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1 **Health, pleasure and fullness: Changing mindset affects brain responses and portion size**
2 **selection in adults with overweight and obesity**

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32 **Short running title:** Changing mindset affects brain and behaviour

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44 **Abstract**

45 **Background:** Increased portion size is an essential contributor to the current obesity
46 epidemic. The decision of how much to eat before a meal begins (i.e. pre-meal planning), and
47 the attention assigned to this task, plays a vital role in our portion control.

48 **Objective:** We investigated whether pre-meal planning can be influenced by a shift in
49 mindset in individuals with overweight and obesity in order to influence portion size selection
50 and brain activity.

51 **Design:** We investigated the neural underpinnings of pre-meal planning in 36 adults of
52 different weight groups ($BMI < 25\text{kg/m}^2$ and $BMI \geq 25\text{kg/m}^2$) by means of functional magnetic
53 resonance imaging. To examine the important role of attentional focus, participants were
54 instructed to focus their mindset on either the health effects of food, expected pleasure, or
55 their intention to stay full until dinnertime, while choosing their portion size for lunch.

56 **Results:** We observed that participants of all weight groups reduced their portion size when
57 adopting a health mindset, which was accompanied by enhanced activation of the self-control
58 network (i.e. left prefrontal cortex). Fullness and pleasure mindsets resulted in contrasting
59 reward responses in individuals with overweight and obesity compared to normal-weight
60 individuals. Under the pleasure mindset, persons with overweight and obesity showed
61 heightened activity in parts of the taste cortex (i.e. right frontal operculum), while the fullness
62 mindset caused reduced activation in the ventral striatum, an important component of the
63 reward system. Moreover, participants with overweight and obesity did not modify their
64 behaviour under the pleasure mindset and selected larger portions than the normal-weight
65 group.

66 **Conclusions:** We were able to identify specific brain response patterns as participants made a
67 final choice of a portion size. The results demonstrate that different brain responses and
68 behaviours during pre-meal planning can inform the development of effective strategies for
69 healthy weight management.

70 **Introduction**

71 Mindsets determine attentional focus when making a choice and they play an
72 important role in everyday decisions. For example, directing attentional focus to healthy
73 thoughts, as a result of walking by a gym during shopping, can influence food choice.
74 Interestingly, healthy choices increase when the attentional focus is directed to healthy
75 features of food¹⁻⁴. This is related to increased activation in parts of the prefrontal cortex,
76 particularly the dorsolateral prefrontal cortex (dlPFC)⁵. The activation pattern of the dlPFC
77 during memory and executive control tasks predict weight loss success in dieters^{6,7} and is
78 reduced in individuals with obesity⁸⁻¹⁰. Moreover, the dlPFC is part of the core network
79 related to dietary self-control, which is defined as a mental process functioning to override
80 temptations to select a goal-oriented action⁸. Besides the prefrontal cortex, the core brain
81 regions related to dietary self-control include parts of the insula, supplementary motor cortex,
82 operculum, parietal cortices and striatal regions. This network captures the process of
83 valuation and action needed during food choice.

84 Although many studies have evaluated the neural representations of food choice, few
85 studies have investigated determinants for the selection of meal size. Nonetheless, besides
86 what we eat, daily food intake might be even more dependent on the portion size we select¹¹.
87 Indeed, the rise in obesity in the U.S. since the 1950s has paralleled with increasing portion
88 sizes¹². The crucial influence of portion size is supported by the fact that we tend to plan our
89 meals and then consume selected portions in their entirety¹³. Moreover, the energy content of
90 selected portions is strongly influenced by the extent to which we expect the meal to deliver
91 satiation¹⁴. We even tend to underestimate the caloric content of high energy density foods
92 based on lower expected satiation, which results in the selection of larger portion sizes¹⁴⁻¹⁶.
93 Hence, the decision of how much to eat before a meal begins, and the attention assigned to
94 this task, plays a vital role in our food intake. We recently investigated in adults with normal-
95 weight the neural underpinnings of portion size selection for lunch before mealtime began,

96 which is referred to as pre-meal planning¹⁷. Participants chose their portion size for lunch by
97 adopting three different mindsets. By switching an individual's attentional focus to health
98 aspects (i.e., health mindset), we were able to reduce portion size selection for lunch, which
99 was accompanied by a specific brain response pattern. This study suggests the opportunity to
100 improve portion control by mindset manipulation. However, it is not known whether pre-meal
101 planning can be influenced by a shift in mindset in individuals with overweight and obesity to
102 encourage healthier portion control.

103 Therefore, we investigated in the current study behavioural responses and neural
104 processes during pre-meal planning in adults with $\text{BMI} \geq 25\text{kg/m}^2$ using functional magnetic
105 resonance imaging (fMRI). During fMRI recording, participants were instructed to focus their
106 mindset on either the health effects of food, expected pleasure, or their intention to stay full
107 until dinnertime, while choosing their portion size for lunch.

108 **Materials and methods**

109 **Participants**

110 Eighteen participants with overweight and obesity were recruited into the study.
111 Fourteen controls with normal-weight were included from a recent study¹⁷ and an additional
112 four healthy controls were recruited to ensure that the groups did not differ in age.
113 Participants were recruited via e-mail and board advertisements, and were screened on
114 exclusion criteria by online questionnaires. Participants were required to fulfill the following
115 inclusion criteria: right handed, between 18 and 35 years of age, having a body mass index
116 (BMI) between 18 and 24 kg/m^2 for the $\text{BMI} < 25\text{ kg/m}^2$ group and a BMI between 25 and 35
117 kg/m^2 for the $\text{BMI} \geq 25\text{ kg/m}^2$ group. Participants were excluded if they had a non-removable
118 metal object in their body, were pregnant, had type 2 diabetes, were taking antidepressants or
119 had a neurological disorder (e.g., epilepsy), were vegetarian or vegan, had a food allergy, or
120 self-reported having an eating disorder. The study was approved by the ethics committee of

121 the University of Tübingen. Written informed consent was obtained prior to the study.

122 Participant characteristics are summarized in **table 1**.

123 **Study design**

124 The study design is described in detail in our recent publication investigating neural
125 correlates of mindset-induced changes in pre-meal planning in adults with normal-weight ¹⁷.
126 Participants were overnight fasted (at least 12 h) and consumed a normal breakfast between
127 7.30 am and 8.00 am. They then abstained from eating and drinking (except water) before
128 arriving in our lab at 10.30 am.

129 Prior to fMRI scanning, participants were familiarized with the experimental
130 procedure and the associated stimuli, as recently reported ¹⁷. Hunger was rated at four time
131 points (upon arrival, after an fMRI scanning session, after lunch, and 1h after lunch) on a
132 visual-analogue scale from 0 to 10 (0: not hungry at all; 10: very hungry). A blood sample
133 was taken after the fMRI scanning session to determine plasma insulin and HbA1c levels (see
134 **table 1**).

