

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

3

4 Jordan D. Beaumont^{a,*}, Natalie C. Smith^a, David Starr^a, Danielle Davis^a, Michelle Dalton^a,
5 Alexander Nowicky^b, Mark Russell^a and Martin J. Barwood^a

6

7 ^a*School of Social and Health Sciences, Leeds Trinity University, Leeds, LS18 5HD, UK*

8 ^b*Centre for Cognitive Neuroscience, Department of Clinical Sciences, College of Health and*
9 *Life Sciences, Brunel University London, Uxbridge, UB8 3PH, UK*

10

11 *** Corresponding author:**

12 Jordan D. Beaumont

13 School of Social and Health Sciences, Leeds Trinity University, Leeds, LS18 5HD, UK

14 Email: j.beaumont@leedstrinity.ac.uk

15

16 **Key words:** Appetite, Food consumption, Food craving, Food reward, Neuromodulation,
17 Non-invasive brain stimulation

18

19 **Running title:** Impact of eating behaviour traits on tDCS

20

21 **Acknowledgements:**

22 The authors would like to thank Rachel Davies for help with defining search terms. The
23 authors would also like to thank Dr. Ann Manzardo and Dr. Maria Kekic for access to their
24 study data for our meta-analysis.

25

26 **Conflicts of interest:** None.

27

28

29 **Abbreviations**

30 AU, arbitrary unit; BED, binge eating disorder; BF_{10} , Bayes factor; BMI, body mass index;
31 CBIT, computer-based image task; CBM, cognitive bias modification; CI, confidence interval;
32 cm, centimetre; COMT, catechol-o-methyl transferase; DLPFC, dorsolateral prefrontal
33 cortex; EBA, extrastriate body area; EDNOS, eating disorder not otherwise specified; F,
34 female; FCI, Food Craving Inventory; FCQ-S, Food Craving Questionnaire-State; GABA,
35 gamma-aminobutyric acid; IAT, implicit association task; IFG, inferior frontal gyrus; kcal,
36 kilocalorie; kg, kilogram; LFPQ, Leeds Food Preference Questionnaire; M, male; mA,
37 milliamperere; met, methionine; min, minute; NR, not reported; PFC, prefrontal cortex; PICO,
38 Population, Intervention, Control and Outcome; PWS, Prader Willi syndrome; RoB, risk of
39 bias; SE, standard error; SEM, standard error of the mean; subBED, subthreshold binge
40 eating disorder; tDCS, transcranial direct current stimulation; tnM1, tongue muscle
41 representation of the primary motor cortex; VAS, visual analogue scale; VNS, visual numeric
42 scale
43

44 **ABSTRACT**

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

62

63 1. INTRODUCTION

64 Obesity is a global health epidemic that is predicted to affect 20% of the worldwide adult
65 population by 2030 ¹, with a higher prevalence predicted for both the United Kingdom (35 to
66 48%) and United States of America (45 to 52%) ^{2,3}. This condition is associated with many
67 comorbid diseases, such as type 2 diabetes and coronary heart disease, which places
68 greater emphasis on the treatment of obesity ^{4,5}. Although it is often diminished to the notion
69 of “eat less, move more”, obesity is multi-faceted and driven by the complex relationship
70 between behavioural, biological and environmental factors ^{6,7}. Despite this complexity, the
71 treatment of obesity typically involves simple changes to the diet and/or physical activity ^{8,9}.
72 Although these treatment modalities produce initial weight loss of up to 10%, this weight loss
73 is not maintained long-term ⁹. Additional treatment options such as behavioural therapy,
74 medications and surgeries also do not result in successful or maintained weight loss for
75 many individuals ¹⁰⁻¹², with extreme forms of treatment such as bariatric surgery associated
76 with 10 to 27% of individuals experiencing weight regain ^{11,13}. These weight loss
77 interventions typically target the symptoms of obesity, such as excess adiposity, and often
78 ignore the important underlying brain-dependent factors that contribute to energy balance ¹⁴.

79

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

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

99

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

115

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

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

125

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

140

141 **2. METHODS**

142 **2.1 Search Strategy**

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

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

156

157 **2.2. Inclusion and Exclusion Criteria**

158 In line with the Population, Intervention, Control and Outcome (PICO) model⁵⁸; articles were
159 included if they were peer-reviewed intervention studies that recruited adult human
160 participants (*population*), applying conventional (i.e. one anode and one cathode) tDCS
161 procedures (*intervention*) using a sham-controlled design (*control*) to determine the effects
162 on hedonic-related eating behaviours (subjective appetite, food craving, consumption or
163 reward) (*outcome*). Results were limited to those written in English and published after 1998
164 to coincide with the development of modern tDCS procedures^{38,59}. Any further articles
165 known to the authors were also considered for inclusion.

166

167 **2.3. Data Extraction**

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

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

178

179 **2.4. Study Quality Assessment**

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

183

184 **2.5. Statistical Analysis**

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

196

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

203
204
205
206
207
208
209
210
211
212
213
214
215
216
217
218
219
220
221
222
223
224
225
226
227
228
229
230

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

Meta-analyses were performed using R⁷¹ with the meta package⁷². Random effects models were used due to the variability in study design and outcomes. A negative effect size indicates that active tDCS reduced the outcome measure compared to sham tDCS, whereas a positive effect size indicates an increase in the outcome measure following active versus sham tDCS. Effect sizes were interpreted as trivial ($g < 0.20$), small ($g = 0.20$), moderate ($g = 0.50$) or large ($g > 0.80$)⁷³. The heterogeneity of effect sizes were assessed using the I^2 index, and interpreted as might not be important (0 to 40%), may represent moderate heterogeneity (30 to 60%), may represent substantial heterogeneity (50 to 90%), or considerable heterogeneity (75 to 100%)⁷⁴. Subgroup analyses were conducted to identify whether participant behaviour traits were moderating the effects of tDCS on eating-related measures. Forest and funnel plots were produced using the meta package for R. To test for publication bias, Egger's regression was used⁷⁵. Where meta-analysis was not possible, a systematic review of the literature is included.

