g., participant characteristics, stimulation parameters) vary greatly between studies. In order to identify an effect of tDCS on consumptive behaviours, more consistent and carefully considered use of feeding practices is required.

6.5 Conclusion

The increased interest in tDCS for the modulation of eating behaviours has led to a wealth of methodological approaches. These varying approaches are important for initially identifying the impact of tDCS across measures and populations, but as this

research area grows it is important that researchers use more consistent methods. This chapter has considered how differences in participant characteristics can shape the effects of tDCS, and there appears a more evident and consistent effect of tDCS in those susceptible to hedonic-driven appetite. This is logical as neuroimaging studies of those with specific traits (e.g., binge eating symptomatology) show reduced activity in the PFC (Karhunen et al., 2000; Boeka and Lokken, 2011), and so these individuals may likely benefit from hyper-activation of this cortical region through tDCS. Several recent studies have acknowledged this trait-dependent effect (Burgess et al., 2016; Ray et al., 2017), and the lack of significant results for participants who do not show susceptibility to the rewarding components of food should not be surprising.

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

1. Focus on recruiting participants who are susceptible to hedonic-driven appetite (e.g., those experiencing frequent food craving or presenting with binge-type behaviour).
2. Recruit participants who have trait susceptibilities for the specific outcome measure of interest (e.g., recruit those with binge eating symptomatology when looking to modulate food reward).
3. To elucidate the potential link between enhanced executive functioning and improved appetite control following tDCS, studies should establish participants' baseline executive functioning capabilities and monitor any changes following stimulation.
4. Limit the information provided to participants during recruitment and screening procedures, as this can drive any effects on eating behaviour outcomes.

5. Incorporate a comprehensive group of validated measures, including explicit liking and explicit and implicit wanting.
6. Control fasting duration and measure baseline subjective appetite, even where subjective appetite is not a measure of interest.

It is acknowledged that the meta-analyses presented in this chapter consider the effects of heterogeneous tDCS parameters on eating behaviours. This may account for some variation in effect sizes, and it is important that the above recommendations are met with the use of effective stimulation parameters and appropriate study design (see Chapter 3). The understanding of population-based differences in tDCS effects is still limited, and more studies are needed to confirm the hypothesis that those with deficits in the control of eating behaviour will be responsive to the effects of tDCS. However, early data suggests this distinction may be apparent. This also highlights the further need for the publication of null effects, which will help identify potential cohorts that are unresponsive to tDCS. This should go hand-in-hand with the reporting of Bayesian statistics so study results can be quantified in terms of their agreement with the alternative or null hypotheses. The chapter that follows will further explore the potential eating behaviour trait-dependent effect of tDCS on eating-related measures, in those with binge-type behaviour.

Chapter 7 Study Two

The effects of prefrontal transcranial direct current stimulation (tDCS) on food preference and craving in participants who are susceptible to overeating and weight gain.

7.1 Chapter Summary

This chapter builds on the prior empirical study (Chapter 5) by exploring the eating behaviour trait-dependent effect of tDCS, as discussed in Chapter 6. The work presented in this chapter focusses on participants displaying binge-type behaviour, as indicated through the BES. This study is the first to compare the effects of tDCS in the fasted and fed states and extended the examination of a comprehensive and reliable measure of food reward under stimulation.

In addition to the BES, participants' eating behaviour traits were measured using the TFEQ, FCQ-T-r and the 7-day CoEQ. In line with the stimulation parameters recommendations in Chapter 3, and following those applied in Chapter 5, the present study applied anodal and sham tDCS over the right DLPFC at 2.0 mA for 20 minutes. Subjective appetite VAS, FCQ-S and the LFPQ were completed at baseline and post-tDCS. Participants were provided with a fixed-energy meal (cheese sandwich), with appetite VAS completed immediately post-meal. Additional VAS, FCQ-S and LFPQ measures repeated 20-minutes post-meal. A 24-hour version of the CoEQ was completed at the end of each test day.

There were no difference in pre- and post-tDCS scores across fullness ($p = 0.275$, $BF_{10} = 0.040$), prospective consumption ($p = 0.127$, $BF_{10} = 0.063$). desire to eat ($p = 0.247$, $BF_{10} = 0.054$) or FCQ-S measures ($p = 0.918$, $BF_{10} = 0.040$) when comparing active and sham tDCS. Only explicit liking ($p = 0.016$, $BF_{10} = 2.391$) and wanting for HFSW foods ($p = 0.008$, $BF_{10} = 0.145$) were significantly different across LFPQ measures, with increased scores following active tDCS. Similarly, hunger increased following active tDCS compared with a decrease following sham ($p = 0.020$, $BF_{10} = 0.188$). Of note, baseline hunger scores were significantly higher in at the start of the sham session; when these were included in covariate analyses for LFPQ scores,

the significant differences for HFSW explicit liking ($p = 0.161$, $BF_{10} = 1.074$) and wanting ($p = 0.138$, $BF_{10} = 0.810$) were removed. When post-meal scores were included in the analyses, similar pattern of effects were seen but effects were more consistently supported by anecdotal-to-extreme evidence in favour of the alternative hypothesis.

This data does not support the eating behaviour trait-dependent effect of tDCS discussed in the previous chapter, and results align with those presented in the prior empirical study. This may suggest that the eating behaviour traits displayed by the participants recruited to the present study did not reach the threshold required to be responsive to the modulatory influence of tDCS. Participants displayed mild-to-moderate binge eating behaviour, with prior work suggesting clinically-relevant binge eating (i.e., BED diagnosis) results in modulation of eating behaviour through tDCS. This may indicate that sub-clinical populations are not responsive to tDCS, and future work should look to directly compare the effects in clinical and sub-clinical populations displaying eating behaviour traits suggesting susceptibility to overconsumption and weight gain.

7.2 Introduction

In the previous empirical study (Chapter 5), no significant effects of tDCS on eating-related measures were found in a healthy weight cohort who displayed no susceptibility to overconsume. As discussed in Chapter 6, there appears to be an eating behaviour trait-dependent effect of tDCS on eating-related measures. Propensity to reward-driven, hedonic appetite can potentiate energy balance dysregulation, with the rewarding components of food overriding homeostatic mechanisms (Boswell and Kober, 2016; Kober and Boswell, 2018). This heightened hedonic appetite is associated with reduced executive functioning, and those exhibiting binge eating behaviours appear to have altered activity within the PFC (Karhunen et al., 2000; Boeka and Lokken, 2011). The right brain hypothesis of obesity proposes that a reduction of right DLPFC activity facilitates obesogenic behaviours through poor executive control of appetite (Alonso-Alonso and Pascual-Leone, 2007). Indeed, reduced activity within the DLPFC has been linked with greater impulsive behaviours and overconsumption (Gluck et al., 2017).

In two recent publications, Burgess and colleagues demonstrate this eating behaviour trait-dependent effect of tDCS with particular focus on those with binge-type behaviour (Burgess et al., 2016; Ray et al., 2017). Thirty participants who were obese and met the diagnostic criteria for BED underwent 20 minutes of 2.0 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, no effects were found 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, as supported by the meta-data presented in Chapter 6.

Consistent with this, previous research has demonstrated that individuals with BED are hyper-responsive to the rewarding aspects of food (Davis et al., 2009; Davis, 2013). The estimated prevalence of BED in the general population ranges from 0.7 to 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 to 20% of individuals with healthy weight, overweight or obesity, and constitutes a trait that can be assessed psychometrically and applied to a non-clinical population (Gormally et al., 1982). Similar to findings in individuals with BED, individuals with eating behaviour trait susceptibility to overconsumption (i.e., binge-type behaviour and emotional eating) have been found to be hyper-responsive to the rewarding aspects of food (Dalton et al., 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.

7.3 Aims and Hypotheses

The present study aimed to extend study one (Chapter 5) by identifying the effects of tDCS on food craving and reward in individuals displaying eating behaviour trait susceptibility to overconsumption, and specifically binge-type behaviours. Based on the findings discussed in Chapter 6, it was hypothesised that: (i) active tDCS would reduce participants' desire to eat and state food craving, and the rewarding valuation of sweet and high-fat foods; (ii) subjective appetite and preference measures will decrease following the consumption on a standardised meal under both active and sham tDCS, with greater reduction seen following active stimulation.

7.4 Method

7.4.1 Participant Recruitment

Total sample size of 17 was determined using an effect size f of 0.33, α error probability of 0.05, one group with three measurements, a correlation among repeated measures equal to 0.5, and non-sphericity correlation Є of 1; power equalled 0.82. A total of 24 participants were recruited via email, poster and participant database advertisements. As a consequence of the COVID-19 pandemic, attrition of seven participants occurred due to these individuals moving away from the Leeds area and being unable to continue with laboratory visits following the regional and national lockdowns. Hence, the retention rate was lower than in study one (Chapter 5).

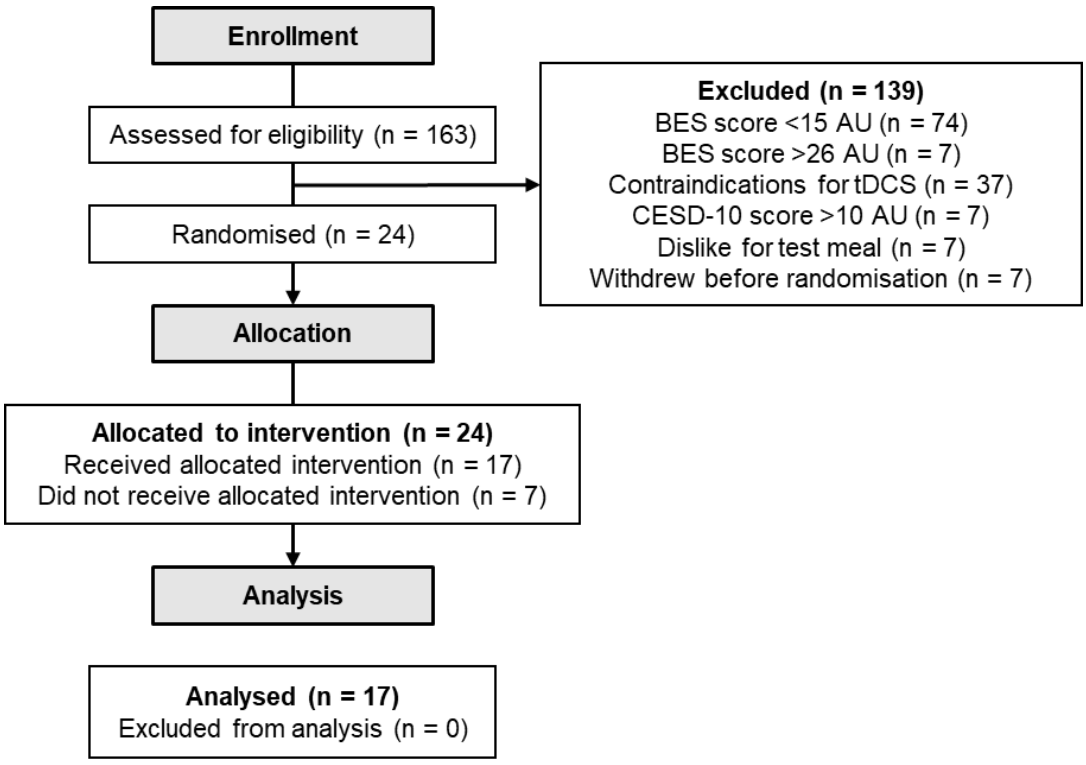


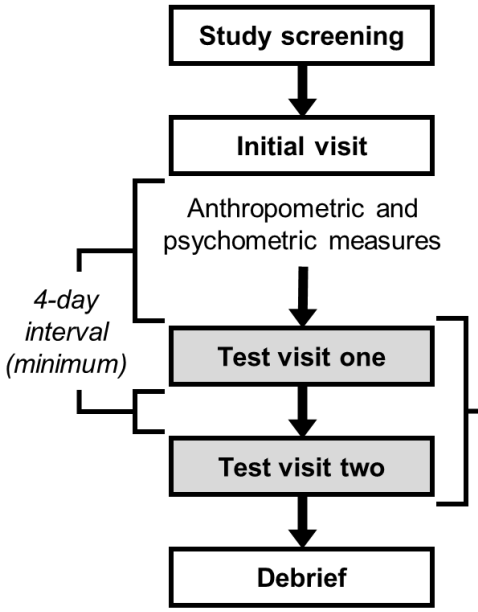
Figure 7-1 CONSORT diagram for recruitment of participants to study two.

Participants were classed as healthy adult participants (Category A; see Table 4-1). Eligible participants were between 18 and 60 years of age and met the generic inclusion criteria (see section 4.4) being: free of brain stimulation-specific contraindications, non-smokers, not pregnant nor wishing to conceive, not on medications, and did not present with depressive symptoms or low mood. In addition, participants were required to score between 15 and 26 on the BES. This highlights mild-to-moderate binge-type behaviour and individual susceptible to overconsumption and weight gain, but does not indicate a clinical disorder (Marcus et al., 1988; Dalton and Finlayson, 2014). Due to apparent differences in eating behaviour between males and females (Rolls et al., 1991), the present study recruited only female participants. The recruitment of female participants is in line with prior research (Kekic et al., 2014; To et al., 2018; Chen et al., 2019; Mattavelli et al., 2019), and allows comparisons of tDCS effects across studies. Finally, participants were required to like the fixed-energy test meal (i.e., a cheese sandwich providing 30% of the participant's RMR), with a score of four or greater for liking of the test meal on a seven-point scale (see section 4.9).

7.4.2 Procedure

Similar to study one (Chapter 5), individuals were initially screened with an online questionnaire, and eligible participants attended the laboratory on three separate occasions. Study procedures are detailed in Figure 7-2, and are similar to the prior empirical study (see 5.4.2) with the addition of a fixed-energy meal and subsequent assessment of appetite VAS, FCQ-S and LFPQ measures. Post-meal measures were conducted 10 minutes after consumption, with additional appetite VAS completed immediately (0 minutes) post-meal. Participants attended two near-identical testing sessions following a four-hour fast. Due to the significant differences found in subjective appetite measures in the prior study, greater control of this

fasting requirement was introduced. To ensure participants attended the test visits in a similar motivational state, they were asked to refrain from consuming any food or drink (other than water) in the four hours prior to attending the laboratory but to consume their normal breakfast before this fasting period (Gibbons et al., 2014; Meule, 2018a). Participants were asked to consume the same food on both test visit days, with adherence self-reported at the start of each visit. Finally, at the end of each test visit day, participants were required to complete a 24-hour CoEQ.



Time (min)	Task
0	Baseline questionnaire (adherence to fasting criteria)
2	Questionnaires (pre-tDCS): Appetite VAS → FCQ-S → LFPQ
17	tDCS preparatory procedures
22	Active or sham tDCS (randomised and counterbalanced)
42	Adverse Events Questionnaire
45	Questionnaires (post-tDCS): Appetite VAS → FCQ-S → LFPQ
60	Adverse Events Questionnaire
63	Standardised meal (cheese sandwich)
73	Appetite VAS (with additional question)
75	10-minute interval
85	Adverse Events Questionnaire
88	Questionnaires (post-meal): Appetite VAS → FCQ-S → LFPQ
103	Adverse Events Questionnaire
At end of day: Control of Eating Questionnaire, 24-hour version	

Figure 7-2 Study two procedure outline. FCQ-S, Food Craving Questionnaire-State; LFPQ, Leeds Food Preference Questionnaire; min, minute; tDCS, transcranial direct current stimulation; VAS, visual analogue scale.

7.4.3 Additional Ethical Considerations and Changes to Study

In light of the COVID-19 pandemic, the present study was adjusted to mitigate the risk of virus transmission while facilitating data collection. An updated risk assessment was completed before continuing with data collection, which was reviewed and approved by an external health and safety consultant. In addition to the recruitment criteria detailed in section 7.4.1, potential participants were screened to determine those at high risk of COVID-related complications; these individuals were not permitted to participate in the present study. As it is unclear how NIBS could interact with COVID-19, anyone with the virus or aftereffects were excluded from participation. In the event that a participant or researcher presented with COVID symptoms, a log of all visits to the laboratory was maintained so that other individuals who had come into contact with the infected individual could be notified. All study procedures followed appropriate institutional and governmental COVID-19 recommendations, including social distancing (where possible), regular handwashing and sanitising, use of face coverings and shields, and thorough cleaning of equipment and touchpoints.

7.4.4 Data Analysis

Mean and SD were calculated for each time point (baseline, post-tDCS and post-meal) under both active and sham conditions. To assess normality of data, Shapiro-Wilks tests were completed. FCQ-S and LFPQ data were analysed using two (condition; active and sham) by three (time point; baseline, post-tDCS and post-meal) repeated measures ANOVA. Appetite VAS scores were analysed using two (condition; active and sham) by four (time point; baseline, post-tDCS, 0 minutes post-meal, and 10 minutes post-meal) repeated measures ANOVA. Additional ANOVAs were completed without the post-meal data to compare the pre- and post-tDCS effects for comparison with the findings discussed in Chapter 5. Partial eta

squared (η_p^2) were used to indicate ANOVA effect size. Pair-wise comparisons with Bonferroni corrections were used to determine post-hoc significant effects.

To control for the observed difference in hunger scores at baseline, ANCOVA were performed to determine whether significant changes in measures were driven by baseline hunger. Paired-samples t-tests were used to compare differences in adverse events. Non-parametric pair-wise comparisons were analysed using Wilcoxon signed-rank test. To interpret findings and assess strength of evidence in support of the experimental or null hypothesis, Bayesian statistics were computed and interpreted using the classification scheme by Lee and Wagenmakers (2013) (Table 4-5). All statistical analyses were performed using JASP version 0.16.2.0 (University of Amsterdam, Amsterdam, The Netherlands).

7.5 Results

7.5.1 Missing Data

Data for the 24-hour CoEQ were missing for three participants due to losing the questionnaire (n = 1 participant, 1 questionnaire), or loss of contact during the COVID-19 pandemic (n = 2 participants, 3 questionnaires). Due to technical issues, data for the LFPQ were missing for the post-tDCS time point in the active session for one participant.

7.5.2 Participant Characteristics

Demographic, anthropometric and eating behaviour trait characteristics are displayed in Table 7-1. Participants were mainly healthy weight (n = 9), with six participants classified as overweight, and two participants classified as obese. All participants had a waist-to-hip ratio above the recommended levels (range: 1.1 to 1.4 AU) (World Health Organisation, 2008). Most participants (n = 12) had FCQ-T-r

scores above the cut-off for clinically relevant trait cravings (range: 44 to 82 AU), with BES scores suggesting mild (n = 2; range: 15 to 17 AU) and moderate (n = 15; range: 18 to 26) binge eating behaviour. In comparison with the participants in study one (Chapter 5), participants in the present study presented with lower craving control scores, and higher craving for sweet foods on the 7-day version of the CoEQ.

Table 7-1 Summary of participant demographic, anthropometric and psychometric characteristics.

		n (%)
Ethnicity	White	12 (70.6)
	Asian or Asian British	3 (17.6)
	Mixed or multiple ethnicity	2 (11.8)
Education	Attained university degree	8 (47.1)
	Not attained university degree	9 (52.9)
		mean ± SD
Age (years)		23 ± 7
Height (cm)		164.8 ± 9.0
Weight (kg)		69.1 ± 12.0
BMI ($kg \cdot m^{-2}$)		25.4 ± 3.8
Body fat (kg)		45.3 ± 4.7
Body fat (%)		33.4 ± 5.9
Waist circumference (cm)		82.2 ± 9.5
Hip circumference (cm)		102.8 ± 8.4
Waist-to-Hip Ratio (AU)		1.3 ± 0.1
CESD-10 (AU)		9 ± 5
BES score (AU)		21 ± 4
FCQ-T-r (AU)		57 ± 10
TFEQ Cognitive Restraint (AU)		10 ± 4
TFEQ Disinhibition (AU)		11 ± 3
TFEQ Hunger (AU)		8 ± 3
CoEQ (7-day) Craving Control (mm)		48 ± 20
CoEQ (7-day) Craving for Sweet Foods (mm)		49 ± 25
CoEQ (7-day) Craving for Savoury Foods (mm)		58 ± 21
CoEQ (7-day) Positive Mood (mm)		45 ± 10

AU, arbitrary unit; BES, Binge Eating Scale BMI, Body Mass Index; CESD-10, Centre for Epidemiologic Studies Short Depression Scale; CoEQ, Control of Eating Questionnaire; FCQ-T-r, Food Craving Questionnaire-Trait reduced form; TFEQ, Three Factor Eating Questionnaire.

7.5.3 Standardised Meal

The composition, energy content and nutritional content of the cheese sandwich are displayed in Table 7-2 and Table 7-3. These values were calculated based on the composition data from each food item provided by the manufacturer (see section 4.9). Overall, participants rated the meal as moderately pleasant (active session 62.3 ± 19.7 mm, sham session 64.4 ± 20.7 mm), with no difference in score between active and sham conditions ($t_{(16)}$ = 0.874, p = 0.395, BF_{10} = 0.348). There was also no difference in consumption of water during both active (346 ± 273 ml) and sham sessions (378 ± 327 ml) (z = 0.052, p = 0.979). Consumption of the test meal had the expected effects on study measures; hunger, prospective consumption, desire to eat and FCQ-S scores were all reduced following consumption, with fullness VAS scores increasing after consumption (see sections 7.5.4 and 7.5.5).

Table 7-2 Ingredient composition and total energy content of the cheese sandwich (mean ± SD).

	Weight (g)	Energy (kcal)	% Total Energy
Total sandwich	136.6 ± 10.6	434.3 ± 43.4	-
White bread	75.9 ± 2.7	181.4 ± 6.6	42.2 ± 4.4
Cheddar cheese	51.7 ± 8.8	214.9 ± 36.7	49.2 ± 3.7
Sunflower spread	9.0 ± 1.5	37.9 ± 6.5	8.7 ± 0.7

g, grams; kcal, kilocalories.

Table 7-3 Composition and nutritional content of the cheese sandwich.

	Weight (g)	Energy (kcal)	% Total Energy
Total fat	23.80 ± 3.78	214.2 ± 34.0	49.0 ± 3.1
Saturated fat	12.64 ± 2.10		
Carbohydrates	35.56 ± 1.26	142.2 ± 5.0	33.1 ± 3.3
Sugar	2.20 ± 0.08		
Fibre	1.75 ± 0.06		
Protein	19.11 ± 2.21	76.4 ± 8.9	17.6 ± 0.3
Salt	1.70 ± 0.18		

g, grams; kcal, kilocalories.

7.5.4 Appetite Visual Analogue Scales

Despite no difference in fasting duration when comparing active (5.39 ± 2.87 hours) and sham conditions (5.08 ± 2.58 hours) ($t_{(16)}$ = 0.888, p = 0.215, BF_{10} = 0.351), hunger scores were significantly higher at baseline in the sham tDCS session (z = −2.130, p = 0.035, BF_{10} = 2.806) (Table 7-4). There were no differences when comparing active to sham protocols for hunger ($F_{(1.953, 29.301)}$ = 2.926, p = 0.071, η_p^2 = 0.163), fullness ($F_{(3, 45)}$ = 0.502, p = 0.683, η_p^2 = 0.045), prospective consumption ($F_{(3, 45)}$ = 0.704, p = 0.554, η_p^2 = 0.032), or desire to eat scores ($F_{(3, 45)}$ = 0.777, p = 0.513, η_p^2 = 0.049) (Table 7-4). However, each of these comparisons is supported by extreme evidence for the alternative hypothesis (hunger BF_{10} = 2.009e+12, fullness BF_{10} = 9.363e+12, prospective consumption BF_{10} = 5.815e+9, and desire to eat BF_{10} = 105,758.472).

Table 7-4 Mean ± SD data for appetite VAS scores (n = 17).

		Hunger (mm)	Fullness (mm)	Prospective Consumption (mm)	Desire to Eat (mm)
Baseline (pre-tDCS)	Active tDCS	49.1 ± 25.9	32.1 ± 18.0	52.9 ± 21.2	50.6 ± 27.8
	Sham tDCS	62.1 ± 18.0	25.0 ± 18.7	57.8 ± 17.2	56.5 ± 28.0
Post-tDCS	Active tDCS	56.3 ± 23.8	28.3 ± 18.2	59.1 ± 17.4	60.4 ± 20.7
	Sham tDCS	56.5 ± 25.9	28.6 ± 20.9	58.8 ± 23.2	56.7 ± 25.9
0 minutes post-meal	Active tDCS	27.9 ± 21.1	61.9 ± 21.7	33.5 ± 18.8	32.6 ± 24.6
	Sham tDCS	30.8 ± 23.1	60.9 ± 20.8	36.0 ± 20.1	34.5 ± 25.7
10 minutes post-meal	Active tDCS	27.0 ± 19.2	64.3 ± 17.5	33.1 ± 18.9	34.8 ± 21.1
	Sham tDCS	29.9 ± 21.2	59.7 ± 18.5	37.0 ± 22.8	31.2 ± 24.4

Of interest, while hunger levels were higher at the start of the sham session, there was a significant change pre- to post-tDCS where hunger levels following active tDCS increased to match those of post-sham stimulation ($F_{(1, 15)}$ = 6.796, p = 0.020, η_p^2 = 0.312, BF_{10} = 0.188). When controlling for baseline hunger, this effect was no longer significant ($F_{(1, 30)}$ = 0.610, p = 0.441, η_p^2 = 0.020, BF_{10} = 0.680). No significant differences were seen when comparing active and sham tDCS for measures of fullness ($F_{(1, 15)}$ = 1.282, p = 0.275, η_p^2 = 0.079, BF_{10} = 0.040), prospective consumption ($F_{(1, 15)}$ = 2.606, p = 0.127, η_p^2 = 0.148, BF_{10} = 0.063) and desire to eat ($F_{(1, 15)}$ = 1.452, p = 0.247, η_p^2 = 0.088, BF_{10} = 0.054), with Bayes factors suggesting moderate-to-strong evidence in favour of the null hypothesis.

7.5.5 Food Craving Questionnaire-State

When comparing data across all three time points, there was no difference in food craving scores following active (baseline 44.2 ± 10.1 AU, post-tDCS 43.5 ± 14.5 AU, post-meal 36.4 ± 10.7 AU) versus sham protocols (baseline 46.5 ± 7.4 AU, post-tDCS 45.4 ± 10.7 AU, post-meal 34.9 ± 8.9 AU) ($F_{(2, 32)}$ = 0.852, p = 0.436, η_p^2 = 0.051) (Figure 7-3). However, Bayes factor analysis revealed extreme evidence in favour of the alternative hypothesis (BF_{10} = 985.182). However, when post-meal data were removed from analyses, the effect remained non-significant ($F_{(1, 16)}$ = 0.011, p = 0.918, η_p^2 < 0.001) but Bayes factors suggest strong evidence in favour of the null hypothesis (BF_{10} = 0.040).

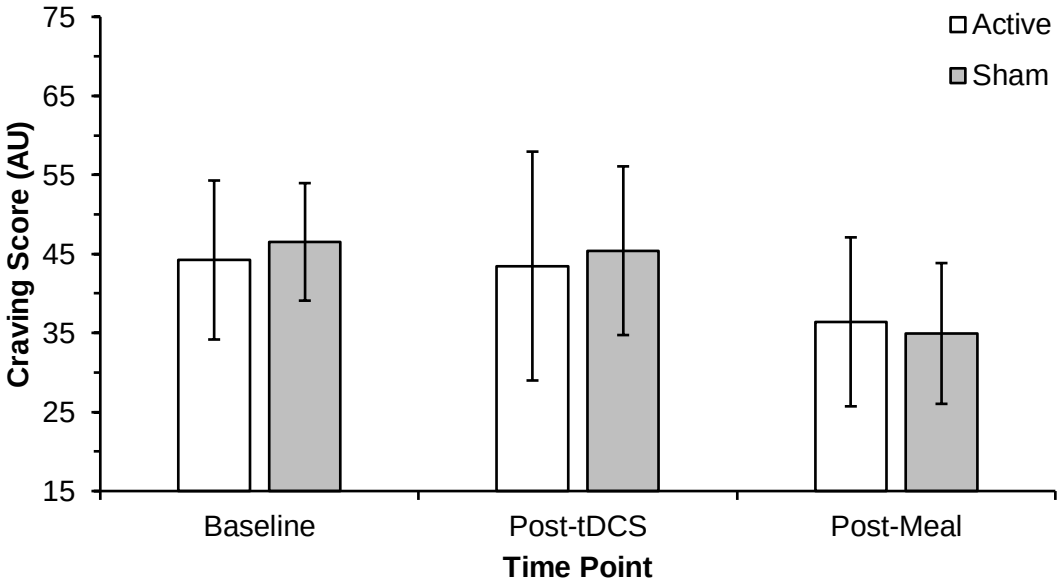


Figure 7-3 Mean ± SD food craving scores (n = 17).

7.5.6 Control of Eating Questionnaire (24-hour version)

Scores for craving control (active 59.1 ± 18.4 mm, sham 59.0 ± 20 mm) ($t_{(13)}$ = 0.494, p = 0.629, BF_{10} = 0.300) and craving for sweet foods (active 38.8 ± 20.1 mm, sham 39.2 ± 20.1 mm) ($t_{(13)}$ = 0.512, p = 0.617, BF_{10} = 0.303) were not significantly different between active and sham conditions (Figure 7-4). Craving for savoury foods approached significance (active 45.3 ± 17.9 mm, sham 49.4 ± 20.6 mm) ($t_{(13)}$ = 2.128, p = 0.053), but the effect was only supported by anecdotal evidence in favour of the alternative hypothesis (BF_{10} = 1.505). However, positive mood scores were significantly lower following active (47.1 ± 10.1 mm) compared with sham tDCS (51.5 ± 11.0 mm) (z = −2.271 13.000, p = 0.025, BF_{10} = 5.023).

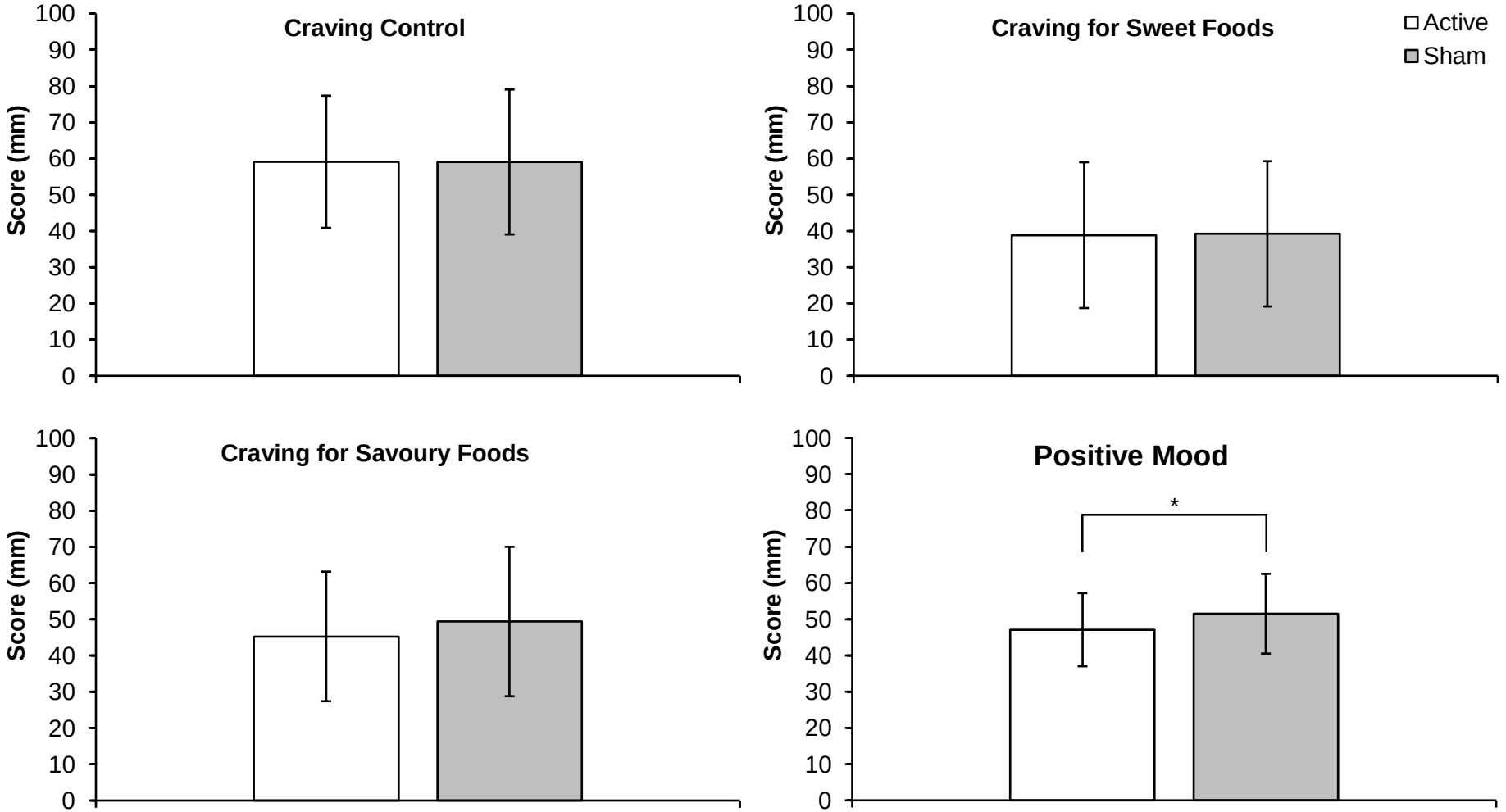


Figure 7-4 Comparison of CoEQ (24-hour version) scores following active and sham tDCS (n = 17). * $p < 0.05$.

7.5.7 Leeds Food Preference Questionnaire

Only explicit liking for HFSW was significantly different between conditions, with scores increasing following active versus sham tDCS ($F_{(2, 30)}$ = 6.814, p = 0.008, η_p^2 = 0.312, BF_{10} = 356.532) (Table 7-5). Explicit wanting for HFSW foods followed a similar pattern as explicit liking scores, but this only neared significance ($F_{(1.460, 21.897)}$ = 3.715, p = 0.053, η_p^2 = 0.199, BF_{10} = 6.273) (Table 7-6). Implicit wanting for this food category did not differ between active and sham conditions ($F_{(1.339, 20.083)}$ = 0.598, p = 0.495, η_p^2 = 0.038, BF_{10} = 0.020) (Table 7-7).

Table 7-5 Mean ± SD data for explicit liking (n = 17).

		Baseline (mm)	Post-tDCS (mm)	Post-meal (mm)
Active	HFSA	65.3 ± 18.9	65.5 ± 20.5	52.8 ± 23.3
	LFSA	52.6 ± 12.5	47.6 ± 19.6	39.0 ± 18.8
	HFSW	57.4 ± 13.7 *	62.1 ± 15.2 *	55.9 ± 14.9 *
	LFSW	63.5 ± 13.1	64.8 ± 13.0	63.5 ± 16.2
	FAB	3.3 ± 17.7	7.7 ± 11.8	3.1 ± 11.7
	TAB	1.5 ± 10.2	6.9 ± 16.6	13.8 ± 19.6
Sham	HFSA	69.2 ± 17.8	70.4 ± 19.9	50.2 ± 24.5
	LFSA	56.7 ± 15.1	55.1 ± 16.6	40.0 ± 18.3
	HFSW	68.4 ± 11.8 *	65.3 ± 15.9 *	51.0 ± 18.6 *
	LFSW	68.7 ± 11.8	66.2 ± 11.3	58.6 ± 14.9
	FAB	6.1 ± 12.8	7.2 ± 15.5	1.4 ± 14.7
	TAB	5.6 ± 13.4	3.0 ± 8.1	9.7 ± 16.4

HFSA, high-fat savoury; LFSA, low-fat savoury; HFSW, high-fat sweet; LFSW, low-fat sweet; FAB, fat appeal bias; TAB, taste appeal bias.

** p < 0.05 for comparison between active and sham protocols.*

Table 7-6 Mean ± SD data for explicit wanting (n = 17).

		Baseline (mm)	Post-tDCS (mm)	Post-meal (mm)
Active	HFSA	62.4 ± 19.7	63.5 ± 23.2	45.6 ± 24.3
	LFSA	49.5 ± 16.8	48.1 ± 18.8	34.2 ± 17.4
	HFSW	52.9 ± 16.6	58.2 ± 16.7	47.2 ± 18.6
	LFSW	60.7 ± 13.9	64.9 ± 13.4	54.9 ± 18.4
	FAB	2.6 ± 15.2	4.4 ± 13.2	1.9 ± 14.9
	TAB	0.9 ± 12.6	5.8 ± 17.2	11.1 ± 17.4
Sham	HFSA	65.9 ± 18.8	67.8 ± 23.5	42.8 ± 27.1
	LFSA	53.0 ± 17.5	54.5 ± 17.2	36.5 ± 20.2
	HFSW	62.0 ± 16.6	57.2 ± 20.5	45.1 ± 22.2
	LFSW	63.3 ± 10.0	61.4 ± 14.3	48.4 ± 21.0
	FAB	5.8 ± 16.4	4.6 ± 15.8	1.5 ± 15.2
	TAB	3.2 ± 11.8	−1.8 ± 10.8	7.1 ± 13.2

HFSA, high-fat savoury; LFSA, low-fat savoury; HFSW, high-fat sweet; LFSW, low-fat sweet; FAB, fat appeal bias; TAB, taste appeal bias.

Table 7-7 Mean ± SD data for implicit wanting (n = 17).

		Baseline (AU)	Post-tDCS (AU)	Post-meal (AU)
Active	HFSA	18.4 ± 24.5	21.5 ± 25.5	7.7 ± 25.7
	LFSA	−20.3 ± 21.6	−14.6 ± 23.9	−16.5 ± 24.3
	HFSW	−8.6 ± 15.6	−10.4 ± 16.0	−5.3 ± 15.4
	LFSW	10.4 ± 27.7	3.5 ± 28.8	14.2 ± 28.7
	FAB	9.9 ± 22.8	11.1 ± 24.2	2.3 ± 26.3
	TAB	1.9 ± 28.3	−6.9 ± 31.5	8.9 ± 32.9
Sham	HFSA	18.6 ± 31.8	22.2 ± 25.0	7.5 ± 25.1
	LFSA	−12.6 ± 23.3	−7.0 ± 19.1	−18.1 ± 21.0
	HFSW	−5.9 ± 22.9	−13.8 ± 14.4	−5.0 ± 25.0
	LFSW	−0.2 ± 24.6	−1.4 ± 22.6	15.7 ± 19.5
	FAB	12.7 ± 28.3	8.5 ± 25.0	2.5 ± 16.8
	TAB	−6.0 ± 35.9	−15.2 ± 24.1	10.7 ± 37.4

AU, arbitrary unit; HFSA, high-fat savoury; LFSA, low-fat savoury; HFSW, high-fat sweet; LFSW, low-fat sweet; FAB, fat appeal bias; TAB, taste appeal bias.

