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

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Short running title: Changing mindset affects brain and behaviour

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Abstract

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

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

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

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

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

Introduction

Mindsets determine attentional focus when making a choice and they play an important role in everyday decisions. For example, directing attentional focus to healthy thoughts, as a result of walking by a gym during shopping, can influence food choice. Interestingly, healthy choices increase when the attentional focus is directed to healthy features of food [1-4]. This is related to increased activation in parts of the prefrontal cortex, particularly the dorsolateral prefrontal cortex (dlPFC) [5]. The activation pattern of the dlPFC during memory and executive control tasks predict weight loss success in dieters [6, 7] and is reduced in individuals with obesity [8-10]. Moreover, the dlPFC is part of the core network related to dietary self-control, which is defined as a mental process functioning to override temptations to select a goal-oriented action [8]. Besides the prefrontal cortex, the core brain regions related to dietary self-control include parts of the insula, supplementary motor cortex, operculum, parietal cortices and striatal regions. This network captures the process of valuation and action needed during food choice.

Although many studies have evaluated the neural representations of food choice, few studies have investigated determinants for the selection of meal size. Nonetheless, besides what we eat, daily food intake might be even more dependent on the portion size we select [11]. Indeed, the rise in obesity in the U.S. since the 1950s has paralleled with increasing portion sizes [12]. The crucial influence of portion size is supported by the fact that we tend to plan our meals and then consume selected portions in their entirety [13]. Moreover, the energy content of selected portions is strongly influenced by the extent to which we expect the meal to deliver satiation [14]. We even tend to underestimate the caloric content of high energy density foods based on lower expected satiation, which results in the selection of larger portion sizes [14-16]. Hence, the decision of how much to eat before a meal begins, and the attention assigned to this task, plays a vital role in our food intake. We recently investigated in adults with normal-weight the neural underpinnings of portion size selection for lunch before mealtime began, which is referred to as pre-meal planning [17]. Participants chose their portion size for lunch by adopting three different mindsets. By switching an individual's attentional focus to health aspects (i.e., health mindset), we were able to reduce portion size selection for lunch, which was accompanied by a specific brain response pattern. This study suggests the opportunity to improve portion control by mindset manipulation. However, it is not known whether pre-meal planning can be influenced by a shift in mindset in individuals with overweight and obesity to encourage healthier portion control.

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

Materials and methods

Participants

Eighteen participants with overweight and obesity were recruited into the study. Fourteen controls with normal-weight were included from a recent study [17] and an additional four healthy controls were recruited to ensure that the groups did not differ in age. Participants were recruited via e-mail and board advertisements, and were screened on exclusion criteria by online questionnaires. Participants were required to fulfill the following inclusion criteria: right handed, between 18 and 35 years of age, having a body mass index (BMI) between 18 and 24 kg/m^2 for the BMI < 25 kg/m^2 group and a BMI between 25 and 35 kg/m^2 for the BMI ≥ 25 kg/m^2 group. Participants were excluded if they had a non-removable metal object in their body, were pregnant, had type 2 diabetes, were taking antidepressants or had a neurological disorder (e.g., epilepsy), were vegetarian or vegan, had a food allergy, or self-reported having an eating disorder. The study was approved by the ethics committee of the University of Tübingen. Written informed consent was obtained prior to the study. Participant characteristics are summarized in **table 1**.

Study design

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

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

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

Stimuli

We selected 10 stimuli (i.e. different meals) from a database that systematically varied in portion sizes [18]. We used 10 pictures per meal showing different portion sizes, starting with 100 kcals and increasing portion sizes in 100 kcal steps. A portion size of 500 kcal was used for the ratings of the meals. Based on the NOVA food classification system, we predict that individual meal stimuli would be classified as either ‘processed’ or ‘ultra-processed’ (group 3 and 4, respectively) [19].

fMRI task

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

For the fMRI task, we used 10 different meals in 10 different portion sizes (starting with a portion size of 100 kcal (418 kilojoules (kJ) and increasing by 100kcal (418 kJ) up to 1000kcal (4184 kJ)). Each of the four task blocks consisted of 30 trials starting with the presentation of a randomly selected meal. For each meal, there were three trials in each task block. Each trial started with an initial meal size once in the lower, middle and upper range of portion sizes. Participants were required to decide whether they wanted to increase or decrease the portion size via button press. Pressing a right button increased the portion size and pressing a left button decreased the portion, i.e. the next larger or smaller portion size was shown after presentation of an inter-stimulus fixation cross for a randomized time between 1 and 2 s. At the end of each trial, when participants reached their desired portion size, the selected portion was shown for 2 s and participants had to confirm the selection by button press. They were then asked if they were satisfied with their final portion size decision (feedback). In the final analyses, we only included decision trials for which participants indicated that they were satisfied with their final portion size selection. Participants performed the task self-paced and were allowed 10.5 minutes to complete the task. Dummy trials were included in the analyses if they needed less time. Stimuli were presented visually projected on a monitor in the scanner room using Presentation (Neurobehavioural Systems, Inc., Albany, CA). The task was recently described in detail [17].