3. RESULTS AND DISCUSSION

3.1 Study Characteristics

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

231 included studies used conventional sham-controlled tDCS procedures (i.e. one anode, one
232 cathode), with 12 between-participant and 16 within-participant designs (Table 1). Eight
233 studies involved repeated sessions of tDCS. Across the reviewed studies, a total of 996
234 participants were recruited, which ranged from 9 to 172 individuals per study. This included
235 individuals with healthy weight (n = 14 studies, 576 participants), overweight or obesity (n =
236 15 studies, 393 participants). One study included those with healthy weight and overweight
237 (n = 27), but the authors did not provide a breakdown for each weight category ⁶⁷.

238

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

240 *** INSERT TABLE 1 HERE ***

241

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

256

257 **3.2 Study Quality**

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

266

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

268

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

279

280 **3.3 Subjective Appetite**

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

286 0.15) (Figure S7), where a lack of change in scores ^{14, 46, 47, 52, 53, 63, 64, 76, 78, 88}, or increase in
287 measures of hunger ^{77, 89}, is often shown. Although Heinitz et al. ⁶⁴ found no difference in
288 subjective appetite scores when delivering daily inpatient tDCS, they did observe reductions
289 in hunger and the urge to eat following outpatient treatment and after adjusting for age and
290 sex. This suggests that long stimulation duration (40 minutes) and regular repetition (15
291 sessions) may affect the subjective appetite sensations of individuals with obesity. A similar
292 effect was shown in participants who were overweight, with reduced desire to eat following
293 single-session active versus sham tDCS, which was further reduced following isocaloric
294 exercise ⁶⁸. Although these studies include participants either considered or assumed to be
295 “healthy”, neither fully measure or report the behaviour traits of their participants, and so it is
296 difficult to identify what impact these traits may have on the change in subjective appetite
297 scores.

298

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

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

301

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

313

314 There appears to be an influence of COMT Val158Met polymorphism, whereby those who
315 are carriers of the methionine (met) allele showed reduced appetite following 16 sessions of
316 active tDCS compared to no change in scores for non-carriers⁶⁶. The COMT enzyme is
317 important for dopaminergic neurotransmission⁹¹, and absence of the met allele is associated
318 with reduced dopamine degradation which can increase the sensitivity to rewarding cues⁹².
319 This altered dopamine transmission impacts activity within the DLPFC and executive
320 functioning capabilities^{93,94}. The findings by Fassini et al.⁶⁶ suggest that absence of the met
321 allele can inhibit the modulatory influence of tDCS. Indeed, COMT Val158Met polymorphism
322 has previously been shown to impact the effects of stimulation⁹⁵. However, when Fassini et
323 al. repeated their study in a further cohort of met carrier and non-carriers, they did not find a
324 difference in subjective appetite scores⁶⁵. Further data are required to fully understand the
325 influence of COMT Val158Met polymorphism on the modulation of eating behaviour by
326 tDCS.

327

328 Across studies, the fasting period and baseline subjective appetite levels were not well
329 controlled. Fasting duration ranged from 2 to 7 hours, with 7 studies either not
330 measuring/reporting fasting duration or not asking participants to fast^{52, 64, 76, 78, 80, 84, 96}.
331 Longer fasting periods can lead to heightened appetite and greater hedonic response to
332 foods and related cues^{97,98}. No study has assessed the effects of differing fasting durations
333 on eating-related outcome measures following tDCS, but the impact of these uncontrolled
334 fasting periods cannot be excluded. It may be that the equivocal effects following tDCS are
335 driven by greater baseline appetite levels, but only two papers have included subjective
336 appetite scores as covariates in statistical analyses^{52,53}. To identify a more consistent effect
337 of tDCS on subjective appetite and other eating-related behaviours, greater control of fasting
338 duration and baseline appetite is required⁹⁹.

339

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

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

350

351 **3.4 Food Craving**

352 Here we focus specifically on the measure of in-the-moment food craving as assessed via
353 the Food Craving Questionnaire-State (FCQ-S) ¹⁰⁵. Food craving was measured in 8 of the
354 reviewed studies (Table 2). An additional 6 studies measured food craving as a proxy of
355 explicit wanting ^{44, 45, 51, 52, 76, 79}; these studies will be discussed in the following section. As
356 with subjective appetite, there is a lack of a consistent overall effect of stimulation on
357 measures of food craving across studies ($g = -0.08$; 95% CI = -0.28, 0.12) (Figure 4). Where
358 these studies recruited those participants considered “healthy”, no change in food craving
359 scores was observed when comparing anodal versus sham tDCS ($g = -0.06$; 95% CI = -0.29,
360 0.17) (Figure 4). Of interest, although Ljubisavljevic et al. ⁶⁷ recruited “healthy” individuals
361 they demonstrated that repeated sessions of tDCS were able to reduce food craving scores,
362 and particularly the craving for fast-food, sweet and high-fat food groups. This may highlight
363 a beneficial impact of multi-sessions designs on eating behaviour measures, which was also
364 demonstrated for subjective appetite ⁶⁴ (see 3.2). Again, the authors did not fully describe
365 the behavioural traits of their participants, and so the impact of these traits cannot be fully
366 identified.