135 The fMRI scanning session started at around 11.15 am and lasted roughly 90 minutes.
136 After the fMRI session, participants were asked to indicate the healthiness, tastiness, and
137 expected satiation of each meal on a laptop. At around 1.00-1.15 pm all participants received
138 spaghetti Bolognese (Barilla Bolognese neu (90kcal/100g), Barilla Spaghettoni no.7
139 (359kcal/100g dry weight)) in the portion size that they selected during the free-choice
140 condition in the fMRI task. Due to organizational limitations, we chose to serve a specific
141 meal to all participants (participants were in fact told that they would receive a randomly
142 selected meal). Participants were left alone to finish their meal and were told to take as long
143 as they needed (typically around 15 min). After lunch, participants remained in the lab for a
144 further hour. Over this period they completed several questionnaires. For an overview of the
145 study procedure, refer to supplementary **Figure 1**.

146

147 **Stimuli**

148 We selected 10 stimuli (i.e. different meals) from a database that systematically varied
149 in portion sizes¹⁸. We used 10 pictures per meal showing different portion sizes, starting with
150 100 kcals and increasing portion sizes in 100 kcal steps. A portion size of 500 kcal was used
151 for the ratings of the meals. Based on the NOVA food classification system, we predict that
152 individual meal stimuli would be classified as either ‘processed’ or ‘ultra-processed’ (group 3
153 and 4, respectively)¹⁹.

154 **fMRI task**

155 The fMRI task was completed four times, starting with a free-choice (baseline)
156 condition followed by different instructions to induce a specific mindset. For the free-choice
157 condition (baseline), participants were instructed to select the portion size for each meal that
158 they wanted to eat for lunch that day. Participants were informed that one meal of this
159 baseline condition would be randomly chosen for lunch in the selected portion size. For the
160 other conditions, they were instructed to imagine selecting their portion sizes under certain
161 considerations. To adopt a pleasure mindset, they were instructed to select a portion size that
162 they would eat with pleasure, for the fullness mindset if they would plan to be full until
163 dinner, and for the health mindset if they would consider health aspects. Except for the free-
164 choice conditions, all other conditions were pseudo-randomized to avoid order effects. We
165 used this harmonized design to increase comparability between participants and between
166 mindsets, and to prevent a potential carry-over effect from the mindset to the free-choice
167 condition.

168 For the fMRI task, we used 10 different meals in 10 different portion sizes (starting
169 with a portion size of 100 kcal (418 kilojoules (kJ)) and increasing by 100kcal (418 kJ) up to
170 1000kcal (4184 kJ)). Each of the four task blocks consisted of 30 trials starting with the
171 presentation of a randomly selected meal. For each meal, there were three trials in each task
172 block. Each trial started with an initial meal size once in the lower, middle and upper range of

173 portion sizes. Participants were required to decide whether they wanted to increase or
174 decrease the portion size via button press. Pressing a right button increased the portion size
175 and pressing a left button decreased the portion, i.e. the next larger or smaller portion size was
176 shown after presentation of an inter-stimulus fixation cross for a randomized time between 1
177 and 2 s. At the end of each trial, when participants reached their desired portion size, the
178 selected portion was shown for 2 s and participants had to confirm the selection by button
179 press. They were then asked if they were satisfied with their final portion size decision
180 (feedback). In the final analyses, we only included decision trials for which participants
181 indicated that they were satisfied with their final portion size selection. Participants performed
182 the task self-paced and were allowed 10.5 minutes to complete the task. Dummy trials were
183 included in the analyses if they needed less time. Stimuli were presented visually projected on
184 a monitor in the scanner room using Presentation (Neurobehavioural Systems, Inc., Albany,
185 CA). The task was recently described in detail ¹⁷.

186 **fMRI data acquisition and preprocessing**

187 Whole brain fMRI data were obtained using a 3 Tesla scanner (Siemens
188 MAGNETOM Prisma, Erlangen, Germany) equipped with a 20-channel head coil. Each task
189 block consisted of 312 scans (repetition time: 2 s, echo time: 30 ms, voxel size 3x3x3 mm³).
190 In addition, we obtained a high resolution T1-weighted anatomical image and a static field
191 map to unwarp geometrically distorted functional scans. As recently described, preprocessing
192 and statistical analyses of the fMRI data were performed in SPM12 (Wellcome Trust Centre
193 for Neuroimaging, London, UK). The anatomical image was normalized to the Montreal
194 Neurological Institute (MNI) template (1x1x1mm³). The functional images were normalized
195 to a voxel size of 3 x 3 x 3 mm³ and smoothed with a three-dimensional isotropic Gaussian
196 kernel (FWHM: 9 mm). FMRI data were high-pass filtered (0.008 Hz) and global AR (1) auto
197 correlation correction was performed.

198 **fMRI data analysis**

199 FMRI data were analyzed in an event-related design using the general linear model
200 (GLM). For the first level model, responses to stimuli were modeled for each participant as
201 events and convolved with a canonical hemodynamic response function and its time
202 derivative. For each subject, four regressors indicating the individual trial events were
203 analyzed using linear regression. The four regressors included the 1) pre-decisions
204 (increase/decrease of portion size), 2) final decision of portion size, 3) feedback trials and 4) a
205 regressor of no interest including the dummy trials and those decisions with which
206 participants were not satisfied. To account for head motion, six realignment parameters were
207 included as regressors to the model. Individual contrast images were computed to estimate the
208 activation changes for the final decision of the portion size in the free choice condition
209 compared to the three mindsets.

210 For the second-level analyses, full-factorial models were calculated using the first-
211 level contrasts of the final decision, with the between-subject factor “body-weight”
212 ($BMI < 25 \text{ kg/m}^2$ group vs. $BMI \geq 25 \text{ kg/m}^2$ group) and a within-subject factor “condition” (free-
213 choice vs mindset). Effects were considered statistically significant using a primary threshold
214 at peak level of $p < 0.001$ uncorrected and a whole brain family wise error correction (FWE) of
215 $p < 0.05$ at cluster level. In addition, we performed a region of interest (ROI) analyses for the
216 dlPFC (inferior frontal gyrus), frontal operculum, and putamen, based on recent publications
217 on food choice and dietary self-control^{5, 8, 17}. All ROIs were created in wfu pick atlas²⁰.

218 **Behavioural data analysis**

219 **Self-rated hunger**

220 Using a mixed-model ANOVA (within-subject factor: time (4 time points); between-
221 subject factor “body-weight” ($BMI < 25 \text{ kg/m}^2$ vs $BMI \geq 25 \text{ kg/m}^2$), we investigated the effect
222 of time on reported hunger and assessed differences in participants with normal-weight and
223 with overweight and obesity.

224 **Portion size selection**

225 Individual energy requirements were calculated based on the Harris Benedict equation
226 ²¹. Portion size selections are expressed as percentages (%) of individual energy requirements
227 [in kilojoules (kJ)]. To investigate mindset-induced portion size selection, we used a mixed-
228 model ANOVA (within-subject factor: mindset (corrected in relation to baseline/free-choice
229 condition), between-subject factor “body-weight” (BMI<25 kg/m² vs BMI≥25 kg/m²) and
230 sex.

231 **Expected satiation**

232 Expected satiation was calculated as recently described ¹⁷. Bivariate correlation was
233 used to investigate the relationship between portion size selection in the baseline condition,
234 energy density, expected satiation, tastiness and healthiness ratings, for the weight groups
235 separately.