When considering explicit liking for the other food categories, there were no differences observed for HFSA ($F_{(2, 30)}$ = 1.113, p = 0.342, η_p^2 = 0.069, BF_{10} = 880.990), LFSA ($F_{(2, 30)}$ = 0.756, p = 0.478, η_p^2 = 0.048, BF_{10} = 10,368.165), or LFSW foods ($F_{(2, 30)}$ = 2.685, p = 0.085, η_p^2 = 0.152, BF_{10} = 0.162). Similarly, there were no significant effects observed for the explicit wanting of HFSA ($F_{(2, 30)}$ = 0.967, p = 0.392, η_p^2 = 0.061, BF_{10} = 31,477.412), LFSA ($F_{(2, 30)}$ = 0.254, p = 0.778, η_p^2 = 0.017, BF_{10} = 1,266.114), or LFSW foods ($F_{(2, 30)}$ = 1.969, p = 0.157, η_p^2 = 0.116, BF_{10} = 8.553). Implicit wanting scores for HFSA ($F_{(2, 30)}$ = 0.016, p = 0.984, η_p^2 = 0.001, BF_{10} = 0.989), LFSA ($F_{(2, 30)}$ = 1.483, p = 0.243, η_p^2 = 0.090, BF_{10} = 0.261), and LFSW foods ($F_{(1.477, 22.148)}$ = 1.586, p = 0.227, η_p^2 = 0.096, BF_{10} = 0.370) were not significantly

different between conditions, and these effects were supported by anecdotal-to-moderate evidence in favour of the null hypothesis.

When considering FAB scores, there were no differences when comparing active and sham tDCS across measures of explicit liking ($F_{(2, 30)}$ = 0.775, p = 0.470, η_p^2 = 0.049, BF_{10} = 0.033), explicit wanting ($F_{(2, 30)}$ = 0.663, p = 0.523, η_p^2 = 0.042, BF_{10} = 0.008), or implicit wanting ($F_{(2, 30)}$ = 0.460, p = 0.636, η_p^2 = 0.030, BF_{10} = 0.027). There were no significant effects observed for TAB scores across explicit liking ($F_{(2, 30)}$ = 2.341, p = 0.114, η_p^2 = 0.135, BF_{10} = 2.053), explicit wanting ($F_{(2, 30)}$ = 2.663, p = 0.086, η_p^2 = 0.151, BF_{10} = 0.644), and implicit wanting measures ($F_{(1.338, 20.007)}$ = 0.807, p = 0.414, η_p^2 = 0.051, BF_{10} = 2.808).

A similar pattern of effects were observed when comparing only pre- and post-tDCS scores across all measures (Table 7-8). No significant effects were observed across measures, with the exception of explicit liking and wanting for HFSW foods. For both explicit liking and wanting, the preference for HFSW foods increased following active tDCS and decreased following sham tDCS. To determine whether these significant effects were driven by the difference in baseline hunger, ANCOVA were performed; the difference between pre- and post-tDCS was no longer significant when controlling for hunger (explicit liking $F_{(1, 30)}$ = 2.061, p = 0.161, η_p^2 = 0.064, BF_{10} = 1.074; explicit wanting $F_{(1, 30)}$ = 2.319, p = 0.138, η_p^2 = 0.072, BF_{10} = 0.810). Across most measures, Bayes factors suggest anecdotal-to-strong evidence in favour of the null hypothesis. Only explicit liking for LFSA and HFSW foods and the implicit wanting for LFSA were supported by evidence in favour of the alternative hypothesis, but the strength of evidence was only anecdotal (Table 7-8).

Table 7-8 Inferential and Bayesian analyses comparing pre- and post-tDCS data across food reward measures.

Measure		df	Residual	F	p	η_p^2	BF_{10}
Explicit liking	HFSA	1	15	0.045	0.834	0.003	0.064
	LFSA	1	15	0.634	0.438	0.041	2.051
	HFSW	1	15	7.314	0.016	0.328	2.391
	LFSW	1	15	1.343	0.265	0.082	0.097
	FAB	1	15	0.784	0.390	0.050	0.058
	TAB	1	15	2.680	0.122	0.152	0.080
Explicit wanting	HFSA	1	15	0.024	0.878	0.002	0.050
	LFSA	1	15	0.360	0.557	0.023	0.086
	HFSW	1	15	9.257	0.008	0.382	0.145
	LFSW	1	15	2.844	0.112	0.159	0.046
	FAB	1	15	1.083	0.315	0.067	0.033
	TAB	1	15	3.484	0.082	0.188	0.112
Implicit wanting	HFSA	1	15	0.017	0.897	0.001	0.032
	LFSA	1	15	<0.001	0.982	<0.001	1.129
	HFSW	1	15	1.431	0.250	0.087	0.073
	LFSW	1	15	1.299	0.272	0.080	0.087
	FAB	1	15	1.287	0.274	0.079	0.027
	TAB	1	15	0.004	0.951	<0.001	0.246

HFSA, high-fat savoury; LFSA, low-fat savoury; HFSW, high-fat sweet; LFSW, low-fat sweet; FAB, fat appeal bias; TAB, taste appeal bias.

7.5.8 Response to tDCS

Stimulation was successfully delivered across all 34 sessions, with mean impedance levels of 8 ± 5 kΩ at the start of stimulation. Participants experienced similar

sensations following both active and sham conditions (Table 7-9), with only itching differing between sessions ($z = 2.366$, $p = 0.011$, $BF_{10} = 4.718$). There were no differences in the severity of adverse events across active and sham protocols (Table 7-10). Unlike in the previous study (Chapter 5), blinding was not successfully achieved in the present study with 70.6% of participants able to identify the correct order of tDCS conditions. Additionally, researcher blinding was not upheld, with correct guess of 75.0%. Although both participants and the researcher were able to correctly identify the active tDCS condition, confidence scores were moderate for both participants (5.3 ± 2.5 AU) and the researcher (4.3 ± 2.7 AU).

Table 7-9 Frequency of adverse events immediately post-stimulation (n = 17).

Sensation	Active tDCS	Sham tDCS	p	BF_{10}
Headache	1 (6%)	3 (18%)	0.424	0.354
Neck pain	1 (6%)	1 (6%)	1.000	0.342
Scalp pain	1 (6%)	1 (6%)	1.000	0.310
Tingling	8 (47%)	5 (29%)	0.233	0.451
Itching	10 (59%)	3 (18%)	0.011	4.718
Burning sensation	5 (29%)	2 (12%)	0.233	0.485
Skin redness	4 (24%)	0 (0%)	-	-
Sleepiness	8 (47%)	12 (71%)	0.129	0.695
Trouble concentrating	4 (24%)	6 (35%)	0.530	0.322
Acute mood change	1 (6%)	2 (12%)	1.000	0.375
Other	0 (0%)	1 (6%) [a]	-	-

[a] *Participant reported a pulsating sensation.*

Table 7-10 Severity scores for adverse events experienced immediately post-tDCS (mean ± SD) [a].

Sensation	Active tDCS	Sham tDCS	p	BF_{10}
Headache	1.0 ± 0.0	1.0 ± 0.0	0.424	0.371
Neck pain	1.0 ± 0.0	1.0 ± 0.0	0.424	0.358
Scalp pain	1.0 ± 0.0	2.0 ± 0.0	1.000	0.321
Tingling	1.5 ± 0.7	1.6 ± 0.8	0.386	0.409
Itching	1.4 ± 0.7	2.0 ± 0.8	0.081	1.170
Burning sensation	1.0 ± 0.0	2.0 ± 1.0	0.824	0.315
Skin redness	1.0 ± 0.0	-	-	-
Sleepiness	1.8 ± 0.7	1.6 ± 0.6	0.120	0.781
Trouble concentrating	2.3 ± 0.4	1.2 ± 0.4	0.708	0.271
Acute mood change	2.0 ± 0.0	1.5 ± 0.5	1.000	0.367
Other	-	1.0 ± 0.0	-	-

[a] *Scored on a four-point scale; 0 = not present, 1 = mild, 2 = moderate, 3 = severe.*

7.6 Discussion

The present study aimed to identify the effects of tDCS applied over the right DLPFC on eating-related measures in those with mild-to-moderate binge-type behaviour. While the study applied those parameters that appear to produce the most consistent modulation of eating behaviour (Chapter 3), and focussed on a population with eating behaviour traits suggesting susceptibility to overconsumption as recommended in Chapter 6, a general lack of significant effects were observed when comparing active and sham tDCS conditions.

While there are limited significant differences observed across the data when analysed using frequentist statistics, Bayesian analyses provides support for an

effect with moderate-to-extreme evidence in favour of the alternative hypothesis (i.e., supporting the hypothesis that tDCS is able to modulate eating-related measures) when including post-meal data in the analyses. When considering mean scores between active and sham protocols, there does appear to be an effect of active tDCS across some measures. For example, while post-tDCS scores are numerically close across measures of hunger, fullness and prospective consumption, post-meal scores suggest active protocols are able to suppress hunger and prospective consumption and enhance fullness sensations. Such effects may explain the large Bayes factors observed for these comparisons. It should be noted, however, that similar patterns are not observed across many of the variables included in the original study hypothesis; namely, food craving, desire to eat and food reward scores.

Pre- and post-tDCS data from the present study largely align with those reported in the prior empirical work presented in Chapter 5. There are limited significant effects in line with the study hypotheses, and active tDCS appeared to increase hunger, and the explicit liking and wanting for sweet foods. These effects were in the opposite direction than hypothesised. While previous studies have demonstrated reduced craving or implicit wanting for sweet foods (Goldman et al., 2011; Burgess et al., 2016; Carvalho et al., 2019), these effects have not been consistent with reduction in the consumption of high-fat and sweet foods (To et al., 2018). There is evidence to suggest that those with binge-type behaviour display heightened liking and wanting for sweet foods, and particularly HFSW foods (Finlayson and Dalton, 2012a; Dalton and Finlayson, 2014). While explicit liking for HFSW food images was significantly lower at baseline in the active session, a reflection of the heightened hunger observed in the sham session, scores were comparable post-tDCS under

both active and sham stimulation. This suggests active tDCS is unable to moderate scores in the present population.

This may indicate the need for further consideration of target populations, and it is possible that the participants recruited to this study, while displaying eating behaviour traits suggesting susceptibility to overconsumption, did not display the full trait profile associated with modulatory impact of tDCS. The change in hunger scores in the present work are similar to those reported by Marron et al. (2019), who applied similar parameters as the present work albeit focussing on left DLPFC stimulation. Marron et al. also recruited “healthy” populations who are unlikely to respond to the modulatory effects of tDCS, as discussed in Chapter 6. The findings of Burgess et al. (2016) suggest active tDCS is able to reduce food craving and consumption compared with sham protocols, and differ to the present study. In reconciling the discrepancies the participants in the study by Burgess et al. (2016) had a BES score of 27 ± 6 AU so were at the clinically-relevant end of the scale, whereas the present study recruited those with sub-clinical binge eating behaviour and a lower BES score (21 ± 4 AU).

A delimitation of the present body of work is the focus on non-patient populations, in line with the standardised NIBS protocol (see Chapter 8 for further consideration). As such, the present study was limited in terms of focussing on those with non-clinically relevant binge eating behaviour. As discussed, a number of studies have demonstrated that only those with BED appear to be responsive to tDCS, where as those with frank obesity are not (Burgess et al., 2016; Ray et al., 2017; Max et al., 2020). It could be that the participants recruited to the present study fall within this latter group, or do not display sufficiently predominant trait behaviours to be considered “responsive” to tDCS. While the BES is a psychometrically valid indicator

of binge-type behaviour that is widely used in research (Gormally et al., 1982; Celio et al., 2004; Grupski et al., 2013), the BES is not intended as a clinical diagnostic tool (Cotter and Kelly, 2016) and does not measure all of the diagnostic criteria for BED (American Psychiatric Association, 2013). Further exploration of the potential eating behaviour trait-dependent effect of tDCS is warranted to directly compare the efficacy in clinical and sub-clinical populations. In line with the evidence from prior studies, it may be that only those displaying clinically-relevant behaviours are responsive to the modulatory influence of tDCS (Bravo et al., 2016; Burgess et al., 2016; Grundeis et al., 2017; Kekic et al., 2017; Chen et al., 2019; Ray et al., 2019; Amo Usanos et al., 2020; Fassini et al., 2020; Max et al., 2020).

It is important to consider whether the lack of significant effects is the result of small sample size which can lead to a lack of statistical power to detect such significant differences. An *a priori* sample size calculation was completed for the present study, which was based on the findings for food craving and explicit wanting scores across a number of recently published studies (Fregni et al., 2008; Goldman et al., 2011; Kekic et al., 2014; Ljubisavljevic et al., 2016), and is aligned with the sample size calculation from the previous study presented in this thesis (Chapter 5). Nevertheless, power calculation conducted *a posteriori* suggest only moderate power was achieved (mean 0.54 ± 0.36; range 0.06 to 1.00). When considering the sample size required to identify a significant effect across measures, based on the effect sizes for pre- and post-tDCS data, this is considerably higher than the number of recruited participants (mean 431 ± 755 individuals), with minimum sample size ranging from 6 to 1963 across variables. Of note, based on these calculations sufficient sample size and power were achieved for appetite VAS measures (achieved power = 0.80 ± 0.18).

An important consideration for the present data, regardless of statistical comparisons, is that change in mean scores for some measures suggests active tDCS altered eating-related measure in the direction opposite to the original hypothesis. For example, it was hypothesised that active protocols would reduce the desire to eat, but hunger, prospective consumption and desire to eat VAS scores all increased following active versus sham tDCS. Indeed, the explicit liking and wanting for HFSW foods significantly increased following active tDCS. This raises several questions around the assumptions made for the effects of anodal versus cathodal tDCS (Jacobson et al., 2012). While the evidence presented in Chapter 3 suggests anodal tDCS produces the most consistent reduction in scores, efficacy of the assumed anodal-excite/cathodal-inhibit dichotomy has been disputed (Bestmann et al., 2015; Fertonani and Miniussi, 2016). Only a small proportion of studies have directly compared the effects of anodal and cathodal tDCS on eating behaviours and while early studies suggest clear anodal-excite/cathodal-inhibit effects this in not consistent across all studies (Fregni et al., 2008; Gluck et al., 2015; Grundeis et al., 2017; Kekic et al., 2017; Carvalho et al., 2019; Vicario et al., 2020). Further comparison of these effects is warranted across different populations, in conjunction with the use of brain imaging tools to clearly demonstrate the impact of tDCS on brain activity under these parameters.

The lack of significant differences across craving control and craving for sweet and savoury food measures of the CoEQ is not surprising. It has been suggested that the effects of tDCS are likely only to be present until up to 90 minutes post-stimulation (Nitsche and Paulus, 2001). The 24-hour version of the CoEQ was completed at the end of the test visit days, which falls outside of this window. As such, the modulatory effects are likely to have diminished by the time participants

complete this questionnaire. In line with this, these effects are only supported by anecdotal evidence as indicated by Bayes factors.

As an adjunct to the present study, it may be possible to promote learning and changes in eating behaviour through the use of online food-based cognitive training tasks (Nitsche and Paulus, 2001; Miniussi et al., 2013). Certainly, under similar tDCS parameters as used in the present study, Max et al. (2020) found faster latencies of correct anti-saccades in an online food-modified task in those with BED. However, as discussed in Chapter 3, there is currently only limited evidence to support the use of online tasks and further consideration for the impact these may have on eating-related measures following tDCS is needed. The use of such online tasks may impact the expected polarity-dependent effects of tDCS (Thair et al., 2017) and as such careful consideration of the applied parameters is needed. As recommended in Chapter 3, where online tasks are used these should address the specific eating-related measure the study aims to modulate.

Finally, despite following the same protocol as the prior study (Chapter 5), participant blinding was not upheld in the present study. A much larger percentage of participants were able to distinguish between active and sham protocols. While confidence scores did not suggest participants were sure of the condition order, qualitative statements collected whilst measuring blinding efficacy suggest that differences in sensations of itching and tingling were the reason for participants guessing correctly. Similarly, while researcher blinding was not upheld, confidence scores did not suggest the researcher was sure of the order of conditions, and qualitative statements were mainly around the sensations experienced by participants. These findings question the previous assumption that sham protocols are an effective blinding tool (Gandiga et al., 2006; Brunoni et al., 2011; Nikolin et

al., 2018), and instead provides further evidence that blinding cannot be upheld where cutaneous sensations are more pronounced (O'Connell et al., 2012).

7.7 Conclusion

The present study looked to identify the impact of tDCS in those with mild-to-moderate binge-type behaviour and is the first study to compare the effects of tDCS in the fasted and fed state. Despite evidence of a potential eating behaviour trait-dependent effect of tDCS (see Chapter 6), the present chapter did not demonstrate clear support for the conclusions discussed in the previous chapter. This may be due to focussing on a non-clinical population with only mild-to-moderate binge eating behaviour while prior studies focus on clinical populations. As such, the present participants' may not have met the threshold required to see the modulatory effects of tDCS. This may also reflect the variability in response to stimulation and future work should aim to introduce brain imaging techniques so an understanding of the impact of applied parameters can be achieved, and further consider individuals who may be responsive to the modulatory effects of tDCS.

Chapter 8 General Discussion

8.1 Thesis Overview

Non-invasive brain stimulation techniques are a novel contribution to the research portfolio at Leeds Trinity University, and the present work describes their first use at the institution. While the exploration of tDCS for the modulation of eating behaviours has seen increasing interest over the last 14 years, this research area is still at a relatively early stage. This thesis looked to establish more consistency in the application of tDCS for the modulation of eating behaviours. Through the systematic review of literature and meta-analyses of available data, effective tDCS parameters were established, and potential individuals who are responsive to the modulatory influence of tDCS were explored. The effective parameters were applied in two empirical studies that looked to further develop the idea of an eating behaviour trait-dependent effect of tDCS. While no significant differences in scores across eating-related measures were found in the empirical work, this provides a clear direction for future work, which will be explored in this chapter. An overview of the thesis and the learnings and progress of work is displayed in Figure 8-1.

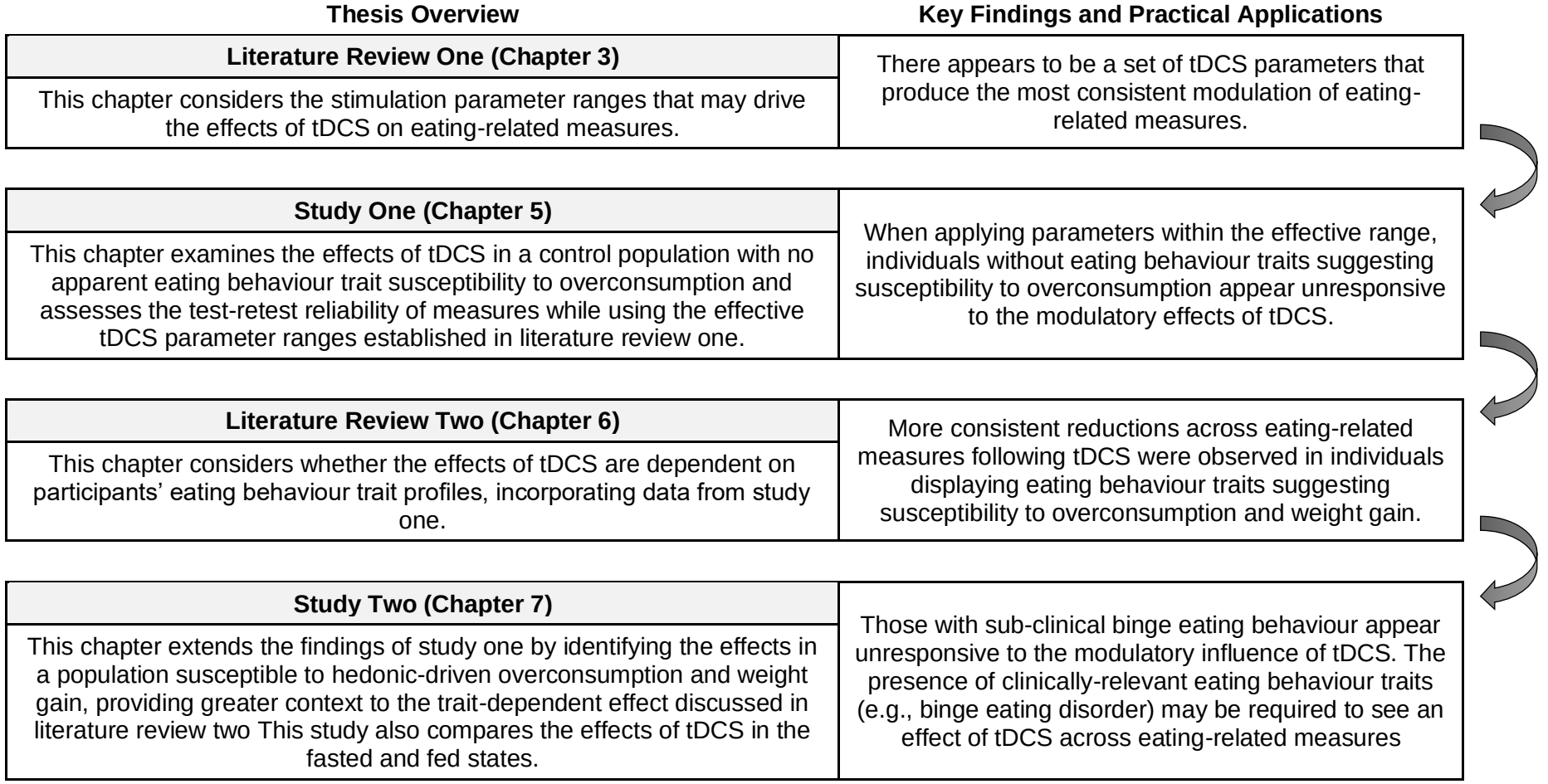


Figure 8-1 An overview of the thesis progression and key findings from each chapter.

8.1.1 Considering Effective Parameter Ranges

When delivering tDCS, it is important to understand the impact of applied parameters as even small changes can impact the expected effects of stimulation (Bikson et al., 2010; Filmer et al., 2014). As such, appropriate tDCS parameters should be established before conducting empirical work. This thesis began with such considerations, through a systematic review and meta-analyses of prior literature using tDCS to modulate eating behaviours (Chapter 3). This chapter built on prior reviews (Hall et al., 2017; Lowe et al., 2017; Mostafavi et al., 2018), and considered a more comprehensive set of tDCS parameters. The prior reviews focus on measures of food craving and consumption, with the review presented in Chapter 3 assessing the impact of tDCS parameters across a wider range of eating-related measures, including subjective appetite (hunger, fullness, prospective consumption, desire to eat), food craving, food reward (explicit liking, implicit and explicit wanting), and food consumption.

While this review provided a comprehensive overview, the paucity of available data and sufficient description of study methods in published work made it difficult to run meta-analyses for all comparisons. In addition, a number of studies applied novel parameters, i.e., deviating from the traditional 2.0 mA delivered to the DLPFC for 20 minutes, with equivocal findings. For example, stimulating the right IFG (To et al., 2018; Chen et al., 2019) or applying tDCS for 40 minutes (Gluck et al., 2015; Heinitz et al., 2017). This emphasises the need for further research into the impact of these alternative parameters. Despite this, there is clear evidence in favour of specific parameters, such as the use of appropriate current intensity and electrode size to achieve current densities of at least 0.057 $mA \cdot cm^{-2}$ at the target region. This review culminated in a series of recommendations for effective parameter ranges (see Table 3-13), which were adhered to in the empirical studies described in this thesis.

8.1.2 Considering the Responsiveness to tDCS

The second systematic review and meta-analysis (Chapter 6) considered individuals who may be “responsive” and “unresponsive” to the effects of tDCS on eating behaviours. This focus was driven by the findings of Burgess et al. (2016) and Ray et al. (2017) who provide evidence for a potential eating behaviour trait-dependent effect of tDCS, where those who present with traits suggesting susceptibility to overconsumption appear to be responsive to the modulatory impact of tDCS across eating-related measures. In Chapter 6, comparison of tDCS effects on measures of eating behaviour were made between those who present with susceptibility to overconsumption (trait group) and those who do not (“healthy” group). In line with Chapter 3, this review considered an extensive set of eating-related measures (subjective appetite, food craving, food reward, food consumption).

The findings presented in Chapter 6 do indeed suggest an eating behaviour trait-dependent effect of tDCS exists. In particular, effects were greater in those who presented with eating behaviour traits associated with the test variable of interest. For example, food craving measures in those who experience frequent food cravings (g = −0.43; 95% CI = −1.11, 0.25), and explicit wanting in those with binge eating behaviour (g = −0.19; 95% CI = −0.57, 0.19). As such, studies should focus on participants displaying eating behaviour traits aligned with test variables (e.g., displaying binge-type behaviour when measuring food reward).

Considering this evidence, further exploration of the potential eating behaviour trait-dependent effect of tDCS was warranted. It should be noted that although many of the participant populations across the reviewed research were deemed “healthy”, the behaviour traits of these participants were not well controlled. This gave need to

assess the effects of tDCS in a more controlled “healthy” population. The first empirical study presented in this thesis looked to apply tDCS in such a population; participants had a BMI within the healthy weight range and presented with low susceptibility to overconsumption, as indicated through validated eating behaviour trait questionnaires. In line with the evidence around executive functioning capabilities (Alonso-Alonso and Pascual-Leone, 2007; Cserjési et al., 2009; Michaud et al., 2017; Blume et al., 2019), these participants were assumed to have sufficient executive control of eating behaviours (i.e., their eating behaviour trait scores did not indicate susceptibility to overconsumption).

Data from this study demonstrated that such “healthy” participants are unresponsive to the effects of tDCS. This may reflect a ceiling effect associated with cortical activity, beyond which no further enhancement is seen (Furuya et al., 2014; da Silva Machado et al., 2021). Comparisons in this study were supported by anecdotal-to-moderate evidence in favour of the null hypothesis, providing further evidence for a potential eating behaviour trait-dependent effect of tDCS. The empirical studies presented in this thesis document the first use of the LFPQ in response to tDCS. With individuals displaying binge eating behaviour appearing more responsive to the rewarding aspects of food (Dalton et al., 2013a) and the modulatory effect of tDCS (Burgess et al., 2016; Max et al., 2020), Chapter 7 focussed on establishing the effects of tDCS in those with mild-to-moderate binge eating behaviour who would speculatively also have lower levels of executive functioning. Despite focussing on those displaying eating behaviour traits associated with overconsumption, no effects of tDCS were observed.

The lack of significant effects for studies presented in this thesis may be driven by a lack of DLPFC hypoactivation in the recruited participants. Focus on stimulation of

the DLPFC was based on observations of reduced activity within this cortical region in those with binge eating behaviour as observed through regional cerebral blood flow and the Frontal Systems Behaviour Scale (Karhunen et al., 2000; Boeka and Lokken, 2011). Of note, participants in these studies presented with more clinically-relevant binge eating behaviour. In particular, individuals displaying these binge eating behaviours show hyper-responsivity to the rewarding aspects of food (Dalton et al., 2013a), which is associated with hypoactivation of the DLPFC (Alonso-Alonso and Pascual-Leone, 2007; Havermans, 2011; Finlayson and Dalton, 2012b; Boswell and Kober, 2016; Kober and Boswell, 2018) and reduced dietary self-regulation (Munsch et al., 2012). To see a change in eating-related measures following tDCS, participants will likely need to present with reduced activity of the DLPFC, associated problematic eating behaviours and poor baseline executive functioning. As such, it is likely that participants will need to be screened using a variety of tools beyond the BES; this should include consideration for both cortical activity and executive functioning.

There is evidence from other domains, particularly studies using tDCS to modulate executive functioning, that individuals can be classed as “responsive” and “unresponsive” to tDCS (Berryhill and Jones, 2012; Learmonth et al., 2015; Perceval et al., 2020). Specifically, those with poorer baseline executive functioning appear to be responsive to tDCS. Much of the theory behind the use of tDCS to modulate eating behaviours is based on deficits in executive functioning (Alonso-Alonso and Pascual-Leone, 2007; Lowe et al., 2019), and it is likely that those who present with poor executive control of eating behaviours may be responsive to tDCS. Recent evidence suggests that those who present with binge eating behaviour show impaired executive functioning (Cserjési et al., 2009; Michaud et al., 2017; Blume et al., 2019). These findings align with the theory behind tDCS (i.e., beneficial in those

with executive functioning deficits), with studies recruiting those presenting with BED showing consistent modulation of eating-related measures (Burgess et al., 2016; Max et al., 2020). This may indicate the difference between clinical (i.e., BED) and sub-clinical (i.e., mild-to-moderate binge-type behaviour identified through the BES) presentation of eating behaviours.

The subthreshold modulation of cortical activity through tDCS occurs by inhibiting neurotransmitters, and particularly GABA and glutamate (see Figure 1-2) (Filmer et al., 2014). Where drug treatments (e.g., topiramate and gabapentin) are used to target these neurotransmitters, successful control of binge eating behaviour has been demonstrated (Guardia et al., 2011; Reas and Grilo, 2014); specifically, such treatments appear able to reduce binge eating frequency and weight, with some evidence supporting improvement in psychiatric comorbidities (e.g., depression). Such impacts, particularly relating to eating behaviour, are not surprising given GABA and glutamate – along with other neurotransmitter systems and pathways (e.g., dopamine and opioid pathways) – are important in appetite control (Blundell and Finlayson, 2004; Blundell, 2006; Abizaid and Horvath, 2008). This may provide a route through which tDCS can improve eating behaviour in this population but may also explain why effects are seen in those displaying trait susceptibility to overconsumption and weight gain.

8.2 Methodological Considerations for tDCS

The focus of this thesis was to identify effective study design, stimulation parameters and participant characteristics that produce consistent changes in eating behaviour following the application of tDCS. With the onward aim of improving the consistency and replicability of research measuring the impact of tDCS on eating behaviours, this section summarises the main recommendations and provides further

considerations for study design, stimulation parameters and participant characteristics.

8.2.1 Study Design

Due to the inter-individual differences in response to tDCS (Chew et al., 2015; Li et al., 2015; Antal et al., 2017; Jamil and Nitsche, 2017), it is recommended that studies follow a within-participant design, where all participants receive active (anodal and/or cathodal) and sham tDCS. Considering the evidence presented in Chapter 3, studies should also adhere to a double-blind, randomised and counterbalanced, crossover design. It is important that both participant and researcher blinding is maintained to ensure the data are not biased by expectation of effects (Horvath et al., 2014; Ray et al., 2019). Other than the empirical studies presented in this thesis, only a small number of tDCS studies focussing on the modulation of eating behaviour utilise these robust designs (Fregni et al., 2008; Kekic et al., 2014; Lapenta et al., 2014; Kekic et al., 2017; To et al., 2018; Max et al., 2020). Following such robust study designs will likely improve the reliability and replicability of the data.

8.2.2 Stimulation Parameters

Standard protocols (e.g., 2.0 mA for 20 minutes) are widely considered to be safe for both adults and children (Matsumoto and Ugawa, 2017). Early into the use of modern tDCS techniques, Nitsche and colleagues published guidance on safe parameters (summarised in Table 8-1) (Nitsche et al., 2003). It is well-documented that tDCS within these safety limits is tolerated well by participants, with no evidence of serious adverse events (e.g., seizures, psychotic symptoms) in more than 33,200 tDCS sessions (Bikson et al., 2016). Certainly, evidence from the empirical work presented in this thesis suggests tDCS within the safe limits is well-tolerated. Of

note, no serious adverse events were reported by the study participants, nor did any participant request that stimulation was terminated early due to experiencing adverse events or for any other reason. Caution should be made for appropriate set-up of equipment and application of parameters, as poor control for these factors can result in moderate adverse events (e.g., skin lesions) (Palm et al., 2008; Frank et al., 2010; Rodríguez et al., 2014; Lu and Lam, 2019).

Table 8-1 tDCS parameter safety limits.

Parameter	Safe Range [a]	Value Used in Thesis
Stimulation Duration	≤40 minutes	20 minutes
Electrode Size	≥9 cm^2	25 cm^2 (anode) 51 cm^2 (cathode)
Stimulation Intensity	≤4.0 mA	2.0 mA
Current Density	25 $mA \cdot cm^{-2}$	0.039 to 0.080 $mA \cdot cm^{-2}$
Total Charge	216 $C \cdot cm^{-2}$	1.6 $C \cdot cm^{-2}$

[a] *Nitsche et al. (2003)*

With delivery of the electrical current, there is a risk of mild adverse events (e.g., itching, tingling, redness under the electrode pads), or a short flash of light in the visual field (Nitsche et al., 2003). There is also a low risk of headache, sensation of burning, nausea, fatigue and insomnia (Poreisz et al., 2007). The presence of such adverse events is not linked with damage to the skin or brain, nor do they result in detrimental changes to cortical activity, learning or behaviour (Nitsche et al., 2003; Bikson et al., 2016). For the present work, the most common adverse events reported by participants were itching, tingling and sleepiness. Severity scores across all sensations show they were mild, again supporting the tolerability of tDCS.

In addition to adherence with safety guidelines, the parameters applied within the current body of work were within effective ranges, as outlined in Chapter 3 (see Table 8-2). These effective ranges are based on studies looking at the impact of tDCS on eating-related measures. While they are similar to the parameters applied for the modulation of other behaviours or tests (e.g., depression, smoking cessation) (Lefaucheur, 2016), the effective ranges established in this thesis should be seen as specific to studies within an eating behaviour domain. The foundations of many tDCS parameter sets comes from work on the motor cortex. For example, early understanding of the anodal-excitatory/cathodal-inhibitory effects of tDCS were demonstrated by stimulating the motor cortex, and then measuring motor evoked potentials of the abductor minimi muscle of the right hand using magnetic fields delivered through transcranial magnetic stimulation (Nitsche and Paulus, 2000; Nitsche and Paulus, 2001). The effects of stimulation directed to motor cortex cannot be easily transferred to other cortical regions and relies on effect measurement by brain imaging techniques (e.g., functional near-infrared spectroscopy [fNIRS] or magnetic resonance imaging [MRI]) (Filmer et al., 2014; Woods et al., 2016). As such, the parameter ranges recommended in Chapter 3 should be applied to and developed in those studies where eating-related variables constitute a main aim, objective or test variable. It is likely as this area of research develops these parameter ranges will change to reflect new knowledge of efficacy; the present ranges should be used as a reference point to explore the efficacy of tDCS for modulating eating behaviours.

Table 8-2 Comparison of applied parameters with the effective ranges discussed in Chapter 3.

Parameter	Effective Range	Parameters Applied in the Present Thesis
Montage	Target: Right DLPFC Reference: Cortical region away from DLPFC, or extracephalic region	Target: Right DLPFC Reference: Occipital lobe
Electrode Size	Target: ≤35 cm^2 Reference: Equal or greater than target electrode	Target: 25 cm^2 Reference: 51 cm^2
Current Intensity	1.5 to 2.0 mA	2.0 mA
Current Density	0.057 to 0.080 $mA \cdot cm^{-2}$ (under anode)	Anode: 0.080 $mA \cdot cm^{-2}$ Cathode: 0.039 $mA \cdot cm^{-2}$
Stimulation Duration	20 minutes	20 minutes
Inter-session Interval	Single session: >48 hours Multi-session: ≤24 hours	≥48 hours • Study one: 120 ± 108 hours • Study two: 165 ± 14 hours
Offline / Online Protocol	Offline, or unrelated media (online task) to standardise thoughts	Offline

DLPFC, dorsolateral prefrontal cortex; mA, milliampere; $mA \cdot cm^{-2}$, milliampere per centimetre squared.

An important consideration in tDCS research is the efficacy of blinding protocols, as this can bias data towards an effect, such as those observed by Ray et al. (2019) where food craving scores and the amount of food consumed were reduced when participants expected to receive active versus sham tDCS, regardless of whether they actually received the active protocol. Sham protocols are assumed to be a successful method of blinding due to similar experience of adverse events during tDCS (Gandiga et al., 2006; Brunoni et al., 2011; Nikolin et al., 2018). However, the efficacy of such protocols have been questioned when applying higher current strengths, due to the greater prevalence of cutaneous sensations (Kessler et al., 2012; O'Connell et al., 2012). This is particularly problematic where there are visual cues (e.g., erythema) (O'Connell et al., 2012; Palm et al., 2013). While study one (Chapter 5) provided evidence in support of sham protocols as blinding techniques, blinding was not upheld in study two (Chapter 7) despite following best practice guidelines (Woods et al., 2016; Thair et al., 2017). This may reflect the inter-individual differences in experience of adverse events, and careful consideration for how to maintain study blinding is warranted (Kessler et al., 2012; Workman et al., 2021).

8.2.3 Participant Characteristics

The meta-data presented in Chapter 6 shows a more consistent reduction across eating-related measures following active tDCS in those who present with eating behaviour traits associated with overconsumption and weight gain. These individuals can be seen as "responsive" to the modulatory impact of tDCS, with "healthy" (i.e., those without eating behaviour traits suggesting susceptibility to overconsumption) appearing unresponsive to stimulation. Data presented in Chapter 5 provides further support that "healthy" individuals are unresponsive to tDCS. While Chapter 7 looked to recruit those who are responsive (i.e., with eating

behaviour traits linked to overconsumption), as indicated by the evidence presented in Chapter 6, data did not provide clear support for the eating behaviour trait-dependent effect of tDCS. As discussed in the previous chapter and in the sections above, this may highlight the difference between clinical and sub-clinical populations with only those presenting with clinically-relevant eating behaviour traits (e.g., BED) being responsive to tDCS and potentially other forms of NIBS.

To determine whether clinical population are indeed responsive to tDCS, compared with sub-clinical and non-clinical populations, it is important to establish baseline executive functioning, particularly for those functions associated with eating behaviour such as inhibitory control (de Klerk et al., 2022; Weydmann et al., 2022). It is also important to establish baseline cortical activity (e.g., through brain imaging techniques). Changes in both of these measures should then be recorded post-tDCS, and ideally with comparison between clinical and sub-clinical populations. While some recent studies have assessed the impact of tDCS on executive functioning and eating behaviours (e.g., Lapenta et al. (2014); Sedgmond et al. (2019)), these studies do not sufficiently establish baseline eating behaviour traits and executive functioning, nor brain activity pre- and post-tDCS. As such, it is difficult to determine the impact of tDCS parameters on cortical activity across populations, and differences in responsiveness to tDCS based on eating behaviour traits and executive functioning capabilities. If clinically-relevant eating behaviours and executive functioning capabilities are drivers of tDCS effects, it is important that studies assess these factors to further this discussion.