367

368

*** INSERT FIGURE 4 HERE ***

369

370 The overall effect for trait groups shows only a trivial effect size ($g = -0.16$; 95% CI = -0.57,
371 0.26) (Figure 4). When we consider the effects of tDCS on state food craving in a population
372 who experience frequent food cravings, there is a more consistent reduction in craving
373 intensity when applying active versus sham stimulation ($g = -0.43$; 95% CI = -1.11, 0.25)
374 (Table S2). However, this effect was not extended to those with disinhibited and restrained
375 eating behaviour ($g = 0.00$; 95% CI = -0.52, 0.52). Finally, COMT Val158Met polymorphism
376 did not appear to influence the effects of repeated-session tDCS on food craving scores,
377 with no change in scores for met carriers and non-carriers when comparing active versus
378 sham tDCS ⁶⁵.

379

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

393

394 **3.5 Food Reward**

395 Food reward can be measured as “liking” (perceived impact of a food or related cue on
396 subject affect or pleasure) and “wanting” (subjective motivation that encompasses the
397 desire, craving or awareness of the ‘lack of something desirable’) responses to food ¹⁰⁶.

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

411

412 The overall effect of active versus sham tDCS on measures of explicit wanting ($g = -0.10$;
413 95% CI = -0.31, 0.11), explicit liking ($g = 0.08$; 95% CI = -0.05, 0.21), and implicit wanting (g
414 = -0.06; 95% CI = -0.50, 0.37) show only trivial effect sizes (Figure 5, Figure S9). These
415 effect sizes are mirrored in “healthy” participant populations ($g = 0.00$ to 0.09) (Figure S8).
416 Although no effect of tDCS was found, Ray et al. ⁷⁶ did show that the expectation of
417 receiving active tDCS led to reduced explicit wanting for foods. When this effect was
418 removed from analyses, the effect size for overall ($g = -0.01$; 95% CI = -0.16, 0.14) (Figure
419 5) and “healthy” groups ($g = 0.09$; 95% CI = -0.04, 0.22) increased, although remained trivial
420 (Figure S8). This emphasises the importance of controlled study designs and limiting the
421 information shared with participants, with the aim of reducing the bias that expectation may
422 have on the dataset.

423

424

*** INSERT FIGURE 5 HERE ***

425

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

437

438 Here we also include studies that measure eye tracking^{44,79,83}, as this can be used as a
439 measure of reward sensitivity^{97,108}. Two studies tracked participants' eye movement while
440 they were presented with a series of food and non-food images on a computer screen, and
441 recruited those with frequent food cravings^{44,79}. Although both studies showed reduced food
442 craving intensity ($g = -0.54$; 95% CI = -1.23, 0.15) (Table S2), the significant reduction in
443 fixation on food by Fregni et al.⁴⁴ was not replicated by Lapenta et al.⁷⁹. An additional study
444 used an anti-saccade task, where participants were sat in front of a computer screen
445 displaying a central cross; a food image was displayed on either the left or right side of the
446 screen, and participants were required to look in the opposite direction as fast as possible⁸³.
447 The authors found a current intensity-dependent effect, where faster latency of anti-
448 saccades were shown following 2.0 mA, but not 1.0 mA, tDCS in participants with BED.

449

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

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

457

458 **3.6 Food Consumption**

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

475

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

482 95% CI = -0.07, 0.17) (Figure 6). In comparison, a greater effect of active versus sham tDCS
483 can be seen in trait groups ($g = -0.12$; 95% CI = -0.76, 0.51) (Figure 6), driven particularly by
484 participants displaying frequent food cravings ($g = -0.30$; 95% CI = -1.32, 0.72) and binge
485 eating traits ($g = -0.23$; 95% CI = -0.74, 0.28) (Table S2).

486

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

488

489 Although two studies found reduced *ad libitum* consumption when comparing active to sham
490 tDCS in those who experience frequent food cravings^{44, 79}, this effect was not shown across
491 further studies recruiting similar populations^{45, 80}, with an increase in chocolate consumption
492 in a cohort with specific cravings for chocolate⁸². It is important to note that food craving is
493 not correlated with food consumption⁵¹. However, where specific behavioural traits are
494 evident (e.g. binge-type behaviour), heightened food cravings can lead to greater food intake
495¹¹². Therefore, it is possible that other eating behaviour traits are also influencing this
496 discrepancy in effects. Burgess et al.⁵¹ recruited participants with BED or subthreshold BED
497 (i.e. meet all BED criteria with the exception of binge eating frequency), and found an 11%
498 reduction in food consumption. However, when the authors replicated their study in
499 participants with frank (non-binge eating) obesity, they did not find a main effect of active
500 versus sham tDCS on food consumption⁵². Only when specific behaviour traits were
501 included as covariates in statistical analyses did an effect appear; males with intent to
502 restrict or non-planning impulsiveness traits had a 13% reduction in the consumption of
503 preferred foods. The studies that recruited participants experiencing frequent food cravings
504 did not measure wider eating behaviour traits, and so a definitive effect of these wider traits
505 on food consumption is not clear.

506

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

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

519

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

536

537 Finally, Fassini et al. ⁶⁵ measured food consumption via recall. To increase the validity of this
538 measure, the authors asked participants to complete a photo record book ⁶⁵. The study did
539 not find any difference in food consumption between stimulation groups. This may be due to
540 the issues with accuracy and bias during food recall if not conducted in a standardised
541 manner ¹¹⁴, but may also be due to an inability of tDCS to modulate food consumption
542 beyond the testing period. This technique has been shown to alter cortical activity for up to
543 90 minutes post-stimulation ³⁷, with the consumption of foods that were recalled likely being
544 outside of this window. The impact of tDCS on food consumption is less clear than other
545 measures discussed in this review, and this efficacy of tDCS to reduce food consumption
546 has previously been questioned ^{64, 115}. Although there is some evidence to suggest tDCS can
547 modulate energy intake for specific food groups, the method of measuring food intake and
548 other methodological considerations (e.g. participant characteristics, stimulation parameters)
549 vary greatly between studies. In order to identify an effect of tDCS on consumptive
550 behaviours, more consistent and carefully considered use of feeding practices is required.