236 **Correlation analyses**

237 Bivariate correlation (Pearson) and partial correlation was used to investigate
238 relationships between hunger, brain response, and questionnaire-based assessments of trait
239 dietary behaviours. Behavioural data were analyzed with the software package SPSS 24.0
240 (SPSS Inc., Illinois; USA). All data are presented as mean±SEM. P-values <0.05 were
241 considered significant.

242 **Results**

243 **Effects of mindset on portion selection**

244 Compared to the free-choice condition, we observed a significant main effect of
245 mindset (F(2,64)= 73.2, p<0.001), significant interactions between mindset and weight group
246 (F(2,64)= 9.29, p<0.001) and a trend between mindset and sex (F(2,64)= 2.9, p= 0.06). No 3-
247 way interaction was observed (p>0.05). Moreover, we observed a main effect of weight group
248 (F(1,32)= 7.5, p= 0.01) and sex (F(1,32)= 5.3, p= 0.027), independent of mindset. No
249 interaction between weight group and sex was observed independent of mindset. Post-hoc
250 analyses showed that both weight groups selected larger portion sizes in the fullness mindset

251 (BMI<25 kg/m²: t(17)= 6.1, p< 0.001; BMI≥25 kg/m²: t(17)= 5.4, p< 0.001) and selected
252 smaller portions in the health mindset (BMI<25 kg/m²: t(17)= -7.1, p<0.001; BMI≥25 kg/m²:
253 t(17)= -5.1, p<0.001). For the pleasure mindset, only participants with normal-weight showed
254 a significant decrease compared to baseline (BMI<25 kg/m²: t(17)= -3.1, p= 0.007; BMI≥25
255 kg/m²: t(17)= 2.00, p= 0.061) (**Figure 2**).

256 In addition, participants with overweight and obesity selected larger portion sizes in
257 the pleasure mindset (compared to free-choice condition) than participants with normal-
258 weight (t(34)= 3.68, p= 0.001) (Figure 2). Women selected larger portion sizes than men in
259 the pleasure condition compared to the free choice condition (t(34)= 2.25, p= 0.03)
260 (**supplementary table 1**).

261 **Hunger rating**

262 No significant effect was observed for hunger over time between weight groups or sex
263 (p> 0.05).

264 **Correlations between portion size selection and hunger**

265 Portion size selection during pleasure compared to baseline correlated significantly
266 with hunger before the start of the experiment (r= -0.431, p= 0.009). Hence, participants who
267 reported less hunger selected larger portions for pleasure compared to the free-choice
268 condition. This correlation was driven primarily by the BMI≥25 kg/m² group (data not
269 shown). No significant associations were observed for portion size selection under health and
270 fullness mindset (p<0.01 corrected for multiple testing).

271 **Expected satiation**

272 As expected and as recently reported^{17, 18}, the energy density of the meals was
273 associated with lower expected satiation, both in participants with normal-weight (r= -0.774,
274 p= 0.009) and with overweight and obesity (r= -0.716, p= 0.02). Expected satiation was also
275 highly correlated with the portion sizes selected in the baseline condition (BMI<25 kg/m² r= -
276 0.867, p= 0.001; BMI≥25 kg/m²r= -0.911, p<0.001). Finally, portion size selection during

277 baseline was not related to tastiness nor healthiness ratings and no group differences were
278 observed for tastiness and healthiness ratings ($p > 0.05$).

279 **Neuroimaging results**

280 **Health mindset**

281 Compared to the free-choice condition (i.e., baseline), the health mindset induced an
282 increase in activation in the left inferior frontal gyrus (dorsolateral prefrontal cortex (dlPFC))
283 and left superior frontal gyrus (dorsolateral medial prefrontal cortex (dlmPFC)), in both
284 weight groups (**Figure 3; supplementary table 2**).

285 **Pleasure mindset**

286 Compared to the free-choice condition, the pleasure mindset induced increased
287 activation in the posterior insula, posterior cingulate, temporal and inferior frontal gyrus (IFG)
288 (**supplementary Figure 1; supplementary table 2**). Moreover, we observed a main effect of
289 group. Participants with overweight and obesity showed enhanced activation in the right
290 inferior frontal operculum (IFO) compared to participants with normal-weight.

291 Furthermore, right inferior frontal operculum activation significantly correlated with
292 the selected portion size during the pleasure mindset (**Figure 4**) (Correlation both weight
293 groups: $r = 0.408$, $p = 0.01$; BMI $< 25 \text{ kg/m}^2$ group: $r = 0.291$, $p = 0.2$; BMI $\geq 25 \text{ kg/m}^2$ group: $r =$
294 0.538 , $p = 0.02$).

295 **Fullness mindset**

296 Compared to the free-choice condition, the fullness mindset induced an increase in the
297 posterior insula. Furthermore, a significant interaction was observed in the putamen (ventral
298 striatum), between group and mindset fullness vs baseline (**Figure 5; supplementary table**
299 **2**). Post hoc analyses showed that participants with normal-weight increased activation in the
300 ventral striatum during the fullness condition ($t(17) = 2.9$, $p = 0.008$), while participants with
301 overweight and obesity decreased their response ($t(17) = -2.6$, $p = 0.01$). Weight groups

302 significantly differed in ventral striatum activation in the fullness ($F(1,35)= 19.6, p<0.001$)
303 but not the baseline condition.

304 Moreover, ventral striatum activation for fullness compared to baseline significantly
305 correlated with Barratt Impulsiveness Scale (BIS) ($r= -0.492, p= 0.002; r_{BMI\ adj}= -0.435, p_{adj}=$
306 0.009).

307 **Discussion**

308 In the current study, we investigated whether mindset manipulations can modulate
309 brain activity and encourage individuals with overweight and obesity to select healthier
310 portion sizes. We observed that participants of all weight groups could be encouraged to
311 reduce their portion size by adopting a health-focused mindset, which was accompanied by
312 enhanced activation of the self-control network. We also found that the fullness and pleasure
313 mindsets resulted in distinct behavioural and brain response patterns. Under the pleasure
314 mindset, persons with overweight and obesity did not modify their behaviour and selected a
315 larger portion size compared to participants of normal-weight. This was correlated with a
316 heightened right frontal operculum response, which is part of the taste-processing region of
317 the brain²². Under the fullness mindset, the $BMI \geq 25\text{kg/m}^2$ group showed a reduced response
318 in the reward-processing region of the brain (i.e., ventral striatum).