fMRI data acquisition and preprocessing

Whole brain fMRI data were obtained using a 3 Tesla scanner (Siemens MAGNETOM Prisma, Erlangen, Germany) equipped with a 20-channel head coil. Each task block consisted of 312 scans (repetition time: 2 s, echo time: 30 ms, voxel size 3x3x3 mm^3). In addition, we obtained a high resolution T1-weighted anatomical image and a static field map to unwarp geometrically distorted functional scans. As recently described, preprocessing and statistical analyses of the fMRI data were performed in SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK). The anatomical image was normalized to the Montreal Neurological Institute (MNI) template (1x1x1mm^3). The functional images were normalized to a voxel size of 3 x 3 x 3 mm^3 and smoothed with a three-dimensional isotropic Gaussian kernel (FWHM: 9 mm). FMRI data were high-pass filtered (0.008 Hz) and global AR (1) auto correlation correction was performed.

fMRI data analysis

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

For the second-level analyses, full-factorial models were calculated using the first-level contrasts of the final decision, with the between-subject factor "body-weight" ($BMI<25 kg/m^2$ group vs. $BMI \geq 25 kg/m^2$ group) and a within-subject factor "condition" (free-choice vs mindset). Effects were considered statistically significant using a primary threshold at peak level of $p<0.001$ uncorrected and a whole brain family wise error correction (FWE) of $p< 0.05$ at cluster level. In addition, we performed a region of interest (ROI) analyses for the dlPFC (inferior frontal gyrus), frontal operculum, and putamen, based on recent publications on food choice and dietary self-control [5, 8, 17]. All ROIs were created in wfu pick atlas [20].

Behavioural data analysis

Self-rated hunger

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

Portion size selection

Individual energy requirements were calculated based on the Harris Benedict equation [21]. Portion size selections are expressed as percentages (%) of individual energy requirements [in kilojoules (kJ)]. To investigate mindset-induced portion size selection, we used a mixed-model ANOVA (within-subject factor: mindset (corrected in relation to baseline/free-choice condition), between-subject factor "body-weight" (BMI<25 kg/m^2 vs BMI≥25 kg/m^2) and sex.

Expected satiation

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

Correlation analyses

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

Results

Effects of mindset on portion selection

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

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

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

Hunger rating

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

Correlations between portion size selection and hunger

Portion size selection during pleasure compared to baseline correlated significantly with hunger before the start of the experiment (r= -0.431, p= 0.009). Hence, participants who reported less hunger selected larger portions for pleasure compared to the free-choice condition. This correlation was driven primarily by the BMI≥25 kg/m^2 group (data not shown). No significant associations were observed for portion size selection under health and fullness mindset (p<0.01 corrected for multiple testing).

Expected satiation

As expected and as recently reported [17, 18], the energy density of the meals was associated with lower expected satiation, both in participants with normal-weight (r= -0.774, p= 0.009) and with overweight and obesity (r= -0.716, p= 0.02). Expected satiation was also highly correlated with the portion sizes selected in the baseline condition (BMI<25 kg/m^2 r= -0.867, p= 0.001; BMI≥25 kg/m^2r= -0.911, p<0.001). Finally, portion size selection during baseline was not related to tastiness nor healthiness ratings and no group differences were observed for tastiness and healthiness ratings ($p > 0.05$).

Neuroimaging results

Health mindset

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

Pleasure mindset

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

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

Fullness mindset

Compared to the free-choice condition, the fullness mindset induced an increase in the posterior insula. Furthermore, a significant interaction was observed in the putamen (ventral striatum), between group and mindset fullness vs baseline (**Figure 5; supplementary table 2**). Post hoc analyses showed that participants with normal-weight increased activation in the ventral striatum during the fullness condition ($t(17)= 2.9$, $p= 0.008$), while participants with overweight and obesity decreased their response ($t(17)= -2.6$, $p= 0.01$). Weight groups significantly differed in ventral striatum activation in the fullness ($F(1,35)= 19.6$, $p<0.001$) but not the baseline condition.