8.3 Limitations and Delimitations

While the work presented in this thesis applied tDCS parameters that have been shown to alter eating-related measures, as discussed in Chapter 3, and

demonstrated successful delivery of these parameters (as indicated through impedance levels), it is not clear what impact these parameters had on participants' cortical activity. In line with prior evidence, it was assumed that the applied parameters would increase activity within the DLPFC through the sub-threshold modulation of resting membrane potentials (Filmer et al., 2014). However, without direct evidence of this effect (e.g., through brain imaging) it is not possible to draw definitive conclusions on the impact of applied parameters. While brain imaging was not possible for the present work, computational modelling shows a clear pattern of current delivery through the DLPFC (Zheng et al., 2016; Zheng et al., 2017; Marron et al., 2019). It should be noted, however, that there are inter-individual differences in cortical structure and function and response to tDCS (López-Alonso et al., 2014; Jamil and Nitsche, 2017; Lowe et al., 2019) that are not captured by computational modelling, and as such the response of the individual will likely deviate from these models.

It may be that single session tDCS is not sufficient to see changes in eating-related outcomes, and instead that multiple sessions of tDCS are needed. The meta-data presenting in this thesis suggests multi-session tDCS is able to produce a larger reduction in food craving and consumption (g = −0.34 to −0.29) compared with single session designs (g = −0.12 to 0.01). A similar observation was made in the meta-analysis by Mostafavi et al. (2018). In addition, where tDCS is delivered across multiple visits, there appears to be a reduction in food consumption (Jauch-Chara et al., 2014) even when parameters are below the thresholds outlined in Chapter 3. Despite the potential benefits of multi-session versus single session tDCS, it is important to establish efficacy of parameters and of tDCS to modulate eating behaviour through single session designs. Although the present work did not find an effect of tDCS following one session of tDCS, prior studies following single session

designs have found significant effects (Fregni et al., 2008; Goldman et al., 2011; Montenegro et al., 2012; Burgess et al., 2016).

As discussed in the previous sections, much of the theory around tDCS is based on observations following stimulation to the motor cortex. While consistent effects are often shown, it is difficult to transfer these effects directly to the PFC (Filmer et al., 2014; Woods et al., 2016). In particular, the anodal-excite/cathodal-inhibit dichotomy is based on observations from stimulation directed to the motor cortex (Nitsche and Paulus, 2000; Nitsche and Paulus, 2001), and this sliding-scale effect may not be supported when tDCS is delivered to other cortical regions (Bestmann et al., 2015; Fertonani and Miniussi, 2016). This further emphasises the need for research into the effects of tDCS to the PFC, and the downward impact on eating behaviours, which incorporate neuroimaging tools. While prior studies in the area of tDCS and eating behaviours have explored some of the effects observed following stimulation to the motor cortex (e.g., effects of anodal versus cathodal stimulation), the evidence is limited.

As indicated in Chapter 7, the present work is delimited to the use of non-clinical populations as directed by institutional ethical standards and resources. Although the present work suggests that tDCS may only be effective in clinical populations, focus on sub-clinical populations should not be seen as a limitation. The data collected in this population provides evidence aligned with null hypothesis (i.e., tDCS is not effective at reducing eating-related measures). This is an important consideration given many tDCS studies focus on healthy individuals, and particularly studies looking to modulate eating behaviours (Jauch-Chara et al., 2014; Ljubisavljevic et al., 2016; Georgii et al., 2017; Carvalho et al., 2019; Sedgmond et al., 2019; Vicario et al., 2020). While studies using healthy populations are important

for initially establishing efficacy and safety thresholds, future work should focus on those who appear to be responsive to tDCS, particularly those who display eating behaviour trait susceptibility to overconsumption and deficits in executive functioning, who would benefit from the use of the technique to modulate behaviour, learning and/or task performance.

8.4 Future Directions

It is important that the efficacy of tDCS for the modulation of eating behaviours is established. There is large heterogeneity across studies, particularly in applied parameters and participant characteristics. As such, these studies provide equivocal findings and it is particularly difficult to demonstrate a consistent pattern of effects (see Chapter 3 and Chapter 6). As discussed, the evidence presented in the present thesis does not provide support for the use of this technique. This evidence was collected following robust study designs, using stimulation parameters shown to modulate eating-related measures in other published work (as outlined in Chapter 3), and using homogenous participants cohorts displaying “healthy” or binge-type behaviour. Particular focus should be made for the comparison between clinical and sub-clinical populations. It is likely that more promising effects are observed when recruiting the former population, as indicated by the current evidence base (Bravo et al., 2016; Burgess et al., 2016; Grundeis et al., 2017; Kekic et al., 2017; Chen et al., 2019; Ray et al., 2019; Amo Usanos et al., 2020; Fassini et al., 2020; Max et al., 2020).

While the guidelines for future research outlined in Chapter 3 (summarised in Table 8-2, also see section 3.4.9) and Chapter 6 (see section 6.5) are not intended as absolute recommendation, they should be used as a point of reference with the aim of establishing greater consistency in the application of tDCS. While these guidelines

are reflective of the current available evidence, it is likely that they will develop as greater knowledge of the effects of tDCS on eating behaviours is established. As such, future work should look to align methods with the guidelines, but also to test the efficacy of parameters outside the effective ranges (e.g., lower current density in combination with repeated sessions of tDCS, montages focussing on alternative cortical regions) and recruit diverse populations. When recruiting participants, it is important to ensure homogeneity in eating behaviour traits and/or other variables (e.g., executive functioning, weight status) that may impact the study variables of interest.

Controlling for variables such as eating behaviour traits will help contextualise the evidence to specific populations, but it is likely that variability in data will be present due to the inter-individual differences in response to tDCS (Chew et al., 2015; Li et al., 2015; Antal et al., 2017; Jamil and Nitsche, 2017). As such, future work should look to incorporate brain imaging tools, such as fNIRS or MRI, to determine the individual impact and neural basis of applied tDCS parameters (Filmer et al., 2014; Woods et al., 2016). Using such tools may also allow individually-tailored parameters, targeting specific cortical regions or applying specific parameters that result in modulation of eating behaviours within-person rather than within-population (Dunlop et al., 2016; Rodella et al., 2021).

8.5 Conclusion

The aim of this thesis was to improve consistency in the application of tDCS, and specifically consistency in study design, stimulations parameters and participant characteristics. While the empirical work presented in this thesis does not show clear support for the use of tDCS to modulate eating behaviours, with no significant differences between active and sham protocols, this may reflect the use of

unresponsive populations as suggested after conducting this empirical work. Despite this, study design and stimulation parameters that produce consistent reduction in eating-related measures have been identified, and potential responsive and unresponsive populations have been considered. Throughout this thesis, a number of recommendations have been made for the direction of future research, with the aim of improving the consistency of tDCS application and the replicability of findings. While submission of this thesis signifies the end of PhD candidature, there are still a number of questions that remain unanswered that can be explored beyond the PhD and in future studies by other research groups.

References

Abizaid, A. and Horvath, T.L. 2008. Brain circuits regulating energy homeostasis. *Regulatory Peptides.* **149**(1), pp.3-10. https://doi.org/10.1016/j.regpep.2007.10.006

Allison, D.B., Kalinsky, L.B. and Gorman, B.S. 1992. A comparison of the psychometric properties of three measures of dietary restraint. *Psychological Assessment.* **4**(3), pp.391-398. http://dx.doi.org/10.1037/1040-3590.4.3.391

Alonso-Alonso, M. 2013. Translating tDCS into the field of obesity: mechanism-driven approaches. *Frontiers in Human Neuroscience.* **7**, 512. https://doi.org/10.3389/fnhum.2013.00512

Alonso-Alonso, M. and Pascual-Leone, A. 2007. The right brain hypothesis for obesity. *JAMA.* **297**(16), pp.1819-1822. https://doi.org/10.1001/jama.297.16.1819

Alonzo, A., Brassil, J., Taylor, J.L., Martin, D. and Loo, C.K. 2012. Daily transcranial direct current stimulation (tDCS) leads to greater increases in cortical excitability than second daily transcranial direct current stimulation. *Brain Stimulation.* **5**(3), pp.208-213. https://doi.org/10.1016/j.brs.2011.04.006

Ambrus, G.G., Al-Moyed, H., Chaieb, L., Sarp, L., Antal, A. and Paulus, W. 2012. The fade-in – Short stimulation – Fade out approach to sham tDCS – Reliable at 1 mA for naïve and experienced subjects, but not investigators. *Brain Stimulation.* **5**(4), pp.499-504. https://doi.org/10.1016/j.brs.2011.12.001

American Psychiatric Association. 2013. *Diagnostic and statistical manual of mental disorders: DSM-5™.* 5th ed. United States: American Psychiatric Publishing, Inc.

Amo Usanos, C., Valenzuela, P.L., de la Villa, P., Navarro, S.M., Melo Aroeira, A.E.d., Amo Usanos, I., Martínez Cancio, L., Cuesta Villa, L., Shah, H., Magerowski, G. and Alonso-Alonso, M. 2020. Neuromodulation of the prefrontal cortex facilitates diet-induced weight loss in midlife women: a randomized, proof-of-concept clinical trial. *International Journal of Obesity.* **44**(3), pp.568-578. https://doi.org/10.1038/s41366-019-0486-x

Andresen, E.M., Malmgren, J.A., Carter, W.B. and Patrick, D.L. 1994. Screening for depression in well older adults: Evaluation of a short form of the CES-D. *American Journal of Preventive Medicine.* **10**(2), pp.77-84. https://doi.org/10.1016/S0749-3797(18)30622-6

Anglé, S., Engblom, J., Eriksson, T., Kautiainen, S., Saha, M.-T., Lindfors, P., Lehtinen, M. and Rimpelä, A. 2009. Three factor eating questionnaire-R18 as a measure of cognitive restraint, uncontrolled eating and emotional eating in a sample of young Finnish females. *International Journal of Behavioral Nutrition and Physical Activity.* **6**(1), 41. https://dx.doi.org/10.1186%2F1479-5868-6-41

Antal, A., Alekseichuk, I., Bikson, M., Brockmöller, J., Brunoni, A.R., Chen, R., Cohen, L.G., Dowthwaite, G., Ellrich, J., Flöel, A., Fregni, F., George, M.S., Hamilton, R., Haueisen, J., Herrmann, C.S., Hummel, F.C., Lefaucheur, J.P., Liebetanz, D., Loo, C.K., McCaig, C.D., Miniussi, C., Miranda, P.C., Moliadze, V., Nitsche, M.A., Nowak, R., Padberg, F., Pascual-Leone, A., Poppendieck, W., Priori, A., Rossi, S., Rossini, P.M., Rothwell, J., Rueger, M.A., Ruffini, G., Schellhorn, K., Siebner, H.R., Ugawa, Y., Wexler, A., Ziemann, U., Hallett, M. and Paulus, W. 2017. Low intensity transcranial electric stimulation: Safety, ethical, legal regulatory and application guidelines. *Clinical Neurophysiology.* **128**(9), pp.1774-1809. https://doi.org/10.1016/j.clinph.2017.06.001

Auvichayapat, P. and Auvichayapat, N. 2011. Basic knowledge of transcranial direct current stimulation. *Journal of the Medical Association of Thailand.* **94**(4), pp.518-527.

Balodis, I.M., Grilo, C.M. and Potenza, M.N. 2015. Neurobiological features of binge eating disorder. *CNS Spectrums.* **20**(6), pp.557-565. https://doi.org/10.1017/s1092852915000814

Batsikadze, G., Rezaee, Z., Chang, D.-I., Gerwig, M., Herlitze, S., Dutta, A., Nitsche, M.A. and Timmann, D. 2019. Effects of cerebellar transcranial direct current stimulation on cerebellar-brain inhibition in humans: A systematic evaluation. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation.* **12**(5), pp.1177-1186. https://doi.org/10.1016/j.brs.2019.04.010

Beaulieu, K., Hopkins, M., Blundell, J. and Finlayson, G. 2017. Impact of physical activity level and dietary fat content on passive overconsumption of energy in non-obese adults. *International Journal of Behavioral Nutrition and Physical Activity.* **14**(1), 14. https://doi.org/10.1186/s12966-017-0473-3

Beaulieu, K., Hopkins, M., Blundell, J. and Finlayson, G. 2018. Homeostatic and non-homeostatic appetite control along the spectrum of physical activity levels: An updated perspective. *Physiology & Behavior.* **192**, pp.23-29. https://doi.org/10.1016/j.physbeh.2017.12.032

Beaumont, J.D., Davis, D., Dalton, M., Nowicky, A., Russell, M. and Barwood, M.J. 2021. The effect of transcranial direct current stimulation (tDCS) on food craving, reward and appetite in a healthy population. *Appetite.* **157**, 105004. https://doi.org/10.1016/j.appet.2020.105004

Beechy, L., Galpern, J., Petrone, A. and Das, S.K. 2012. Assessment tools in obesity — Psychological measures, diet, activity, and body composition. *Physiology & Behavior.* **107**(1), pp.154-171. https://doi.org/10.1016/j.physbeh.2012.04.013

Berg, K.C., Frazier, P. and Sherr, L. 2009. Change in eating disorder attitudes and behavior in college women: Prevalence and predictors. *Eating Behaviors.* **10**(3), pp.137-142. https://doi.org/10.1016/j.eatbeh.2009.03.003

Berryhill, M.E. and Jones, K.T. 2012. tDCS selectively improves working memory in older adults with more education. *Neuroscience Letters.* **521**(2), pp.148-151. https://doi.org/10.1016/j.neulet.2012.05.074

Best, M., Barsalou, L.W. and Papies, E.K. 2018. Studying human eating behaviour in the laboratory: Theoretical considerations and practical suggestions. *Appetite.* **130**, pp.339-343. https://doi.org/10.1016/j.appet.2018.06.001

Bestmann, S., de Berker, A.O. and Bonaiuto, J. 2015. Understanding the behavioural consequences of noninvasive brain stimulation. *Trends in Cognitive Sciences.* **19**(1), pp.13-20. https://doi.org/10.1016/j.tics.2014.10.003

Bikson, M., Datta, A., Rahman, A. and Scaturro, J. 2010. Electrode montages for tDCS and weak transcranial electrical stimulation: Role of "return" electrode's position and size. *Clinical Neurophysiology.* **121**(12), pp.1976-1978. https://doi.org/10.1016/j.clinph.2010.05.020

Bikson, M., Grossman, P., Thomas, C., Zannou, A.L., Jiang, J., Adnan, T., Mourdoukoutas, A.P., Kronberg, G., Truong, D., Boggio, P., Brunoni, A.R., Charvet, L., Fregni, F., Fritsch, B., Gillick, B., Hamilton, R.H., Hampstead, B.M., Jankord, R., Kirton, A., Knotkova, H., Liebetanz, D., Liu, A., Loo, C., Nitsche, M.A., Reis, J., Richardson, J.D., Rotenberg, A., Turkeltaub, P.E. and Woods, A.J. 2016. Safety of transcranial direct current stimulation: Evidence based update 2016. *Brain Stimulation.* **9**(5), pp.641-661. https://doi.org/10.1016/j.brs.2016.06.004

Björgvinsson, T., Kertz, S.J., Bigda-Peyton, J.S., McCoy, K.L. and Aderka, I.M. 2013. Psychometric properties of the CES-D-10 in a psychiatric sample. *Assessment.* **20**(4), pp.429-436. https://doi.org/10.1177/1073191113481998

Blume, M., Schmidt, R. and Hilbert, A. 2019. Executive functioning in obesity, food addiction, and binge-eating disorder. *Nutrients.* **11**(1). https://doi.org/10.3390/nu11010054

Blundell, J., De Graaf, C., Hulshof, T., Jebb, S., Livingstone, B., Lluch, A., Mela, D., Salah, S., Schuring, E., Van Der Knaap, H. and Westerterp, M. 2010. Appetite control: methodological aspects of the evaluation of foods. *Obesity Reviews.* **11**(3), pp.251-270. https://doi.org/10.1111/j.1467-789X.2010.00714.x

Blundell, J.E. 2006. Perspective on the central control of appetite. *Obesity.* **14**(Supp. 7), pp.s160-s163. https://doi.org/10.1038/oby.2006.298

Blundell, J.E. and Finlayson, G. 2004. Is susceptibility to weight gain characterized by homeostatic or hedonic risk factors for overconsumption? *Physiology & Behavior.* **82**(1), pp.21-25. https://doi.org/10.1016/j.physbeh.2004.04.021

Boeka, A.G. and Lokken, K.L. 2011. Prefrontal systems involvement in binge eating. *Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity.* **16**(2), pp.e121-e126. https://doi.org/10.1007/bf03325317

Borenstein, M., Hedges, L.V., Higgins, J.P.T. and Rothstein, H.R. 2021. *Introduction to Meta-Analysis.* United Kingdom: Wiley.

Boswell, R.G. and Kober, H. 2016. Food cue reactivity and craving predict eating and weight gain: a meta-analytic review. *Obesity Reviews.* **17**(2), pp.159-177. https://doi.org/10.1111/obr.12354

Bravo, G.L., Poje, A.B., Perissinotti, I., Marcondes, B.F., Villamar, M.F., Manzardo, A.M., Luque, L., LePage, J.F., Stafford, D., Fregni, F. and Butler, M.G. 2016. Transcranial direct current stimulation reduces food-craving and measures of hyperphagia behavior in participants with Prader-Willi syndrome. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics.* **171**(2), pp.266-275. https://doi.org/10.1002/ajmg.b.32401

Brockmeyer, T., Simon, J.J., Becker, A. and Friederich, H.-C. 2017. Reward-related decision making and long-term weight loss maintenance. *Physiology & Behavior.* **181**, pp.69-74. https://doi.org/10.1016/j.physbeh.2017.09.008

Brownley, K.A., Berkman, N.D., Sedway, J.A., Lohr, K.N. and Bulik, C.M. 2007. Binge eating disorder treatment: A systematic review of randomized controlled trials. *International Journal of Eating Disorders.* **40**(4), pp.337-348. https://doi.org/10.1002/eat.20370

Bruce, B. and Wilfley, D. 1996. Binge eating among the overweight population: A serious and prevalent problem. *Journal of the American Dietetic Association.* **96**(1), pp.58-61. https://doi.org/10.1016/S0002-8223(96)00016-8

Brunoni, A.R., Amadera, J., Berbel, B., Volz, M.S., Rizzerio, B.G. and Fregni, F. 2011. A systematic review on reporting and assessment of adverse effects associated with transcranial direct current stimulation. *International Journal of Neuropsychopharmacology.* **14**(8), pp.1133-1145. https://doi.org/10.1017/s1461145710001690

Buckland, N.J. and Dalton, M. 2018. Commentary: Methodological and reporting practices for laboratory studies assessing food intake using fixed and ad libitum test meals. *Appetite.* **130**, pp.336-338. https://doi.org/10.1016/j.appet.2018.06.007

Burgess, E.E., Sylvester, M.D., Morse, K.E., Amthor, F.R., Mrug, S., Lokken, K.L., Osborn, M.K., Soleymani, T. and Boggiano, M.M. 2016. Effects of transcranial direct current stimulation (tDCS) on binge-eating disorder. *International Journal of Eating Disorders.* **49**(10), pp.930-936. https://doi.org/10.1002/eat.22554

Butland, B.K., Jebb, S.A., Kopelman, P.G., McPherson, K., Thomas, S., Mardell, J. and Parry, V. 2007. *Tackling Obesities: Future Choices (Foresight Report).* United Kingdom.

Butler, M.G. and Thompson, T. 2000. Prader-Willi Syndrome: Clinical and genetic findings. *The Endocrinologist.* **10**(4, Supp. 1), pp.s3-s16. https://doi.org/10.1097/00019616-200010041-00002

Cameron, J.D., Goldfield, G.S., Finlayson, G., Blundell, J.E. and Doucet, É. 2014. Fasting for 24 hours heightens reward from food and food-related cues. *PLOS ONE.* **9**(1), e85970. https://dx.doi.org/10.1371%2Fjournal.pone.0085970

Carvalho, S., Sampaio, A., Mendes, A.J., Lema, A., Vieira, D., Goncalves, O.F. and Leite, J. 2019. Polarity specific effects of cross-hemispheric tDCS coupled with approach-avoidance training on chocolate craving. *Frontiers in Pharmacology.* **9**, 1500. https://doi.org/10.3389/fphar.2018.01500

Castellanos, E.H., Charboneau, E., Dietrich, M.S., Park, S., Bradley, B.P., Mogg, K. and Cowan, R.L. 2009. Obese adults have visual attention bias for food cue images: evidence for altered reward system function. *International Journal of Obesity.* **33**(9), pp.1063-1073. https://doi.org/10.1038/ijo.2009.138

Caton, S.J., Ball, M., Ahern, A. and Hetherington, M.M. 2004. Dose-dependent effects of alcohol on appetite and food intake. *Physiology & Behavior.* **81**(1), pp.51-58. https://doi.org/10.1016/j.physbeh.2003.12.017

Ceaser, A., Csernansky, J.G. and Barch, D.M. 2013. COMT influences on prefrontal and striatal blood oxygenation level-dependent responses during working memory among individuals with schizophrenia, their siblings, and healthy controls. *Cognitive Neuropsychiatry.* **18**(4), pp.257-283. https://doi.org/10.1080/13546805.2012.698100

Celio, A.A., Wilfley, D.E., Crow, S.J., Mitchell, J. and Walsh, B.T. 2004. A comparison of the binge eating scale, questionnaire for eating and weight patterns-revised, and eating disorder examination questionnaire with instructions with the eating disorder examination in the assessment of binge eating disorder and its symptoms. *International Journal of Eating Disorders.* **36**(4), pp.434-444. https://doi.org/10.1002/eat.20057

Cepeda-Benito, A., Gleaves, D.H., Williams, T.L. and Erath, S.A. 2000. The development and validation of the state and trait food-cravings questionnaires. *Behavior Therapy.* **31**(1), pp.151-173. https://doi.org/10.1016/S0005-7894(00)80009-X

Chen, S., Jackson, T., Dong, D., Zhang, X. and Chen, H. 2019. Exploring effects of single-session anodal tDCS over the inferior frontal gyrus on responses to food cues and food cravings among highly disinhibited restrained eaters: A preliminary study. *Neuroscience Letters.* **706**, pp.211-216. https://doi.org/10.1016/j.neulet.2019.05.035

Chew, T., Ho, K.-A. and Loo, C.K. 2015. Inter- and intra-individual variability in response to transcranial direct current stimulation (tDCS) at varying current intensities. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation.* **8**(6), pp.1130-1137. https://doi.org/10.1016/j.brs.2015.07.031

Cohen, J. 1992. A power primer. *Psychological Bulletin.* **112**(1), pp.155-159. https://doi.org/10.1037//0033-2909.112.1.155

Cornier, M.-A. 2011. Is your brain to blame for weight regain? *Physiology & Behavior.* **104**(4), pp.608-612. https://doi.org/10.1016/j.physbeh.2011.04.003

Cotter, E.W. and Kelly, N.R. 2016. Binge Eating Scale (BES). In: Wade, T. ed. *Encyclopedia of Feeding and Eating Disorders.* Singapore: Springer Singapore, pp.1-5.

Cserjési, R., Luminet, O., Poncelet, A.-S. and Lénárd, L. 2009. Altered executive function in obesity. Exploration of the role of affective states on cognitive abilities. *Appetite.* **52**(2), pp.535-539. https://doi.org/10.1016/j.appet.2009.01.003

da Silva Machado, D.G., Bikson, M., Datta, A., Caparelli-Dáquer, E., Unal, G., Baptista, A.F., Cyrino, E.S., Li, L.M., Morya, E., Moreira, A. and Okano, A.H. 2021. Acute effect of high-definition and conventional tDCS on exercise performance and psychophysiological responses in endurance athletes: a randomized controlled trial. *Scientific Reports.* **11**(1), 13911. https://doi.org/10.1038/s41598-021-92670-6

Dalton, M., Blundell, J. and Finlayson, G. 2013a. Effect of BMI and binge eating on food reward and energy intake: Further evidence for a binge eating subtype of obesity. *Obesity Facts.* **6**(4), pp.348-359. https://doi.org/10.1159/000354599

Dalton, M., Blundell, J. and Finlayson, G. 2013b. Examination of food reward and energy intake under laboratory and free-living conditions in a trait binge eating subtype of obesity. *Frontiers in Psychology.* **4**, 757. https://doi.org/10.3389/fpsyg.2013.00757

Dalton, M. and Finlayson, G. 2014. Psychobiological examination of liking and wanting for fat and sweet taste in trait binge eating females. *Physiology & Behavior.* **136**, pp.128-134. https://doi.org/10.1016/j.physbeh.2014.03.019

Dalton, M., Finlayson, G., Hill, A. and Blundell, J. 2015. Preliminary validation and principal components analysis of the Control of Eating Questionnaire (CoEQ) for the experience of food craving. *European Journal Of Clinical Nutrition.* **69**, pp.1313-1317. https://doi.org/10.1038/ejcn.2015.57

DaSilva, A.F., Volz, M.S., Bikson, M. and Fregni, F. 2011. *Electrode Positioning and Montage in Transcranial Direct Current Stimulation.* [Online]. [Accessed 20 June 2022]. Available from: https://www.jove.com/video/2744/electrode-positioning-montage-transcranial-direct-current

Davis, C. 2013. Compulsive overeating as an addictive behavior: Overlap between food addiction and binge eating disorder. *Current Obesity Reports.* **2**(2), pp.171-178. https://doi.org/10.1007/s13679-013-0049-8

Davis, C., Levitan, R.D., Reid, C., Carter, J.C., Kaplan, A.S., Patte, K.A., King, N., Curtis, C. and Kennedy, J.L. 2009. Dopamine for "wanting" and opioids for "liking": A comparison of obese adults with and without binge eating. *Obesity.* **17**(6), pp.1220-1225. https://doi.org/10.1038/oby.2009.52

Davis, C., Levitan, R.D., Yilmaz, Z., Kaplan, A.S., Carter, J.C. and Kennedy, J.L. 2012. Binge eating disorder and the dopamine D2 receptor: Genotypes and sub-phenotypes. *Progress in Neuro-Psychopharmacology and Biological Psychiatry.* **38**(2), pp.328-335. https://doi.org/10.1016/j.pnpbp.2012.05.002

de Graaf, T.A. and Sack, A.T. 2018. When and how to interpret null results in NIBS: A taxonomy based on prior expectations and experimental design. *Frontiers in Neuroscience.* **12**, 915. https://doi.org/10.3389/fnins.2018.00915

de Klerk, M.T., Smeets, P.A.M. and la Fleur, S.E. 2022. [Post-print]. Inhibitory control as a potential treatment target for obesity. *Nutritional Neuroscience.* https://doi.org/10.1080/1028415X.2022.2053406

De Lauzon-Guillain, B., Romon, M., Musher-Eizenman, D., Heude, B., Basdevant, A., Charles, M.A. and the Fleurbaix-Laventie Ville Santé Study Group. 2009. Cognitive restraint, uncontrolled eating and emotional eating: correlations between parent and adolescent. *Maternal & Child Nutrition.* **5**(2), pp.171-178. https://doi.org/10.1111/j.1740-8709.2008.00164.x

Dedoncker, J., Brunoni, A.R., Baeken, C. and Vanderhasselt, M.-A. 2016. A systematic review and meta-analysis of the effects of transcranial direct current stimulation (tDCS) over the dorsolateral prefrontal cortex in healthy and neuropsychiatric samples: Influence of stimulation parameters. *Brain Stimulation.* **9**(4), pp.501-517. https://doi.org/10.1016/j.brs.2016.04.006

Deeks, J.J., Higgins, J.P.T. and Altman, D.G. 2021. Analysing data and undertaking meta-analyses. In: Higgins, J.P.T., et al. eds. *Cochrane Handbook for Systematic Reviews of Interventions.* [Online]. Cochrane Statistical Methods Group. [Accessed 20 June 2022]. Available from: https://training.cochrane.org/handbook/current/chapter-10

Dohle, S., Diel, K. and Hofmann, W. 2018. Executive functions and the self-regulation of eating behavior: A review. *Appetite.* **124**, pp.4-9. https://doi.org/10.1016/j.appet.2017.05.041

Dreher, J.-C., Kohn, P., Kolachana, B., Weinberger, D.R. and Berman, K.F. 2009. Variation in dopamine genes influences responsivity of the human reward system. *Proceedings of the National Academy of Sciences of the United States of America.* **106**(2), pp.617-622. https://doi.org/10.1073/pnas.0805517106

Duarte, C., Pinto-Gouveia, J. and Ferreira, C. 2015. Expanding binge eating assessment: Validity and screening value of the Binge Eating Scale in women from the general population. *Eating Behaviors.* **18**, pp.41-47. https://doi.org/10.1016/j.eatbeh.2015.03.007

Dunlop, K.A., Woodside, B. and Downar, J. 2016. Targeting neural endophenotypes of eating disorders with non-invasive brain stimulation. *Frontiers in Neuroscience.* **10**, 30. https://doi.org/10.3389/fnins.2016.00030

Egger, M., Smith, G.D., Schneider, M. and Minder, C. 1997. Bias in meta-analysis detected by a simple, graphical test. *BMJ.* **315**, pp.629-639. https://doi.org/10.1136/bmj.315.7109.629

Embling, R., Pink, A.E., Gatzemeier, J., Price, M., Lee, M.D. and Wilkinson, L.L. 2021. Effect of food variety on intake of a meal: a systematic review and meta-analysis. *The American Journal of Clinical Nutrition.* **113**(3), pp.716-741. https://doi.org/10.1093/ajcn/nqaa352

Fassi, L. and Cohen Kadosh, R. 2020. [Pre-print]. Is it all in our head? When subjective beliefs about receiving an intervention are better predictors of experimental results than the intervention itself. *bioRxiv.* https://doi.org/10.1101/2020.12.06.411850

Fassi, L. and Cohen Kadosh, R. 2021. Letter to the editor: How some brain stimulation studies fail to evaluate blinding adequately. *Journal of Psychiatric Research.* **137**, pp.452-453. https://doi.org/10.1016/j.jpsychires.2021.03.020

Fassini, P.G., Das, S.K., Magerowski, G., Marchini, J.S., da Silva Junior, W.A., da Silva, I.R., de Souza Ribeiro Salgueiro, R., Machado, C.D., Suen, V.M.M. and Alonso-Alonso, M. 2020. Noninvasive neuromodulation of the prefrontal cortex in young women with obesity: a randomized clinical trial. *International Journal of Obesity.* **44**(6), pp.1279-1290. https://doi.org/10.1038/s41366-020-0545-3

Fassini, P.G., Das, S.K., Suen, V.M.M., Magerowski, G., Marchini, J.S., da Silva Junior, W.A., Changyu, S. and Alonso-Alonso, M. 2019. Appetite effects of prefrontal stimulation depend on COMT Val158Met polymorphism: A randomized clinical trial. *Appetite.* **140**, pp.142-150. https://doi.org/10.1016/j.appet.2019.05.015

Faul, F., Erdfelder, E., Lang, A.-G. and Buchner, A. 2007. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical

sciences. *Behavior Research Methods.* **39**(2), pp.175-191. https://doi.org/10.3758/bf03193146

Fertonani, A. and Miniussi, C. 2016. Transcranial electrical stimulation: What we know and do not know about mechanisms. *The Neuroscientist.* **23**(2), pp.109-123. https://doi.org/10.1177/1073858416631966

Filmer, H.L., Dux, P.E. and Mattingley, J.B. 2014. Applications of transcranial direct current stimulation for understanding brain function. *Trends in Neurosciences.* **37**(12), pp.742-753. https://doi.org/10.1016/j.tins.2014.08.003

Finlayson, G., Arlotti, A., Dalton, M., King, N. and Blundell, J.E. 2011. Implicit wanting and explicit liking are markers for trait binge eating. A susceptible phenotype for overeating. *Appetite.* **57**(3), pp.722-728. https://doi.org/10.1016/j.appet.2011.08.012

Finlayson, G. and Dalton, M. 2012a. Current progress in the assessment of 'liking' vs. 'wanting' food in human appetite. Comment on '"You Say it's Liking, I Say it's Wanting...". On the difficulty of disentangling food reward in man'. *Appetite.* **58**(1), pp.373-378. https://doi.org/10.1016/j.appet.2011.10.011

Finlayson, G. and Dalton, M. 2012b. Hedonics of food consumption: Are food 'liking' and 'wanting' viable targets for appetite control in the obese? *Current Obesity Reports.* **1**(1), pp.42-49. https://doi.org/10.1007/s13679-011-0007-2

Finlayson, G., King, N. and Blundell, J. 2008. The role of implicit wanting in relation to explicit liking and wanting for food: Implications for appetite control. *Appetite.* **50**(1), pp.120-127. https://doi.org/10.1016/j.appet.2007.06.007

Finlayson, G., King, N. and Blundell, J.E. 2007. Is it possible to dissociate 'liking' and 'wanting' for foods in humans? A novel experimental procedure. *Physiology & Behavior.* **90**(1), pp.36-42. https://doi.org/10.1016/j.physbeh.2006.08.020

Fleurbaix Laventie Ville Sante Study Group. 2004. The Three-Factor Eating Questionnaire-R18 is able to distinguish among different eating patterns in a general population. *The Journal of Nutrition.* **134**(9), pp.2372-2380. https://doi.org/10.1093/jn/134.9.2372

Foster, G.D., Wadden, T.A., Swain, R.M., Stunkard, A.J., Platte, P. and Vogt, R.A. 1998. The Eating Inventory in obese women: clinical correlates and relationship to weight loss. *International Journal of Obesity and Related Metabolic Disorders.* **22**(8), pp.778-785. https://doi.org/10.1038/sj.ijo.0800659

Frank, E., Wilfurth, S., Landgrebe, M., Eichhammer, P., Hajak, G. and Langguth, B. 2010. Anodal skin lesions after treatment with transcranial direct current

stimulation. *Brain Stimulation.* **3**(1), pp.58-59. https://doi.org/10.1016/j.brs.2009.04.002

Frankenfield, D., Roth-Yousey, L. and Compher, C. 2005. Comparison of predictive equations for resting metabolic rate in healthy nonobese and obese adults: A systematic review. *Journal of the American Dietetic Association.* **105**(5), pp.775-789. https://doi.org/10.1016/j.jada.2005.02.005

Fregni, F., Orsati, F., Pedrosa, W., Fecteau, S., Tome, F.A.M., Nitsche, M.A., Mecca, T., Macedo, E.C., Pascual-Leone, A. and Boggio, P.S. 2008. Transcranial direct current stimulation of the prefrontal cortex modulates the desire for specific foods. *Appetite.* **51**(1), pp.34-41. https://doi.org/10.1016/j.appet.2007.09.016

French, S.A., Mitchell, N.R., Finlayson, G., Blundell, J.E. and Jeffery, R.W. 2014. Questionnaire and laboratory measures of eating behavior. Associations with energy intake and BMI in a community sample of working adults. *Appetite.* **72**, pp.50-58. https://doi.org/10.1016/j.appet.2013.09.020

Fricke, K., Seeber, A.A., Thirugnanasambandam, N., Paulus, W., Nitsche, M.A. and Rothwell, J.C. 2010. Time course of the induction of homeostatic plasticity generated by repeated transcranial direct current stimulation of the human motor cortex. *Journal of Neurophysiology.* **105**(3), pp.1141-1149. https://doi.org/10.1152/jn.00608.2009

Furuya, S., Klaus, M., Nitsche, M.A., Paulus, W. and Altenmüller, E. 2014. Ceiling effects prevent further improvement of transcranial stimulation in skilled musicians. *The Journal of Neuroscience.* **34**(41), pp.13834-13839. https://doi.org/10.1523/JNEUROSCI.1170-14.2014

Galetta, S.L. 2017. Occipital Lobe. *Reference Module in Neuroscience and Biobehavioral Psychology.* [Online]. USA: Elsevier. Available from: http://www.sciencedirect.com/science/article/pii/B9780128093245038104

Gálvez, V., Alonzo, A., Martin, D. and Loo, C.K. 2013. Transcranial direct current stimulation treatment protocols: should stimulus intensity be constant or incremental over multiple sessions? *International Journal of Neuropsychopharmacology.* **16**(1), pp.13-21. https://doi.org/10.1017/s1461145712000041

Gandiga, P.C., Hummel, F.C. and Cohen, L.G. 2006. Transcranial DC stimulation (tDCS): A tool for double-blind sham-controlled clinical studies in brain stimulation. *Clinical Neurophysiology.* **117**(4), pp.845-850. https://doi.org/10.1016/j.clinph.2005.12.003

Georgii, C., Goldhofer, P., Meule, A., Richard, A. and Blechert, J. 2017. Food craving, food choice and consumption: The role of impulsivity and sham-controlled tDCS stimulation of the right dlPFC. *Physiology & Behavior.* **177**, pp.20-26. https://doi.org/10.1016/j.physbeh.2017.04.004

Gibbons, C., Finlayson, G., Dalton, M., Caudwell, P. and Blundell, J.E. 2014. Metabolic Phenotype Guidelines: Studying eating behaviour in humans. *Journal of Endocrinology.* **222**(2), pp.G1-G12. https://doi.org/10.1530/joe-14-0020

Gilhooly, C.H., Das, S.K., Golden, J.K., McCrory, M.A., Dallal, G.E., Saltzman, E., Kramer, F.M. and Roberts, S.B. 2007. Food cravings and energy regulation: the characteristics of craved foods and their relationship with eating behaviors and weight change during 6 months of dietary energy restriction. *International Journal of Obesity.* **31**(12), pp.1849-1858. https://doi.org/10.1038/sj.ijo.0803672

Gill, J., Shah-Basak, P.P. and Hamilton, R. 2015. It's the thought that counts: Examining the task-dependent effects of transcranial direct current stimulation on executive function. *Brain Stimulation.* **8**(2), pp.253-259. https://doi.org/10.1016/j.brs.2014.10.018

Gluck, M.E., Alonso-Alonso, M., Piaggi, P., Weise, C.M., Jumpertz-von Schwartzenberg, R., Reinhardt, M., Wassermann, E.M., Venti, C.A., Votruba, S.B. and Krakoff, J. 2015. Neuromodulation targeted to the prefrontal cortex induces changes in energy intake and weight loss in obesity. *Obesity.* **23**(11), pp.2149-2156. https://doi.org/10.1002/oby.21313

Gluck, M.E., Viswanath, P. and Stinson, E.J. 2017. Obesity, appetite, and the prefrontal cortex. *Current Obesity Reports.* **6**(4), pp.380-388. https://doi.org/10.1007/s13679-017-0289-0

Goldman, R.L., Borckardt, J.J., Frohman, H.A., O'Neil, P.M., Madan, A., Campbell, L.K., Budak, A. and George, M.S. 2011. Prefrontal cortex transcranial direct current stimulation (tDCS) temporarily reduces food cravings and increases the self-reported ability to resist food in adults with frequent food craving. *Appetite.* **56**(3), pp.741-746. https://doi.org/10.1016/j.appet.2011.02.013

Goldman, R.L., Canterberry, M., Borckardt, J.J., Madan, A., Byrne, T.K., George, M.S., O'Neil, P.M. and Hanlon, C.A. 2013. Executive control circuitry differentiates degree of success in weight loss following gastric-bypass surgery. *Obesity.* **21**(11), pp.2189-2196. https://doi.org/10.1002/oby.20575

Goldstone, A.P., Prechtl de Hernandez, C.G., Beaver, J.D., Muhammed, K., Croese, C., Bell, G., Durighel, G., Hughes, E., Waldman, A.D., Frost, G. and Bell, J.D. 2009. Fasting biases brain reward systems towards high-calorie foods. *European Journal of Neuroscience.* **30**(8), pp.1625-1635. https://doi.org/10.1111/j.1460-9568.2009.06949.x

Gormally, J., Black, S., Daston, S. and Rardin, D. 1982. The assessment of binge eating severity among obese persons. *Addictive Behaviors.* **7**(1), pp.47-55. https://doi.org/10.1016/0306-4603(82)90024-7

Griffioen-Roose, S., Mars, M., Finlayson, G., Blundell, J.E. and de Graaf, C. 2011. The effect of within-meal protein content and taste on subsequent food

choice and satiety. *British Journal of Nutrition.* **106**(5), pp.779-788. https://doi.org/10.1017/s0007114511001012

Grundeis, F., Brand, C., Kumar, S., Rullmann, M., Mehnert, J. and Pleger, B. 2017. Non-invasive prefrontal/frontal brain stimulation is not effective in modulating food reappraisal abilities or calorie consumption in obese females. *Frontiers in Neuroscience.* **11**, 334. https://doi.org/10.3389/fnins.2017.00334

Grupski, A.E., Hood, M.M., Hall, B.J., Azarbad, L., Fitzpatrick, S.L. and Corsica, J.A. 2013. Examining the Binge Eating Scale in screening for binge eating disorder in bariatric surgery candidates. *Obesity Surgery.* **23**(1), pp.1-6. https://doi.org/10.1007/s11695-011-0537-4

Guardia, D., Rolland, B., Karila, L. and Cottencin, O. 2011. GABAergic and glutamatergic modulation in binge eating: therapeutic approach. *Current Pharmaceutical Design.* **17**(14), pp.1396-1409. https://doi.org/10.2174/138161211796150828

Guarienti, F., Caumo, W., Shiozawa, P., Cordeiro, Q., Boggio, P.S., Benseñor, I.M., Lotufo, P.A., Bikson, M. and Brunoni, A.R. 2015. Reducing transcranial direct current stimulation-induced erythema with skin pretreatment: Considerations for sham-controlled clinical trials. *Neuromodulation: Technology at the Neural Interface.* **18**(4), pp.261-265. https://doi.org/10.1111/ner.12230

Hall, K.D., Sacks, G., Chandramohan, D., Chow, C.C., Wang, Y.C., Gortmaker, S.L. and Swinburn, B.A. 2011. Quantification of the effect of energy imbalance on bodyweight. *The Lancet.* **378**(9793), pp.826-837. https://doi.org/10.1016/S0140-6736(11)60812-X

Hall, P.A., Lowe, C. and Vincent, C. 2017. Brain stimulation effects on food cravings and consumption: An update on Lowe et al. (2017) and a response to Generoso et al. (2017). *Psychosomatic Medicine.* **79**(7), pp.839-842. https://doi.org/10.1097/PSY.0000000000000504

Hall, P.A. and Lowe, C.J. 2018. Cravings, currents and cadavers: What is the magnitude of tDCS effects on food craving outcomes? *Nutritional Neuroscience.* **23**(6), pp.1-4. https://doi.org/10.1080/1028415x.2018.1513678

Hall, P.A., Vincent, C.M. and Burhan, A.M. 2018. Non-invasive brain stimulation for food cravings, consumption, and disorders of eating: A review of methods, findings and controversies. *Appetite.* **124**, pp.78-88. https://doi.org/10.1016/j.appet.2017.03.006

Harpaz, E., Tamir, S., Weinstein, A. and Weinstein, Y. 2017. The effect of caffeine on energy balance. *Journal of Basic and Clinical Physiology and Pharmacology.* **28**(1), pp.1-10. https://doi.org/10.1515/jbcpp-2016-0090

Hassanzahraee, M., Nitsche, M.A., Zoghi, M. and Jaberzadeh, S. 2020. Determination of anodal tDCS duration threshold for reversal of corticospinal excitability: An investigation for induction of counter-regulatory mechanisms. *Brain Stimulation.* **13**(3), pp.832-839. https://doi.org/10.1016/j.brs.2020.02.027

Havermans, R.C. 2011. “You Say it's Liking, I Say it's Wanting …”. On the difficulty of disentangling food reward in man. *Appetite.* **57**(1), pp.286-294. https://doi.org/10.1016/j.appet.2011.05.310

Heinitz, S., Reinhardt, M., Piaggi, P., Weise, C.M., Diaz, E., Stinson, E.J., Venti, C., Votruba, S.B., Wassermann, E.M., Alonso-Alonso, M., Krakoff, J. and Gluck, M.E. 2017. Neuromodulation directed at the prefrontal cortex of subjects with obesity reduces snack food intake and hunger in a randomized trial. *The American Journal of Clinical Nutrition.* **106**(6), pp.1347-1357. https://doi.org/10.3945/ajcn.117.158089

Herman, C.P., Roth, D.A. and Polivy, J. 2003. Effects of the presence of others on food intake: A normative interpretation. *Psychological Bulletin.* **129**(6), pp.873-886. https://doi.org/10.1037/0033-2909.129.6.873

Hetherington, M.M., Foster, R., Newman, T., Anderson, A.S. and Norton, G. 2006. Understanding variety: Tasting different foods delays satiation. *Physiology & Behavior.* **87**(2), pp.263-271. https://doi.org/10.1016/j.physbeh.2005.10.012

Higgins, J.P.T., Thomas, J., Chandler, J., Cumpston, M., Li, T., Page, M.J. and Welch, V.A. 2020. *Cochrane Handbook for Systematic Reviews of Interventions.* 6.1 ed. Chichester, UK: John Wiley & Sons.