319 Changing the perspective to health aspects resulted in a reduction in portion size
320 selection with enhanced activation of the self-control network, including parts of the
321 dorsolateral prefrontal cortex (dlPFC) and dorsolateral medial prefrontal cortex (dlmPFC).
322 The dlPFC is known to be important for anticipatory cognitive control, including dietary self-
323 control and food choice. The dlmPFC also plays a role in mentalization²³, assigning valence
324 and tracking health value independent of attentional focus¹. Obesity is related to a diminished
325 response of the left dlPFC, particularly in a food choice and dietary self-control setting⁸.
326 Nonetheless, we found that all weight groups successfully recruited the dlPFC when changing
327 mindset. Hence, our findings are promising in showing that young adults with obesity can

328 enhance left dlPFC activity to influence eating behaviour. Similarly, cognitive reappraisal
329 approaches, thinking of the health benefits and suppressing craving, showed that individuals
330 with obesity can increase the dlPFC²⁴⁻²⁶; however, without any long lasting effects on body
331 weight²⁷. Moreover, persons with obesity can learn to upregulate the dlPFC using
332 neurofeedback training²⁸, which results in healthier food choices³. Recent advances in non-
333 invasive brain stimulation revealed that targeting the left dlPFC is effective in decreasing food
334 intake and facilitating weight loss²⁹⁻³¹ (although to date no study has evaluated long-term
335 effects of altering dlPFC activity on eating behaviour). Therefore, it could be that a mindset-
336 induced change in dlPFC activity forms the neural basis for short-term dieting success in the
337 overweight population.

338 Under the pleasure mindset, participants with normal-weight modified their choice by
339 selecting smaller portions, which is consistent with results of a study by Cornil and Chandon
340³². They found that drawing attention to the orosensory aspects of eating can cause
341 participants to select smaller food portions, apparently because orosensory pleasure peaks
342 during the early part of a meal^{32,33}. In our study, however, while the pleasure mindset
343 reduced portion size selection in participants with normal-weight, it failed to do so in
344 participants with overweight and obesity. On a neural level, persons with overweight and
345 obesity showed enhanced activation in the right inferior frontal operculum (IFO) (i.e., the pars
346 opercularis of the inferior frontal gyrus) during the pleasure mindset. The right inferior frontal
347 gyrus is activated whenever an important/salient cue is detected; hence, it plays an important
348 role in the framework of attention^{34,35}. Regarding its functional role in eating behaviour, it is
349 important to recognize the role of the IFO in discriminating different taste cue properties, as
350 part of the taste cortex^{36,37}. In people with obesity, palatable food cues and tastes are found to
351 generate particularly strong activation of the right inferior frontal operculum^{9,38}. Moreover,
352 anticipated food intake and increased food desire results in higher reactivity of the frontal
353 operculum in obesity^{39,40}. Together, this could lead to greater failure to suppress response

354 tendencies to salient food cues. In the current study, individuals with overweight and obesity
355 reported feeling less hungry. In light of the above-mentioned findings, for people with
356 overweight and obesity, shifting attentional focus to pleasure might increase the salience of
357 food, leading to the selection of larger portion sizes, even in the relative absence of hunger.

358 Under the fullness mindset, we identified a group specific pattern in the ventral
359 striatum, which is a key region for processing incentive value and the anticipation of
360 pleasurable outcomes ⁴¹. This novel finding demonstrates how it is possible to tweak the
361 brain's reward system simply by shifting attention to fullness. Previous studies have shown
362 that ventral striatal activity is particularly sensitive to the anticipation of food intake,
363 processing of food cues ^{42, 43}, metabolic state, sensory modality and food consumption ^{39, 44-46}.
364 It is still under discussion, however, whether overeating is caused by greater reward
365 sensitivity or reward deficiency in people with obesity ^{39, 46}. Alternatively, it has been
366 proposed that obesity is associated with reduced reward-related learning, particularly with an
367 impairment in negative outcome learning ^{47, 48}. This is reflected by the negative reward
368 prediction error, encoding the negative discrepancy between expected and actual reward ⁴⁹- a
369 process that is largely driven by dopaminergic neurons in the striatum ^{47, 49}. Accordingly, our
370 findings could point to a shift in the reward prediction error to the initial portion size (portion
371 size at the beginning of the experimental block) in the BMI ≥ 25 kg/m² group. Thus, the final
372 portion size decision under the fullness mindset might be 'worse' than expected (i.e. less
373 rewarding), resulting in a decreased response in the ventral striatum particularly in persons
374 with high impulsivity. This is in accordance with previous behavioural studies showing that
375 eating itself is rewarding, but fullness is not ³³.

376 A possible limitation of our study is the 'real' versus 'hypothetical' setting of the
377 study design. During the free-choice (baseline) condition, participants made a 'real' choice
378 (with an actual outcome); however, the mindset-induced choices were merely hypothetical in
379 nature. A recent study showed that people with overweight make the same hypothetical but

380 not real-world healthy food choices ⁵⁰. Hence, the potential to improve portion control by
381 using a health mindset might be different in real life, where other factors, such as price, also
382 impact decision making. Moreover, and in relation to this idea, we note that a recent weight-
383 loss program incorporating a portion-control strategy failed to show sustained weight loss ⁵¹.
384 Another potential limitation is that we did not evaluate participants on their individual
385 strategies after each mindset induction. Although participants were guided to develop
386 different mindsets, we cannot say with confidence that these mindsets were always adopted.
387 Individuals may differ in this regard and this issue might be addressed in future studies.

388 In conclusion, our study demonstrates that switching an individual's mindset during
389 pre-meal planning has the potential to improve portion size control. The encouraging message
390 from this study is that people of all weights responded positively to a healthy mindset
391 instruction. Hence, the approach can be considered in strategies for healthy weight
392 management. Maintaining a lower weight after successfully completing a dietary intervention
393 is, however, a very significant challenge. We postulate that individuals with obesity may
394 adapt temporarily to a health-focused mindset during a diet but, over time, and perhaps due in
395 part to greater impulsivity, may shift back to a pleasure-focused mindset, making them
396 vulnerable to the selection of larger portions. This might help to explain weight cycling after a
397 diet. Further research is necessary to evaluate strategies to induce long-lasting changes to
398 encourage healthier food choice and portion control.

399 Supplementary information is available at the International Journal of Obesity website.

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 413

414 **References**

- 415 1. Bhanji JP, Beer JS. Taking a different perspective: mindset influences neural regions that
 416 represent value and choice. *Soc Cogn Affect Neurosci* 2012; **7**(7): 782-93.
- 417
 418 2. Hare TA, Malmaud J, Rangel A. Focusing attention on the health aspects of foods changes value
 419 signals in vmPFC and improves dietary choice. *J Neurosci* 2011; **31**(30): 11077-87.
- 420
 421 3. Spetter MS, Malekshahi R, Birbaumer N, Luhrs M, van der Veer AH, Scheffler K *et al.* Volitional
 422 regulation of brain responses to food stimuli in overweight and obese subjects: A real-time
 423 fMRI feedback study. *Appetite* 2017; **112**: 188-195.
- 424
 425 4. Petit O, Merunka D, Anton JL, Nazarian B, Spence C, Cheok AD *et al.* Health and Pleasure in
 426 Consumers' Dietary Food Choices: Individual Differences in the Brain's Value System. *PLoS One*
 427 2016; **11**(7): e0156333.
- 428
 429 5. Hare TA, Camerer CF, Rangel A. Self-control in decision-making involves modulation of the
 430 vmPFC valuation system. *Science* 2009; **324**(5927): 646-8.
- 431
 432 6. Goldman RL, Canterberry M, Borckardt JJ, Madan A, Byrne TK, George MS *et al.* Executive
 433 control circuitry differentiates degree of success in weight loss following gastric-bypass
 434 surgery. *Obesity (Silver Spring)* 2013.
- 435
 436 7. Hege MA, Stingl KT, Ketterer C, Haring HU, Heni M, Fritsche A *et al.* Working memory-related
 437 brain activity is associated with outcome of lifestyle intervention. *Obesity (Silver Spring)* 2013;
 438 **21**(12): 2488-94.
- 439
 440 8. Han JE, Boachie N, Garcia-Garcia I, Michaud A, Dagher A. Neural correlates of dietary self-
 441 control in healthy adults: A meta-analysis of functional brain imaging studies. *Physiol Behav*
 442 2018; **192**: 98-108.