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

Discussion

In the current study, we investigated whether mindset manipulations can modulate brain activity and encourage individuals with overweight and obesity to select healthier portion sizes. We observed that participants of all weight groups could be encouraged to reduce their portion size by adopting a health-focused mindset, which was accompanied by enhanced activation of the self-control network. We also found that the fullness and pleasure mindsets resulted in distinct behavioural and brain response patterns. Under the pleasure mindset, persons with overweight and obesity did not modify their behaviour and selected a larger portion size compared to participants of normal-weight. This was correlated with a heightened right frontal operculum response, which is part of the taste-processing region of the brain [22]. Under the fullness mindset, the BMI≥25kg/m^2 group showed a reduced response in the reward-processing region of the brain (i.e., ventral striatum).

Changing the perspective to health aspects resulted in a reduction in portion size selection with enhanced activation of the self-control network, including parts of the dorsolateral prefrontal cortex (dlPFC) and dorsolateral medial prefrontal cortex (dlmPFC). The dlPFC is known to be important for anticipatory cognitive control, including dietary self-control and food choice. The dlmPFC also plays a role in mentalization [23], assigning valence and tracking health value independent of attentional focus [1]. Obesity is related to a diminished response of the left dlPFC, particularly in a food choice and dietary self-control setting [8]. Nonetheless, we found that all weight groups successfully recruited the dlPFC when changing mindset. Hence, our findings are promising in showing that young adults with obesity can enhance left dlPFC activity to influence eating behaviour. Similarly, cognitive reappraisal approaches, thinking of the health benefits and suppressing craving, showed that individuals with obesity can increase the dlPFC [24-26]; however, without any long lasting effects on body weight[27]. Moreover, persons with obesity can learn to upregulate the dlPFC using neurofeedback training[28], which results in healthier food choices [3]. Recent advances in non-invasive brain stimulation revealed that targeting the left dlPFC is effective in decreasing food intake and facilitating weight loss [29-31] (although to date no study has evaluated long-term effects of altering dlPFC activity on eating behaviour). Therefore, it could be that a mindset-induced change in dlPFC activity forms the neural basis for short-term dieting success in the overweight population.

Under the pleasure mindset, participants with normal-weight modified their choice by selecting smaller portions, which is consistent with results of a study by Cornil and Chandon [32]. They found that drawing attention to the orosensory aspects of eating can cause participants to select smaller food portions, apparently because orosensory pleasure peaks during the early part of a meal [32, 33]. In our study, however, while the pleasure mindset reduced portion size selection in participants with normal-weight, it failed to do so in participants with overweight and obesity. On a neural level, persons with overweight and obesity showed enhanced activation in the right inferior frontal operculum (IFO) (i.e., the pars opercularis of the inferior frontal gyrus) during the pleasure mindset. The right inferior frontal gyrus is activated whenever an important/salient cue is detected; hence, it plays an important role in the framework of attention [34, 35]. Regarding its functional role in eating behaviour, it is important to recognize the role of the IFO in discriminating different taste cue properties, as part of the taste cortex [36, 37]. In people with obesity, palatable food cues and tastes are found to generate particularly strong activation of the right inferior frontal operculum [9, 38]. Moreover, anticipated food intake and increased food desire results in higher reactivity of the frontal operculum in obesity [39, 40]. Together, this could lead to greater failure to suppress response tendencies to salient food cues. In the current study, individuals with overweight and obesity reported feeling less hungry. In light of the above-mentioned findings, for people with overweight and obesity, shifting attentional focus to pleasure might increase the salience of food, leading to the selection of larger portion sizes, even in the relative absence of hunger.