Higuera-Hernández, M.F., Reyes-Cuapio, E., Gutiérrez-Mendoza, M., Rocha, N.B., Veras, A.B., Budde, H., Jesse, J., Zaldívar-Rae, J., Blanco-Centurión, C., Machado, S. and Murillo-Rodríguez, E. 2018. Fighting obesity: Non-pharmacological interventions. *Clinical Nutrition ESPEN.* **25**, pp.50-55. https://doi.org/10.1016/j.clnesp.2018.04.005

Hill, A.T., Fitzgerald, P.B. and Hoy, K.E. 2016. Effects of anodal transcranial direct current stimulation on working memory: A systematic review and meta-analysis of findings from healthy and neuropsychiatric populations. *Brain Stimulation.* **9**(2), pp.197-208. https://doi.org/10.1016/j.brs.2015.10.006

Hill, J.O. 2006. Understanding and addressing the epidemic of obesity: An energy balance perspective. *Endocrine Reviews.* **27**(7), pp.750-761. https://doi.org/10.1210/er.2006-0032

Holsen, L.M., Savage, C.R., Martin, L.E., Bruce, A.S., Lepping, R.J., Ko, E., Brooks, W.M., Butler, M.G., Zarcone, J.R. and Goldstein, J.M. 2012. Importance of reward and prefrontal circuitry in hunger and satiety: Prader–Willi syndrome vs simple obesity. *International Journal of Obesity.* **36**(5), pp.638-647. https://doi.org/10.1038/ijo.2011.204

Horvath, J., Carter, O. and Forte, J. 2014. Transcranial direct current stimulation: five important issues we aren't discussing (but probably should be). *Frontiers in Systems Neuroscience.* **8**, 2. https://dx.doi.org/10.3389%2Ffnsys.2014.00002

Horvath, J.C. 2015. Are current blinding methods for transcranial direct current stimulation (tDCS) effective in healthy populations? *Clinical Neurophysiology.* **126**(11), pp.2045-2046. https://doi.org/10.1016/j.clinph.2015.04.001

Hruby, A. and Hu, F.B. 2015. The epidemiology of obesity: A big picture. *PharmacoEconomics.* **33**(7), pp.673-689. https://doi.org/10.1007/s40273-014-0243-x

Hudson, J.I., Hiripi, E., Pope, H.G. and Kessler, R.C. 2007. The prevalence and correlates of eating disorders in the National Comorbidity Survey replication. *Biological Psychiatry.* **61**(3), pp.348-358. https://doi.org/10.1016/j.biopsych.2006.03.040

Im, C.-H., Park, J.-H., Shim, M., Chang, W.H. and Kim, Y.-H. 2012. Evaluation of local electric fields generated by transcranial direct current stimulation with an extracephalic reference electrode based on realistic 3D body modeling. *Physics in Medicine and Biology.* **57**(8), pp.2137-2150. https://doi.org/10.1088/0031-9155/57/8/2137

Imburgio, M.J. and Orr, J.M. 2018. Effects of prefrontal tDCS on executive function: Methodological considerations revealed by meta-analysis. *Neuropsychologia.* **117**, pp.156-166. https://doi.org/10.1016/j.neuropsychologia.2018.04.022

Jacobson, L., Koslowsky, M. and Lavidor, M. 2012. tDCS polarity effects in motor and cognitive domains: a meta-analytical review. *Experimental Brain Research.* **216**(1), pp.1-10. https://doi.org/10.1007/s00221-011-2891-9

Jamil, A. and Nitsche, M.A. 2017. What effect does tDCS have on the brain? Basic physiology of tDCS. *Current Behavioral Neuroscience Reports.* **4**(4), pp.331-340. https://doi.org/10.1007/s40473-017-0134-5

Jauch-Chara, K., Kistenmacher, A., Herzog, N., Schwarz, M., Schweiger, U. and Oltmanns, K.M. 2014. Repetitive electric brain stimulation reduces food intake in humans. *The American Journal of Clinical Nutrition.* **100**(4), pp.1003-1009. https://doi.org/10.3945/ajcn.113.075481

Joseph, R.J., Alonso-Alonso, M., Bond, D.S., Pascual-Leone, A. and Blackburn, G.L. 2011. The neurocognitive connection between physical activity and eating behaviour. *Obesity Reviews.* **12**(10), pp.800-812. https://doi.org/10.1111/j.1467-789X.2011.00893.x

Karhunen, L.J., Vanninen, E.J., Kuikka, J.T., Lappalainen, R.I., Tiihonen, J. and Uusitupa, M.I.J. 2000. Regional cerebral blood flow during exposure to food in obese binge eating women. *Psychiatry Research: Neuroimaging.* **99**(1), pp.29-42. https://doi.org/10.1016/S0925-4927(00)00053-6

Karlsson, J., Persson, L.O., Sjöström, L. and Sullivan, M. 2000. Psychometric properties and factor structure of the Three-Factor Eating Questionnaire (TFEQ) in obese men and women. Results from the Swedish Obese Subjects (SOS) study. *International Journal of Obesity.* **24**(12), pp.1715-1725. https://doi.org/10.1038/sj.ijo.0801442

Katwala, A. 2019. High-flying CEOs are trying to brain-zap their way to happiness. *WIRED*.

Kekic, M., McClelland, J., Bartholdy, S., Boysen, E., Musiat, P., Dalton, B., Tiza, M., David, A.S., Campbell, I.C. and Schmidt, U. 2017. Single-session transcranial direct current stimulation temporarily improves symptoms, mood, and self-regulatory control in bulimia nervosa: A randomised controlled trial. *PLOS ONE.* **12**(1), e0167606. https://doi.org/10.1371/journal.pone.0167606

Kekic, M., McClelland, J., Campbell, I., Nestler, S., Rubia, K., David, A.S. and Schmidt, U. 2014. The effects of prefrontal cortex transcranial direct current stimulation (tDCS) on food craving and temporal discounting in women with frequent food cravings. *Appetite.* **78**, pp.55-62. https://doi.org/10.1016/j.appet.2014.03.010

Keller, K.L. 2017. Brain stimulation for treatment of obesity: will stimulating the prefrontal cortex reduce overeating? *American Journal of Clinical Nutrition.* **106**(6), pp.1331-1332. https://doi.org/10.3945/ajcn.117.169631

Kelly, J. and Metcalfe, J. 2012. Validity and reliability of body composition analysis using the Tanita BC418-MA. *Journal of Exercise Physiology Online.* [Online]. **15**(6), pp.74-83. Available from: http://www.asep.org/asep/asep/JEPonlineDECEMBER2012_Kelly.pdf

Kessler, R.C., Berglund, P.A., Chiu, W.T., Deitz, A.C., Hudson, J.I., Shahly, V., Aguilar-Gaxiola, S., Alonso, J., Angermeyer, M.C., Benjet, C., Bruffaerts, R., de Girolamo, G., de Graaf, R., Maria Haro, J., Kovess-Masfety, V., O'Neill, S., Posada-Villa, J., Sasu, C., Scott, K., Viana, M.C. and Xavier, M. 2013. The prevalence and correlates of Binge Eating Disorder in the World Health Organization World Mental Health surveys. *Biological Psychiatry.* **73**(9), pp.904-914. https://doi.org/10.1016/j.biopsych.2012.11.020

Kessler, S.K., Turkeltaub, P.E., Benson, J.G. and Hamilton, R.H. 2012. Differences in the experience of active and sham transcranial direct current stimulation. *Brain Stimulation.* **5**(2), pp.155-162. https://doi.org/10.1016/j.brs.2011.02.007

Kissileff, H.R., Wentzlaff, T.H., Guss, J.L., Walsh, B.T., Devlin, M.J. and Thornton, J.C. 1996. A direct measure of satiety disturbance in patients with bulimia nervosa. *Physiology & Behavior.* **60**(4), pp.1077-1085. https://doi.org/10.1016/0031-9384(96)00086-8

Klem, G.H., Lüders, H.O., Jasper, H.H. and Elger, C. 1999. The ten-twenty electrode system of the International Federation. The International Federation of Clinical Neurophysiology. *Electroencephalography and Clinical Neurophysiology Supplement.* **52**, pp.3-6.

Kober, H. and Boswell, R.G. 2018. Potential psychological and neural mechanisms in binge eating disorder: Implications for treatment. *Clinical Psychology Review.* **60**, pp.32-44. https://doi.org/10.1016/j.cpr.2017.12.004

Krause, B. and Kadosh, R.C. 2014. Not all brains are created equal: the relevance of individual differences in responsiveness to transcranial electrical stimulation. *Frontiers in Systems Neuroscience.* **8**, 25. https://doi.org/10.3389/fnsys.2014.00025

Lapenta, O.M., Di Sierve, K., de Macedo, E.C., Fregni, F. and Boggio, P.S. 2014. Transcranial direct current stimulation modulates ERP-indexed inhibitory control and reduces food consumption. *Appetite.* **83**, pp.42-48. https://doi.org/10.1016/j.appet.2014.08.005

Le, D.S.N.T., Pannacciulli, N., Chen, K., Del Parigi, A., Salbe, A.D., Reiman, E.M. and Krakoff, J. 2006. Less activation of the left dorsolateral prefrontal cortex in response to a meal: a feature of obesity. *The American Journal of Clinical Nutrition.* **84**(4), pp.725-731. https://doi.org/10.1093/ajcn/84.4.725

Le, D.S.N.T., Pannacciulli, N., Chen, K., Salbe, A.D., Hill, J.O., Wing, R.R., Reiman, E.M. and Krakoff, J. 2007. Less activation in the left dorsolateral prefrontal cortex in the reanalysis of the response to a meal in obese than in lean women and its association with successful weight loss. *The American Journal of Clinical Nutrition.* **86**(3), pp.573-579. https://doi.org/10.1093/ajcn/86.3.573

Learmonth, G., Thut, G., Benwell, C.S.Y. and Harvey, M. 2015. The implications of state-dependent tDCS effects in aging: Behavioural response is determined by baseline performance. *Neuropsychologia.* **74**, pp.108-119. https://doi.org/10.1016/j.neuropsychologia.2015.01.037

Lee, M. and Wagenmakers, E. 2013. *Bayesian Cognitive Modeling: A Practical Course.* United Kingdom: Cambridge University Press.

Lefaucheur, J.P. 2016. A comprehensive database of published tDCS clinical trials (2005-2016). *Clinical Neurophysiology.* **46**(6), pp.319-398. https://doi.org/10.1016/j.neucli.2016.10.002

Leite, J., Gonçalves, Ó.F., Pereira, P., Khadka, N., Bikson, M., Fregni, F. and Carvalho, S. 2018. The differential effects of unihemispheric and bihemispheric tDCS over the inferior frontal gyrus on proactive control. *Neuroscience Research.* **130**, pp.39-46. https://doi.org/10.1016/j.neures.2017.08.005

Li, L.M., Uehara, K. and Hanakawa, T. 2015. The contribution of interindividual factors to variability of response in transcranial direct current stimulation studies. *Frontiers in Cellular Neuroscience.* **9**, 181. https://doi.org/10.3389/fncel.2015.00181

Lipsey, M.W. and Wilson, D.B. 2000. *Practical Meta-Analysis.* United States: SAGE Publications.

Ljubisavljevic, M., Maxood, K., Bjekic, J., Oommen, J. and Nagelkerke, N. 2016. Long-term effects of repeated prefrontal cortex transcranial direct current stimulation (tDCS) on food craving in normal and overweight young adults. *Brain Stimulation.* **9**(6), pp.826-833. https://doi.org/10.1016/j.brs.2016.07.002

Lobstein, T., Brinsden, H. and Neveux, M. 2022. *World Obesity Atlas 2022.* London, UK.

López-Alonso, V., Cheeran, B., Río-Rodríguez, D. and Fernández-del-Olmo, M. 2014. Inter-individual variability in response to non-invasive brain stimulation paradigms. *Brain Stimulation: Basic, Translational, and Clinical Research in Neuromodulation.* **7**(3), pp.372-380. https://doi.org/10.1016/j.brs.2014.02.004

Lowe, C.J., Reichelt, A.C. and Hall, P.A. 2019. The prefrontal cortex and obesity: A health neuroscience perspective. *Trends in Cognitive Sciences.* **23**(4), pp.349-361. https://doi.org/10.1016/j.tics.2019.01.005

Lowe, C.J., Vincent, C. and Hall, P.A. 2017. Effects of noninvasive brain stimulation on food cravings and consumption: A meta-analytic review. *Psychosomatic Medicine.* **79**(1), pp.2-13. https://doi.org/10.1097/psy.0000000000000368

Lu, H. and Lam, L. 2019. Cathodal skin lesions induced by transcranial direct current stimulation (tDCS). *Neuromodulation: Technology at the Neural Interface.* **22**, pp.989–991. https://doi.org/10.1111/ner.12892

Marcus, M.D., Wing, R.R. and Hopkins, J. 1988. Obese binge eaters: Affect, cognitions, and response to behavioral weight control. *Journal of Consulting and Clinical Psychology.* **56**(3), pp.433-439. https://doi.org/10.1037/0022-006x.56.3.433

Marron, E.M., Viejo-Sobera, R., Cuatrecasas, G., Redolar-Ripoll, D., Lorda, P.G., Datta, A., Bikson, M., Magerowski, G. and Alonso-Alonso, M. 2019. Prefronto-cerebellar neuromodulation affects appetite in obesity.

International Journal of Obesity. **43**(10), pp.2119-2124. https://doi.org/10.1038/s41366-018-0278-8

Martin, D.M., Liu, R., Alonzo, A., Green, M. and Loo, C.K. 2014. Use of transcranial direct current stimulation (tDCS) to enhance cognitive training: effect of timing of stimulation. *Experimental Brain Research.* **232**(10), pp.3345-3351. https://doi.org/10.1007/s00221-014-4022-x

Matsumoto, H. and Ugawa, Y. 2017. Adverse events of tDCS and tACS: A review. *Clinical Neurophysiology Practice.* **2**, pp.19-25. https://doi.org/10.1016/j.cnp.2016.12.003

Mattavelli, G., Gallucci, A., Schiena, G., D'Agostino, A., Sassetti, T., Bonora, S., Bertelli, S., Benetti, A., Tugnoli, E., Ruggiero, G.M., Sassaroli, S., Lauro, L.R., Gambini, O. and Papagno, C. 2019. Transcranial direct current stimulation modulates implicit attitudes towards food in eating disorders. *International Journal of Eating Disorders.* **52**(5), pp.576-581. https://doi.org/10.1002/eat.23046

Max, S.M., Plewnia, C., Zipfel, S., Giel, K.E. and Schag, K. 2020. Combined antisaccade task and transcranial direct current stimulation to increase response inhibition in binge eating disorder. *European Archives of Psychiatry and Clinical Neuroscience.* **271**, pp.17-28. https://doi.org/10.1007/s00406-020-01164-5

McCreery, D.B., Agnew, W.F., Yuen, T.G.H. and Bullara, L. 1990. Charge density and charge per phase as cofactors in neural injury induced by electrical stimulation. *IEEE Transactions on Biomedical Engineering.* **37**(10), pp.996-1001. https://doi.org/10.1109/10.102812

McLaren, M.E., Nissim, N.R. and Woods, A.J. 2018. The effects of medication use in transcranial direct current stimulation: A brief review. *Brain Stimulation.* **11**(1), pp.52-58. https://doi.org/10.1016/j.brs.2017.10.006

Mehta, S., Melhorn, S.J., Smeraglio, A., Tyagi, V., Grabowski, T., Schwartz, M.W. and Schur, E.A. 2012. Regional brain response to visual food cues is a marker of satiety that predicts food choice. *The American Journal of Clinical Nutrition.* **96**(5), pp.989-999. https://doi.org/10.3945/ajcn.112.042341

Meule, A. 2018a. Assessment of Food Cravings. In: Preuss, H.G., et al. eds. *Processed Food Addiction: Foundations, Assessment, and Recovery.* United States: CRC Press, pp.137-145.

Meule, A. 2018b. Food cravings in food addiction: exploring a potential cut-off value of the Food Cravings Questionnaire-Trait-reduced. *Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity.* **23**(1), pp.39-43. https://doi.org/10.1007/s40519-017-0452-3

Meule, A., Hermann, T. and Kübler, A. 2014a. A short version of the Food Cravings Questionnaire—Trait: the FCQ-T-reduced. *Frontiers in Psychology.* **5**, 190. https://dx.doi.org/10.3389%2Ffpsyg.2014.00190

Meule, A., Teran, C.B., Berker, J., Gründel, T., Mayerhofer, M. and Platte, P. 2014b. On the differentiation between trait and state food craving: Half-year retest-reliability of the Food Cravings Questionnaire-Trait-reduced (FCQ-T-r) and the Food Cravings Questionnaire-State(FCQ-S). *Journal of Eating Disorders.* **2**(1), 25. https://doi.org/10.1186/s40337-014-0025-z

Michaud, A., Vainik, U., Garcia-Garcia, I. and Dagher, A. 2017. Overlapping neural endophenotypes in addiction and obesity. *Frontiers in Endocrinology.* **8**, 127. https://doi.org/10.3389/fendo.2017.00127

Mifflin, M.D., St Jeor, S.T., Hill, L.A., Scott, B.J., Daugherty, S.A. and Koh, Y.O. 1990. A new predictive equation for resting energy expenditure in healthy individuals. *The American Journal of Clinical Nutrition.* **51**(2), pp.241-247. https://doi.org/10.1093/ajcn/51.2.241

Miller, E.K. and Cohen, J.D. 2001. An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience.* **24**(1), pp.167-202. https://doi.org/10.1146/annurev.neuro.24.1.167

Miller, W.C., Anton, H.A. and Townson, A.F. 2008. Measurement properties of the CESD scale among individuals with spinal cord injury. *Spinal Cord.* **46**(4), pp.287-292. https://doi.org/10.1038/sj.sc.3102127

Miniussi, C., Harris, J.A. and Ruzzoli, M. 2013. Modelling non-invasive brain stimulation in cognitive neuroscience. *Neuroscience & Biobehavioral Reviews.* **37**(8), pp.1702-1712. https://doi.org/10.1016/j.neubiorev.2013.06.014

Miranda, P.C., Lomarev, M. and Hallett, M. 2006. Modeling the current distribution during transcranial direct current stimulation. *Clinical Neurophysiology.* **117**(7), pp.1623-1629. https://doi.org/10.1016/j.clinph.2006.04.009

Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G. and The, P.G. 2009. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA statement. *PLOS Medicine.* **6**(7), e1000097. https://doi.org/10.1371/journal.pmed.1000097

Moliadze, V., Antal, A. and Paulus, W. 2010. Electrode-distance dependent after-effects of transcranial direct and random noise stimulation with extracephalic reference electrodes. *Clinical Neurophysiology.* **121**(12), pp.2165-2171. https://doi.org/10.1016/j.clinph.2010.04.033

Monte-Silva, K., Kuo, M.-F., Hessenthaler, S., Fresnoza, S., Liebetanz, D., Paulus, W. and Nitsche, M.A. 2013. Induction of late LTP-like plasticity in the human

motor cortex by repeated non-invasive brain stimulation. *Brain Stimulation.* **6**(3), pp.424-432. https://doi.org/10.1016/j.brs.2012.04.011

Montenegro, R.A., Farinatti, P.d.T.V., Fontes, E.B., Soares, P.P.d.S., Cunha, F.A.d., Gurgel, J.L., Porto, F., Cyrino, E.S. and Okano, A.H. 2011. Transcranial direct current stimulation influences the cardiac autonomic nervous control. *Neuroscience Letters.* **497**(1), pp.32-36. https://doi.org/10.1016/j.neulet.2011.04.019

Montenegro, R.A., Okano, A.H., Cunha, F.A., Gurgel, J.L., Fontes, E.B. and Farinatti, P.T.V. 2012. Prefrontal cortex transcranial direct current stimulation associated with aerobic exercise change aspects of appetite sensation in overweight adults. *Appetite.* **58**(1), pp.333-338. https://doi.org/10.1016/j.appet.2011.11.008

Moshfegh, A.J., Rhodes, D.G., Baer, D.J., Murayi, T., Clemens, J.C., Rumpler, W.V., Paul, D.R., Sebastian, R.S., Kuczynski, K.J., Ingwersen, L.A., Staples, R.C. and Cleveland, L.E. 2008. The US Department of Agriculture Automated Multiple-Pass Method reduces bias in the collection of energy intakes. *American Journal of Clinical Nutrition.* **88**(2), pp.324-332. https://doi.org/10.1093/ajcn/88.2.324

Mostafavi, S.-A., Khaleghi, A., Mohammadi, M.R. and Akhondzadeh, S. 2018. Is transcranial direct current stimulation an effective modality in reducing food craving? A systematic review and meta-analysis. *Nutritional Neuroscience.* **23**(1), pp.1-13. https://doi.org/10.1080/1028415x.2018.1470371

Munsch, S., Meyer, A.H., Quartier, V. and Wilhelm, F.H. 2012. Binge eating in binge eating disorder: A breakdown of emotion regulatory process? *Psychiatry Research.* **195**(3), pp.118-124. https://doi.org/10.1016/j.psychres.2011.07.016

Ng, L. and Davis, C. 2013. Cravings and food consumption in binge eating disorder. *Eating Behaviors.* **14**(4), pp.472-475. https://doi.org/10.1016/j.eatbeh.2013.08.011

Nikolin, S., Huggins, C., Martin, D., Alonzo, A. and Loo, C.K. 2018. Safety of repeated sessions of transcranial direct current stimulation: A systematic review. *Brain Stimulation.* **11**(2), pp.278-288. https://doi.org/10.1016/j.brs.2017.10.020

Nitsche, M.A., Boggio, P.S., Fregni, F. and Pascual-Leone, A. 2009. Treatment of depression with transcranial direct current stimulation (tDCS): A review. *Experimental Neurology.* **219**(1), pp.14-19. https://doi.org/10.1016/j.expneurol.2009.03.038

Nitsche, M.A., Cohen, L.G., Wassermann, E.M., Priori, A., Lang, N., Antal, A., Paulus, W., Hummel, F., Boggio, P.S., Fregni, F. and Pascual-Leone, A. 2008. Transcranial direct current stimulation: State of the art 2008. *Brain Stimulation.* **1**(3), pp.206-223. https://doi.org/10.1016/j.brs.2008.06.004

Nitsche, M.A., Doemkes, S., Karaköse, T., Antal, A., Liebetanz, D., Lang, N., Tergau, F. and Paulus, W. 2007. Shaping the effects of transcranial direct current stimulation of the human motor cortex. *Journal of Neurophysiology.* **97**(4), pp.3109-3117. https://doi.org/10.1152/jn.01312.2006

Nitsche, M.A., Liebetanz, D., Lang, N., Antal, A., Tergau, F. and Paulus, W. 2003. Safety criteria for transcranial direct current stimulation (tDCS) in humans. *Clinical Neurophysiology.* **114**(11), pp.2220-2222. https://doi.org/10.1016/S1388-2457(03)00235-9

Nitsche, M.A. and Paulus, W. 2000. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of Physiology.* **527**(3), pp.633-639. https://doi.org/10.1111/j.1469-7793.2000.t01-1-00633.x

Nitsche, M.A. and Paulus, W. 2001. Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. *Neurology.* **57**(10), pp.1899-1901. https://doi.org/10.1212/wnl.57.10.1899

Nitsche, M.A. and Paulus, W. 2011. Transcranial direct current stimulation – update 2011. *Restorative Neurology and Neuroscience.* **29**, pp.463-492. https://doi.org/10.3233/rnn-2011-0618

Noetscher, G.M., Yanamadala, J., Makarov, S.N. and Pascual-Leone, A. 2014. Comparison of cephalic and extracephalic montages for transcranial direct current stimulation – a numerical study. *IEEE Transactions on Biomedical Engineering.* **61**(9), pp.2488-2498. https://doi.org/10.1109/tbme.2014.2322774

O'Connell, N.E., Cossar, J., Marston, L., Wand, B.M., Bunce, D., Moseley, G.L. and De Souza, L.H. 2012. Rethinking clinical trials of transcranial direct current stimulation: Participant and assessor blinding is inadequate at intensities of 2mA. *PLOS ONE.* **7**(10), e47514. https://doi.org/10.1371/journal.pone.0047514

Oustric, P., Thivel, D., Dalton, M., Beaulieu, K., Gibbons, C., Hopkins, M., Blundell, J. and Finlayson, G. 2020. Measuring food preference and reward: Application and cross-cultural adaptation of the Leeds Food Preference Questionnaire in human experimental research. *Food Quality and Preference.* **80**, 103824. https://doi.org/10.1016/j.foodqual.2019.103824

Palm, U., Keeser, D., Schiller, C., Fintescu, Z., Nitsche, M., Reisinger, E. and Padberg, F. 2008. Skin lesions after treatment with transcranial direct current stimulation (tDCS). *Brain Stimulation.* **1**(4), pp.386-387. https://doi.org/10.1016/j.brs.2008.04.003

Palm, U., Reisinger, E., Keeser, D., Kuo, M.-F., Pogarell, O., Leicht, G., Mulert, C., Nitsche, M.A. and Padberg, F. 2013. Evaluation of sham transcranial direct current stimulation for randomized, placebo-controlled clinical trials. *Brain*

Stimulation: Basic, Translational, and Clinical Research in Neuromodulation. **6**(4), pp.690-695. https://doi.org/10.1016/j.brs.2013.01.005

Perceval, G., Martin, A.K., Copland, D.A., Laine, M. and Meinzer, M. 2020. Multisession transcranial direct current stimulation facilitates verbal learning and memory consolidation in young and older adults. *Brain and Language.* **205**, 104788. https://doi.org/10.1016/j.bandl.2020.104788

Pignatti, R., Bertella, L., Albani, G., Mauro, A., Molinari, E. and Semenza, C. 2006. Decision-making in obesity: A study using the Gambling Task. *Eating and Weight Disorders - Studies on Anorexia, Bulimia and Obesity.* **11**(3), pp.126-132. https://doi.org/10.1007/BF03327557

Pleger, B. 2018. Invasive and non-invasive stimulation of the obese human brain. *Frontiers in Neuroscience.* **12**, 884. https://dx.doi.org/10.3389%2Ffnins.2018.00884

Pomarol-Clotet, E., Fatjó-Vilas, M., McKenna, P.J., Monté, G.C., Sarró, S., Ortiz-Gil, J., Aguirre, C., Gomar, J.J., Guerrero, A., Landin, R., Capdevila, A., Fañanás, L. and Salvador, R. 2010. COMT Val158Met polymorphism in relation to activation and de-activation in the prefrontal cortex: A study in patients with schizophrenia and healthy subjects. *NeuroImage.* **53**(3), pp.899-907. https://doi.org/10.1016/j.neuroimage.2010.04.018

Poreisz, C., Boros, K., Antal, A. and Paulus, W. 2007. Safety aspects of transcranial direct current stimulation concerning healthy subjects and patients. *Brain Research Bulletin.* **72**(4), pp.208-214. https://doi.org/10.1016/j.brainresbull.2007.01.004

Priori, A., Berardelli, A., Rona, S., Accornero, N. and Manfredi, M. 1998. Polarization of the human motor cortex through the scalp. *NeuroReport.* **9**(10), pp.2257-2260. https://doi.org/10.1097/00001756-199807130-00020

Pull, C.B. 2004. Binge eating disorder. *Current Opinion in Psychiatry.* **17**(1), pp.43-48.

Quintana, D.S. and Williams, D.R. 2018. Bayesian alternatives for common null-hypothesis significance tests in psychiatry: a non-technical guide using JASP. *BMC Psychiatry.* **18**(1), 178. https://doi.org/10.1186/s12888-018-1761-4

Radloff, L.S. 1977. The CES-D scale: A self-report depression scale for research in the general population. *Applied Psychological Measurement.* **1**(3), pp.385-401. https://doi.org/10.1177/014662167700100306

Ray, M.K., Sylvester, M.D., Helton, A., Pittman, B.R., Wagstaff, L.E., McRae, T.R., Turan, B., Fontaine, K.R., Amthor, F.R. and Boggiano, M.M. 2019. The effect of expectation on transcranial direct current stimulation (tDCS) to suppress

food craving and eating in individuals with overweight and obesity. *Appetite.* **136**, pp.1-7. https://doi.org/10.1016/j.appet.2018.12.044

Ray, M.K., Sylvester, M.D., Osborn, L., Helms, J., Turan, B., Burgess, E.E. and Boggiano, M.M. 2017. The critical role of cognitive-based trait differences in transcranial direct current stimulation (tDCS) suppression of food craving and eating in frank obesity. *Appetite.* **116**, pp.568-574. https://doi.org/10.1016/j.appet.2017.05.046

Reas, D.L. and Grilo, C.M. 2014. Current and emerging drug treatments for binge eating disorder. *Expert Opinion on Emerging Drugs.* **19**(1), pp.99-142. https://doi.org/10.1517/14728214.2014.879291

Rodella, C., Cespón, J., Repetto, C. and Pellicciari, M.C. 2021. Customized application of tDCS for clinical rehabilitation in Alzheimer's disease. *Frontiers in Human Neuroscience.* **15**, 687968. https://doi.org/10.3389/fnhum.2021.687968

Rodríguez, N., Opisso, E., Pascual-Leone, Á. and Soler, M.D. 2014. Skin lesions induced by transcranial direct current stimulation (tDCS). *Brain Stimulation.* **7**(5), pp.765-767. https://doi.org/10.1016/j.brs.2014.06.005

Rohatgi, A. 2020. *WebPlotDigitizer.* [Online]. [Accessed 20 June 2022]. Available from: https://automeris.io/WebPlotDigitizer

Rolls, B.J., Andersen, A.E., Moran, T.H., McNelis, A.L., Baier, H.C. and Fedoroff, I.C. 1992. Food intake, hunger, and satiety after preloads in women with eating disorders. *American Journal of Clinical Nutrition.* **55**(6), pp.1093-1103. https://doi.org/10.1093/ajcn/55.6.1093

Rolls, B.J., Fedoroff, I.C. and Guthrie, J.F. 1991. Gender differences in eating behavior and body weight regulation. *Health Psychology.* **10**(2), pp.133-142. https://doi.org/10.1037/0278-6133.10.2.133

Rossi, S., Hallett, M., Rossini, P.M. and Pascual-Leone, A. 2009. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clinical Neurophysiology.* **120**(12), pp.2008-2039. https://doi.org/10.1016/j.clinph.2009.08.016

RStudio Team. 2022. *RStudio: Integrated Development for R.* [Online]. [Accessed 20 June 2022]. Available from: http://www.rstudio.com/

Rush, S. and Driscoll, D.A. 1968. Current distribution in the brain from surface electrodes. *Anesthesia & Analgesia.* **47**(6), pp.717-723.

Russo, R., Wallace, D., Fitzgerald, P.B. and Cooper, N.R. 2013. Perception of comfort during active and sham transcranial direct current stimulation: A double blind study. *Brain Stimulation: Basic, Translational, and Clinical*

Research in Neuromodulation. **6**(6), pp.946-951. https://doi.org/10.1016/j.brs.2013.05.009

Santos, V.S.d.S.d., Zortea, M., Alves, R.L., Naziazeno, C.C.d.S., Saldanha, J.S., Carvalho, S.d.C.R.d., Leite, A.J.d.C., Torres, I.L.d.S., Souza, A.d., Calvetti, P.Ü., Fregni, F. and Caumo, W. 2018. Cognitive effects of transcranial direct current stimulation combined with working memory training in fibromyalgia: a randomized clinical trial. *Scientific Reports.* **8**(1), 12477. https://doi.org/10.1038/s41598-018-30127-z

Schag, K., Teufel, M., Junne, F., Preissl, H., Hautzinger, M., Zipfel, S. and Giel, K.E. 2013. Impulsivity in binge eating disorder: food cues elicit increased reward responses and disinhibition. *PLOS ONE.* **8**(10), pp.e76542-e76542. https://doi.org/10.1371/journal.pone.0076542

Schubert, M.M., Irwin, C., Seay, R.F., Clarke, H.E., Allegro, D. and Desbrow, B. 2017. Caffeine, coffee, and appetite control: a review. *International Journal of Food Science and Nutrition.* **68**(8), pp.901-912. https://doi.org/10.1080/09637486.2017.1320537

Schwarzer, G., Carpenter, J.R. and Rücker, G. 2015. *Meta-Analysis with R.* Switzerland: Springer International Publishing.