443

- 444 9. Brooks SJ, Cedernaes J, Schioth HB. Increased prefrontal and parahippocampal activation with
445 reduced dorsolateral prefrontal and insular cortex activation to food images in obesity: a meta-
446 analysis of fMRI studies. *PLoS One* 2013; **8**(4): e60393.
- 447
448 10. Hege MA, Stingl KT, Kullmann S, Schag K, Giel KE, Zipfel S *et al.* Attentional impulsivity in binge
449 eating disorder modulates response inhibition performance and frontal brain networks. *Int J*
450 *Obes (Lond)* 2015; **39**(2): 353-60.
- 451
452 11. Brunstrom JM. Mind over platter: pre-meal planning and the control of meal size in humans.
453 *Int J Obes (Lond)* 2014; **38 Suppl 1**: S9-12.
- 454
455 12. Labbe D, Rytz A, Brunstrom JM, Forde CG, Martin N. Influence of BMI and dietary restraint on
456 self-selected portions of prepared meals in US women. *Appetite* 2017; **111**: 203-207.
- 457
458 13. Fay SH, Ferriday D, Hinton EC, Shakeshaft NG, Rogers PJ, Brunstrom JM. What determines real-
459 world meal size? Evidence for pre-meal planning. *Appetite* 2011; **56**(2): 284-9.
- 460
461 14. Wilkinson LL, Hinton EC, Fay SH, Ferriday D, Rogers PJ, Brunstrom JM. Computer-based
462 assessments of expected satiety predict behavioural measures of portion-size selection and
463 food intake. *Appetite* 2012; **59**(3): 933-8.
- 464
465 15. Brunstrom JM, Shakeshaft NG. Measuring affective (liking) and non-affective (expected
466 satiety) determinants of portion size and food reward. *Appetite* 2009; **52**(1): 108-14.
- 467
468 16. Brunstrom JM, Shakeshaft NG, Scott-Samuel NE. Measuring 'expected satiety' in a range of
469 common foods using a method of constant stimuli. *Appetite* 2008; **51**(3): 604-14.
- 470
471 17. Hege MA, Veit R, Krumsiek J, Kullmann S, Heni M, Rogers PJ *et al.* Eating less or more - Mindset
472 induced changes in neural correlates of pre-meal planning. *Appetite* 2018; **125**: 492-501.
- 473
474 18. Brunstrom JM, Rogers PJ. How many calories are on our plate? Expected fullness, not liking,
475 determines meal-size selection. *Obesity (Silver Spring)* 2009; **17**(10): 1884-90.
- 476
477 19. Monteiro CA, Cannon G, Moubarac JC, Levy RB, Louzada MLC, Jaime PC. The UN Decade of
478 Nutrition, the NOVA food classification and the trouble with ultra-processing. *Public Health*
479 *Nutr* 2018; **21**(1): 5-17.
- 480
481 20. Maldjian JA, Laurienti PJ, Kraft RA, Burdette JH. An automated method for neuroanatomic and
482 cytoarchitectonic atlas-based interrogation of fMRI data sets. *Neuroimage* 2003; **19**(3): 1233-
483 9.
- 484
485 21. Harris JA, Benedict FG. A Biometric Study of Human Basal Metabolism. *Proc Natl Acad Sci U S*
486 *A* 1918; **4**(12): 370-3.
- 487

- 488 22. Frank S, Kullmann S, Veit R. Food related processes in the insular cortex. *Front Hum Neurosci*
489 2013; **7**: 499.
- 490
491 23. Amodio DM, Frith CD. Meeting of minds: the medial frontal cortex and social cognition. *Nat*
492 *Rev Neurosci* 2006; **7**(4): 268-77.
- 493
494 24. Siep N, Roefs A, Roebroek A, Havermans R, Bonte M, Jansen A. Fighting food temptations: the
495 modulating effects of short-term cognitive reappraisal, suppression and up-regulation on
496 mesocorticolimbic activity related to appetitive motivation. *Neuroimage* 2012; **60**(1): 213-20.
- 497
498 25. Yokum S, Stice E. Cognitive regulation of food craving: effects of three cognitive reappraisal
499 strategies on neural response to palatable foods. *Int J Obes (Lond)* 2013; **37**(12): 1565-70.
- 500
501 26. Kumar S, Grundeis F, Brand C, Hwang HJ, Mehnert J, Pleger B. Differences in Insula and Pre-
502 /Frontal Responses during Reappraisal of Food in Lean and Obese Humans. *Front Hum*
503 *Neurosci* 2016; **10**: 233.
- 504
505 27. Stice E, Yokum S, Burger K, Rohde P, Shaw H, Gau JM. A pilot randomized trial of a cognitive
506 reappraisal obesity prevention program. *Physiol Behav* 2015; **138**: 124-32.
- 507
508 28. Kohl SH, Veit R, Spetter MS, Gunther A, Rina A, Luhrs M *et al*. Real-time fMRI neurofeedback
509 training to improve eating behavior by self-regulation of the dorsolateral prefrontal cortex: A
510 randomized controlled trial in overweight and obese subjects. *Neuroimage* 2019; **191**: 596-
511 609.
- 512
513 29. Kim SH, Chung JH, Kim TH, Lim SH, Kim Y, Lee YA *et al*. The effects of repetitive transcranial
514 magnetic stimulation on eating behaviors and body weight in obesity: A randomized controlled
515 study. *Brain Stimul* 2018; **11**(3): 528-535.
- 516
517 30. Gluck ME, Viswanath P, Stinson EJ. Obesity, Appetite, and the Prefrontal Cortex. *Curr Obes Rep*
518 2017; **6**(4): 380-388.
- 519
520 31. Heinitz S, Reinhardt M, Piaggi P, Weise CM, Diaz E, Stinson EJ *et al*. Neuromodulation directed
521 at the prefrontal cortex of subjects with obesity reduces snack food intake and hunger in a
522 randomized trial. *Am J Clin Nutr* 2017; **106**(6): 1347-1357.
- 523
524 32. Cornil Y, Chandon P. Pleasure as a Substitute for Size: How Multisensory Imagery Can Make
525 People Happier with Smaller Food Portions. *J Marketing Res* 2016; **53**(5): 847-864.
- 526
527 33. Rogers PJ. Combating Excessive Eating: A Role for Four Evidence-Based Remedies. *Obesity*
528 2018; **26**: S18-S24.
- 529
530 34. Hampshire A, Chamberlain SR, Monti MM, Duncan J, Owen AM. The role of the right inferior
531 frontal gyrus: inhibition and attentional control. *Neuroimage* 2010; **50**(3): 1313-9.
- 532