Under the fullness mindset, we identified a group specific pattern in the ventral striatum, which is a key region for processing incentive value and the anticipation of pleasurable outcomes [41]. This novel finding demonstrates how it is possible to tweak the brain's reward system simply by shifting attention to fullness. Previous studies have shown that ventral striatal activity is particularly sensitive to the anticipation of food intake, processing of food cues [42, 43], metabolic state, sensory modality and food consumption [39, 44-46]. It is still under discussion, however, whether overeating is caused by greater reward sensitivity or reward deficiency in people with obesity [39, 46]. Alternatively, it has been proposed that obesity is associated with reduced reward-related learning, particularly with an impairment in negative outcome learning [47, 48]. This is reflected by the negative reward prediction error, encoding the negative discrepancy between expected and actual reward [49]- a process that is largely driven by dopaminergic neurons in the striatum [47, 49]. Accordingly, our findings could point to a shift in the reward prediction error to the initial portion size (portion size at the beginning of the experimental block) in the BMI ≥ 25 kg/m^2 group. Thus, the final portion size decision under the fullness mindset might be 'worse' than expected (i.e. less rewarding), resulting in a decreased response in the ventral striatum particularly in persons with high impulsivity. This is in accordance with previous behavioural studies showing that eating itself is rewarding, but fullness is not [33].

A possible limitation of our study is the 'real' versus 'hypothetical" setting of the study design. During the free-choice (baseline) condition, participants made a 'real' choice (with an actual outcome); however, the mindset-induced choices were merely hypothetical in nature. A recent study showed that people with overweight make the same hypothetical but not real-world healthy food choices [50]. Hence, the potential to improve portion control by using a health mindset might be different in real life, where other factors, such as price, also impact decision making. Moreover, and in relation to this idea, we note that a recent weight-loss program incorporating a portion-control strategy failed to show sustained weight loss [51]. Another potential limitation is that we did not evaluate participants on their individual strategies after each mindset induction. Although participants were guided to develop different mindsets, we cannot say with confidence that these mindsets were always adopted. Individuals may differ in this regard and this issue might be addressed in future studies.

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

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

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References

1. Bhanji JP, Beer JS. Taking a different perspective: mindset influences neural regions that represent value and choice. *Soc Cogn Affect Neurosci* 2012; **7**(7)**:** 782-93.

2. Hare TA, Malmaud J, Rangel A. Focusing attention on the health aspects of foods changes value signals in vmPFC and improves dietary choice. *J Neurosci* 2011; **31**(30)**:** 11077-87.

3. Spetter MS, Malekshahi R, Birbaumer N, Luhrs M, van der Veer AH, Scheffler K *et al.* Volitional regulation of brain responses to food stimuli in overweight and obese subjects: A real-time fMRI feedback study. *Appetite* 2017; **112:** 188-195.

4. Petit O, Merunka D, Anton JL, Nazarian B, Spence C, Cheok AD *et al.* Health and Pleasure in Consumers' Dietary Food Choices: Individual Differences in the Brain's Value System. *PLoS One* 2016; **11**(7)**:** e0156333.

5. Hare TA, Camerer CF, Rangel A. Self-control in decision-making involves modulation of the vmPFC valuation system. *Science* 2009; **324**(5927)**:** 646-8.

6. Goldman RL, Canterberry M, Borckardt JJ, Madan A, Byrne TK, George MS *et al.* Executive control circuitry differentiates degree of success in weight loss following gastric-bypass surgery. *Obesity (Silver Spring)* 2013.

7. Hege MA, Stingl KT, Ketterer C, Haring HU, Heni M, Fritsche A *et al.* Working memory-related brain activity is associated with outcome of lifestyle intervention. *Obesity (Silver Spring)* 2013; **21**(12)**:** 2488-94.

8. Han JE, Boachie N, Garcia-Garcia I, Michaud A, Dagher A. Neural correlates of dietary self-control in healthy adults: A meta-analysis of functional brain imaging studies. *Physiol Behav* 2018; **192:** 98-108.

9. Brooks SJ, Cedernaes J, Schioth HB. Increased prefrontal and parahippocampal activation with reduced dorsolateral prefrontal and insular cortex activation to food images in obesity: a meta-analysis of fMRI studies. *PLoS One* 2013; **8**(4)**:** e60393.

10. Hege MA, Stingl KT, Kullmann S, Schag K, Giel KE, Zipfel S *et al.* Attentional impulsivity in binge eating disorder modulates response inhibition performance and frontal brain networks. *Int J Obes (Lond)* 2015; **39**(2)**:** 353-60.

11. Brunstrom JM. Mind over platter: pre-meal planning and the control of meal size in humans. *Int J Obes (Lond)* 2014; **38 Suppl 1:** S9-12.

12. Labbe D, Rytz A, Brunstrom JM, Forde CG, Martin N. Influence of BMI and dietary restraint on self-selected portions of prepared meals in US women. *Appetite* 2017; **111:** 203-207.

13. Fay SH, Ferriday D, Hinton EC, Shakeshaft NG, Rogers PJ, Brunstrom JM. What determines real-world meal size? Evidence for pre-meal planning. *Appetite* 2011; **56**(2)**:** 284-9.