Sedgmond, J., Lawrence Natalia, S., Verbruggen, F., Morrison, S., Chambers Christopher, D. and Adams Rachel, C. 2019. Prefrontal brain stimulation during food-related inhibition training: effects on food craving, food consumption and inhibitory control. *Royal Society Open Science.* **6**(1), 181186. https://doi.org/10.1098/rsos.181186

Sterne, J.A.C., Savović, J., Page, M.J., Elbers, R.G., Blencowe, N.S., Boutron, I., Cates, C.J., Cheng, H.-Y., Corbett, M.S., Eldridge, S.M., Emberson, J.R., Hernán, M.A., Hopewell, S., Hróbjartsson, A., Junqueira, D.R., Jüni, P., Kirkham, J.J., Lasserson, T., Li, T., McAleenan, A., Reeves, B.C., Shepperd, S., Shrier, I., Stewart, L.A., Tilling, K., White, I.R., Whiting, P.F. and Higgins, J.P.T. 2019. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ.* **366**, l4898. https://doi.org/10.1136/bmj.l4898

Stice, E., Spoor, S., Bohon, C., Veldhuizen, M.G. and Small, D.M. 2008. Relation of reward from food intake and anticipated food intake to obesity: a functional magnetic resonance imaging study. *Journal of Abnormal Psychology.* **117**(4), pp.924-935. https://doi.org/10.1037/a0013600

Striegel-Moore, R.H., Rosselli, F., Perrin, N., DeBar, L., Wilson, G.T., May, A. and Kraemer, H.C. 2009. Gender difference in the prevalence of eating disorder symptoms. *International Journal of Eating Disorders.* **42**(5), pp.471-474. https://doi.org/10.1002/eat.20625

Stubbs, R.J., Duarte, C., O'Driscoll, R., Turicchi, J., Kwasnicka, D., Sniehotta, F.F., Marques, M.M., Horgan, G., Larsen, S., Palmeira, A., Santos, I., Teixeira, P.J., Halford, J. and Heitmann, B.L. 2021. The H2020 "NoHoW Project": A

position statement on behavioural approaches to longer-term weight management. *Obesity Facts.* **14**(2), pp.246-258. https://doi.org/10.1159/000513042

Stunkard, A.J. and Messick, S. 1985. The Three-Factor Eating Questionnaire to measure dietary restraint, disinhibition and hunger. *Journal of Psychosomatic Research.* **29**(1), pp.71-83. https://doi.org/10.1016/0022-3999(85)90010-8

Sun, W. and Kober, H. 2020. Regulating food craving: From mechanisms to interventions. *Physiology & Behavior.* **222**, 112878. https://doi.org/10.1016/j.physbeh.2020.112878

Tanita. 2018. *BC-418 Segmental Body Composition Analyzer.* [Online]. [Accessed 20 June 2022]. Available from: https://www.tanita.com/en/bc-418/

Thair, H., Holloway, A.L., Newport, R. and Smith, A.D. 2017. Transcranial direct current stimulation (tDCS): A beginner's guide for design and implementation. *Frontiers in Neuroscience.* **11**, 641. https://doi.org/10.3389/fnins.2017.00641

The R Foundation. 2022. *The R Project for Statistical Computing.* [Online]. [Accessed 20 June 2022]. Available from: https://www.r-project.org/

To, C., Falcone, M., Loughead, J., Logue-Chamberlain, E., Hamilton, R., Kable, J., Lerman, C. and Ashare, R.L. 2018. Got chocolate? Bilateral prefrontal cortex stimulation augments chocolate consumption. *Appetite.* **131**, pp.28-35. https://doi.org/10.1016/j.appet.2018.08.032

Tremblay, S., Lepage, J.-F., Latulipe-Loiselle, A., Fregni, F., Pascual-Leone, A. and Théoret, H. 2014. The uncertain outcome of prefrontal tDCS. *Brain Stimulation.* **7**(6), pp.773-783. https://doi.org/10.1016/j.brs.2014.10.003

Truong, D.Q., Magerowski, G., Blackburn, G.L., Bikson, M. and Alonso-Alonso, M. 2013. Computational modeling of transcranial direct current stimulation (tDCS) in obesity: Impact of head fat and dose guidelines. *NeuroImage: Clinical.* **2**, pp.759-766. https://doi.org/10.1016/j.nicl.2013.05.011

Tunbridge, E.M., Lane, T.A. and Harrison, P.J. 2007. Expression of multiple catechol-o-methyltransferase (COMT) mRNA variants in human brain. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics.* **144B**(6), pp.834-839. https://doi.org/10.1002/ajmg.b.30539

University of Edinburgh. 2014. *Guidelines for Non-Invasive Brain Stimulation (NIBS) studies.* [Online]. [Accessed 20 June 2022]. Available from: https://www.ed.ac.uk/files/atoms/files/tms_tcs_edinburgh_ethics_guidelines.docx

Van den Noortgate, W., López-López, J.A., Marín-Martínez, F. and Sánchez-Meca, J. 2013. Three-level meta-analysis of dependent effect sizes. *Behavior Research Methods.* **45**(2), pp.576-594. https://doi.org/10.3758/s13428-012-0261-6

Van den Noortgate, W., López-López, J.A., Marín-Martínez, F. and Sánchez-Meca, J. 2015. Meta-analysis of multiple outcomes: a multilevel approach. *Behavior Research Methods.* **47**(4), pp.1274-1294. https://doi.org/10.3758/s13428-014-0527-2

Venti, C.A., Votruba, S.B., Franks, P.W., Krakoff, J. and Salbe, A.D. 2010. Reproducibility of ad libitum energy intake with the use of a computerized vending machine system. *American Journal of Clinical Nutrition.* **91**(2), pp.343-348. https://doi.org/10.3945/ajcn.2009.28315

Vicario, C.M., Salehinejad, M.A., Mosayebi-Samani, M., Maezawa, H., Avenanti, A. and Nitsche, M.A. 2020. Transcranial direct current stimulation over the tongue motor cortex reduces appetite in healthy humans. *Brain Stimulation.* **13**(4), pp.1121-1123. https://doi.org/10.1016/j.brs.2020.05.008

Villarejo, C., Fernández-Aranda, F., Jiménez-Murcia, S., Peñas-Lledó, E., Granero, R., Penelo, E., Tinahones, F.J., Sancho, C., Vilarrasa, N., Montserrat-Gil de Bernabé, M., Casanueva, F.F., Fernández-Real, J.M., Frühbeck, G., De la Torre, R., Treasure, J., Botella, C. and Menchón, J.M. 2012. Lifetime obesity in patients with eating disorders: Increasing prevalence, clinical and personality correlates. *European Eating Disorders Review.* **20**(3), pp.250-254. https://doi.org/10.1002/erv.2166

Vitor-Costa, M., Okuno, N.M., Bortolotti, H., Bertollo, M., Boggio, P.S., Fregni, F. and Altimari, L.R. 2015. Improving cycling performance: Transcranial direct current stimulation increases time to exhaustion in cycling. *PLOS ONE.* **10**(12), e0144916. https://doi.org/10.1371/journal.pone.0144916

Wagenmakers, E.-J., Marsman, M., Jamil, T., Ly, A., Verhagen, J., Love, J., Selker, R., Gronau, Q.F., Šmíra, M., Epskamp, S., Matzke, D., Rouder, J.N. and Morey, R.D. 2018. Bayesian inference for psychology. Part I: Theoretical advantages and practical ramifications. *Psychonomic Bulletin & Review.* **25**(1), pp.35-57. https://doi.org/10.3758/s13423-017-1343-3

Wallace, D.L., Aarts, E., d'Oleire Uquillas, F., Dang, L.C., Greer, S.M., Jagust, W.J. and D'Esposito, M. 2015. Genotype status of the dopamine-related catechol-O-methyltransferase (COMT) gene corresponds with desirability of "unhealthy" foods. *Appetite.* **92**, pp.74-80. https://doi.org/10.1016/j.appet.2015.05.004

Wang, G.-J., Volkow, N.D., Telang, F., Jayne, M., Ma, J., Rao, M., Zhu, W., Wong, C.T., Pappas, N.R., Geliebter, A. and Fowler, J.S. 2004. Exposure to appetitive food stimuli markedly activates the human brain. *NeuroImage.* **21**(4), pp.1790-1797. https://doi.org/10.1016/j.neuroimage.2003.11.026

Wang, Y.C., McPherson, K., Marsh, T., Gortmaker, S.L. and Brown, M. 2011. Health and economic burden of the projected obesity trends in the USA and the UK. *The Lancet.* **378**(9793), pp.815-825. https://doi.org/10.1016/S0140-6736(11)60814-3

Ward, Z.J., Bleich, S.N., Cradock, A.L., Barrett, J.L., Giles, C.M., Flax, C., Long, M.W. and Gortmaker, S.L. 2019. Projected U.S. state-level prevalence of adult obesity and severe obesity. *New England Journal of Medicine.* **381**(25), pp.2440-2450. https://doi.org/10.1056/NEJMsa1909301

Wardle, R.A., Thapaliya, G., Nowak, A., Radford, S., Dalton, M., Finlayson, G. and Moran, G.W. 2018. An examination of appetite and disordered eating in active Crohn's disease. *Journal of Crohn's and Colitis.* **12**(7), pp.819-825. https://doi.org/10.1093/ecco-jcc/jjy041

Weydmann, G., Hauck, N., Decker, R., Holland, H., Corrêa, L.L., de Oliveira, A.A. and Bizarro, L. 2022. [Post-print]. Reinforcement sensitivity personality factors, BMI, and lack of inhibitory control as predictors of trait food craving. *Trends in Psychology.* https://doi.org/10.1007/s43076-021-00124-9

Wiegand, A., Nieratschker, V. and Plewnia, C. 2016. Genetic modulation of transcranial direct current stimulation effects on cognition. *Frontiers in Human Neuroscience.* **10**, 651. https://doi.org/10.3389/fnhum.2016.00651

Woods, A.J., Antal, A., Bikson, M., Boggio, P.S., Brunoni, A.R., Celnik, P., Cohen, L.G., Fregni, F., Herrmann, C.S., Kappenman, E.S., Knotkova, H., Liebetanz, D., Miniussi, C., Miranda, P.C., Paulus, W., Priori, A., Reato, D., Stagg, C., Wenderoth, N. and Nitsche, M.A. 2016. A technical guide to tDCS, and related non-invasive brain stimulation tools. *Clinical Neurophysiology.* **127**(2), pp.1031-1048. https://doi.org/10.1016/j.clinph.2015.11.012

Workman, C.D., Fietsam, A.C., Kamholz, J. and Rudroff, T. 2021. Women report more severe sensations from 2 mA and 4 mA transcranial direct current stimulation than men. *European Journal of Neuroscience.* **53**(8), pp.2696-2702. https://doi.org/10.1111/ejn.15070

World Health Organisation. 2008. *Waist circumference and waist-hip ratio: report of a WHO expert consultation.* Geneva.

World Health Organisation. 2021. *Obesity and Overweight.* [Online]. [Accessed 20 June 2022]. Available from: https://www.who.int/en/news-room/fact-sheets/detail/obesity-and-overweight

Wurzman, R., Hamilton, R.H., Pascual-Leone, A. and Fox, M.D. 2016. An open letter concerning do-it-yourself users of transcranial direct current stimulation. *Annals of Neurology.* **80**(1), pp.1-4. https://doi.org/10.1002/ana.24689

Yeomans, M.R., Caton, S. and Hetherington, M.M. 2003. Alcohol and food intake. *Current Opinion in Clinical Nutrition & Metabolic Care.* **6**(6), pp.639-644.

Zheng, H., Huang, D., Chen, S., Wang, S., Guo, W., Luo, J., Ye, H. and Chen, Y. 2016. Modulating the activity of ventromedial prefrontal cortex by anodal tDCS enhances the trustee's repayment through altruism. *Frontiers in Psychology.* **7**, 1437. https://dx.doi.org/10.3389%2Ffpsyg.2016.01437

Zheng, H., Wang, S., Guo, W., Chen, S., Luo, J., Ye, H. and Huang, D. 2017. Enhancing the activity of the DLPFC with tDCS alters risk preference without changing interpersonal trust. *Frontiers in Neuroscience.* **11**, 52. https://dx.doi.org/10.3389%2Ffnins.2017.00052

Appendices

Appendix 1 PRISMA Checklist for the Literature Review in Chapter 3

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	12
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	13 to 14
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	15 to 16
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	16
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	17 to 18
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	16 to 17
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	17
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	17 to 18

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	18
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	18
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	18
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	18 to 20
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	18 to 20
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	18
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	18 to 20
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 3-1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	20 to 21, Table 3-6, Appendix 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 3-4
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	25 to 55
Synthesis of results	21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency	25 to 55
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	22 to 23
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	19 to 20, 22

DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	55 to 59
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	55 to 59
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	59 to 60
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

Appendix 2 Studies Incorporated into the Meta-Analysis for Chapter 3

	Montage	Montage Type	Current Intensity	Current Density	Blinding Protocol	Blinding Success	Online/Offline Protocol	Number of Sessions
Amo Usanos et al. (2020)								
Bravo et al. (2016)	X	X	X	X	X		X	
Burgess et al. (2016)	X	X	X	X	X		X	X
Carvalho et al. (2019)			X	X	X	X	X	
Chen et al. (2019)	X	X	X	X	X	X	X	X
Fassini et al. (2019)								
Fassini et al. (2020)								X
Fregni et al. (2008)			X	X	X		X	X
Georgii et al. (2017)	X	X	X	X	X	X	X	X
Gluck et al. (2015)			X	X	X		X	
Goldman et al. (2011)	X	X	X	X	X	X	X	X

Table continued

	Montage	Montage Type	Current Intensity	Current Density	Blinding Protocol	Blinding Success	Online/Offline Protocol	Number of Sessions
Grundeis et al. (2017)			X	X	X		X	X
Heinitz et al. (2017)								X
Jauch-Chara et al. (2014)	X	X	X	X	X		X	X
Kekic et al. (2014)	X	X	X	X	X		X	X
Kekic et al. (2017)			X	X	X	X	X	
Lapenta et al. (2014)	X	X	X	X	X		X	X
Ljubisavljevic et al. (2016)								
Marron et al. (2019)	X	X	X	X	X		X	
Mattavelli et al. (2019)			X	X		X	X	
Max et al. (2020)	X	X			X	X	X	
Montenegro et al. (2012)								
Ray et al. (2017)	X	X	X	X	X		X	X
Ray et al. (2019)								

Table continued

	Montage	Montage Type	Current Intensity	Current Density	Blinding Protocol	Blinding Success	Online/Offline Protocol	Number of Sessions
Sedgmond et al. (2019)	X	X	X	X	X	X	X	X
To et al. (2018)	X	X	X	X	X	X	X	X
Vicario et al. (2020)			X	X	X		X	
Study n	14	14	20	20	20	10	21	15
Participant n	493	493	716	716	671	524	743	545

Appendix 3 Output of the Multi-Level Modelling

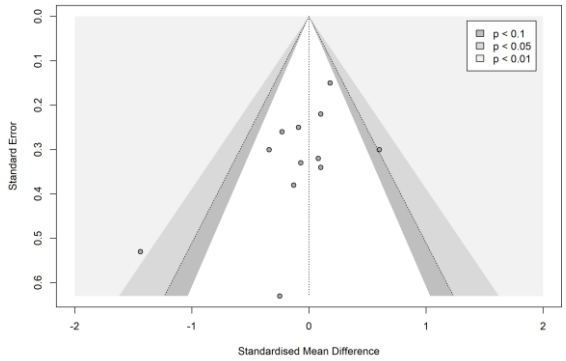
Model level	Added higher level	Model-fit index		Model-comparison index			Variance		
		AIC	Log likelihood	Model	LRT	p	σ^2_1	σ^2_2	σ^2_3
1		60.0577	-29.0288						
2	Participant Sample	62.0577	-29.0288	1 vs. 2	0.0000	1.0000	0.000		
3	Study	64.0577	-29.0288	2 vs. 3	0.0000	1.0000	0.000	0.000	
4	Research group	66.0577	-29.0288	3 vs. 4	0.0000	1.0000	0.000	0.000	0.000

AIC, Akaike information criterion; LRT, likelihood ratio test

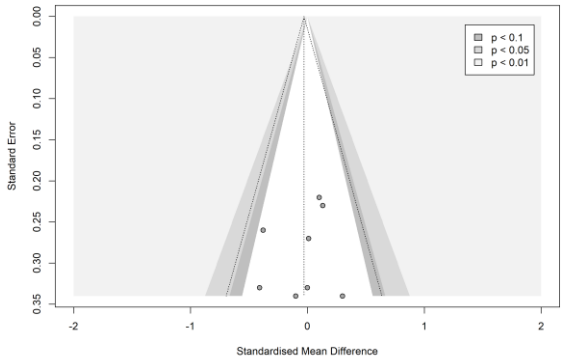
NOTE: To perform multi-level modelling, each unique participant group, individual study, and unique research group were coded, starting from 1. Research groups were identified via corresponding author address.

Appendix 4 Funnel Plots for the Literature Review in Chapter 3

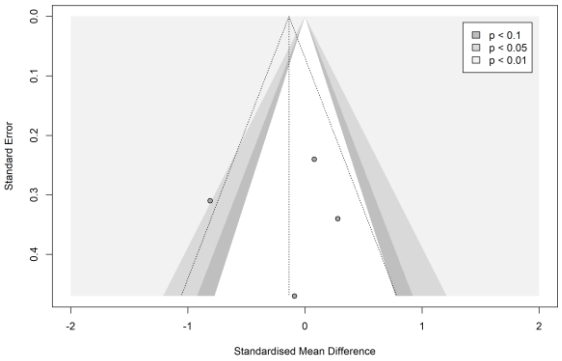
Food Consumption



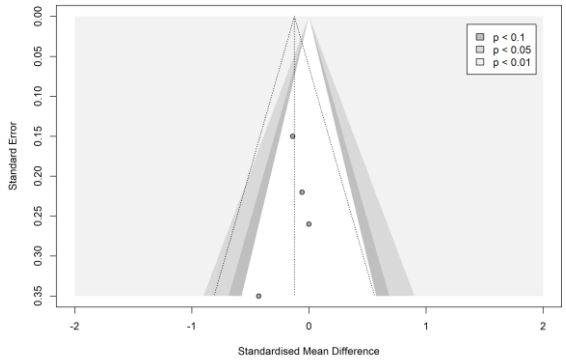
Explicit Wanting



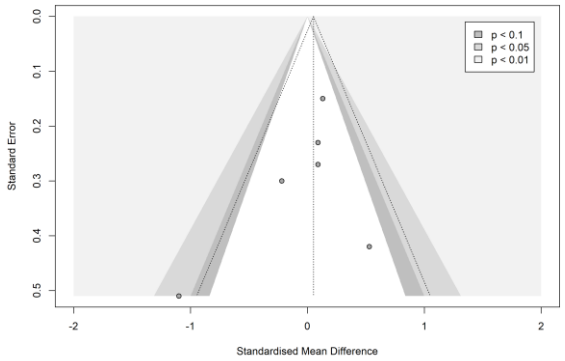
Implicit Wanting



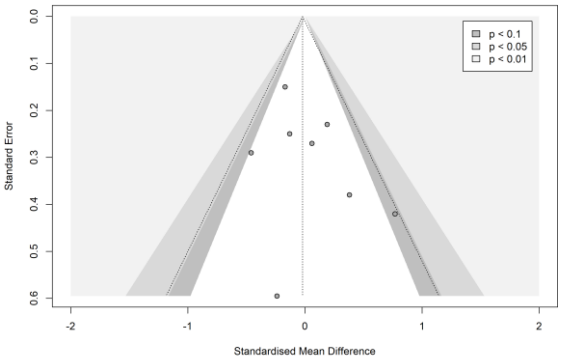
Food Craving



Desire to Eat



Hunger



Appendix 5 Forest Plot for the Literature Review in Chapter 3

Appendix 5.1 Individual forest plots for montage

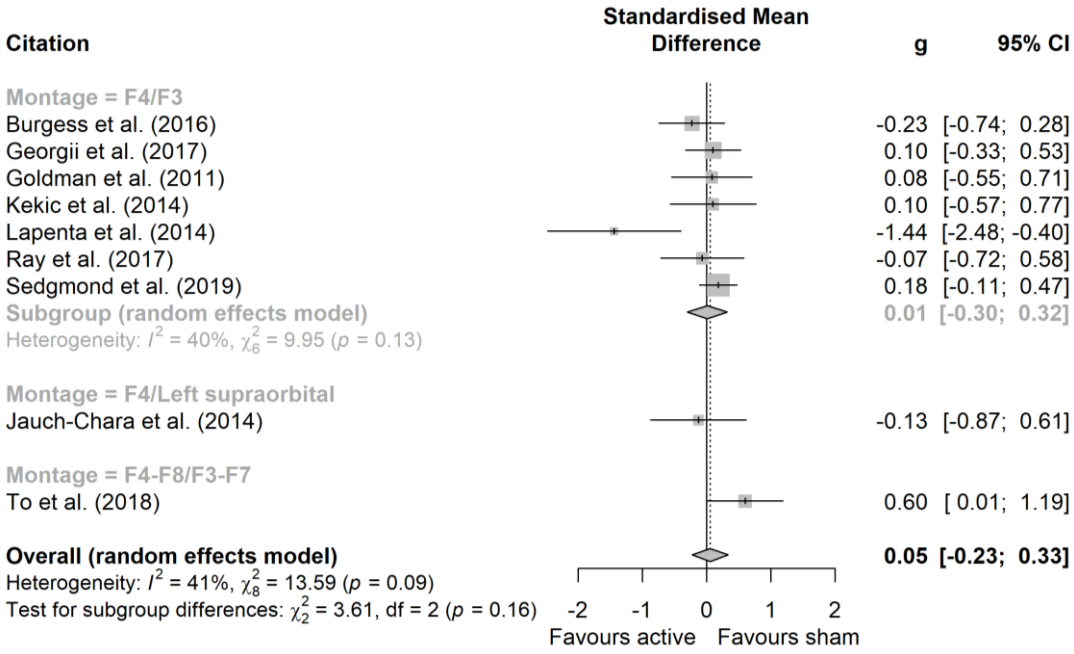


Figure A5.1 Forest plot comparing montages for food consumption.

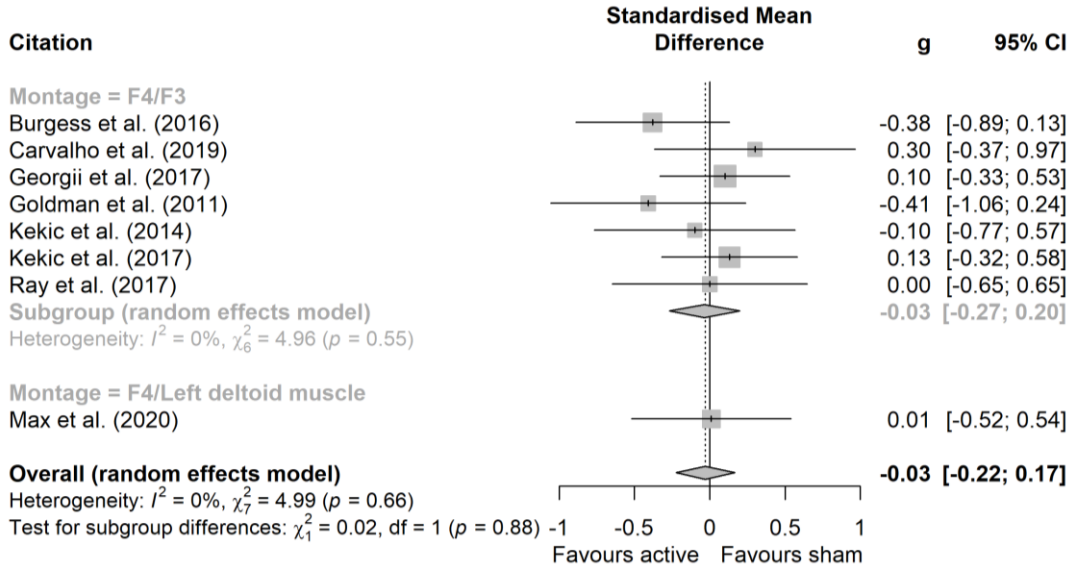


Figure A5.2 Forest plot comparing montages for explicit wanting.

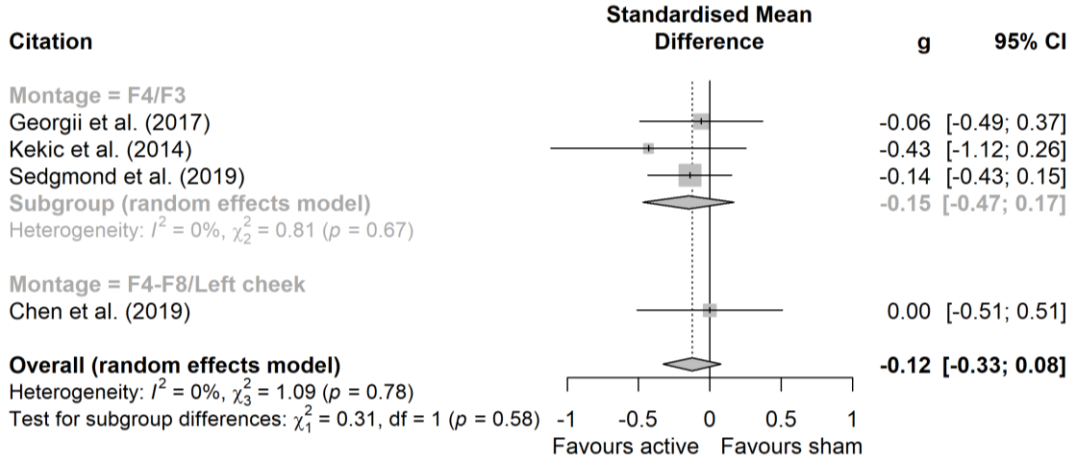


Figure A5.3 Forest plot comparing montages for food craving.

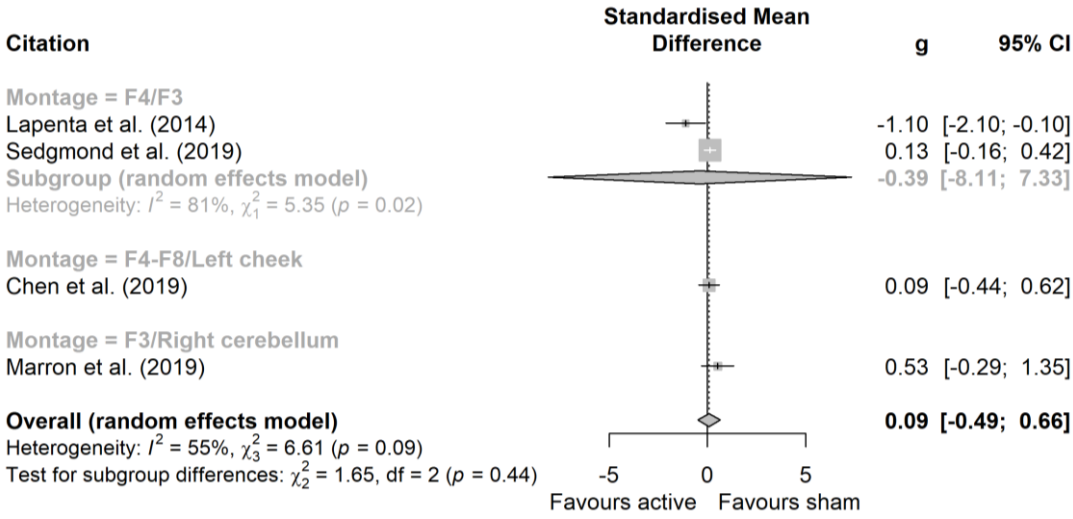


Figure A5.4 Forest plot comparing montages for desire to eat.

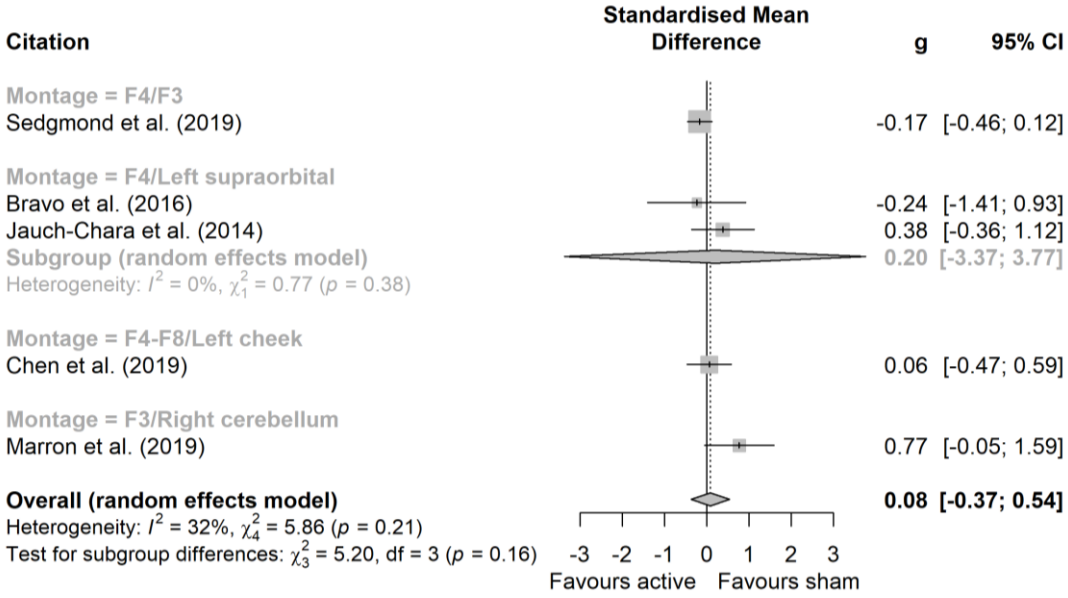


Figure A5.5 Forest plot comparing montages for hunger.

Appendix 5.2 Individual forest plots for montage type

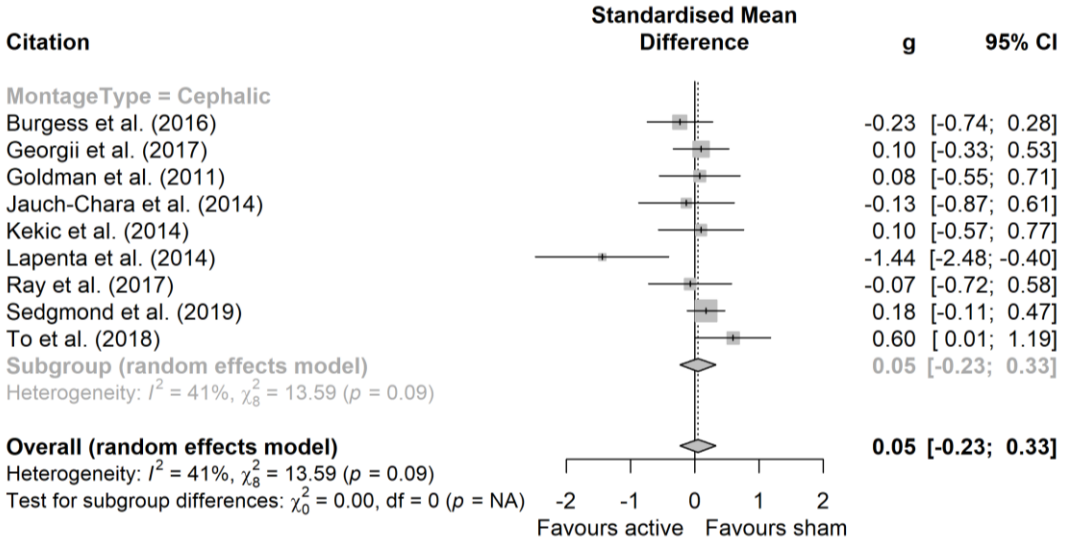


Figure A5.6 Forest plot comparing cephalic versus extracephalic montage for food consumption.

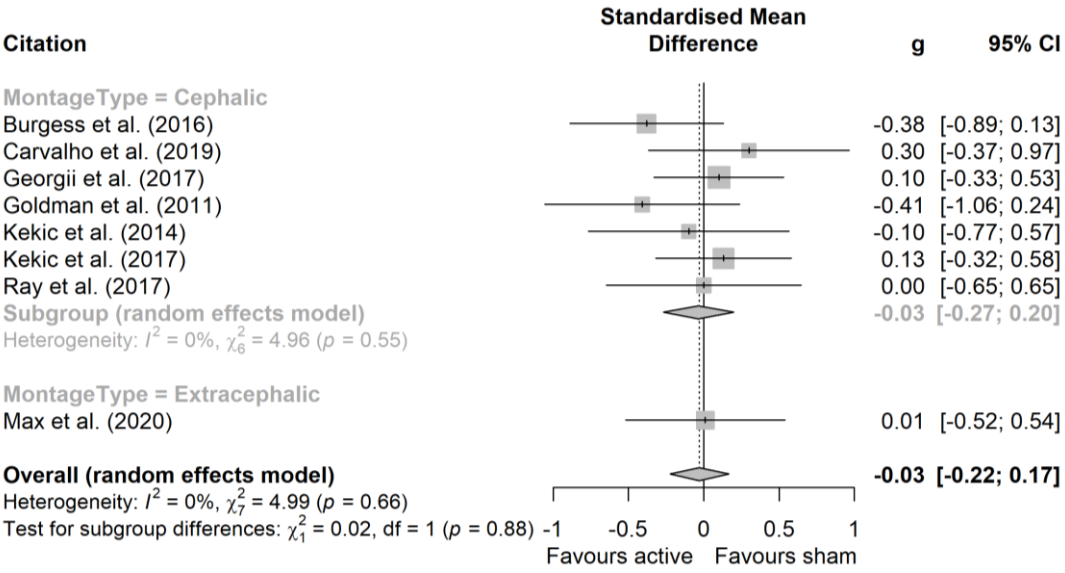


Figure A5.7 Forest plot comparing cephalic versus extracephalic montage for explicit wanting.

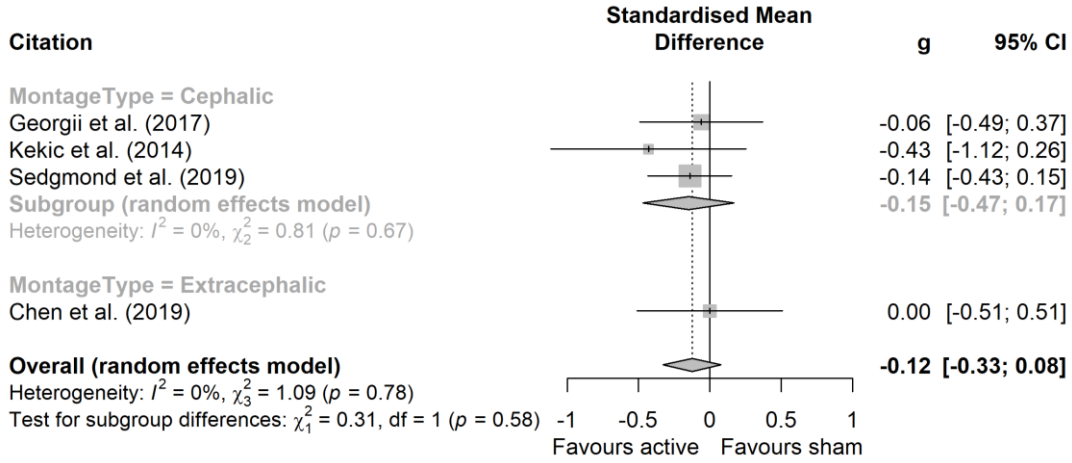


Figure A5.8 Forest plot comparing cephalic versus extracephalic montage for food craving.

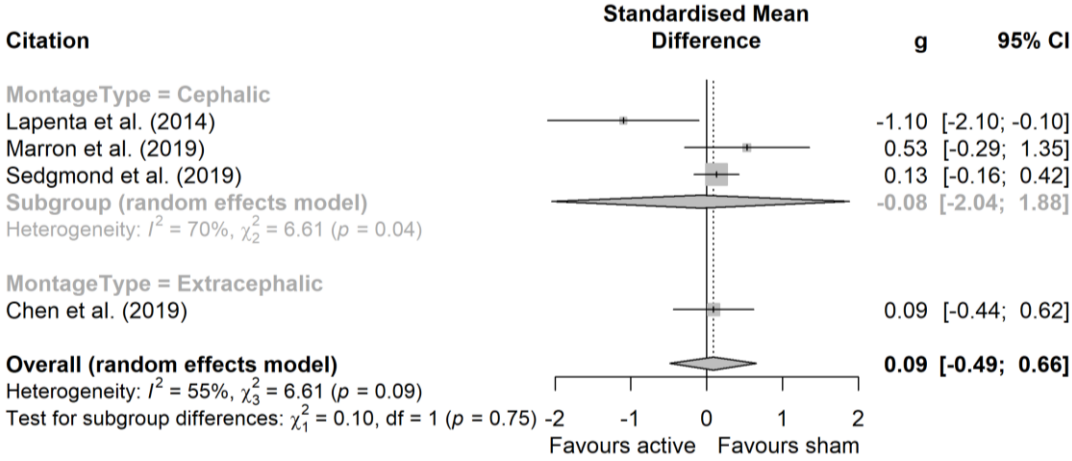


Figure A5.9 Forest plot comparing cephalic versus extracephalic montage for desire to eat.

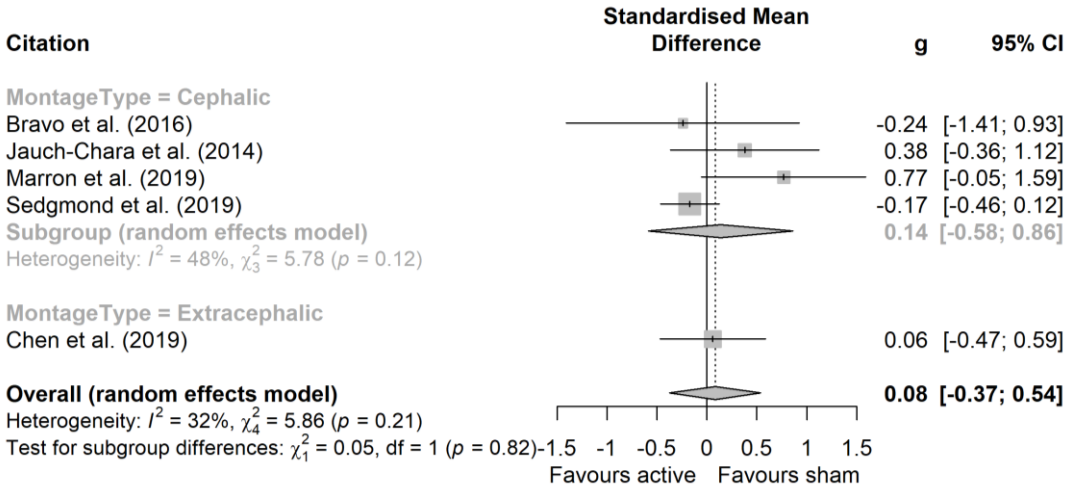


Figure A5.10 Forest plot comparing cephalic versus extracephalic montage for hunger.