551

552 **4. CONCLUSION**

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

565

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

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

582

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

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

594

595 **AUTHOR CONTRIBUTIONS**

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

604

605 **REFERENCES**

- 606 1 Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and
607 projections to 2030. *International Journal of Obesity*. 2008; 32: 1431-37.
- 608 2 Wang YC, McPherson K, Marsh T, Gortmaker SL, Brown M. Health and economic
609 burden of the projected obesity trends in the USA and the UK. *The Lancet*. 2011; 378: 815-
610 25.
- 611 3 Ward ZJ, Bleich SN, Cradock AL, Barrett JL, Giles CM, Flax C, *et al*. Projected U.S.
612 State-Level Prevalence of Adult Obesity and Severe Obesity. *New England Journal of*
613 *Medicine*. 2019; 381: 2440-50.
- 614 4 World Health Organisation. Obesity and Overweight. 2020.
- 615 5 National Institute for Health and Care Excellence. Obesity: identification, assessment
616 and management (CG189). London 2014.
- 617 6 Hill JO. Understanding and Addressing the Epidemic of Obesity: An Energy Balance
618 Perspective. *Endocrine Reviews*. 2006; 27: 750-61.
- 619 7 Hruby A, Hu FB. The Epidemiology of Obesity: A Big Picture. *PharmacoEconomics*.
620 2015; 33: 673-89.
- 621 8 Fabricatore AN, Wadden TA. Obesity. *Annual Review of Clinical Psychology*. 2006;
622 2: 357-77.
- 623 9 Mann T, Tomiyama AJ, Westling E, Lew A-M, Samuels B, Chatman J. Medicare's
624 search for effective obesity treatments: Diets are not the answer. *American Psychologist*.
625 2007; 62: 220-33.
- 626 10 Maleckas A, Gudaitytė R, Petereit R, Venclauskas L, Veličkienė D. Weight regain
627 after gastric bypass: etiology and treatment options. *Gland Surg*. 2016; 5: 617-24.
- 628 11 Wijngaarden LH, Jonker FHW, van den Berg JW, van Rossem CC, van der Harst E,
629 Klaassen RA. Impact of initial response of laparoscopic adjustable gastric banding on
630 outcomes of revisional laparoscopic Roux-en-Y gastric bypass for morbid obesity. *Surgery*
631 *for Obesity and Related Diseases*. 2017; 13: 594-99.
- 632 12 Higuera-Hernández MF, Reyes-Cuapio E, Gutiérrez-Mendoza M, Rocha NB, Veras
633 AB, Budde H, *et al*. Fighting obesity: Non-pharmacological interventions. *Clinical Nutrition*
634 *ESPEN*. 2018; 25: 50-55.
- 635 13 Lee DJ, Elias GJB, Lozano AM. Neuromodulation for the treatment of eating
636 disorders and obesity. *Therapeutic Advances in Psychopharmacology*. 2017; 8: 73-92.
- 637 14 Grundeis F, Brand C, Kumar S, Rullmann M, Mehnert J, Pleger B. Non-invasive
638 Prefrontal/Frontal Brain Stimulation Is Not Effective in Modulating Food Reappraisal Abilities
639 or Calorie Consumption in Obese Females. *Frontiers in Neuroscience*. 2017; 11: 334.

- 640 15 Alonso-Alonso M, Pascual-Leone A. The Right Brain Hypothesis for Obesity. *JAMA*.
641 2007; 297: 1819-22.
- 642 16 Havermans RC. "You Say it's Liking, I Say it's Wanting ...". On the difficulty of
643 disentangling food reward in man. *Appetite*. 2011; 57: 286-94.
- 644 17 Boswell RG, Kober H. Food cue reactivity and craving predict eating and weight gain:
645 a meta-analytic review. *Obesity Reviews*. 2016; 17: 159-77.
- 646 18 Kober H, Boswell RG. Potential psychological & neural mechanisms in binge eating
647 disorder: Implications for treatment. *Clinical Psychology Review*. 2018; 60: 32-44.
- 648 19 Blundell JE. Perspective on the Central Control of Appetite. *Obesity*. 2006; 14: 160S-
649 63S.
- 650 20 Lowe CJ, Reichelt AC, Hall PA. The Prefrontal Cortex and Obesity: A Health
651 Neuroscience Perspective. *Trends in Cognitive Sciences*. 2019; 23: 349-61.
- 652 21 Casanova N, Beaulieu K, Finlayson G, Hopkins M. Metabolic adaptations during
653 negative energy balance and their potential impact on appetite and food intake. *Proceedings*
654 *of the Nutrition Society*. 2019; 78: 279-89.
- 655 22 Budak AR, Thomas SE. Food Craving as a Predictor of "Relapse" in the Bariatric
656 Surgery Population: A Review with Suggestions. *Bariatric Nursing and Surgical Patient Care*.
657 2009; 4: 115-21.
- 658 23 Odom J, Zalesin KC, Washington TL, Miller WW, Hakmeh B, Zaremba DL, *et al*.
659 Behavioral Predictors of Weight Regain after Bariatric Surgery. *Obesity Surgery*. 2010; 20:
660 349-56.
- 661 24 Cornier M-A. Is your brain to blame for weight regain? *Physiology & Behavior*. 2011;
662 104: 608-12.
- 663 25 Miller EK, Cohen JD. An Integrative Theory of Prefrontal Cortex Function. *Annual*
664 *Review of Neuroscience*. 2001; 24: 167-202.
- 665 26 Pignatti R, Bertella L, Albani G, Mauro A, Molinari E, Semenza C. Decision-making in
666 obesity: A study using the Gambling Task. *Eating and Weight Disorders - Studies on*
667 *Anorexia, Bulimia and Obesity*. 2006; 11: 126-32.
- 668 27 Joseph RJ, Alonso-Alonso M, Bond DS, Pascual-Leone A, Blackburn GL. The
669 neurocognitive connection between physical activity and eating behaviour. *Obesity Reviews*.
670 2011; 12: 800-12.
- 671 28 Karhunen LJ, Vanninen EJ, Kuikka JT, Lappalainen RI, Tiihonen J, Uusitupa MJ.
672 Regional cerebral blood flow during exposure to food in obese binge eating women.
673 *Psychiatry Research: Neuroimaging*. 2000; 99: 29-42.