14. Wilkinson LL, Hinton EC, Fay SH, Ferriday D, Rogers PJ, Brunstrom JM. Computer-based assessments of expected satiety predict behavioural measures of portion-size selection and food intake. *Appetite* 2012; **59**(3)**:** 933-8.

15. Brunstrom JM, Shakeshaft NG. Measuring affective (liking) and non-affective (expected satiety) determinants of portion size and food reward. *Appetite* 2009; **52**(1)**:** 108-14.

16. Brunstrom JM, Shakeshaft NG, Scott-Samuel NE. Measuring 'expected satiety' in a range of common foods using a method of constant stimuli. *Appetite* 2008; **51**(3)**:** 604-14.

17. Hege MA, Veit R, Krumsiek J, Kullmann S, Heni M, Rogers PJ *et al.* Eating less or more - Mindset induced changes in neural correlates of pre-meal planning. *Appetite* 2018; **125:** 492-501.

18. Brunstrom JM, Rogers PJ. How many calories are on our plate? Expected fullness, not liking, determines meal-size selection. *Obesity (Silver Spring)* 2009; **17**(10)**:** 1884-90.

19. Monteiro CA, Cannon G, Moubarac JC, Levy RB, Louzada MLC, Jaime PC. The UN Decade of Nutrition, the NOVA food classification and the trouble with ultra-processing. *Public Health Nutr* 2018; **21**(1)**:** 5-17.

20. Maldjian JA, Laurienti PJ, Kraft RA, Burdette JH. An automated method for neuroanatomic and cytoarchitectonic atlas-based interrogation of fMRI data sets. *Neuroimage* 2003; **19**(3)**:** 1233-9.

21. Harris JA, Benedict FG. A Biometric Study of Human Basal Metabolism. *Proc Natl Acad Sci U S A* 1918; **4**(12)**:** 370-3.

22. Frank S, Kullmann S, Veit R. Food related processes in the insular cortex. *Front Hum Neurosci* 2013; **7:** 499.

23. Amodio DM, Frith CD. Meeting of minds: the medial frontal cortex and social cognition. *Nat Rev Neurosci* 2006; **7**(4)**:** 268-77.

24. Siep N, Roefs A, Roebroeck A, Havermans R, Bonte M, Jansen A. Fighting food temptations: the modulating effects of short-term cognitive reappraisal, suppression and up-regulation on mesocorticolimbic activity related to appetitive motivation. *Neuroimage* 2012; **60**(1)**:** 213-20.

25. Yokum S, Stice E. Cognitive regulation of food craving: effects of three cognitive reappraisal strategies on neural response to palatable foods. *Int J Obes (Lond)* 2013; **37**(12)**:** 1565-70.

26. Kumar S, Grundeis F, Brand C, Hwang HJ, Mehnert J, Pleger B. Differences in Insula and Pre-/Frontal Responses during Reappraisal of Food in Lean and Obese Humans. *Front Hum Neurosci* 2016; **10:** 233.

27. Stice E, Yokum S, Burger K, Rohde P, Shaw H, Gau JM. A pilot randomized trial of a cognitive reappraisal obesity prevention program. *Physiol Behav* 2015; **138:** 124-32.

28. Kohl SH, Veit R, Spetter MS, Gunther A, Rina A, Luhrs M *et al.* Real-time fMRI neurofeedback training to improve eating behavior by self-regulation of the dorsolateral prefrontal cortex: A randomized controlled trial in overweight and obese subjects. *Neuroimage* 2019; **191:** 596-609.

29. Kim SH, Chung JH, Kim TH, Lim SH, Kim Y, Lee YA *et al.* The effects of repetitive transcranial magnetic stimulation on eating behaviors and body weight in obesity: A randomized controlled study. *Brain Stimul* 2018; **11**(3)**:** 528-535.

30. Gluck ME, Viswanath P, Stinson EJ. Obesity, Appetite, and the Prefrontal Cortex. *Curr Obes Rep* 2017; **6**(4)**:** 380-388.

31. Heinitz S, Reinhardt M, Piaggi P, Weise CM, Diaz E, Stinson EJ *et al.* Neuromodulation directed at the prefrontal cortex of subjects with obesity reduces snack food intake and hunger in a randomized trial. *Am J Clin Nutr* 2017; **106**(6)**:** 1347-1357.