Appendix 5.3 Individual forest plots for current intensity

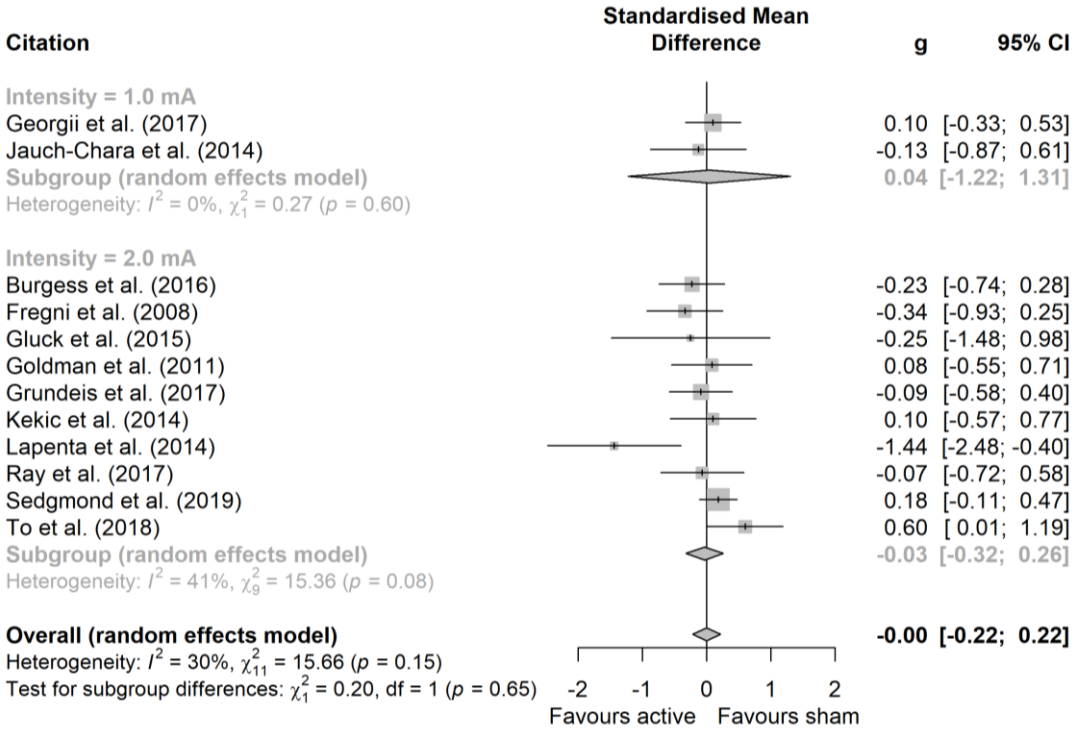


Figure A5.11 Forest plot comparing current intensities for food consumption.

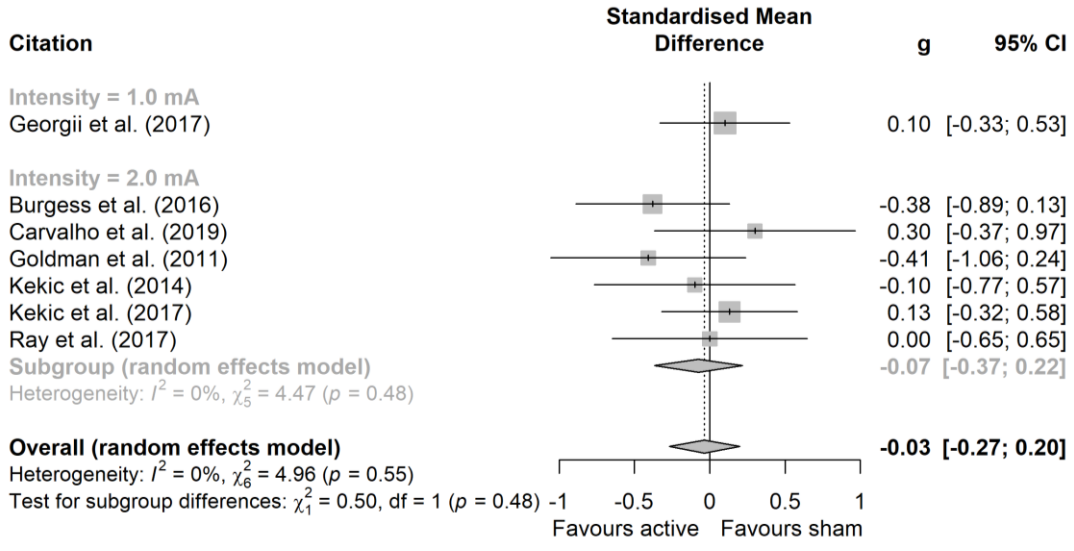


Figure A5.12 Forest plot comparing current intensities for food explicit wanting.

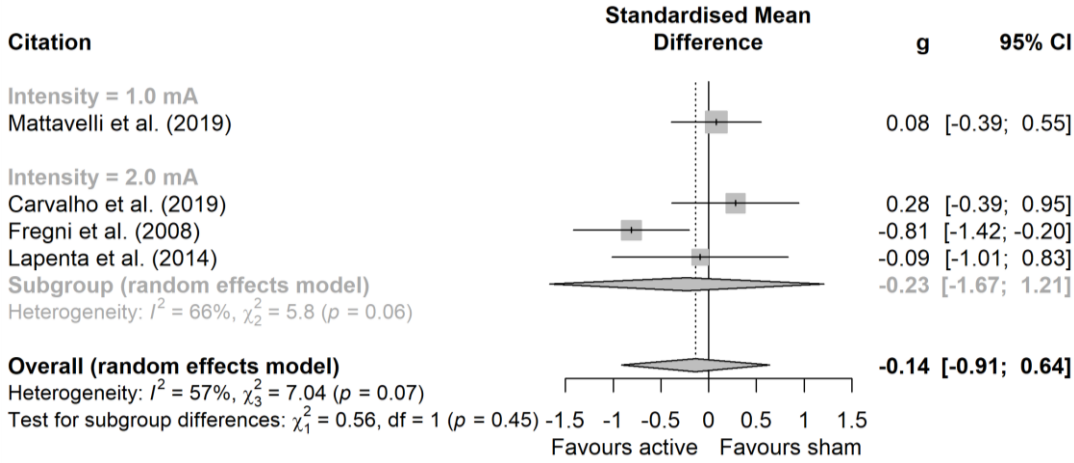


Figure A5.13 Forest plot comparing current intensities for implicit wanting.

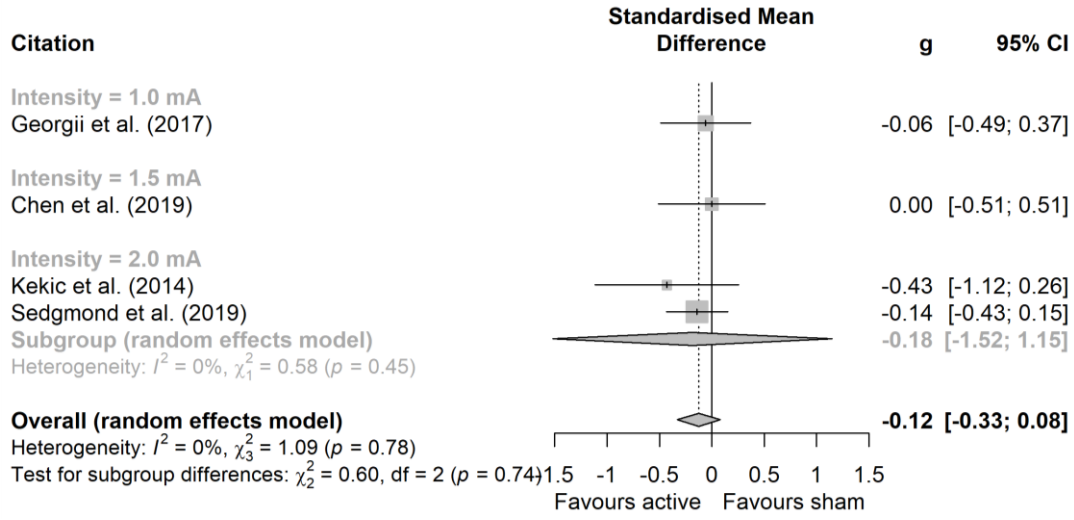


Figure A5.14 Forest plot comparing current intensities for food craving.

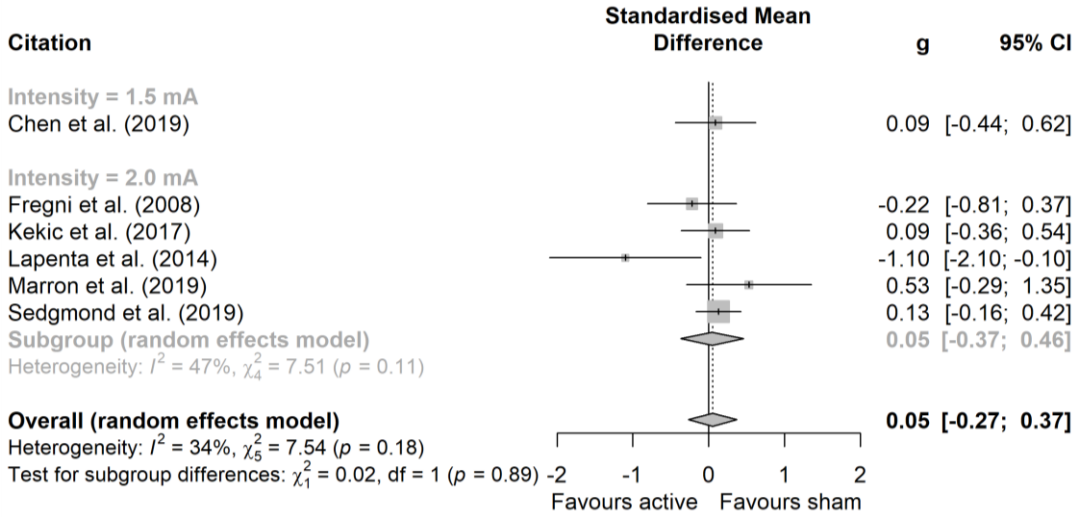


Figure A5.15 Forest plot comparing current intensities for desire to eat.

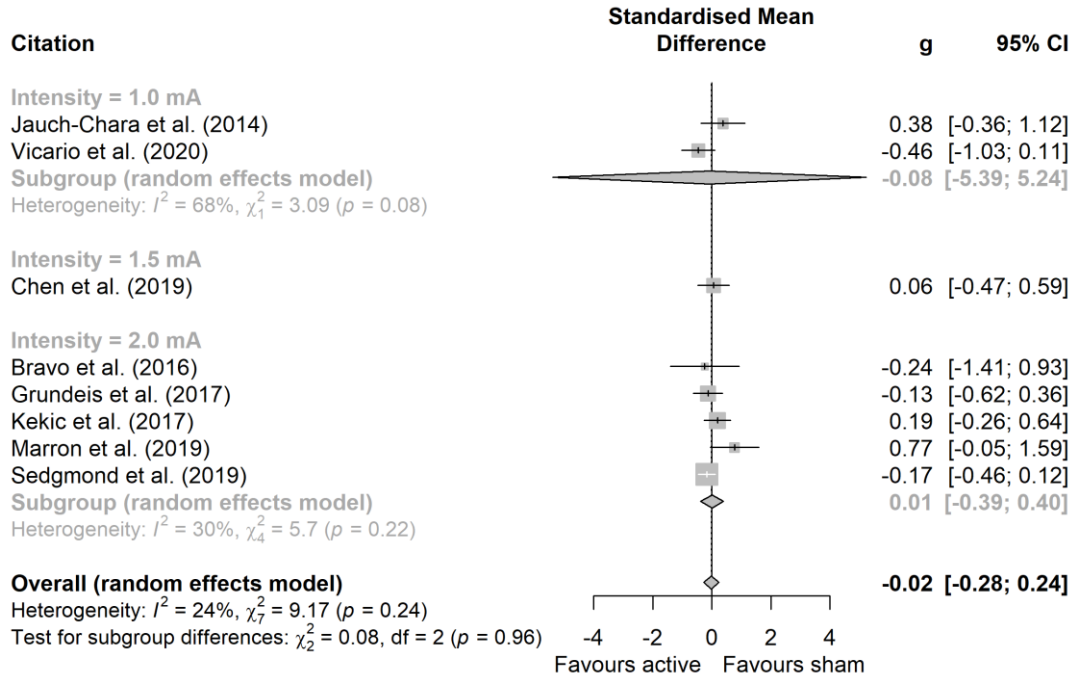


Figure A5.16 Forest plot comparing current intensities for hunger.

Appendix 5.4 Individual forest plots for current density

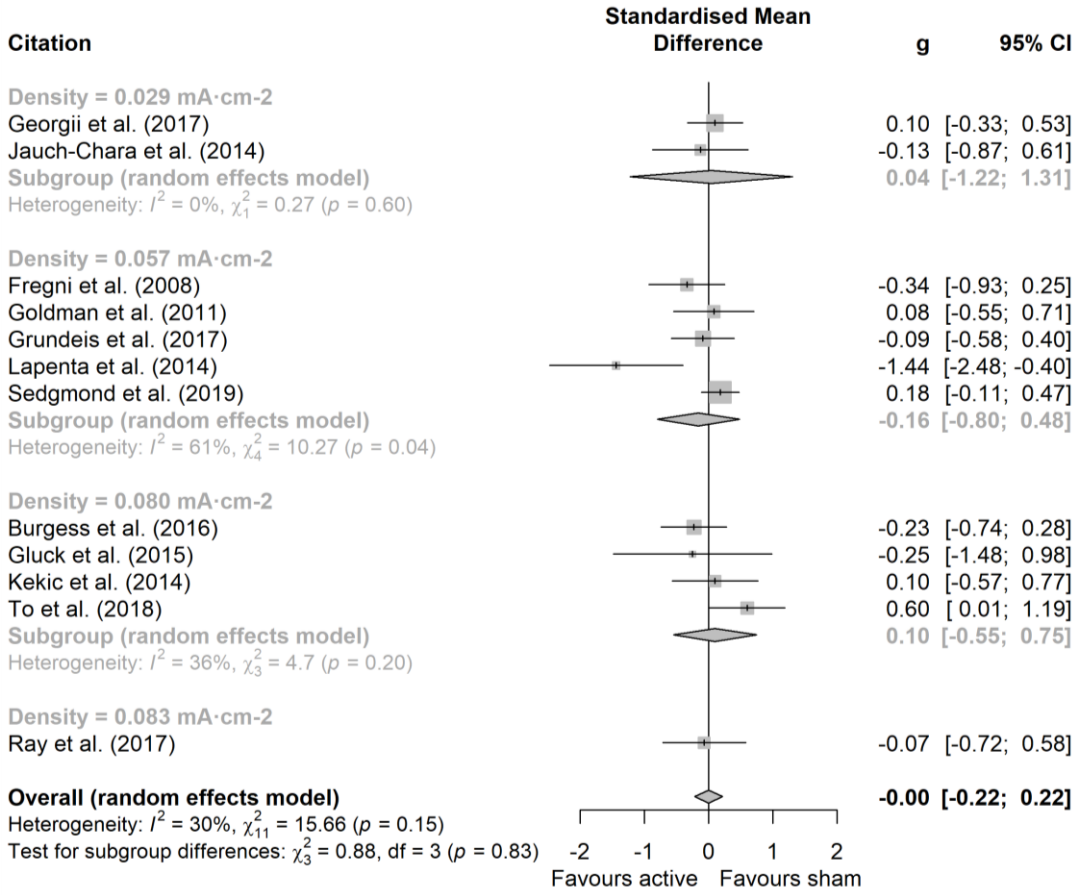


Figure A5.17 Forest plot comparing current densities for food consumption.

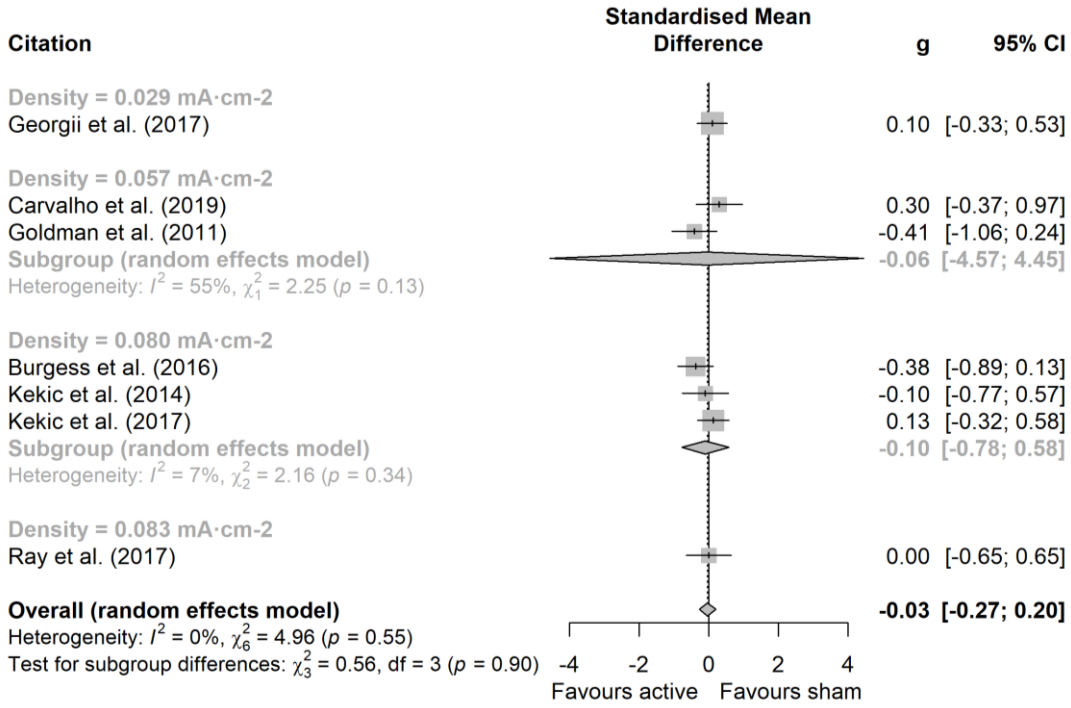


Figure A5.18 Forest plot comparing current densities for explicit wanting.

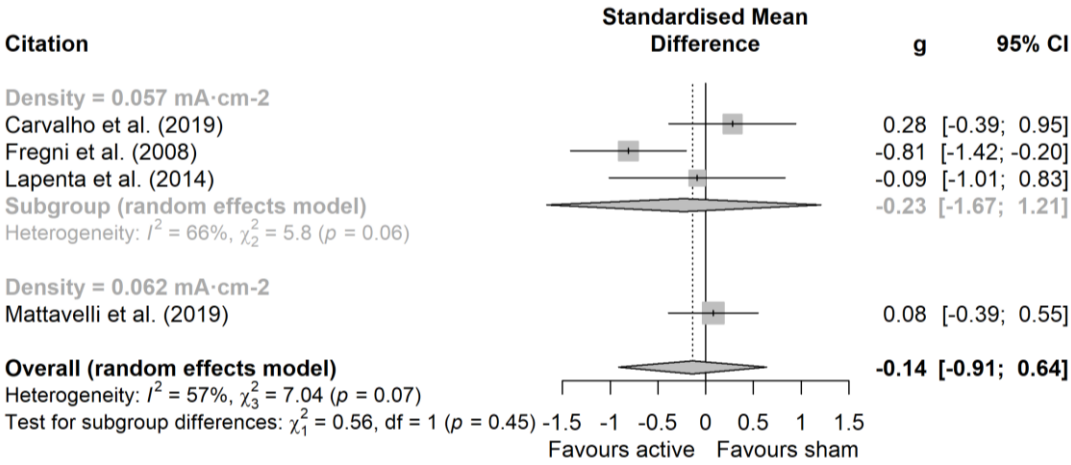


Figure A5.19 Forest plot comparing current densities for implicit wanting.

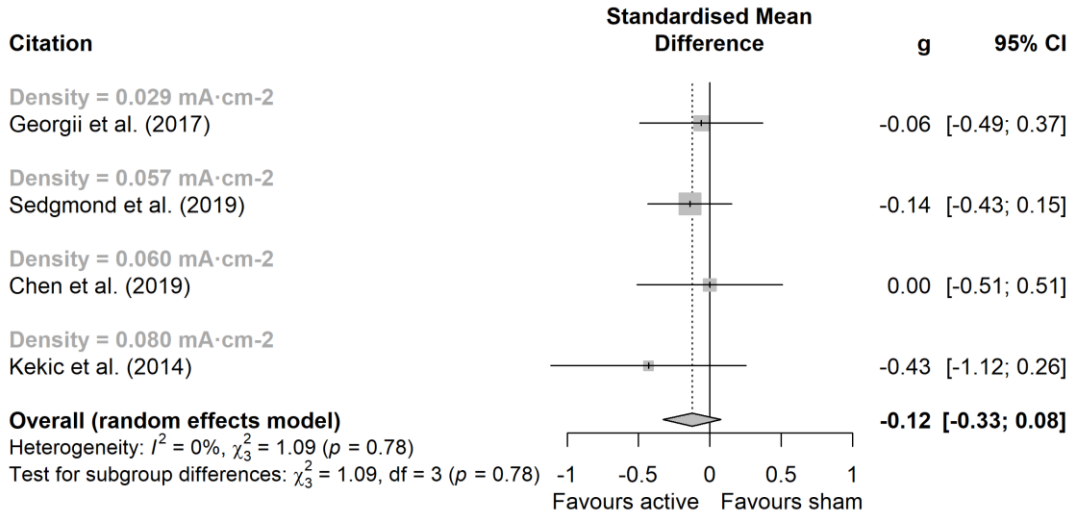


Figure A5.20 Forest plot comparing current densities for food craving.

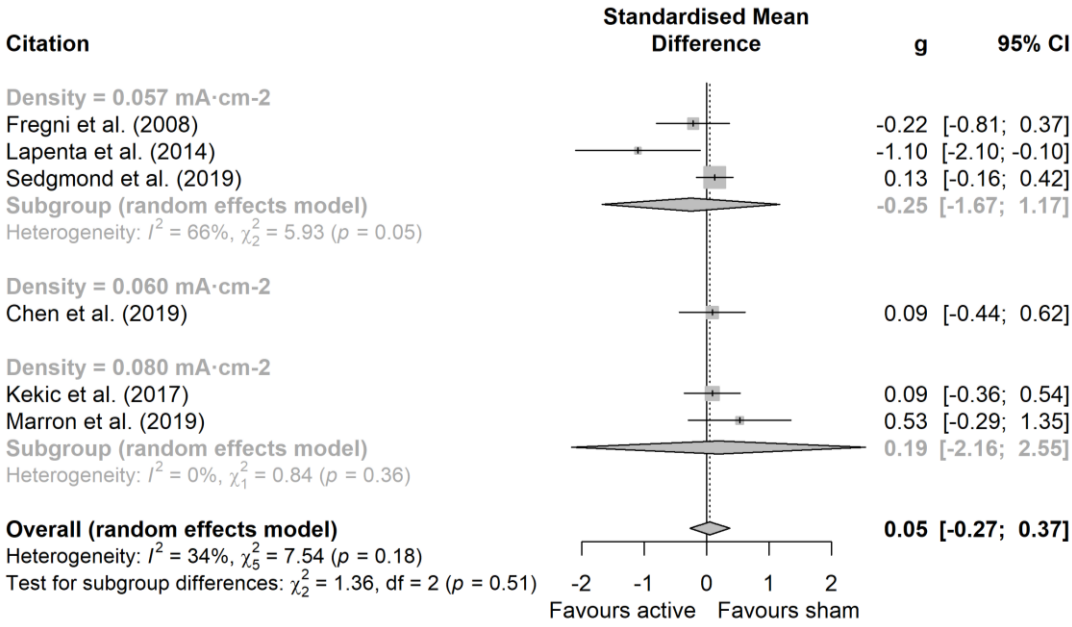


Figure A5.21 Forest plot comparing current densities for desire to eat.

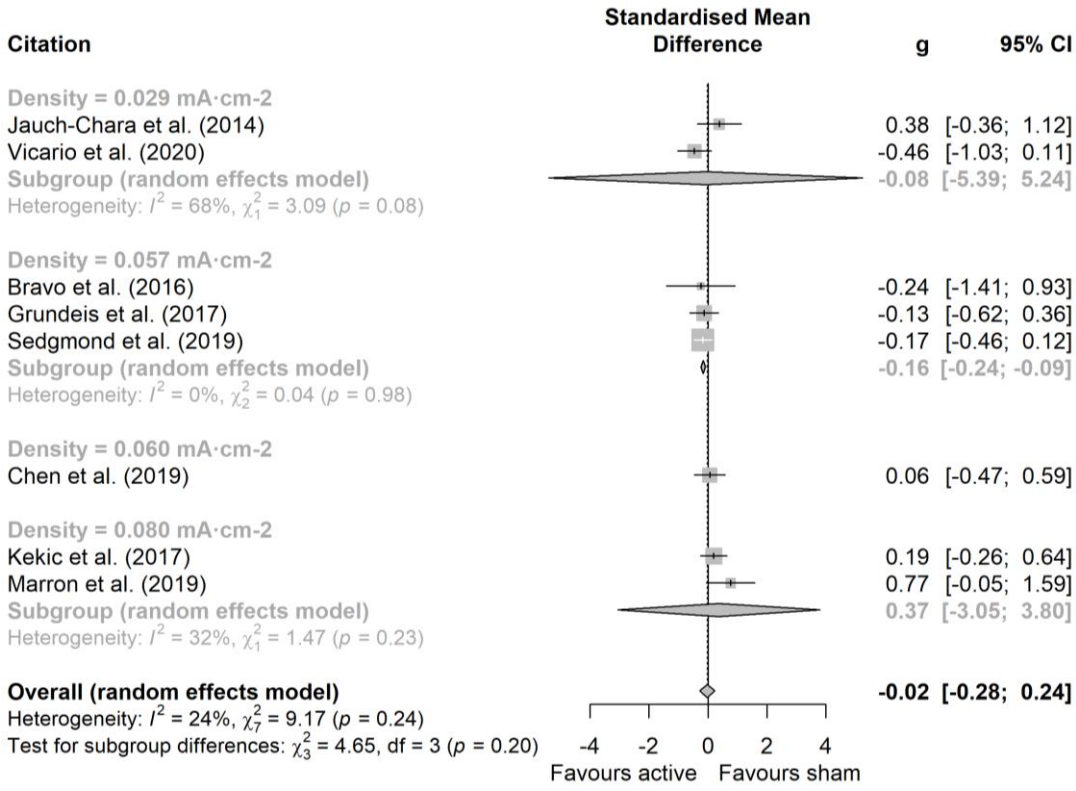


Figure A5.22 Forest plot comparing current densities for hunger.

Appendix 5.5 Individual forest plots for blinding success

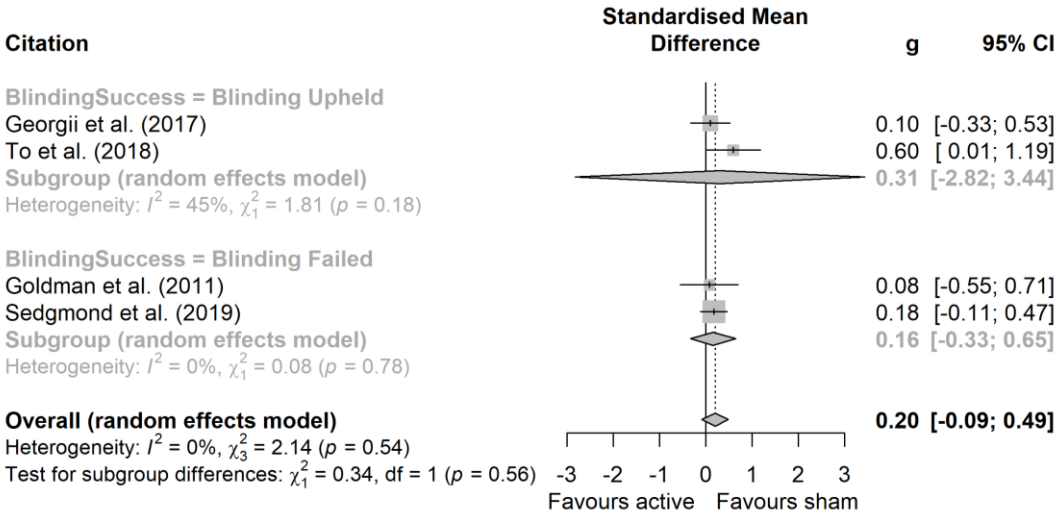


Figure A5.23 Forest plot comparing blinding success for food consumption.

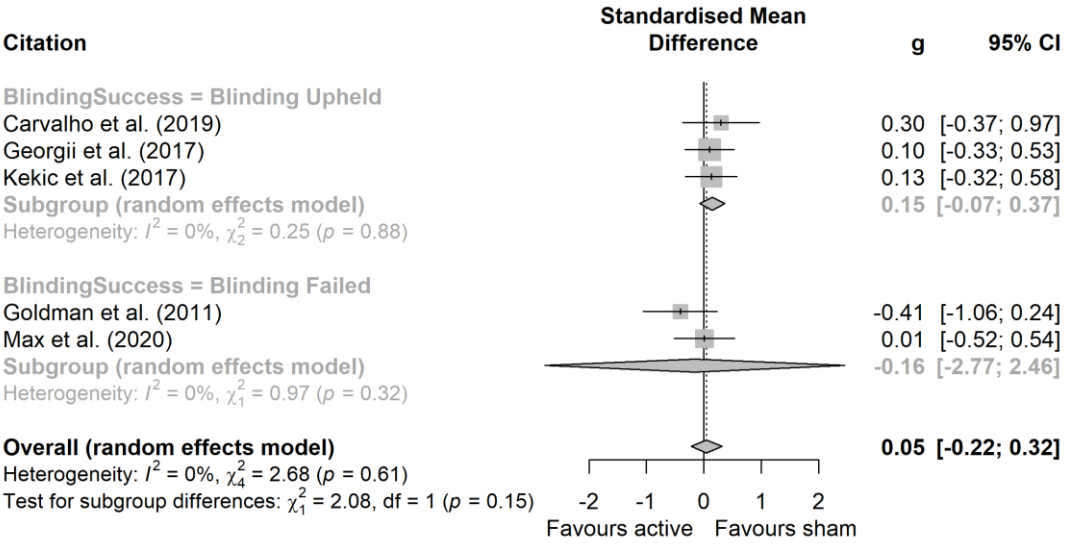


Figure A5.24 Forest plot comparing blinding success for explicit wanting.

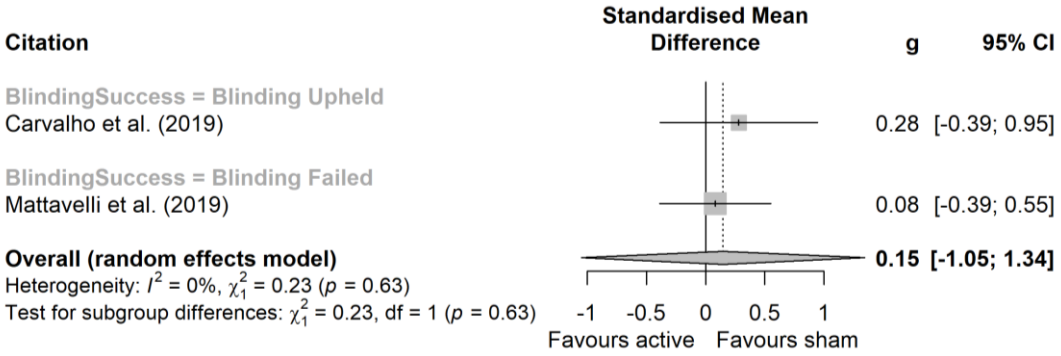


Figure A5.25 Forest plot comparing blinding success for implicit wanting.

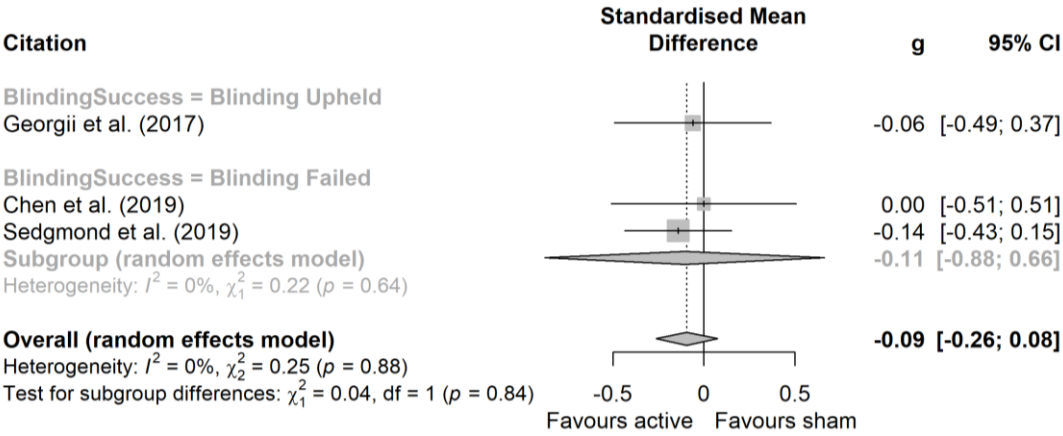


Figure A5.26 Forest plot comparing blinding success for food craving.

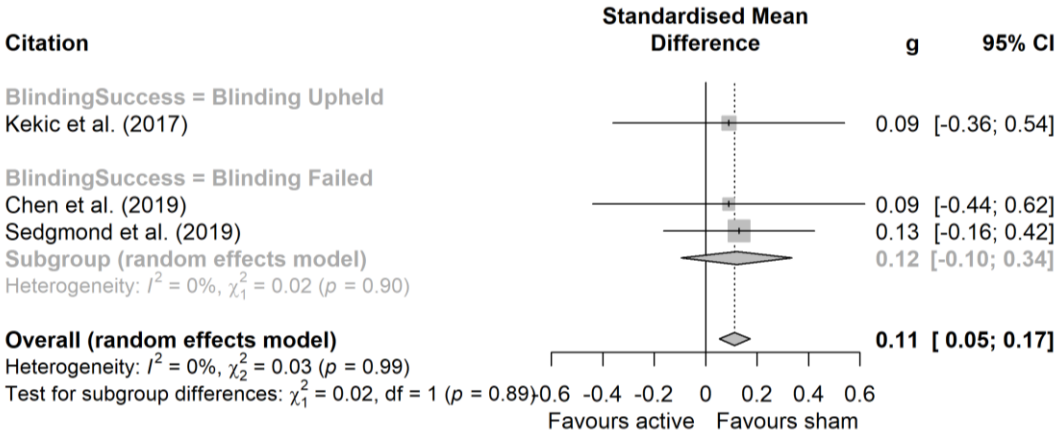


Figure A5.27 Forest plot comparing blinding success for desire to eat.

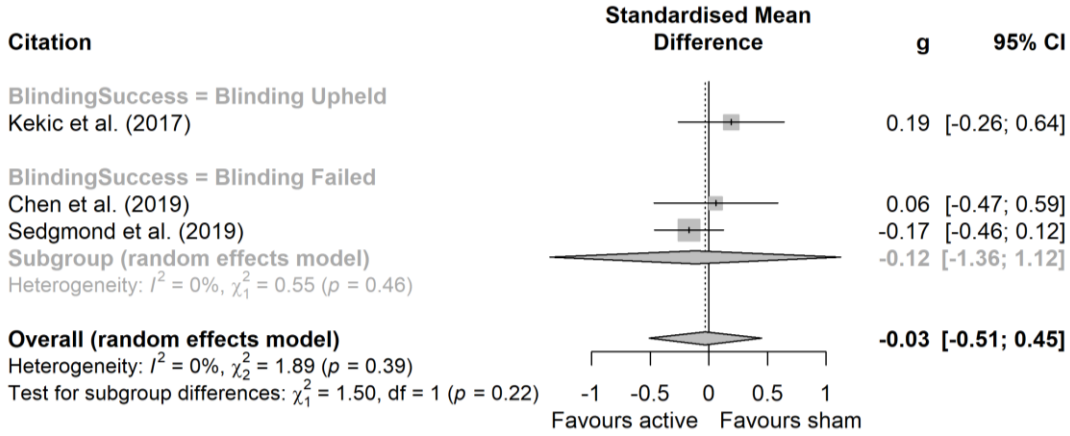


Figure A5.28 Forest plot comparing blinding success for hunger.

Appendix 5.6 Individual forest plots for blinding protocols

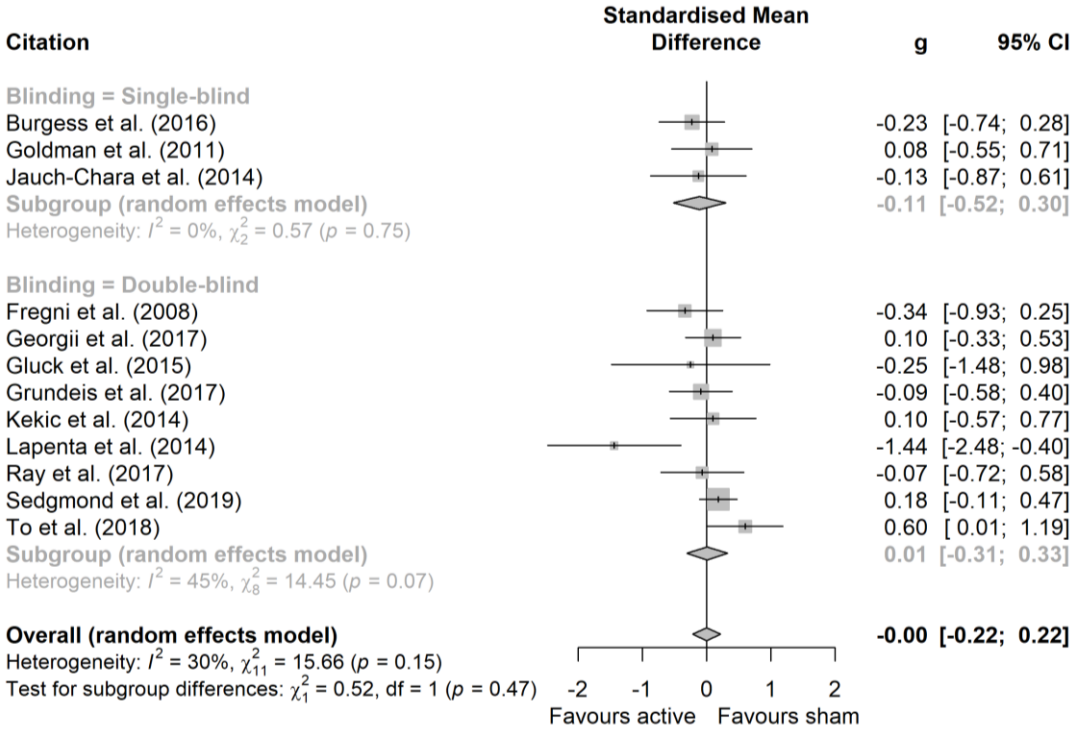


Figure A5.29 Forest plot comparing single- versus double-blind protocols for food consumption.