- 674 29 Boeka AG, Lokken KL. Prefrontal systems involvement in binge eating. *Eating and*
675 *Weight Disorders - Studies on Anorexia, Bulimia and Obesity*. 2011; 16: e121-e26.
- 676 30 Cserjési R, Luminet O, Poncelet A-S, Lénárd L. Altered executive function in obesity.
677 Exploration of the role of affective states on cognitive abilities. *Appetite*. 2009; 52: 535-39.
- 678 31 Michaud A, Vainik U, Garcia-Garcia I, Dagher A. Overlapping Neural
679 Endophenotypes in Addiction and Obesity. *Frontiers in Endocrinology*. 2017; 8: 127.
- 680 32 Blume M, Schmidt R, Hilbert A. Executive Functioning in Obesity, Food Addiction,
681 and Binge-Eating Disorder. *Nutrients*. 2019; 11.
- 682 33 Stice E, Spoor S, Bohon C, Veldhuizen MG, Small DM. Relation of reward from food
683 intake and anticipated food intake to obesity: a functional magnetic resonance imaging
684 study. *Journal of abnormal psychology*. 2008; 117: 924-35.
- 685 34 Gluck ME, Viswanath P, Stinson EJ. Obesity, Appetite, and the Prefrontal Cortex.
686 *Current Obesity Reports*. 2017; 6: 380-88.
- 687 35 Goldman RL, Canterberry M, Borckardt JJ, Madan A, Byrne TK, George MS, *et al*.
688 Executive control circuitry differentiates degree of success in weight loss following gastric-
689 bypass surgery. *Obesity*. 2013; 21: 2189-96.
- 690 36 Thair H, Holloway AL, Newport R, Smith AD. Transcranial Direct Current Stimulation
691 (tDCS): A Beginner's Guide for Design and Implementation. *Frontiers in Neuroscience*.
692 2017; 11: 641.
- 693 37 Nitsche MA, Paulus W. Sustained excitability elevations induced by transcranial DC
694 motor cortex stimulation in humans. *Neurology*. 2001; 57: 1899.
- 695 38 Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by
696 weak transcranial direct current stimulation. *The Journal of Physiology*. 2000; 527: 633-39.
- 697 39 Filmer HL, Dux PE, Mattingley JB. Applications of transcranial direct current
698 stimulation for understanding brain function. *Trends in Neurosciences*. 2014; 37: 742-53.
- 699 40 Jamil A, Nitsche MA. What Effect Does tDCS Have on the Brain? Basic Physiology of
700 tDCS. *Current Behavioral Neuroscience Reports*. 2017; 4: 331-40.
- 701 41 Matsumoto H, Ugawa Y. Adverse events of tDCS and tACS: A review. *Clinical*
702 *Neurophysiology Practice*. 2017; 2: 19-25.
- 703 42 Alonso-Alonso M. Translating tDCS into the field of obesity: mechanism-driven
704 approaches. *Frontiers in Human Neuroscience*. 2013; 7: 512.
- 705 43 Lefaucheur JP. A comprehensive database of published tDCS clinical trials (2005-
706 2016). *Neurophysiol Clin*. 2016; 46: 319-98.

- 707 44 Fregni F, Orsati F, Pedrosa W, Fecteau S, Tome FAM, Nitsche MA, *et al.*
708 Transcranial direct current stimulation of the prefrontal cortex modulates the desire for
709 specific foods. *Appetite*. 2008; 51: 34-41.
- 710 45 Goldman RL, Borckardt JJ, Frohman HA, O'Neil PM, Madan A, Campbell LK, *et al.*
711 Prefrontal cortex transcranial direct current stimulation (tDCS) temporarily reduces food
712 cravings and increases the self-reported ability to resist food in adults with frequent food
713 craving. *Appetite*. 2011; 56: 741-46.
- 714 46 Sedgmond J, Lawrence Natalia S, Verbruggen F, Morrison S, Chambers Christopher
715 D, Adams Rachel C. Prefrontal brain stimulation during food-related inhibition training:
716 effects on food craving, food consumption and inhibitory control. *Royal Society Open*
717 *Science*. 2019; 6: 181186.
- 718 47 Georgii C, Goldhofer P, Meule A, Richard A, Blechert J. Food craving, food choice
719 and consumption: The role of impulsivity and sham-controlled tDCS stimulation of the right
720 dlPFC. *Physiology & Behavior*. 2017; 177: 20-26.
- 721 48 Gluck ME, Alonso-Alonso M, Piaggi P, Weise CM, Jumpertz-von Schwartzberg R,
722 Reinhardt M, *et al.* Neuromodulation targeted to the prefrontal cortex induces changes in
723 energy intake and weight loss in obesity. *Obesity*. 2015; 23: 2149-56.
- 724 49 Krause B, Kadosh RC. Not all brains are created equal: the relevance of individual
725 differences in responsiveness to transcranial electrical stimulation. *Frontiers in Systems*
726 *Neuroscience*. 2014; 8: 25.
- 727 50 Carvalho S, Sampaio A, Mendes AJ, Lema A, Vieira D, Goncalves OF, *et al.* Polarity
728 specific effects of cross-hemispheric tDCS coupled with approach-avoidance training on
729 chocolate craving. *Frontiers in Pharmacology*. 2019; 9.
- 730 51 Burgess EE, Sylvester MD, Morse KE, Amthor FR, Mrug S, Lokken KL, *et al.* Effects
731 of transcranial direct current stimulation (tDCS) on binge-eating disorder. *International*
732 *Journal of Eating Disorders*. 2016; 49: 930-36.
- 733 52 Ray MK, Sylvester MD, Osborn L, Helms J, Turan B, Burgess EE, *et al.* The critical
734 role of cognitive-based trait differences in transcranial direct current stimulation (tDCS)
735 suppression of food craving and eating in frank obesity. *Appetite*. 2017; 116: 568-74.
- 736 53 Beaumont JD, Davis D, Dalton M, Nowicky A, Russell M, Barwood MJ. The effect of
737 transcranial direct current stimulation (tDCS) on food craving, reward and appetite in a
738 healthy population. *Appetite*. 2021; 157: 105004.
- 739 54 Berryhill ME, Jones KT. tDCS selectively improves working memory in older adults
740 with more education. *Neuroscience Letters*. 2012; 521: 148-51.
- 741 55 Perceval G, Martin AK, Copland DA, Laine M, Meinzer M. Multisession transcranial
742 direct current stimulation facilitates verbal learning and memory consolidation in young and
743 older adults. *Brain and Language*. 2020; 205: 104788.