- 533 35. Erika-Florence M, Leech R, Hampshire A. A functional network perspective on response
534 inhibition and attentional control. *Nat Commun* 2014; **5**: 4073.
- 535
536 36. Veldhuizen MG, Bender G, Constable RT, Small DM. Trying to detect taste in a tasteless
537 solution: modulation of early gustatory cortex by attention to taste. *Chem Senses* 2007; **32**(6):
538 569-81.
- 539
540 37. Veldhuizen MG, Gitelman DR, Small DM. An fMRI Study of the Interactions Between the
541 Attention and the Gustatory Networks. *Chemosens Percept* 2012; **5**(1): 117-127.
- 542
543 38. Stice E, Yokum S. Relation of neural response to palatable food tastes and images to future
544 weight gain: Using bootstrap sampling to examine replicability of neuroimaging findings.
545 *Neuroimage* 2018; **183**: 522-531.
- 546
547 39. Stice E, Spoor S, Bohon C, Veldhuizen MG, Small DM. Relation of reward from food intake and
548 anticipated food intake to obesity: a functional magnetic resonance imaging study. *J Abnorm*
549 *Psychol* 2008; **117**(4): 924-35.
- 550
551 40. Ng J, Stice E, Yokum S, Bohon C. An fMRI study of obesity, food reward, and perceived caloric
552 density. Does a low-fat label make food less appealing? *Appetite* 2011.
- 553
554 41. Knutson B, Greer SM. Anticipatory affect: neural correlates and consequences for choice.
555 *Philos Trans R Soc Lond B Biol Sci* 2008; **363**(1511): 3771-86.
- 556
557 42. Simon JJ, Skunde M, Hamze Sinno M, Brockmeyer T, Herpertz SC, Bendszus M *et al.* Impaired
558 Cross-Talk between Mesolimbic Food Reward Processing and Metabolic Signaling Predicts
559 Body Mass Index. *Frontiers in behavioral neuroscience* 2014; **8**: 359.
- 560
561 43. van der Laan LN, de Ridder DT, Viergever MA, Smeets PA. The first taste is always with the
562 eyes: a meta-analysis on the neural correlates of processing visual food cues. *Neuroimage*
563 2011; **55**(1): 296-303.
- 564
565 44. Smeets PA, de Graaf C, Stafleu A, van Osch MJ, Nievelstein RA, van der Grond J. Effect of satiety
566 on brain activation during chocolate tasting in men and women. *Am J Clin Nutr* 2006; **83**(6):
567 1297-305.
- 568
569 45. Yousuf M, Heldmann M, Gottlich M, Munte TF, Donamayor N. Neural processing of food and
570 monetary rewards is modulated by metabolic state. *Brain Imaging Behav* 2017.
- 571
572 46. Devoto F, Zapparoli L, Bonandrini R, Berlingeri M, Ferrulli A, Luzi L *et al.* Hungry Brains: A Meta-
573 Analytical Review of Brain Activation Imaging Studies On Food Perception and Appetite in
574 Obese Individuals. *Neurosci Biobehav Rev* 2018.
- 575
576 47. Kroemer NB, Small DM. Fuel not fun: Reinterpreting attenuated brain responses to reward in
577 obesity. *Physiol Behav* 2016; **162**: 37-45.

- 578
579 48. Mathar D, Neumann J, Villringer A, Horstmann A. Failing to learn from negative prediction
580 errors: Obesity is associated with alterations in a fundamental neural learning mechanism.
581 *Cortex* 2017; **95**: 222-237.
- 582
583 49. Schultz W. Dopamine reward prediction error coding. *Dialogues Clin Neurosci* 2016; **18**(1): 23-
584 32.
- 585
586 50. Medic N, Ziauddeen H, Forwood SE, Davies KM, Ahern AL, Jebb SA *et al.* The Presence of Real
587 Food Usurps Hypothetical Health Value Judgment in Overweight People. *eNeuro* 2016; **3**(2).
- 588
589 51. Rolls BJ, Roe LS, James BL, Sanchez CE. Does the incorporation of portion-control strategies in
590 a behavioral program improve weight loss in a 1-year randomized controlled trial? *Int J Obes*
591 *(Lond)* 2017; **41**(3): 434-442.
- 592
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612 **Figure legends**

613 **Figure 1.** Illustration of the study procedure.

614 **Figure 2.** Portion size (kJ) selected by study participants expressed in % of individual energy
615 requirement. Values (mean \pm SEM) are stratified by condition. A) Plot shows significant within
616 group mindset induced changes in portion size selection. B) Plot shows, in relation to
617 baseline, significant group differences for the pleasure mindset.

618 **Figure 3.** Health induced changes in brain activity compared to baseline in all weight groups.
619 Shown are clusters in the in the left superior frontal gyrus and left inferior frontal gyrus with
620 increased activity for the final decision to select a portion size while adopting the health
621 mindset compared to baseline ($p < 0.001$ uncorrected for display).

622 **Figure 4.** Pleasure mindset induced changes in brain activity and selected portion size.
623 Cluster shows an increase in the right inferior frontal operculum activation in the BMI ≥ 25
624 kg/m² group compared to the BMI < 25 kg/m² group ($P_{FWE} < 0.05$, whole brain-corrected).
625 Correlation plot shows significant relationship between the portion size under the pleasure
626 mindset and activation of the right inferior frontal operculum (For both weight groups: $r =$
627 0.408; $p = 0.01$). Solid regression line for BMI ≥ 25 kg/m² group; dashed regression line for
628 BMI < 25 kg/m² group.

629 **Figure 5.** Fullness mindset induced changes in brain activity compared to baseline. Image on
630 the right shows cluster in the left ventral striatum revealing a significant interaction between
631 group and condition (fullness mindset vs. baseline) ($P_{FWE} < 0.05$ small volume corrected). Bar
632 plot, on the left, shows in participants with normal-weight a significant increase in ventral
633 striatal activation in the fullness mindset compared to baseline, while participants with
634 overweight and obesity show a significant decrease ($*p < 0.01$).