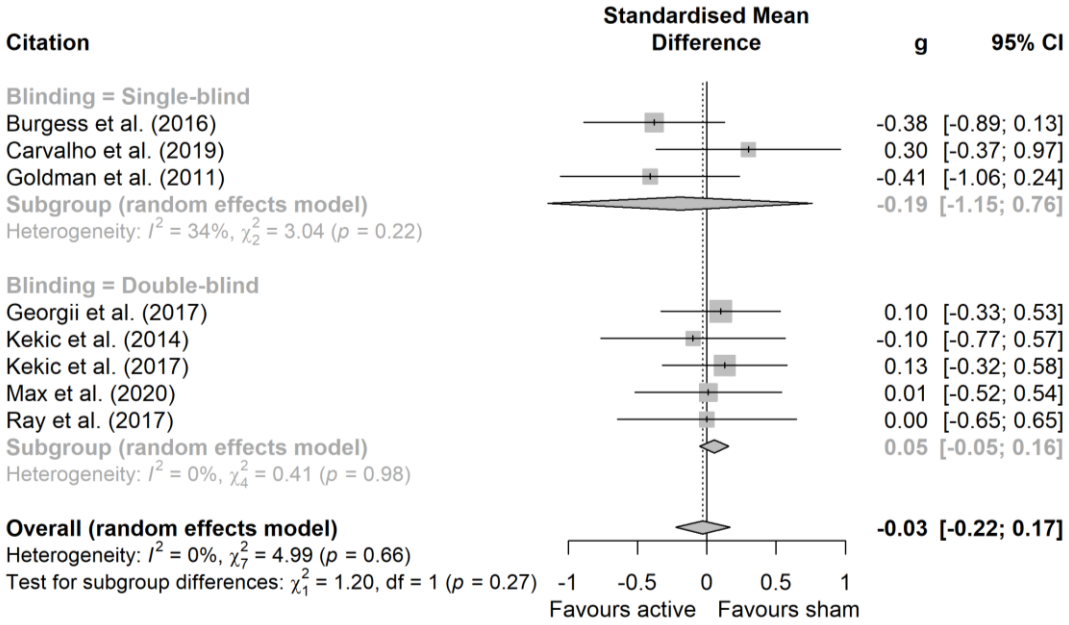


Figure A5.30 Forest plot comparing single- versus double-blind protocols for explicit wanting.

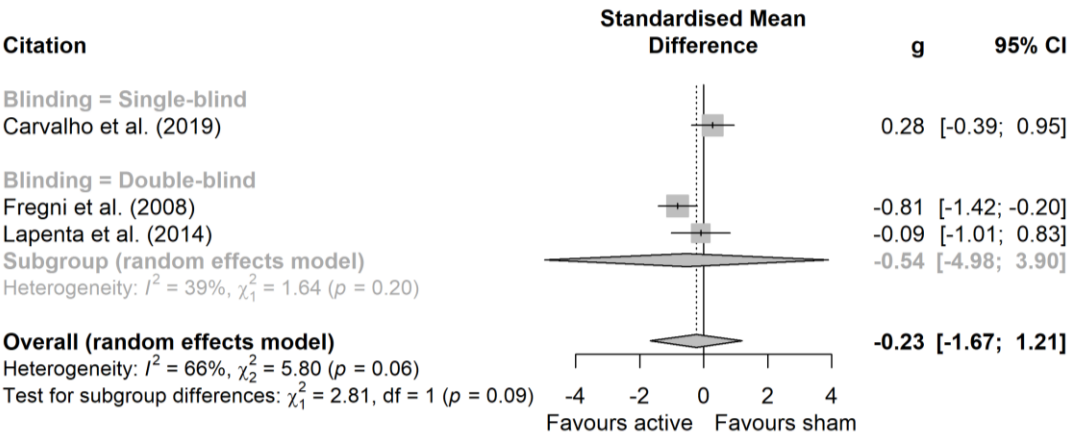


Figure A5.31 Forest plot comparing single- versus double-blind protocols for implicit wanting.

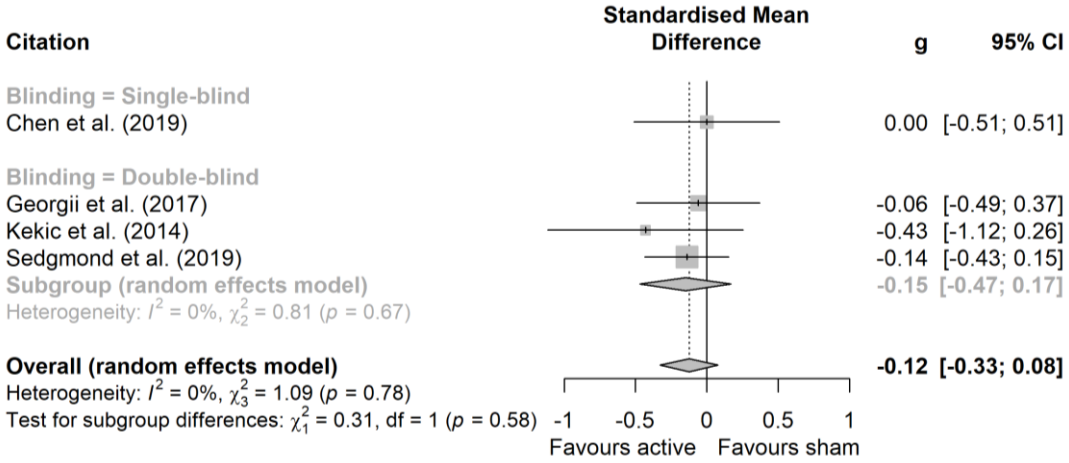


Figure A5.32 Forest plot comparing single- versus double-blind protocols for food craving.

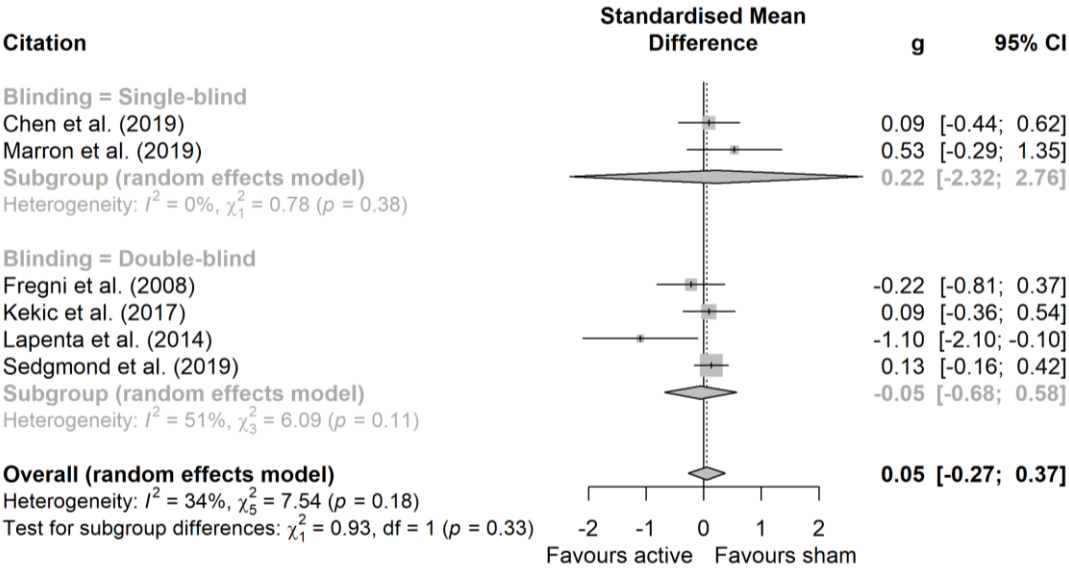


Figure A5.33 Forest plot comparing single- versus double-blind protocols for desire to eat.

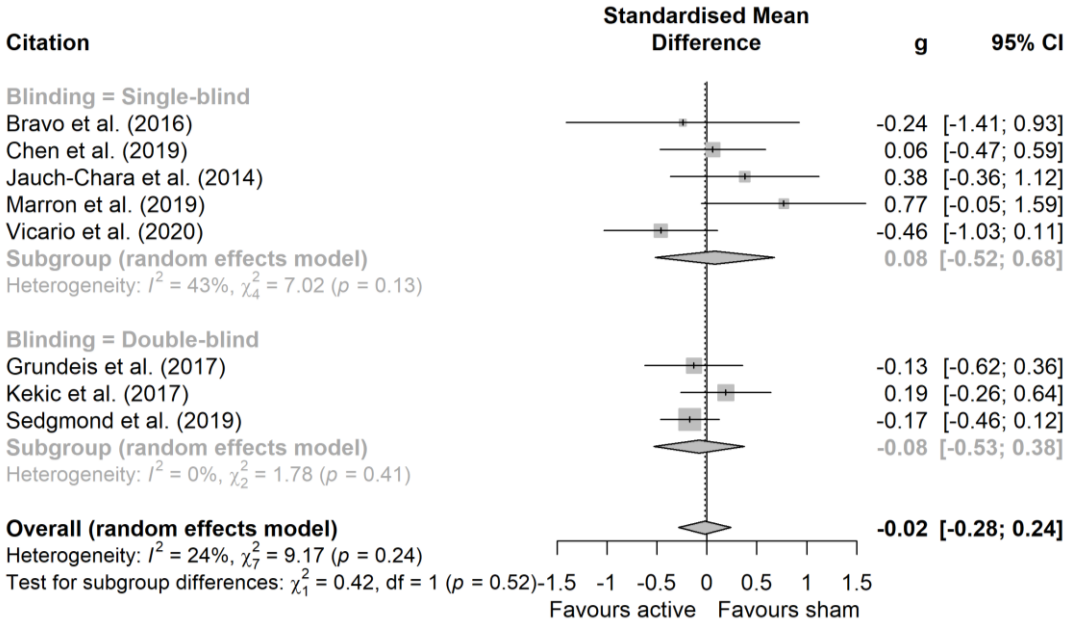


Figure A5.34 Forest plot comparing single- versus double-blind protocols for hunger.

Appendix 5.7 Individual forest plots for offline versus online protocols

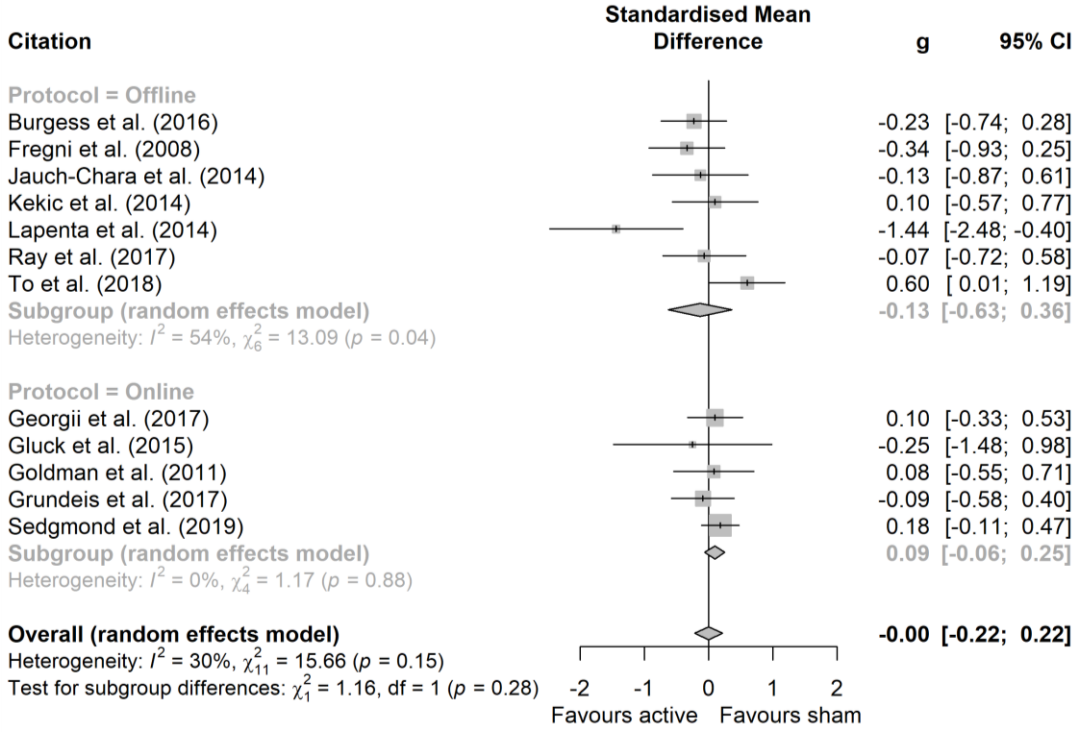


Figure A5.35 Forest plot comparing online versus offline protocols for food consumption.

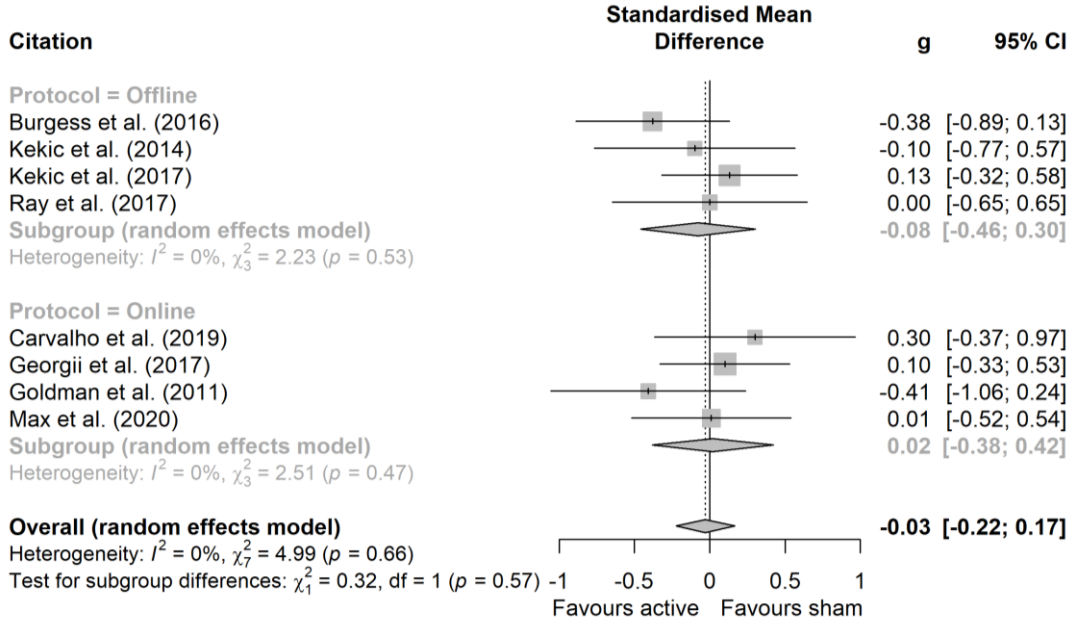


Figure A5.36 Forest plot comparing online versus offline protocols for explicit wanting.

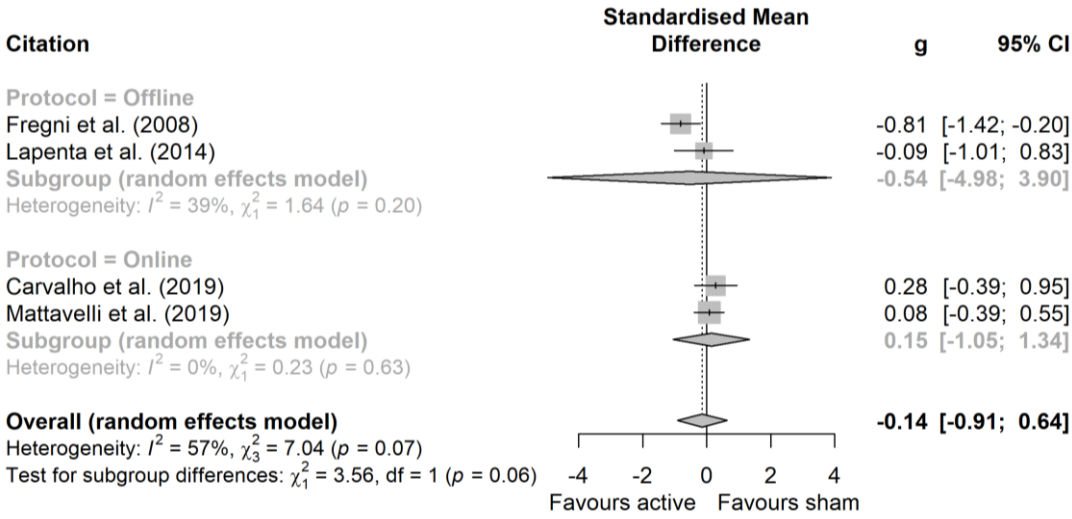


Figure A5.37 Forest plot comparing online versus offline protocols for implicit wanting.

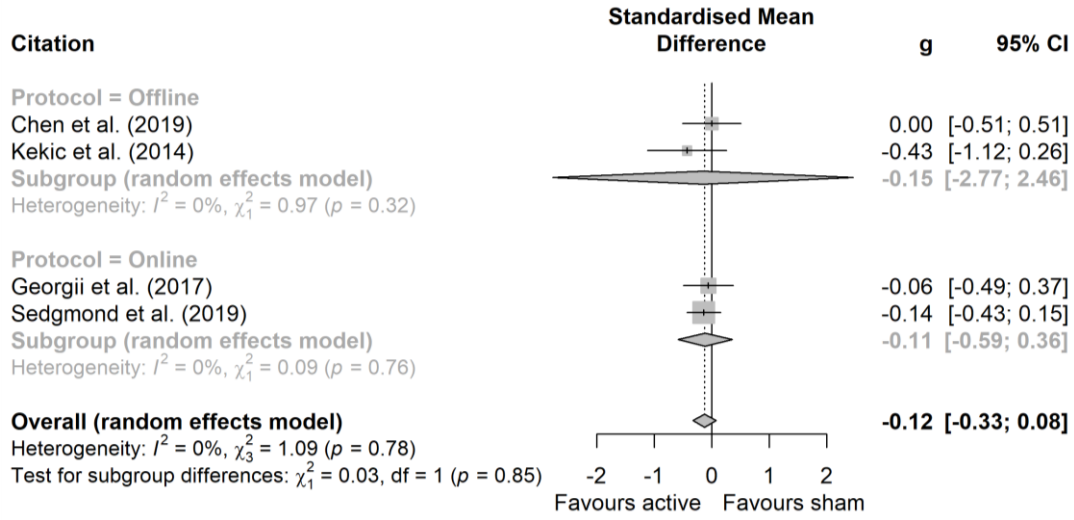


Figure A5.38 Forest plot comparing online versus offline protocols for food craving.

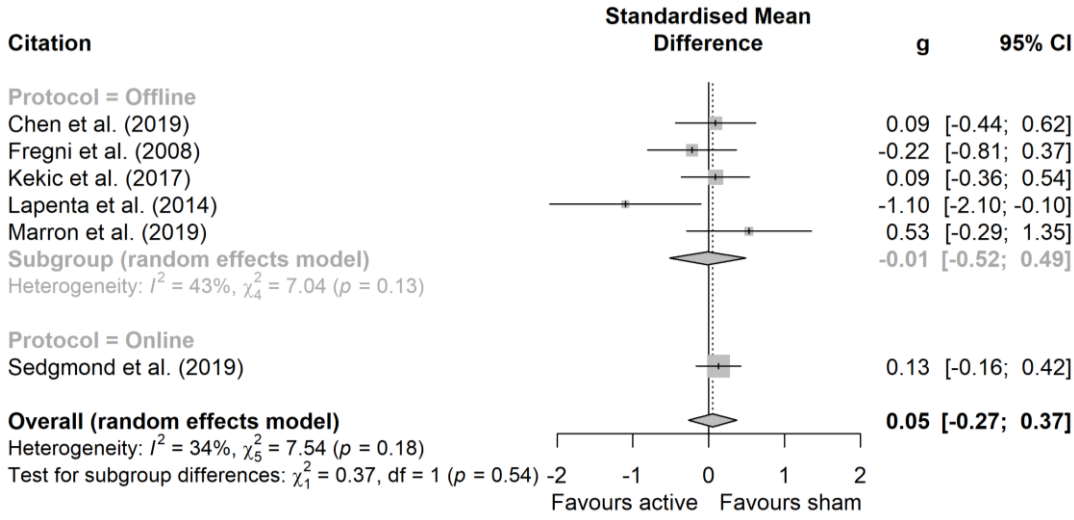


Figure A5.39 Forest plot comparing online versus offline protocols for desire to eat.

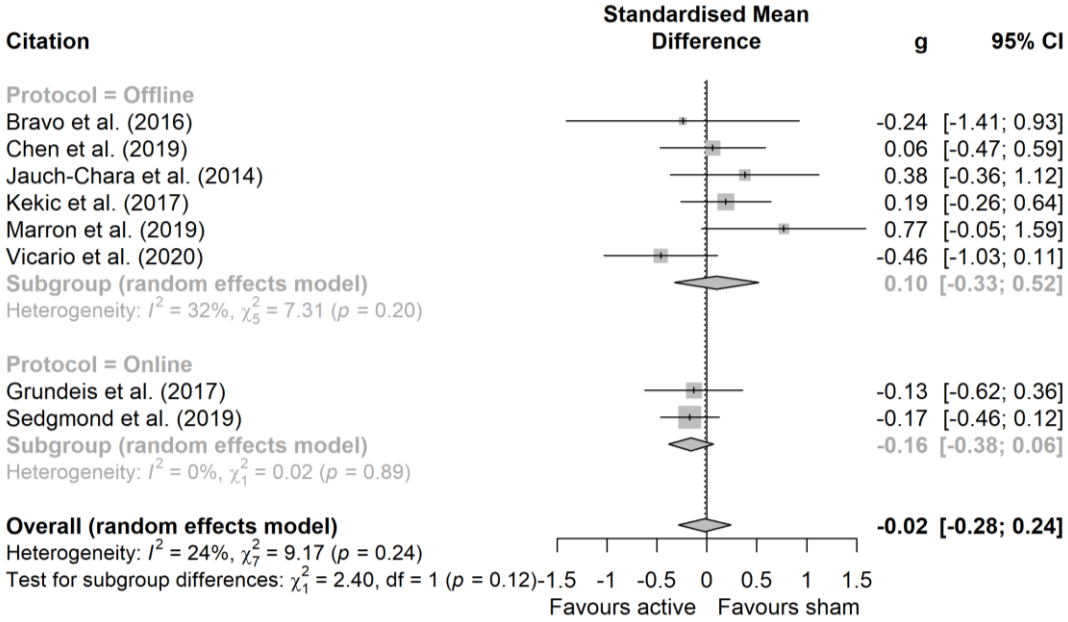


Figure A5.40 Forest plot comparing online versus offline protocols for hunger.

Appendix 6 Non-Invasive Brain Stimulation (NIBS) Guidelines

Non-Invasive Brain Stimulation (NIBS) Research Guidelines

School of Social and Health Sciences Ethics Committee, Leeds Trinity University

February 2018 (v 1.0)

Executive summary

For Leeds Trinity University, the use of non-invasive brain stimulation (NIBS) techniques represents a new and exciting opportunity to embed safe and established practices into the research, teaching and knowledge exchange activities conducted at the institution. As this technique is new to the institution it is pertinent to establish best practice recommendations prior to any test implementation.

Specifically, NIBS is a general name for research techniques in which magnetic or electric stimulation is applied to the external surface of the head of research participants with the aim of providing insight into the functional organization of the living brain. Transcranial direct current stimulation (tDCS) is a form of NIBS which is a neurostimulatory technique that modifies neuronal activity by delivering a weak electrical current to neural tissues through the scalp (Voarino et al., 2017). Many research groups around the world currently use tDCS.

This document serves to outline proposed guidelines for activities incorporating NIBS techniques (specifically tDCS) which require ethical scrutiny at Leeds Trinity University. These guidelines have been drafted in consultation with publicly available documents from the University of Edinburgh (https://www.ed.ac.uk/ppls/psychology/current/postgraduate/research-ethics/tms-tdcs), authoritative safety statements from the journal Brain Stimulation (Bikson et

al., 2016) and in consultation with the most recent regulatory and application guidelines (Antal et al., 2017).

Safety

In short, there is direct support for the safety of tDCS as applied thus far in controlled human trials (Bikson et al., 2016). A meta-analysis of the aggregate number of tDCS sessions failed to identify even a single record of a Serious Adverse Effect related to tDCS across more than 33,200 sessions. Among these over 1000 subjects received tDCS repeatedly (multiple sessions across days) without an instance of Serious Adverse Effect. Furthermore, data on individual patients exists who have received over 100 treatment sessions of tDCS without any indication of adverse effects arising from cumulative exposure, including a patient with schizophrenia who received tDCS daily over 36 months (i.e., more than 1000 sessions; Andrade, 2013) and patients with depression receiving multiple tDCS exposures safely (more than 100 sessions in total; Tadini et al., 2011).

As of the date above, the adverse event reporting database MedWatch in the USA (https://www.fda.gov/Safety/MedWatch/default.htm) returns no reports for the terms “tDCS” or “transcranial Direct Current Stimulation” or “transcranial” or “transcranial Direct Current Stimulator.” Notably, based upon incorporating the principles and guidelines outlined below, the university insurers (UM Association Limited) have granted clinical trials indemnity insurance for a specific programme of tDCS research (reference: Q803; supplementary material).

Guidelines:

In agreement with the more detailed information presented below, ethical applications seeking to incorporate the use of tDCS must explicitly include the

following information in addition to the standard information required by eligible ethical applications submitted to the School of Social and Health Sciences Ethics Committee.

1. Specification of the type of participants to be recruited (i.e., healthy adult participants - category A, non-patient special populations – category B, or patient populations – category C).
2. Enhanced pre-participation screening of all potential participants using the Brain Stimulation Study Suitability Questionnaire (BSSSQ), consideration of potential interacting drugs, and consultant with a medical doctor if deemed a category B or C participant.
3. Explicit statement of the relevant stimulation parameters of the protocol (i.e., paradigm, duration, frequency, intensity).
4. Clear description of additional measures being taken that may interact with the protocol and elicit additive effects (for example, additional environmental stimuli, prior fatigue, nutritional interventions).
5. Clear statement that general and procedure-specific guidelines will be adhered to (including identification of the names of qualified users on the application and details regarding the management of adverse events).

Non-Invasive Brain Stimulation (NIBS) Research Guidelines

School of Social and Health Sciences Ethics Committee, Leeds Trinity University

February 2018 (v 1.0)

These guidelines are intended for use by research groups working within Leeds Trinity University and covers research conducted at the institution and any future campus extensions where NIBS equipment may be used. In addition to the standard requirements of ethical approval by the School of Social and Health Sciences (SSHS) Ethics Committee, these guidelines specify the procedures and study attributes required for approval of new NIBS studies conducted at, or in collaboration with, Leeds Trinity University.

Guideline 1: Specification of the type of participants recruited

Brain stimulation studies will fall into one of the three participant-type study categories described below. The category determines the procedure for approving candidates for participation in the study. Therefore, all applications for ethical approval must state explicitly which of these categories the proposed study belongs to, and follow the appropriate procedure, detailed below, for recruitment.

A) Healthy adult participants

For studies requiring healthy participants aged 18-60 years, recruitment will initially follow the usual procedures employed at Leeds Trinity University. Candidates for participation will be recruited from the general public and Leeds Trinity student population, by advertising and word-of-mouth. For each study, a recruitment poster will be placed on university noticeboards. Prospective participants who express an interest in being considered for eligibility for the study will be sent a recruitment email encouraging them to make further contact with the named members of the research

team specified on the advertising materials. The email will include basic screening criteria, a brief overview of the sessions required for the study and any details of compensation associated with study participation. Respondents will be invited to a screening interview.

At the screening interview, specific information and questionnaires (Appendix 6.1 and Appendix 6.2) will be used to assess the candidate's suitability for brain stimulation studies. The questionnaires require that candidates divulge personal and medical information; therefore, before collecting responses to the questionnaires the candidate will be given an information sheet and consent form. The researcher will check that the participant reads the sheet carefully before signing the form.

B) Non-patient special populations

Some brain stimulation studies require participants who are not patients, but do fall into a special group; including, but not limited to people with severe visual, hearing or other perceptual deficits, people above the age of 60 years or below the age of 18 years, amputees, and people with Autism Spectrum Disorder.

For studies requiring the recruitment of non-patient special populations, a medical doctor who is knowledgeable about brain stimulation will be consulted while the study is being designed. This consultation may result in a list of additional criteria that will be applied to recruitment in addition to those specified for Category A above. The ethics application must detail whether the consulting medic has decided on such criteria, and if so, what these criteria are. Once the ethics committee approves the study, participants meeting all the requirements defined in the application will be approved for participation.

C) Patient populations

Candidates for studies that investigate patients must meet all the requirements set for Category A above; in addition, a medical doctor who is knowledgeable about brain stimulation will be consulted while the study is being designed; this consultation may result in a list of additional criteria that will be applied to recruitment. The ethics application must detail whether the consulting physician has decided on such criteria, and if so, what these criteria are. Furthermore, each candidate for the study will have to be approved individually by a medical doctor who is knowledgeable about brain stimulation; depending on the specific criteria determined for the study, this approval may follow examination of the candidate's questionnaire responses or (if the criteria deem it necessary) a personal examination by the medical doctor involved in the study.

Studies in which patients are recruited through the NHS require that researchers obtain NHS ethics approval before recruitment can begin; to avoid unnecessary duplication of effort, if NHS ethics approval has already been obtained, this will be sufficient for carrying out the study, without requirement for further approval by the SSHS Ethics Committee.

Guideline 2: Pre-participation screening using the Brain Stimulation Study Suitability Questionnaire (BSSSQ) and consideration of potential interacting drugs

In addition to the information above, the following guidelines apply to studies where participants are healthy adults (category A); non-patient special populations (category B) and patients (category C). All candidates for participation in NIBS experiments will complete the BSSSQ questionnaire (Appendix 6.2) to examine their suitability. The detailed guidelines below specify the conditions under which a

subject may be approved based on the questionnaire, and the conditions under which further consultation with a medical professional that is knowledgeable about brain stimulation would be required. Furthermore, screening for drugs that may have interaction effects with NIBS techniques will be completed (Appendix 6.1). Generally, any individual taking any antidepressants, antipsychotics, antivirals, antibiotics, anticonvulsants, antimetabolites, antimalarials, immunosuppressants or chemotherapy drugs will be excluded (Rossi et al., 2009).

BSSSQ: Brain Stimulation Study Suitability Questionnaire

After signing an initial consent form, all candidates will complete the Brain Stimulation Study Suitability Questionnaire (BSSSQ; Appendix 6.2). These guidelines are based on those that are in use at other universities and are mentioned specifically in the documentation generated by the University of Edinburgh. Participants who meet the criteria set by this questionnaire (see below for exclusion criteria and further considerations), in addition to any specific criteria of the study will be approved for participation.

- Answering “yes” to any of the following questions will disqualify a candidate from participating: 1, 2, 3, 5, 6, 7, 8, 9, 10, 14.
- Answering “yes” to any of the following questions will require consultation with a medical professional who is knowledgeable about brain stimulation: 4, 11, 12, 13, 15, 17, 19.
- Answering “yes” to question 20 will require consultation with a medical professional who is knowledgeable about brain stimulation.

If a candidate’s answers to the questionnaire does not disqualify them and do not require consultation with a medical professional who is knowledgeable about brain

stimulation, the participant will be approved for participation in the study. If a candidate is not disqualified based on the questionnaires, but does require consultation with a medical professional, such consultation may result in the candidate being approved or disqualified, based on the medical professional's judgment.

Guideline 3: Explicit statement of the relevant stimulation parameters of the protocol

The modification of spontaneous cortical activity by tDCS involves passing a weak electric current in the order of 1.0 to 2.0 mA through the skull and the underlying cortex via electrodes attached to the scalp. The active electrode is placed over the target region (e.g., left motor cortex) and the reference electrode is placed in task neutral position (e.g., over the contralateral supraorbital ridge). The polarity of the current flow induces a focal, prolonged but reversible change in the excitability of the stimulated brain area. Anodal tDCS (where the positive electrode is placed over the target region) increases excitability; cathodal tDCS (where the negative electrode is placed over the target) decreases excitability. The current is generated by a battery-powered stimulator and passed through rubber electrodes and conductive material (gel or saline-soaked sponges). At least one electrode is attached to the scalp whereas the other electrode may be positioned on the scalp also, or on the body (e.g., shoulder). The electrode size of the stimulators in use by research groups at present is large (~25 to 35 cm^2) and the current strengths used are low (~1.0 to 3.0 mA) resulting in very low current densities (0.029 to 0.120 $mA \cdot cm^{-2}$). Typical protocols apply no more than 20 minutes of stimulation in a single session.

‘Sham’ stimulation is often used as a control condition, where the current is applied for a sufficiently brief duration to avoid any change in cortical excitability (up to 30 seconds), but long enough to produce the transitory sensation on the skin associated with tDCS. Sham stimulation allows the participants to perform tasks ‘blind’ to (i.e., unaware of) whether they are being stimulated, as participants habituate to the tingling sensation caused by stimulation within a shorter period than the duration of the sham stimulation, making it hard to tell the difference between stimulation and sham conditions.

Studies that incorporate tDCS and are carried out under these guidelines will use current strengths not exceeding 2.0 mA, electrode sizes not smaller than 9 cm^2 (3 by 3 cm) and the duration of stimulation in a single session will not exceed 20 min. Clear statement of such parameters is required throughout the ethical approval application.

Guideline 4: Clear description of additional measures being taken

The tDCS procedure described here may be performed in conjunction with other measurement or stimulation techniques. It is anticipated that due to the nature of the intervention that most tDCS studies will incorporate some form of additional behavioural measure (e.g., captured by keyboard responses, eye-tracking, motion-tracking, or any other relevant method). The use of behavioural measures is straightforward and safe with all tDCS paradigms and parameters described above. The ethical approval application must specify what other measures or stimulation methods (if any) will be employed in conjunction with tDCS.

Most tDCS paradigms aim to induce effects in cognitive functioning lasting beyond the period of stimulation. Therefore, participants’ involvement in studies may last an

entire morning/afternoon and measurements of effects may take place in sessions separated by hours, days, weeks or even months. For durations of stimulation that result in long-lasting aftereffects (one hour or more), an intersession interval in excess of 48 h is recommended (Nitsche et al., 2008).

In line with the recommendations of Antal et al (2017), stimulation intensity should not exceed 4.0 mA at any time and should not exceed 60 minutes duration per day.

Guideline 5: Clear statements that general and procedure-specific guidelines will be adhered to

Below are both general guidelines for safeguards to be used in all NIBS studies, as well as additional guidelines for parameters and safeguards specific to tDCS. Explicit mention of these safeguarding practices should be made in the ethical approval documentation.

- Two researchers must be available to respond to any adverse event at all experimental sessions. One of these researchers must have qualified in first aid training within the last three years. The qualified first aider should be notified of testing and available throughout all testing sessions.
- Researchers must be qualified users of the relevant technique and listed on the Leeds Trinity University list of approved tDCS researchers having satisfied the criteria in Appendix 6.3. Such approval must follow training in safety procedures and appropriate use of the brain stimulation equipment. The ethics application must specify the names of the qualified users on the research team.
- Researchers using NIBS should undergo an external training course to ensure 1) correct use of the device and 2) to ensure relevant safety issues

are considered for experiments and the occurrence of adverse effects (Antal et al., 2017).

- A variety of national and international training courses are available. The costs and time commitment to attend a one-day (minimum) course which enable points 1 and 2 above to be addressed is between £300 to £1000 pounds.
- A NIBS user can be re-qualified by a) satisfying the criteria in Appendix 6.3; b) attending an external refresher course on NIBS or c) completion of a research study using NIBS in a calendar year.
- Participants will be informed of all potential risks during the consent process.
- As in all experiments, participants will be free to stop their participation at any time and for any reason.
- Following each NIBS session, participants will complete an Adverse Effects Questionnaire (Appendix 6.4), which requires participants to rate occurrence of any adverse effects such as headaches. Participants will remain in the laboratory for 45 min after NIBS stimulation has ended. If they feel unwell, local emergency procedures will be followed and they will be monitored until the adverse effects subside.
- Before using NIBS, participants should be informed about unusual sensations that they may experience (e.g., for tDCS: tingling and warmth). If the participant reports experiencing pain or significant discomfort, or if there are any safety concerns, the stimulation should be terminated immediately.
- Safety of researchers: There are no known risks to researchers associated with administering tDCS. However, to be consistent with pregnancy as a contraindication for volunteers in NIBS studies, researchers who are pregnant should not deliver NIBS. The potential for harm to the unborn child is unknown, however.

Additional issues relating to best practice

Potential adverse effects of tDCS and their management

Large meta-analyses of the adverse effects of tDCS have shown no such effects. Indeed, a meta-analysis of the aggregate number of tDCS sessions failed to identify even a single record of a Serious Adverse Effect related to tDCS across more than 33,200 sessions (Bikson et al., 2016). Among these over 1000 subjects received tDCS repeatedly (multiple sessions across days) without an instance of Serious Adverse Effect. Furthermore, data on individual patients exists who have received over 100 treatment sessions of tDCS without any indication of adverse effects arising from cumulative exposure, including a patient with schizophrenia who received tDCS daily over 36 months (i.e., more than 1000 sessions; Andrade, 2013) and patients with depression receiving multiple tDCS exposures safely (more than 100 sessions in total; Tadini et al., 2011). Additionally, as of the date above, the adverse event reporting database MedWatch in the USA (https://www.fda.gov/Safety/MedWatch/default.htm) returns no reports for the terms “tDCS” or “transcranial Direct Current Stimulation” or “transcranial” or “transcranial Direct Current Stimulator.”

With respect to the skin contact, the use of water-soaked sponge electrodes should minimize any chemical reactions at the interface; however, participants should as part of the interview process be asked about pre-existing skin conditions. The condition of the skin under the electrodes should be inspected before and after stimulation. Researchers will inform participants of the likely irritation caused in sensitive individuals and assess on a case-by-case basis whether to proceed with the experiment. Proneness to skin reactions is not a contra-indication.

For tDCS studies with healthy subjects, general exclusion criteria available for electrical and magnetic stimulation apply: subjects should be free of medical conditions, or any illness that may increase the risk of stimulation, for example, neurological diseases such as epilepsy. Furthermore, subjects should have no metallic implants near the electrodes. They should be informed about the possible side effects of tDCS, such as headache, dizziness, nausea, and an itching sensation as well as skin irritation under the electrodes. The ethics application must specify these guidelines and participants must complete the neurophysiological physical activity readiness questionnaire prior to undertaking any tDCS study (NPAR-Q; Appendix 6.5). Affirmative answers to any questions indicating, for example but not restricted to, the presence of epilepsy, history of seizures, the existence of medical implants, embedded metallic plates and existing skin conditions will immediately exclude participants.

Significant Adverse Effects (as defined by Bikson et al. 2016) will be reported to the SSHS Ethics Committee, which approved the study, to inform future revisions of these guidelines. Following an adverse effect, the study will be suspended whilst the SSHS ethics committee investigates and will only recommence following permission to do so from the SSHS ethics committee. In agreement with the published safety guidelines, in the case of a seizure or other significant adverse effect that is possibly related to a NIBS session, details will be forwarded to the editor of the journal Brain Stimulation.

Data protection and privacy

All written materials (i.e., consent forms, questionnaires) will be kept in locked filing cabinets whereas all electronic data will be kept on password-protected computers. Both types of data will only be accessible to members of the research team and will

be under the direct responsibility of the principal investigator. Data storage and safety will be in accordance with the Leeds Trinity University data protection policy.