- 744 56 Learmonth G, Thut G, Benwell CSY, Harvey M. The implications of state-dependent
745 tDCS effects in aging: Behavioural response is determined by baseline performance.
746 *Neuropsychologia*. 2015; 74: 108-19.
- 747 57 Moher D, Liberati A, Tetzlaff J, Altman DG, The PG. Preferred Reporting Items for
748 Systematic Reviews and Meta-Analyses: The PRISMA Statement. *PLOS Medicine*. 2009; 6:
749 e1000097.
- 750 58 Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, *et al*. Cochrane
751 Handbook for Systematic Reviews of Interventions. Version 6.1 edn: Cochrane 2020.
- 752 59 Priori A, Berardelli A, Rona S, Accornero N, Manfredi M. Polarization of the human
753 motor cortex through the scalp. *NeuroReport*. 1998; 9.
- 754 60 Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, *et al*. RoB 2: a
755 revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019; 366: 14898.
- 756 61 Rohatgi A. WebPlotDigitizer. 2020.
- 757 62 Lipsey MW, Wilson DB. Practical Meta-Analysis: SAGE Publications 2000.
- 758 63 Amo Usanos C, Valenzuela PL, de la Villa P, Navarro SM, Melo Aroeira AEd, Amo
759 Usanos I, *et al*. Neuromodulation of the prefrontal cortex facilitates diet-induced weight loss
760 in midlife women: a randomized, proof-of-concept clinical trial. *International Journal of*
761 *Obesity*. 2020; 44: 568-78.
- 762 64 Heinitz S, Reinhardt M, Piaggi P, Weise CM, Diaz E, Stinson EJ, *et al*.
763 Neuromodulation directed at the prefrontal cortex of subjects with obesity reduces snack
764 food intake and hunger in a randomized trial. *The American Journal of Clinical Nutrition*.
765 2017; 106: 1347-57.
- 766 65 Fassini PG, Das SK, Magerowski G, Marchini JS, da Silva Junior WA, da Silva IR, *et*
767 *al*. Noninvasive neuromodulation of the prefrontal cortex in young women with obesity: a
768 randomized clinical trial. *International journal of obesity (2005)*. 2020; 44: 1279-90.
- 769 66 Fassini PG, Das SK, Suen VMM, Magerowski G, Marchini JS, da Silva Junior WA, *et*
770 *al*. Appetite effects of prefrontal stimulation depend on COMT Val158Met polymorphism: A
771 randomized clinical trial. *Appetite*. 2019; 140: 142-50.
- 772 67 Ljubisavljevic M, Maxood K, Bjekic J, Oommen J, Nagelkerke N. Long-Term Effects
773 of Repeated Prefrontal Cortex Transcranial Direct Current Stimulation (tDCS) on Food
774 Craving in Normal and Overweight Young Adults. *Brain Stimulation*. 2016; 9: 826-33.
- 775 68 Montenegro RA, Okano AH, Cunha FA, Gurgel JL, Fontes EB, Farinatti PTV.
776 Prefrontal cortex transcranial direct current stimulation associated with aerobic exercise
777 change aspects of appetite sensation in overweight adults. *Appetite*. 2012; 58: 333-38.