Figure 1

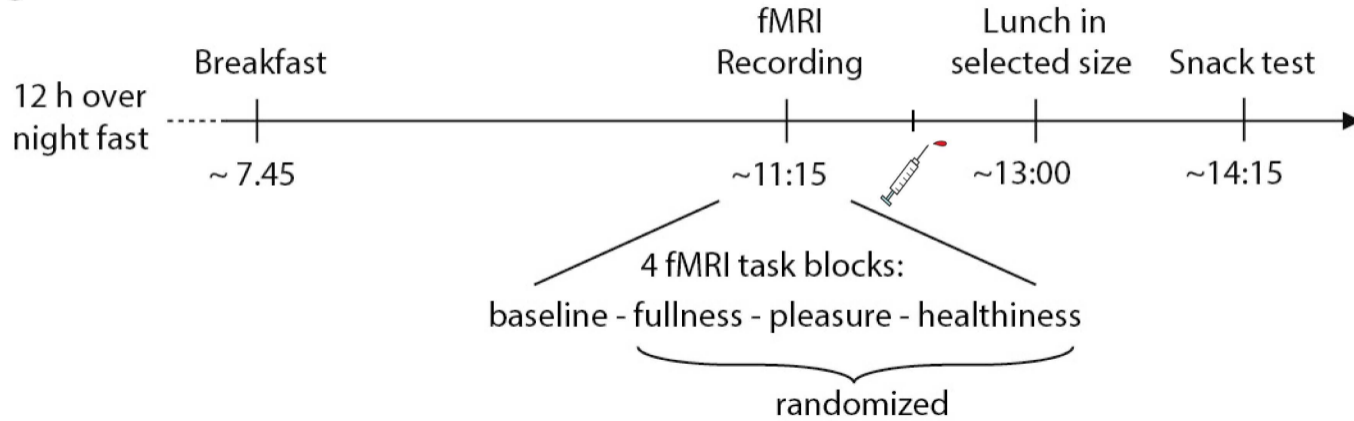
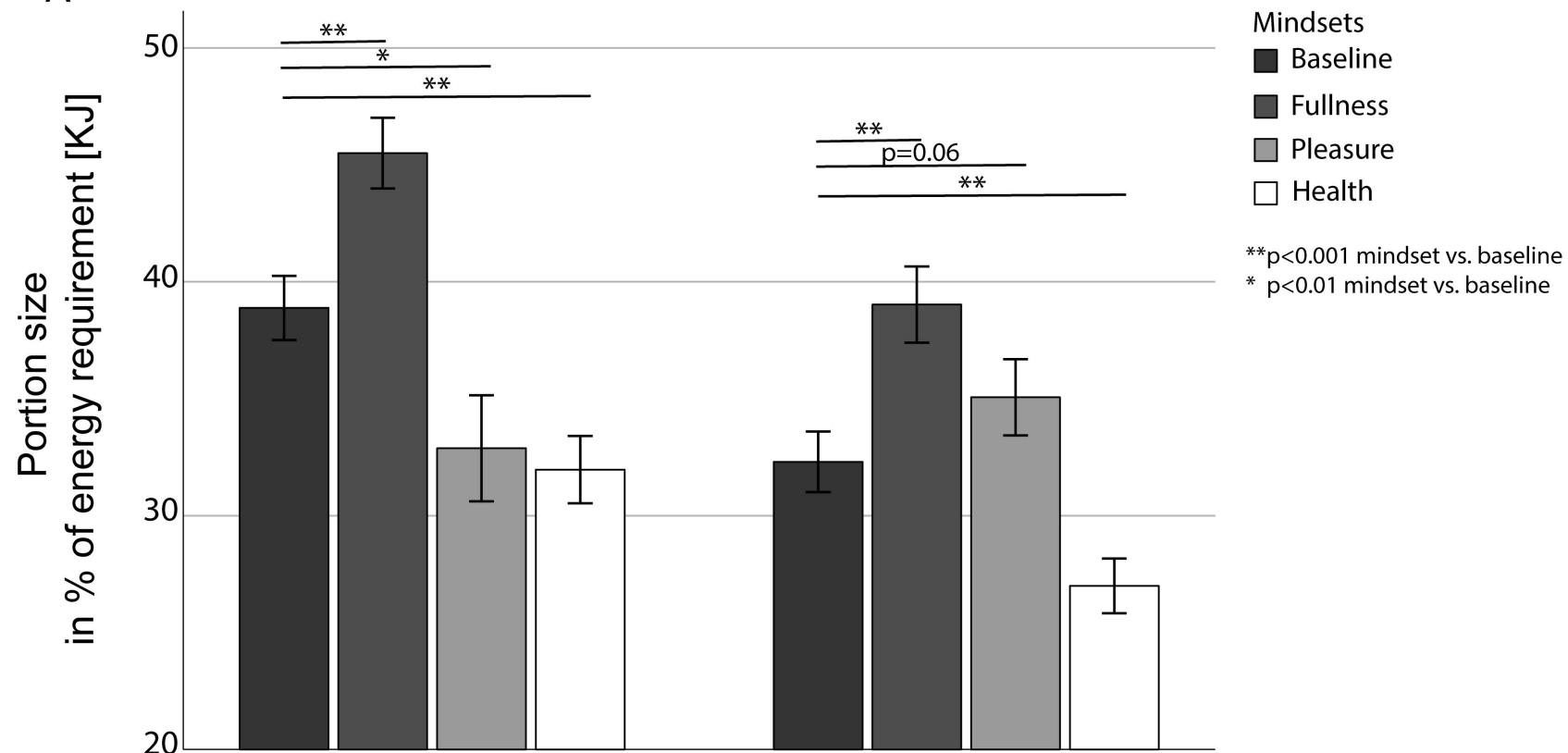