Participant anonymity will be maintained by assigning each participant a unique participant reference number. This number will only appear alongside the participant's name on the consent form, which will be stored separately from all other materials. All other materials will only state the participant reference number.

Data collected in each study will be aggregated for the purpose of performing statistical analyses across participants. Findings may be reported in peer-reviewed journal articles, conference presentations, or as part of dissertations. In all cases, average data across participants will be reported; if individual data are reported for illustrative purposes, they will never be accompanied by information that would enable identification of the individual participant.

Security and equipment maintenance

Equipment for administering tDCS will be housed in a locked laboratory at Leeds Trinity University. Scheduled servicing and equipment maintenance will be logged and recorded and be required as per the manufacturer guidelines.

References

Andrade C. (2013). Once- to twice-daily, 3-year domiciliary maintenance transcranial direct current stimulation for severe, disabling, clozapine-refractory continuous auditory hallucinations in schizophrenia. J ECT;29:239–242.

Antal A, Alekseichuk I, Bikson M, et al. (2017). Low intensity transcranial electric stimulation: Safety, ethical, legal regulatory and application guidelines. Clin Neurophysiol;128:1774-1809.

Bikson M, Grossman P, Thomas C, et al. (2016). Safety of Transcranial Direct Current Stimulation: Evidence based update 2016. Brain Stim;9:641-661.

Nitsche MA, Cohen LG, Wassermann EM, et al. (2008) Transcranial direct current stimulation: State of the art. Brain Stim;1:206-223.

Rossi S, Hallett M, Rossini, PM, et al. (2009). The Safety of TMS Consensus Group. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clinical Neuropsychology; 120: 2008-2039.

Tadini L, El-Nazer R, Brunoni AR, et al. (2011). Cognitive, mood, and electroencephalographic effects of noninvasive cortical stimulation with weak electrical currents. J ECT;27:134–40.

Voarino N, Dublejevic V, Racine E, (2017). tDCS for memory enhancement: Analysis of the speculative aspects of ethical issues. Front. Hum. Neurosci; 10:678.

Appendix 6.1 Potentially Hazardous Drugs

The following drugs are a potential hazard when using repetitive TMS. If the participant is taking or in withdrawal of the following drugs, they are not eligible for testing when using all TMS/tDCS protocols.

1. Intake of the following drugs provide a **strong** potential hazard:

Alcohol	Doxepine	Amphetamines
Amphetamines	Imipramine	Cocaine
Theophylline (asthma treatment)	Maprotiline	Gamma-hydroxybutyrate (GHB)
Antipsychotics:	Nortriptyline	Ketamine
Chlorpromazine	Antivirals:	MDMA, ecstasy
Clozapine	Foscarnet	Phencyclidine (PCP, angel's dust)
Antidepressants:	Ganciclovir	
Amitriptyline	Ritonavir	
	Recreational:	

2. Intake of the following drugs provides a **relative** potential hazard:

Anticholinergics	Pimozide	Venlafaxine
Antihistamines	Quetiapine	Antimalarials
Sympathomimetics	Risperidone	Chloroquine
Antibiotics:	Ziprasidone	Mefloquine
Ampicillin	Antidepressants:	Chemotherapy:
Cephalosporins	Aripiprazole	BCNU
Imipenem	Bupropion	Chlorambucil
Isoniazid	Citalopram	Cytosine arabinoside
Levofloxacin	Duloxetine	Vincristine
Metronidazole	Fluoxetine	Antimetabolites:
Penicillin	Lithium	Methotrexate
Antipsychotics:	Mianserin	Immunosuppressants:
Aripiprazole	Mirtazapine	Cyclosporin
Fluphenazine	Paroxetine	
Haloperidol	Reboxetine	
Olanzapine	Sertraline	

3. **Withdrawal** from the following drugs forms a **strong relative** hazard:

Alcohol	Benzodiazepines	Meprobamate
Barbiturates	Chloralhydrate	

As a general precaution, any individual taking ANY antidepressants, antipsychotics, antivirals, antibiotics, anticonvulsants, antimetabolites, antimalarials, immunosuppressants or chemotherapy drugs are excluded.

Adapted from Rossi et al. (2009).

Appendix 6.2 Brain Stimulation Study Suitability Questionnaire (BSSSQ)

Study Title: [INSERT STUDY TITLE]

Please read the statements carefully and circle YES or NO opposite the question if it applies to you.

1. Do you have epilepsy, or have you ever had a convulsion or a seizure?	YES	NO
2. Have you ever had a fainting spell, “blackout” or syncope? If YES, please describe on which occasion(s):	YES	NO
3. Have you ever had severe (i.e., followed by loss of consciousness) head trauma or neurological illness?	YES	NO
4. Do you have any hearing problems or ringing in your ears?	YES	NO
5. Are you pregnant or is there any chance that you might be?	YES	NO
6. Do you have metal in your brain/skull (except titanium)? (e.g., splinters, fragments, clips, etc.)	YES	NO
7. Do you have cochlear implants?	YES	NO
8. Do you have an implanted neurostimulator (e.g., DBS, epidural/subdural, VNS)?	YES	NO
9. Do you have a cardiac pacemaker or intracardiac lines or metal in your body?	YES	NO
10. Do you have a medication infusion device?	YES	NO
11. Are you taking any medications or recreational drugs, other than oral contraceptives or anti-allergy medicine? If YES, please list:	YES	NO
12. Did you ever have surgical procedures to your spinal cord?	YES	NO
13. Do you have spinal or ventricular derivations?	YES	NO

14. Have you ever had a stroke?	YES	NO
15. Do you suffer from frequent or severe headaches?	YES	NO
16. Did you ever undergo TMS/tDCS in the past? If YES, please list: when did the procedure take place? What was the exposure duration and intensity?	YES	NO
17. Have you ever had an adverse reaction to brain stimulation in the past?	YES	NO
18. Did you ever undergo MRI in the past?	YES	NO
19. Do you suffer from claustrophobia?	YES	NO
20. Do you suffer from any skin condition or disease (e.g., eczema)?	YES	NO

The information I have given is, to the best of my knowledge, correct at the time of completion.

Participant	Witness
Name:	Name:
_____	_____
Date:	Date:
____ / ____ / _____	____ / ____ / _____
Signature:	Signature:
_____	_____

Appendix 6.3 Training Checklist

To use the transcranial direct current stimulation (tDCS) equipment experimenters must meet the requirement listed in the following training checklist. On completion of training, the practice of the experimenter must be approved by a fully trained member of staff to establish that the equipment is being used appropriately and safely.

Checklist:
Confirm the experimenter has been shown and made aware of the following procedures

1. The experimenter has familiarised themselves with the Risk Assessment and Standard Operating Procedures for tDCS and have read the research articles referred to in these documents.	☐
2. The experimenter is competent administering the health screening questionnaire. Undergraduates should know to consult a fully trained member of staff if any questions arise from the pre-screening prior to testing.	☐
3. The experimenter is familiar with the equipment: HDCprog – stimulator programmer. HDCstim – battery driven stimulator. Electrodes, sponges, electrode connector cables. Red electrode (anode/positive stimulation), black electrode (cathode/negative stimulation). Physiological saline solution (~9 gram of sodium chloride (NaCl) dissolved in 1 litre of water). *Additional equipment:* towels, tape measure, Lycra swimming cap.	☐
The experimenter has demonstrated they can perform the following procedures:	
4. Programming the stimulation protocol using the **HCDprog** a. Stimulation setting – define intensity, duration, intervals between consecutive stimulation. b. Treatment manager – observe stimulations concluded, failures, aborts, impedance, and delete protocol after stimulation. c. Stimulus waveform – set the stimulation type (active-mono-channel or bi-channel; sham).	☐ ☐ ☐
5. Administering the stimulation protocol using the **HDCstim** a. Turn HDCstim on; begin stimulation; end/abort stimulation. b. Check battery charge level and replace if necessary.	☐ ☐

c. Screen – number of programmed stimulations and time that must elapse before new stimulation can start; countdown until end of stimulation; number of failures occurred during current stimulation; impedance levels.	☐
d. LED light – green: HDCstim ON; blue: stimulation ON; flashing blue: current of stimulation increasing to 100%.	☐
e. Stimulation failure – turn HDCstim OFF and verify electrode's contact with skin is adequate; electrodes connected properly; electrodes sufficiently wet.	☐
6. Electrode placement	
a. Electrode connector cables – red (anode/positive stimulation); black (cathode/negative stimulation).	☐
b. Soak the electrode sponges in saline solution prior to testing (15 minutes is ideal).	☐
c. Measure the participant's head and mark the desired electrode positions.	☐
d. Place the electrodes in position under the stimulation cap the middle of the electrode should be over the desire location.	☐
e. Confirm electrode pads are soaked sufficiently; ensure regions adjacent to the electrodes are as dry as possible in order to minimise the spread of stimulation sensation.	☐
f. Attach electrode cables to HDCstim.	☐
7. General practice	
a. Participant log – participant details should be kept in the lab to note: name of participant, date of birth, date of testing, any adverse reactions, and any general issues during testing. This must be kept up to date.	☐
b. Cleaning – it is essential the equipment is cleaned and put away properly to avoid damage, such as corrosion due to salt water. Equipment to be cleaned: electrodes, sponges, caps, towels.	☐
c. Equipment inspection – electrodes, sponges and connector cables should be inspected for damage before stimulation occurs, any damaged equipment must not be used.	☐

I confirm that _____ has completed the training checklist and is authorised to use the tDCS equipment.

Name of researcher: _____

Signature: _____

Date: _____

Appendix 6.4 Adverse Events Questionnaire

Study Title: [INSERT STUDY TITLE]

Listed are a variety of adverse events associated with non-invasive brain stimulation. Please highlight which are present, if any, and the severity of the event. Also indicate whether this is related to the stimulation or has been worsened by stimulation.

Symptom	Is it present? 0 = no 1 = mildly 2 = moderately 3 = severely	If present, is it related to stimulation? 0 = no 1 = remotely 2 = possibly 3 = probably 4 = yes	Notes
Headache			
Neck pain			
Scalp pain			
Tingling			
Itching			
Burning sensation			
Skin redness			
Sleepiness			
Trouble concentrating			
Acute mood change			
Other (please specify)			

_____ _____ ___ / ___ / ____

PRINT NAME *SIGNATURE* *DATE*

Witnessed by:

_____ _____ ___ / ___ / ____

PRINT NAME *SIGNATURE* *DATE*

Appendix 6.5 Neurological Conditions Physical Activity Readiness Questionnaire (NPAR-Q)

Study Title: [INSERT STUDY TITLE]

Please read the questions carefully and circle YES or NO opposite the question if it applies to you. If you answer YES to any of the following questions, you are not eligible to take part in the study.

Have you ever broken a bone in your arm and/or hand?	YES	NO
Do you have pain in your arms or your hands?	YES	NO
Have you ever been diagnosed with a neurological disorder (e.g., epilepsy)?	YES	NO
Have you ever had convulsions or seizures?	YES	NO
Have you ever been diagnosed with a brain disorder (e.g., Parkinson's disease)?	YES	NO
Have you ever had brain surgery?	YES	NO
Have you ever had a stroke?	YES	NO
Are you taking any medications that you know would affect neuronal conduction? If YES, please explain:	YES	NO
Do you have a pacemaker?	YES	NO
Have you had any operations involving your heart?	YES	NO
Do you have a metal plate in your skull, or metal objects in the eye or skull (e.g., after brain surgery or shrapnel wounds)?	YES	NO
Are you pregnant or seeking to become pregnant in the near future?	YES	NO
Have you ever had brain stimulation, whether electrical or magnetic?	YES	NO

The information I have given is, to the best of my knowledge, correct at the time of completion.

_____	_____	___ / ___ / ____
PRINT NAME	SIGNATURE	DATE

Appendix 7 Correlation Matrix for Eating Behaviour Trait Questionnaires

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
1. TFEQ Restraint [a]	-										
2. TFEQ Disinhibition [a]	−0.200 ***	-									
3. TFEQ Hunger [a]	−0.320 ***	0.690 ***	-								
4. TFEQ-r18 Restraint [a]	0.890 ***	−0.250 ***	−0.340 ***	-							
5. TFEQ-r18 Uncontrolled eating [a]	−0.310 ***	0.770 ***	0.890 ***	−0.340 ***	-						
6. TFEQ-r18 Emotional eating [a]	−0.020	0.690 ***	0.410 ***	−0.060	0.390 ***	-					
7. CoEQ Craving control [b]	−0.005	−0.487 ***	−0.458 ***	ND	ND	ND	-				
8. CoEQ Positive mood [b]	−0.157	−0.357 ***	−0.095	ND	ND	ND	0.244 **	-			
9. CoEQ Craving for sweet foods [b]	0.020	0.338 ***	0.396 ***	ND	ND	ND	−0.576 ***	−0.139	-		

Table continued

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.
10. CoEQ Craving for savoury foods [b]	−0.130	0.223 **	0.322 ***	ND	ND	ND	−0.365 ***	−0.185	0.173 *	-	
11. BES [b, c]	−0.250 ***	0.700 ***	0.460 ***	ND	ND	ND	−0.518 ***	−0.302 ***	0.408 ***	0.242 ***	-

BES, Binge Eating Scale; CoEQ, Control of Eating Questionnaire; FCQ-T-r, Food Craving Questionnaire-Trait reduced form; ND, no data available; TFEQ, Three Factor Eating Questionnaire; TFEQ-r18, Three Factor Eating Questionnaire reduced form.

** p < 0.05, ** p < 0.01, *** p < 0.001*

[a] Karlsson et al. (2000); n = 4,377 females (n = 2603) and males (n = 1774) with obesity

[b] Dalton et al. (2015); n = 215 females (n = 171) and males (n = 44) with healthy weight, overweight and obesity

[c] Foster et al. (1998); n = 233 females with obesity

NB: No data is available for correlation between the Food Craving Questionnaire-Trait reduced form (FCQ-T-r) and other psychometric questionnaires included here; the FCQ-T-r has been excluded from this table.

Appendix 8 PRISMA Checklist for the Literature Review in Chapter 6

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	125
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	126 to 127
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	128 to 129
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	129
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	17 to 18, 129 to 130
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	16 to 17, 129 to 130
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	17
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	17 to 18

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	18
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	18
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	18
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	18 to 20, 130
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	18 to 20, 130
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	18
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	18 to 20, 130
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 6-1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	130 to 137, Table 6-1, Table 6-3, Appendix 9
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	Table 6-4
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	148 to 170
Synthesis of results	21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency	148 to 170
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	146

Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	19 to 20, 137 to 138
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	170 to 172
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	170 to 172
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	170 to 172
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	N/A

Appendix 9 Studies Incorporated into the Meta-Analysis for Chapter 6

	Hunger	Fullness	Prospective Consumption	Desire to Eat	Food Craving	Explicit Wanting	Implicit Wanting	Explicit Liking	Food Consumption
Amo Usanos et al. (2020)									
Beaumont et al. (2021)	X	X	X	X	X	X	X	X	
Bravo et al. (2016)	X								
Burgess et al. (2016)						X			X
Carvalho et al. (2019)						X	X		
Chen et al. (2019)	X			X	X				
Fassini et al. (2019)									
Fassini et al. (2020)									
Fregni et al. (2008)				X			X		X
Georgii et al. (2017)					X	X			X
Gluck et al. (2015)									X
Goldman et al. (2011)						X			X

Table continued

	Hunger	Fullness	Prospective Consumption	Desire to Eat	Food Craving	Explicit Wanting	Implicit Wanting	Explicit Liking	Food Consumption
Grundeis et al. (2017)	X	X							X
Heinitz et al. (2017)									
Jauch-Chara et al. (2014)	X								X
Kekic et al. (2014)					X	X			X
Kekic et al. (2017)	X			X		X		X	
Lapenta et al. (2014)				X			X		X
Ljubisavljevic et al. (2016)									
Marron et al. (2019)	X	X	X	X					
Mattavelli et al. (2019)							X		
Max et al. (2020)						X			
Montenegro et al. (2012)									
Ray et al. (2017)						X		X	X
Ray et al. (2019)						X			X

Table continued

	Hunger	Fullness	Prospective Consumption	Desire to Eat	Food Craving	Explicit Wanting	Implicit Wanting	Explicit Liking	Food Consumption
Sedgmond et al. (2019)	X	X		X	X				X
To et al. (2018)									X
Vicario et al. (2020)	X								
Study n	9	4	2	7	5	10	5	3	13
Participant n	402	237	33	333	309	338	176	78	483

Appendix 10 Funnel Plots for the Literature Review in Chapter 6

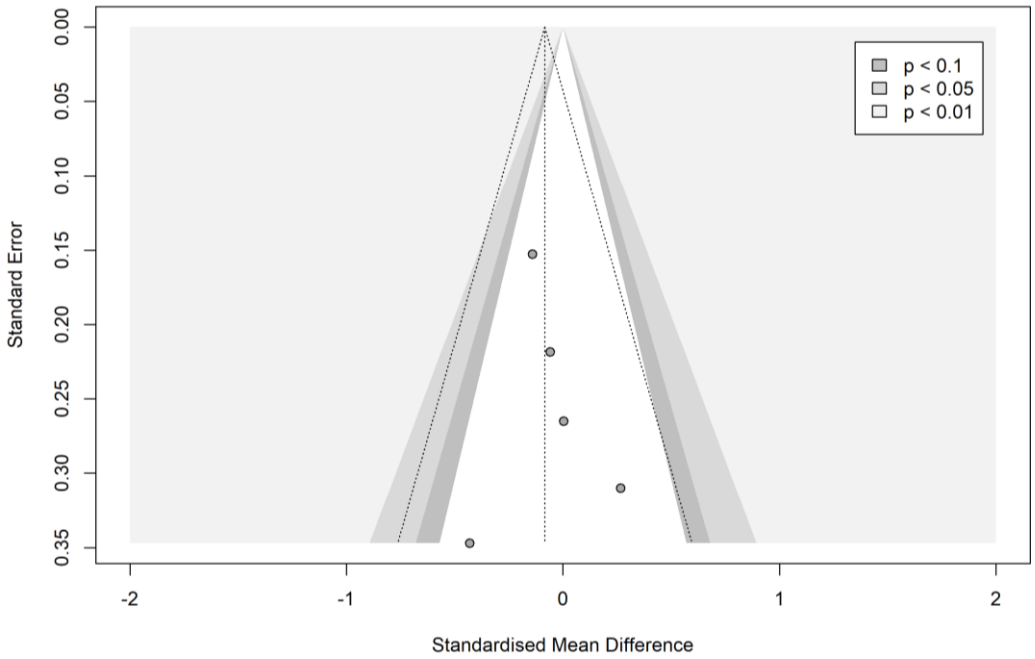


Figure A9.1 Funnel plot for studies measuring food craving via the Food Craving Questionnaire-State.

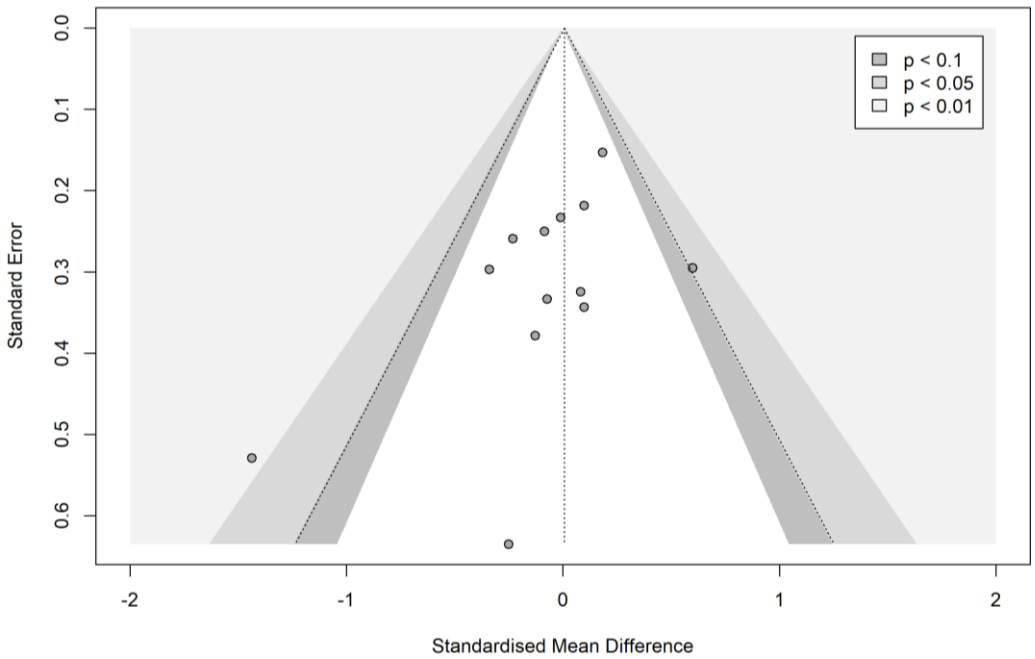


Figure A9.2 Funnel plot for studies measuring food consumption.

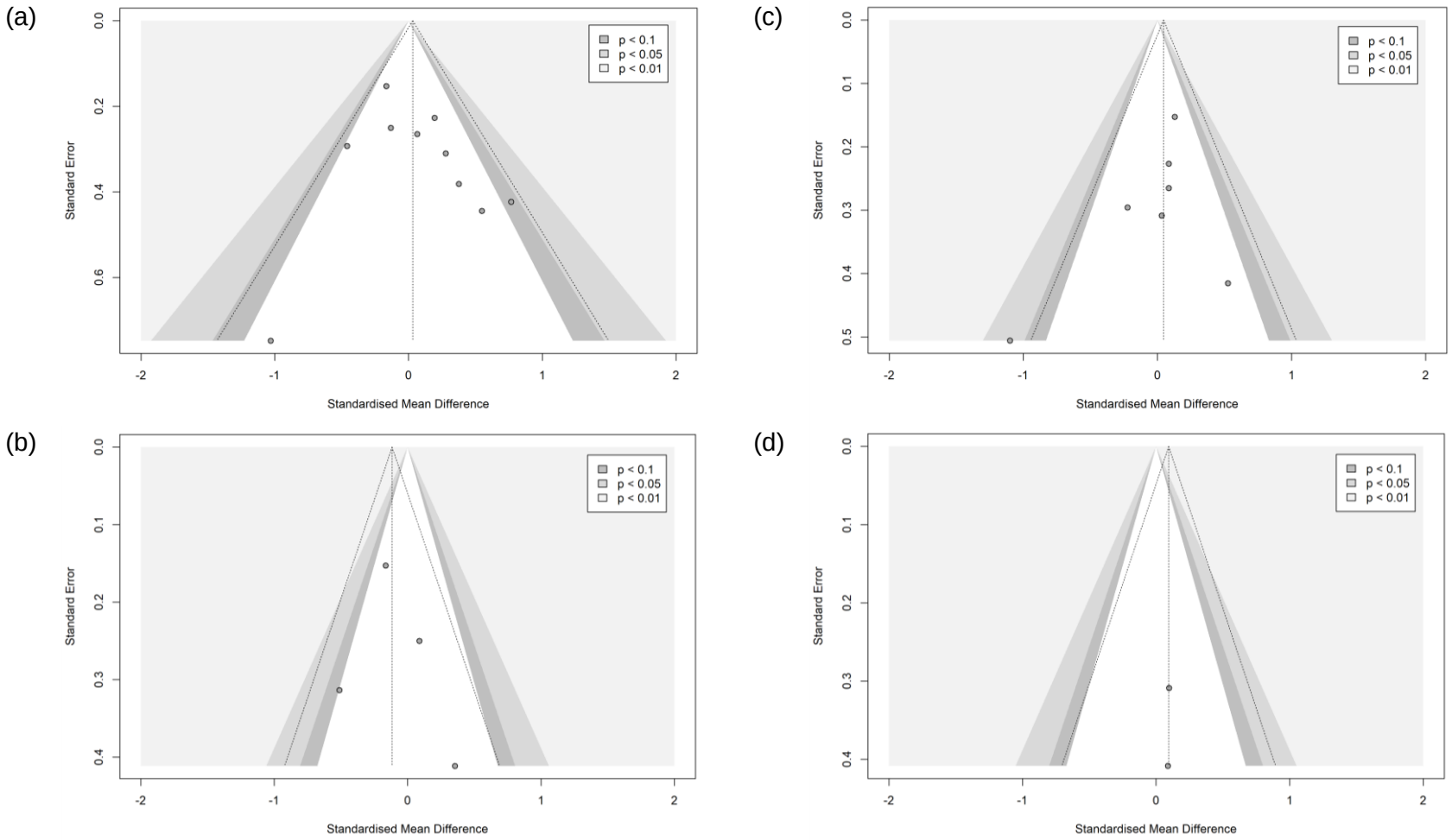
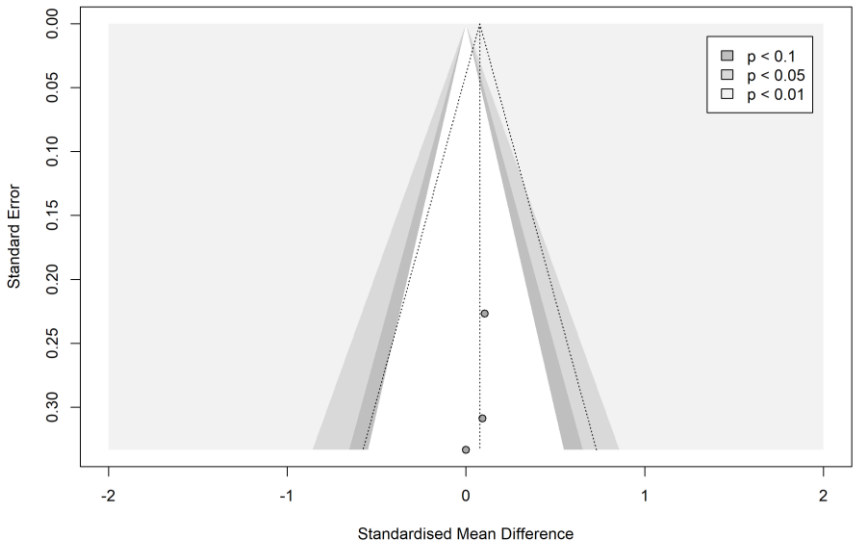
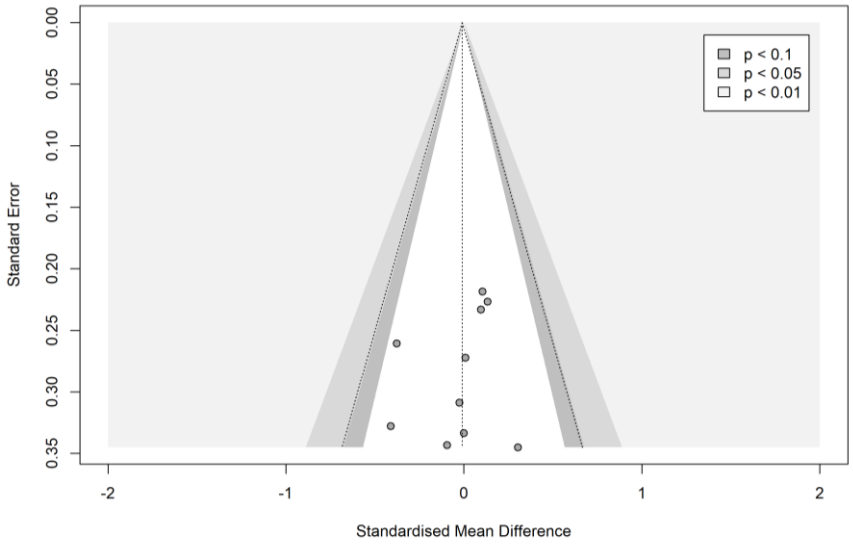


Figure A9.3 Funnel plots for studies measuring (a) hunger, (b) fullness, (c) desire to eat, and (d) prospective consumption.

(a)



(b)



(c)

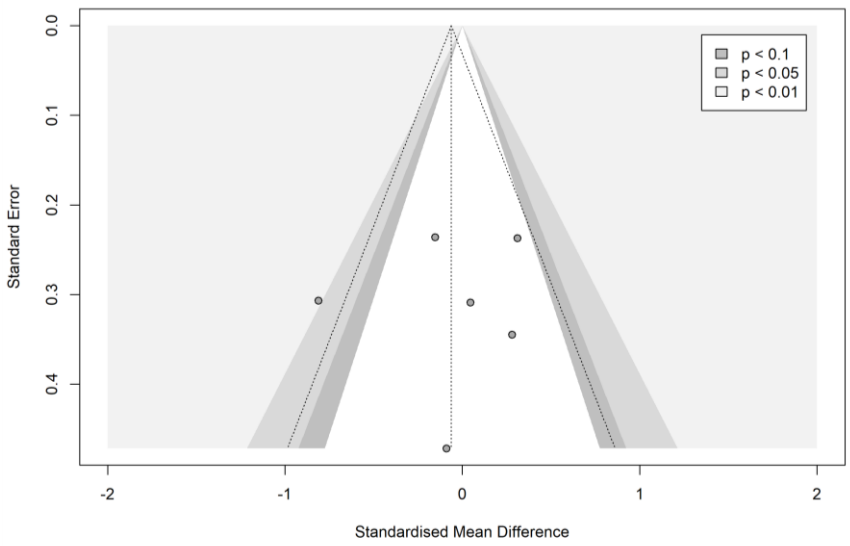


Figure A9.4 Funnel plots for studies measuring (a) explicit liking, (b) explicit wanting, and (c) implicit wanting.

Appendix 11 Candidate's Training Checklist

To use the transcranial direct current stimulation (tDCS) equipment experimenters must meet the requirement listed in the following training checklist. On completion of training, the practice of the experimenter must be approved by a fully trained member of staff to establish that the equipment is being used appropriately and safely.

Checklist:
Confirm the experimenter has been shown and made aware of the following procedures

1. The experimenter has familiarised themselves with the Risk Assessment and Standard Operating Procedures for tDCS and have read the research articles referred to in these documents.	☒
2. The experimenter is competent administering the health screening questionnaire. Undergraduates should know to consult a fully trained member of staff if any questions arise from the pre-screening prior to testing.	☒
3. The experimenter is familiar with the equipment: HDCprog – stimulator programmer. HDCstim – battery driven stimulator. Electrodes, sponges, electrode connector cables. Red electrode (anode/positive stimulation), black electrode (cathode/negative stimulation). Physiological saline solution (~9 gram of sodium chloride (NaCl) dissolved in 1 litre of water). *Additional equipment:* towels, tape measure, Lycra swimming cap.	☒
The experimenter has demonstrated they can perform the following procedures:	
4. Programming the stimulation protocol using the **HCDprog** a. Stimulation setting – define intensity, duration, intervals between consecutive stimulation. b. Treatment manager – observe stimulations concluded, failures, aborts, impedance, and delete protocol after stimulation. c. Stimulus waveform – set the stimulation type (active-mono-channel or bi-channel; sham).	☒ ☒ ☒
5. Administering the stimulation protocol using the **HDCstim** a. Turn HDCstim on; begin stimulation; end/abort stimulation. b. Check battery charge level and replace if necessary.	☒ ☒

c. Screen – number of programmed stimulations and time that must elapse before new stimulation can start; countdown until end of stimulation; number of failures occurred during current stimulation; impedance levels.	☒
d. LED light – green: HDCstim ON; blue: stimulation ON; flashing blue: current of stimulation increasing to 100%.	☒
e. Stimulation failure – turn HDCstim OFF and verify electrode's contact with skin is adequate; electrodes connected properly; electrodes sufficiently wet.	☒
6. Electrode placement	
a. Electrode connector cables – red (anode/positive stimulation); black (cathode/negative stimulation).	☒
b. Soak the electrode sponges in saline solution prior to testing (15 minutes is ideal).	☒
c. Measure the participant's head and mark the desired electrode positions.	☒
d. Place the electrodes in position under the stimulation cap the middle of the electrode should be over the desire location.	☒
e. Confirm electrode pads are soaked sufficiently; ensure regions adjacent to the electrodes are as dry as possible in order to minimise the spread of stimulation sensation.	☒
f. Attach electrode cables to HDCstim.	☒
7. General practice	
a. Participant log – participant details should be kept in the lab to note: name of participant, date of birth, date of testing, any adverse reactions, and any general issues during testing. This must be kept up to date.	☒
b. Cleaning – it is essential the equipment is cleaned and put away properly to avoid damage, such as corrosion due to salt water. Equipment to be cleaned: electrodes, sponges, caps, towels.	☒
c. Equipment inspection – electrodes, sponges and connector cables should be inspected for damage before stimulation occurs, any damaged equipment must not be used.	☒

I confirm that JORDAN BEAUMONT has completed the training checklist and is authorised to use the tDCS equipment.

Name of researcher: Dr MARTIN BARWOOD

Signature:

Date: 07/12/2017

Appendix 12 Debrief Form

Study Code:	
Participant ID Number:	
Date:	

Were you able to tell any difference between the stimulation sessions?

☐ YES ☐ NO

If YES, please give additional information:

Which session do you believe involved ACTIVE tDCS?

☐ Session 1 ☐ Session 2 ☐ I don't know

How confident are you that this session involved ACTIVE tDCS? [4]
(Please circle a number)

Not confident at all | 1 2 3 4 5 6 7 8 9 10 | Very confident

Why do you think this session was the ACTIVE condition?

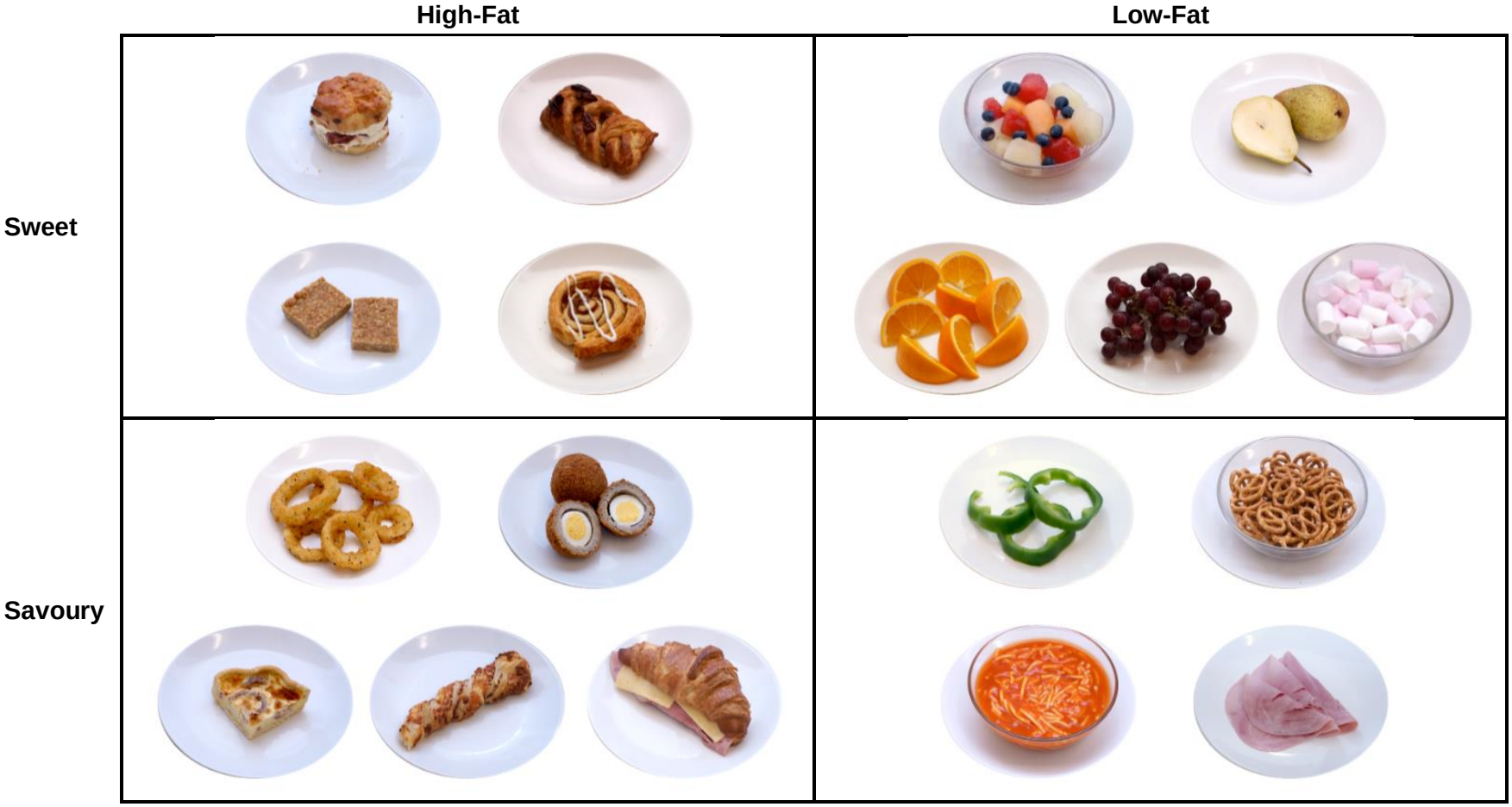
Have you experienced any adverse events in the days following stimulation?

☐ YES ☐ NO

If YES, please give additional information:

[4] This question was only added for study two (Chapter 7)

Appendix 13 Additional LFPQ Images



Appendix 14 Changes to Standardised LFPQ Images

Study	Participant ID	Food Category	Original Image	New Image
Study 1 (Chapter 5)	S2/02	HFSA	Sausage roll	Quiche
	S2/03	LFSW	Haribo	Marshmallow
	S2/05	LFSW	Haribo	Marshmallow
		HFSW	Doughnut	Scone
		HFSA	Sausage roll	Onion rings
	S2/13	HFSA	Garlic bread	Cheese twist
Study 2 (Chapter 7)	S3/01	LFSW	Haribo	Grapes
			Skittles	Oranges
		HFSW	Doughnut	Flapjack
	S3/02	HFSA	Sausage roll	Onion rings
	S3/06	HFSW	Doughnut	Flapjack
	S3/13	HFSW	Chocolate fingers	Flapjack
			Chocolate	Scone
	S3/14	LFSW	Skittles	Grapes
			Banana	Oranges
	S3/15	LFSA	Broccoli	Pepper
			Salad	Pretzel
	S3/17	HFSA	Sausage roll	Onion rings
	S3/19	LFSW	Haribo	Grapes
			Skittles	Marshmallows
	S3/20	LFSA	Rice	Pretzels
	S3/21	LFSW	Haribo	Oranges
			Skittles	Grapes
		HFSW	Chocolate fingers	Cinnamon roll
		HFSA	Sausage roll	Onion rings
	S3/22	HFSW	Chocolate fingers	Cinnamon roll
		HFSA	Sausage roll	Onion rings
		LFSA	Bread roll	Spaghetti
	S3/23	HFSA	Sausage roll	Cheese twist
	S3/24	HFSA	Sausage roll	Cheese twist

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