- 778 69 Van den Noortgate W, López-López JA, Marín-Martínez F, Sánchez-Meca J. Three-
779 level meta-analysis of dependent effect sizes. *Behavior Research Methods*. 2013; 45: 576-
780 94.
- 781 70 Van den Noortgate W, López-López JA, Marín-Martínez F, Sánchez-Meca J. Meta-
782 analysis of multiple outcomes: a multilevel approach. *Behavior Research Methods*. 2015; 47:
783 1274-94.
- 784 71 The R Foundation. The R Project for Statistical Computing. 2021.
- 785 72 Schwarzer G, Carpenter JR, Rücker G. Meta-Analysis with R: Springer International
786 Publishing 2015.
- 787 73 Cohen J. A power primer. *Psychol Bull*. 1992; 112: 155-9.
- 788 74 Deeks JJ, Higgins JPT, Altman DG. Analysing data and undertaking meta-analyses.
789 In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page M, *et al.* (eds.). *Cochrane*
790 *Handbook for Systematic Reviews of Interventions*. Cochrane Statistical Methods Group:
791 2021.
- 792 75 Egger M, Smith GD, Schneider M, Minder C. Bias in meta-analysis detected by a
793 simple, graphical test. *BMJ*. 1997; 315: 629.
- 794 76 Ray MK, Sylvester MD, Helton A, Pittman BR, Wagstaff LE, McRae TR, *et al.* The
795 effect of expectation on transcranial direct current stimulation (tDCS) to suppress food
796 craving and eating in individuals with overweight and obesity. *Appetite*. 2019; 136: 1-7.
- 797 77 Vicario CM, Salehinejad MA, Mosayebi-Samani M, Maezawa H, Avenanti A, Nitsche
798 MA. Transcranial direct current stimulation over the tongue motor cortex reduces appetite in
799 healthy humans. *Brain stimulation*. 2020; 13: 1121-23.
- 800 78 Bravo GL, Poje AB, Perissinotti I, Marcondes BF, Villamar MF, Manzardo AM, *et al.*
801 Transcranial direct current stimulation reduces food-craving and measures of hyperphagia
802 behavior in participants with Prader-Willi syndrome. *American Journal of Medical Genetics*
803 *Part B: Neuropsychiatric Genetics*. 2016; 171: 266-75.
- 804 79 Lapenta OM, Di Sierve K, de Macedo EC, Fregni F, Boggio PS. Transcranial direct
805 current stimulation modulates ERP-indexed inhibitory control and reduces food consumption.
806 *Appetite*. 2014; 83: 42-48.
- 807 80 Kekic M, McClelland J, Campbell I, Nestler S, Rubia K, David AS, *et al.* The effects of
808 prefrontal cortex transcranial direct current stimulation (tDCS) on food craving and temporal
809 discounting in women with frequent food cravings. *Appetite*. 2014; 78: 55-62.
- 810 81 Chen S, Jackson T, Dong D, Zhang X, Chen H. Exploring effects of single-session
811 anodal tDCS over the inferior frontal gyrus on responses to food cues and food cravings
812 among highly disinhibited restrained eaters: A preliminary study. *Neuroscience Letters*.
813 2019; 706: 211-16.

- 814 82 To C, Falcone M, Loughead J, Logue-Chamberlain E, Hamilton R, Kable J, *et al.* Got
815 chocolate? Bilateral prefrontal cortex stimulation augments chocolate consumption. *Appetite*.
816 2018; 131: 28-35.
- 817 83 Max SM, Plewnia C, Zipfel S, Giel KE, Schag K. Combined antisaccade task and
818 transcranial direct current stimulation to increase response inhibition in binge eating
819 disorder. *European archives of psychiatry and clinical neuroscience*. 2020.
- 820 84 Kekic M, McClelland J, Bartholdy S, Boysen E, Musiat P, Dalton B, *et al.* Single-
821 Session Transcranial Direct Current Stimulation Temporarily Improves Symptoms, Mood,
822 and Self-Regulatory Control in Bulimia Nervosa: A Randomised Controlled Trial. *PLoS one*.
823 2017; 12: e0167606.
- 824 85 Mattavelli G, Gallucci A, Schiena G, D'Agostino A, Sasseti T, Bonora S, *et al.*
825 Transcranial direct current stimulation modulates implicit attitudes towards food in eating
826 disorders. *International Journal of Eating Disorders*. 2019; 52: 576-81.
- 827 86 Li LM, Uehara K, Hanakawa T. The contribution of interindividual factors to variability
828 of response in transcranial direct current stimulation studies. *Frontiers in Cellular*
829 *Neuroscience*. 2015; 9: 181.
- 830 87 de Graaf TA, Sack AT. When and How to Interpret Null Results in NIBS: A Taxonomy
831 Based on Prior Expectations and Experimental Design. *Frontiers in Neuroscience*. 2018; 12:
832 915.
- 833 88 Jauch-Chara K, Kistenmacher A, Herzog N, Schwarz M, Schweiger U, Oltmanns KM.
834 Repetitive electric brain stimulation reduces food intake in humans. *The American Journal of*
835 *Clinical Nutrition*. 2014; 100: 1003-09.
- 836 89 Marron EM, Viejo-Sobera R, Cuatrecasas G, Redolar-Ripoll D, Lorda PG, Datta A, *et*
837 *al.* Prefronto-cerebellar neuromodulation affects appetite in obesity. *International Journal of*
838 *Obesity*. 2019; 43: 2119-24.
- 839 90 Holsen LM, Savage CR, Martin LE, Bruce AS, Lepping RJ, Ko E, *et al.* Importance of
840 reward and prefrontal circuitry in hunger and satiety: Prader–Willi syndrome vs simple
841 obesity. *International Journal of Obesity*. 2012; 36: 638-47.
- 842 91 Tunbridge EM, Lane TA, Harrison PJ. Expression of multiple catechol-o-
843 methyltransferase (COMT) mRNA variants in human brain. *American Journal of Medical*
844 *Genetics Part B: Neuropsychiatric Genetics*. 2007; 144B: 834-39.
- 845 92 Dreher J-C, Kohn P, Kolachana B, Weinberger DR, Berman KF. Variation in
846 dopamine genes influences responsivity of the human reward system. *Proceedings of the*
847 *National Academy of Sciences of the United States of America*. 2009; 106: 617-22.
- 848 93 Ceaser A, Csernansky JG, Barch DM. COMT influences on prefrontal and striatal
849 blood oxygenation level-dependent responses during working memory among individuals
850 with schizophrenia, their siblings, and healthy controls. *Cognitive Neuropsychiatry*. 2013; 18:
851 257-83.