Figure 2

A



B

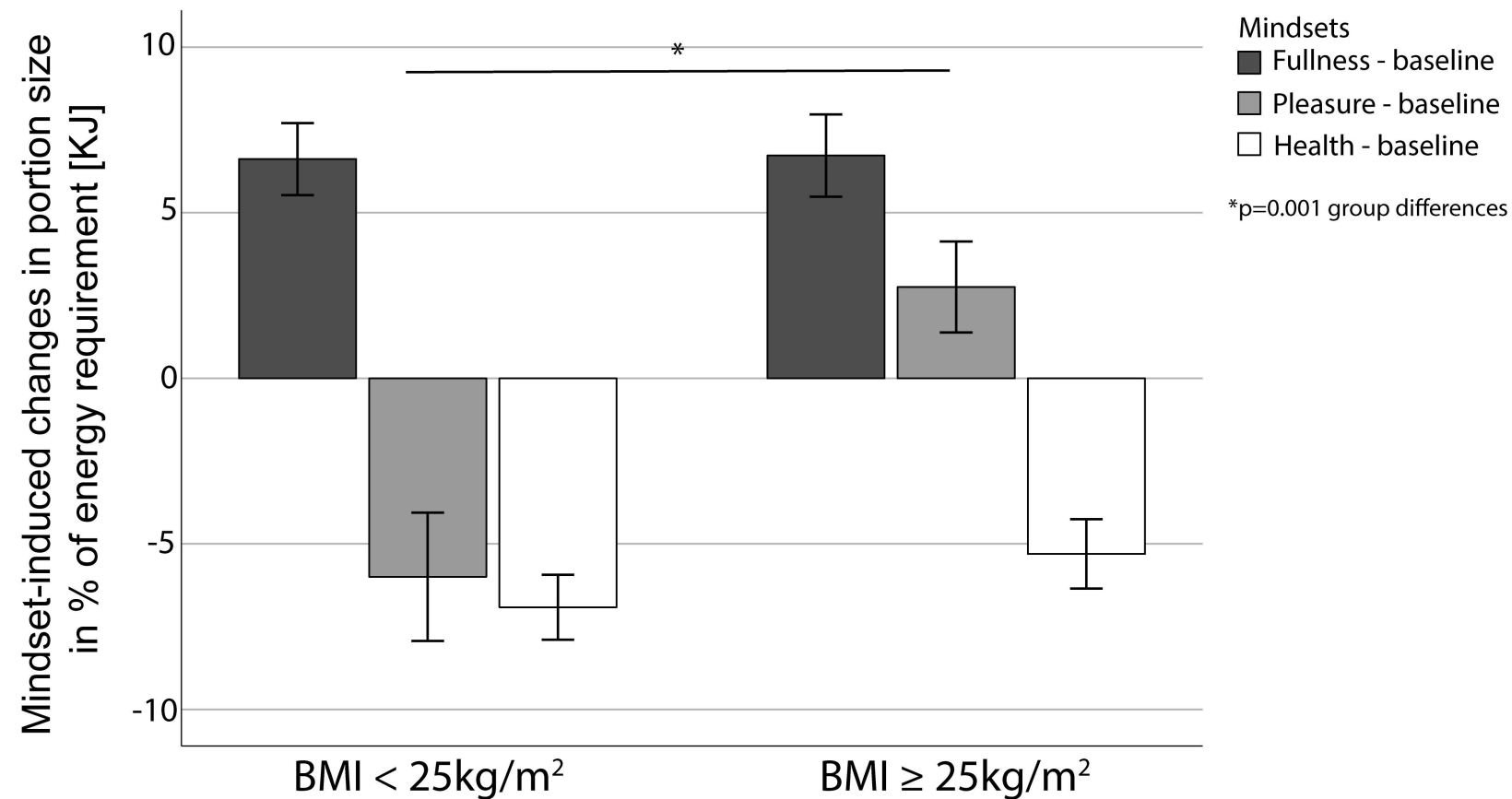


Figure 3

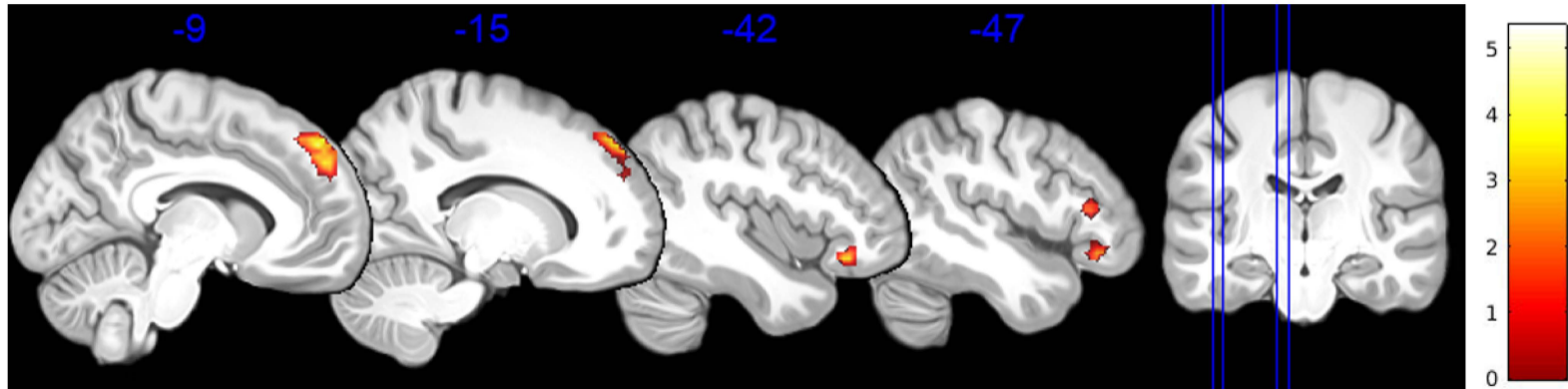


Figure 4

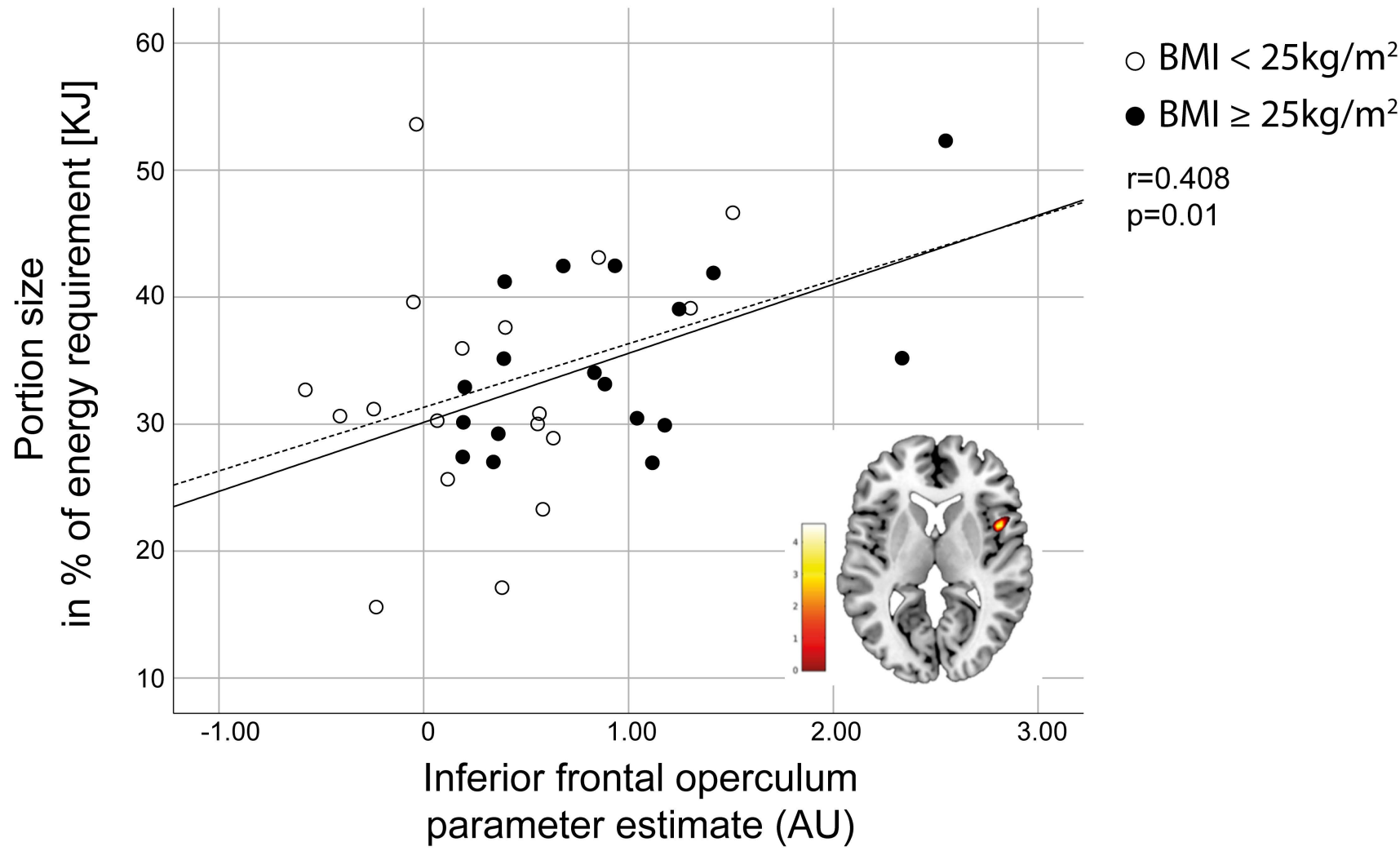


Figure 5