- 852 94 Pomarol-Clotet E, Fatjó-Vilas M, McKenna PJ, Monté GC, Sarró S, Ortiz-Gil J, *et al.*
853 COMT Val158Met polymorphism in relation to activation and de-activation in the prefrontal
854 cortex: A study in patients with schizophrenia and healthy subjects. *NeuroImage*. 2010; 53:
855 899-907.
- 856 95 Wiegand A, Nieratschker V, Plewnia C. Genetic Modulation of Transcranial Direct
857 Current Stimulation Effects on Cognition. *Frontiers in Human Neuroscience*. 2016; 10: 651.
- 858 96 Montenegro RA, Farinatti PdTV, Fontes EB, Soares PPdS, Cunha FAd, Gurgel JL, *et*
859 *al.* Transcranial direct current stimulation influences the cardiac autonomic nervous control.
860 *Neuroscience Letters*. 2011; 497: 32-36.
- 861 97 Castellanos EH, Charboneau E, Dietrich MS, Park S, Bradley BP, Mogg K, *et al.*
862 Obese adults have visual attention bias for food cue images: evidence for altered reward
863 system function. *International Journal of Obesity*. 2009; 33: 1063-73.
- 864 98 Goldstone AP, Prechtel de Hernandez CG, Beaver JD, Muhammed K, Croese C, Bell
865 G, *et al.* Fasting biases brain reward systems towards high-calorie foods. *European Journal*
866 *of Neuroscience*. 2009; 30: 1625-35.
- 867 99 Gibbons C, Finlayson G, Dalton M, Caudwell P, Blundell JE. METABOLIC
868 PHENOTYPING GUIDELINES: Studying eating behaviour in humans. *Journal of*
869 *Endocrinology*. 2014; 222: G1-G12.
- 870 100 Butler MG, Thompson T. Prader-Willi Syndrome: Clinical and Genetic Findings.
871 *Endocrinologist*. 2000; 10: 3S-16S.
- 872 101 Kissileff HR, Wentzlaff TH, Guss JL, Walsh BT, Devlin MJ, Thornton JC. A direct
873 measure of satiety disturbance in patients with bulimia nervosa. *Physiol Behav*. 1996; 60:
874 1077-85.
- 875 102 Rolls BJ, Andersen AE, Moran TH, McNelis AL, Baier HC, Fedoroff IC. Food intake,
876 hunger, and satiety after preloads in women with eating disorders. *Am J Clin Nutr*. 1992; 55:
877 1093-103.
- 878 103 Wallace DL, Aarts E, d'Oleire Uquillas F, Dang LC, Greer SM, Jagust WJ, *et al.*
879 Genotype status of the dopamine-related catechol-O-methyltransferase (COMT) gene
880 corresponds with desirability of "unhealthy" foods. *Appetite*. 2015; 92: 74-80.
- 881 104 Keller KL. Brain stimulation for treatment of obesity: will stimulating the prefrontal
882 cortex reduce overeating? *The American Journal of Clinical Nutrition*. 2017; 106: 1331-32.
- 883 105 Cepeda-Benito A, Gleaves DH, Williams TL, Erath SA. The development and
884 validation of the state and trait food-cravings questionnaires. *Behavior Therapy*. 2000; 31:
885 151-73.
- 886 106 Finlayson G, Dalton M. Hedonics of Food Consumption: Are Food 'Liking' and
887 'Wanting' Viable Targets for Appetite Control in the Obese? *Current Obesity Reports*. 2012;
888 1: 42-49.

- 889 107 Dalton M, Finlayson G. Psychobiological examination of liking and wanting for fat and
890 sweet taste in trait binge eating females. *Physiology & Behavior*. 2014; 136: 128-34.
- 891 108 Schag K, Teufel M, Junne F, Preissl H, Hautzinger M, Zipfel S, *et al.* Impulsivity in
892 binge eating disorder: food cues elicit increased reward responses and disinhibition. *PloS*
893 *one*. 2013; 8: e76542-e42.
- 894 109 Buckland NJ, Dalton M. Commentary: Methodological and reporting practices for
895 laboratory studies assessing food intake using fixed and ad libitum test meals. *Appetite*.
896 2018; 130: 336-38.
- 897 110 Hetherington MM, Foster R, Newman T, Anderson AS, Norton G. Understanding
898 variety: Tasting different foods delays satiation. *Physiology & Behavior*. 2006; 87: 263-71.
- 899 111 Blundell J, De Graaf C, Hulshof T, Jebb S, Livingstone B, Lluch A, *et al.* Appetite
900 control: methodological aspects of the evaluation of foods. *Obesity Reviews*. 2010; 11: 251-
901 70.
- 902 112 Ng L, Davis C. Cravings and food consumption in binge eating disorder. *Eating*
903 *Behaviors*. 2013; 14: 472-75.
- 904 113 Venti CA, Votruba SB, Franks PW, Krakoff J, Salbe AD. Reproducibility of ad libitum
905 energy intake with the use of a computerized vending machine system. *The American*
906 *Journal of Clinical Nutrition*. 2010; 91: 343-48.
- 907 114 Moshfegh AJ, Rhodes DG, Baer DJ, Murayi T, Clemens JC, Rumpler WV, *et al.* The
908 US Department of Agriculture Automated Multiple-Pass Method reduces bias in the
909 collection of energy intakes. *Am J Clin Nutr*. 2008; 88: 324-32.
- 910 115 Lowe CJ, Vincent C, Hall PA. Effects of Noninvasive Brain Stimulation on Food
911 Cravings and Consumption: A Meta-Analytic Review. *Psychosomatic Medicine*. 2017; 79.
- 912 116 Beaumont JD, Starr D, Smith N, Davis D, Dalton M, Nowicky A, *et al.* Effective
913 transcranial direct current stimulation (tDCS) parameters for the modulation of eating
914 behaviour: A systematic literature review. *Manuscript under review*. 2021.
915
916

917 **TABLE LEGENDS**

918

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

920

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

922

923 **FIGURE LEGENDS**

924

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

927

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

930

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

933

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

936

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

939

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