32. Cornil Y, Chandon P. Pleasure as a Substitute for Size: How Multisensory Imagery Can Make People Happier with Smaller Food Portions. *J Marketing Res* 2016; **53**(5)**:** 847-864.

33. Rogers PJ. Combating Excessive Eating: A Role for Four Evidence-Based Remedies. *Obesity* 2018; **26:** S18-S24.

34. Hampshire A, Chamberlain SR, Monti MM, Duncan J, Owen AM. The role of the right inferior frontal gyrus: inhibition and attentional control. *Neuroimage* 2010; **50**(3)**:** 1313-9.

35. Erika-Florence M, Leech R, Hampshire A. A functional network perspective on response inhibition and attentional control. *Nat Commun* 2014; **5:** 4073.

36. Veldhuizen MG, Bender G, Constable RT, Small DM. Trying to detect taste in a tasteless solution: modulation of early gustatory cortex by attention to taste. *Chem Senses* 2007; **32**(6)**:** 569-81.

37. Veldhuizen MG, Gitelman DR, Small DM. An fMRI Study of the Interactions Between the Attention and the Gustatory Networks. *Chemosens Percept* 2012; **5**(1)**:** 117-127.

38. Stice E, Yokum S. Relation of neural response to palatable food tastes and images to future weight gain: Using bootstrap sampling to examine replicability of neuroimaging findings. *Neuroimage* 2018; **183:** 522-531.

39. Stice E, Spoor S, Bohon C, Veldhuizen MG, Small DM. Relation of reward from food intake and anticipated food intake to obesity: a functional magnetic resonance imaging study. *J Abnorm Psychol* 2008; **117**(4)**:** 924-35.

40. Ng J, Stice E, Yokum S, Bohon C. An fMRI study of obesity, food reward, and perceived caloric density. Does a low-fat label make food less appealing? *Appetite* 2011.

41. Knutson B, Greer SM. Anticipatory affect: neural correlates and consequences for choice. *Philos Trans R Soc Lond B Biol Sci* 2008; **363**(1511)**:** 3771-86.

42. Simon JJ, Skunde M, Hamze Sinno M, Brockmeyer T, Herpertz SC, Bendszus M *et al.* Impaired Cross-Talk between Mesolimbic Food Reward Processing and Metabolic Signaling Predicts Body Mass Index. *Frontiers in behavioral neuroscience* 2014; **8:** 359.

43. van der Laan LN, de Ridder DT, Viergever MA, Smeets PA. The first taste is always with the eyes: a meta-analysis on the neural correlates of processing visual food cues. *Neuroimage* 2011; **55**(1)**:** 296-303.

44. Smeets PA, de Graaf C, Stafleu A, van Osch MJ, Nievelstein RA, van der Grond J. Effect of satiety on brain activation during chocolate tasting in men and women. *Am J Clin Nutr* 2006; **83**(6)**:** 1297-305.

45. Yousuf M, Heldmann M, Gottlich M, Munte TF, Donamayor N. Neural processing of food and monetary rewards is modulated by metabolic state. *Brain Imaging Behav* 2017.

46. Devoto F, Zapparoli L, Bonandrini R, Berlingeri M, Ferrulli A, Luzi L *et al.* Hungry Brains: A Meta-Analytical Review of Brain Activation Imaging Studies On Food Perception and Appetite in Obese Individuals. *Neurosci Biobehav Rev* 2018.

47. Kroemer NB, Small DM. Fuel not fun: Reinterpreting attenuated brain responses to reward in obesity. *Physiol Behav* 2016; **162:** 37-45.

48. Mathar D, Neumann J, Villringer A, Horstmann A. Failing to learn from negative prediction errors: Obesity is associated with alterations in a fundamental neural learning mechanism. *Cortex* 2017; **95:** 222-237.

49. Schultz W. Dopamine reward prediction error coding. *Dialogues Clin Neurosci* 2016; **18**(1)**:** 23-32.

50. Medic N, Ziauddeen H, Forwood SE, Davies KM, Ahern AL, Jebb SA *et al.* The Presence of Real Food Usurps Hypothetical Health Value Judgment in Overweight People. *eNeuro* 2016; **3**(2).

51. Rolls BJ, Roe LS, James BL, Sanchez CE. Does the incorporation of portion-control strategies in a behavioral program improve weight loss in a 1-year randomized controlled trial? *Int J Obes (Lond)* 2017; **41**(3)**:** 434-442.

Figure legends

Figure 1. Illustration of the study procedure.

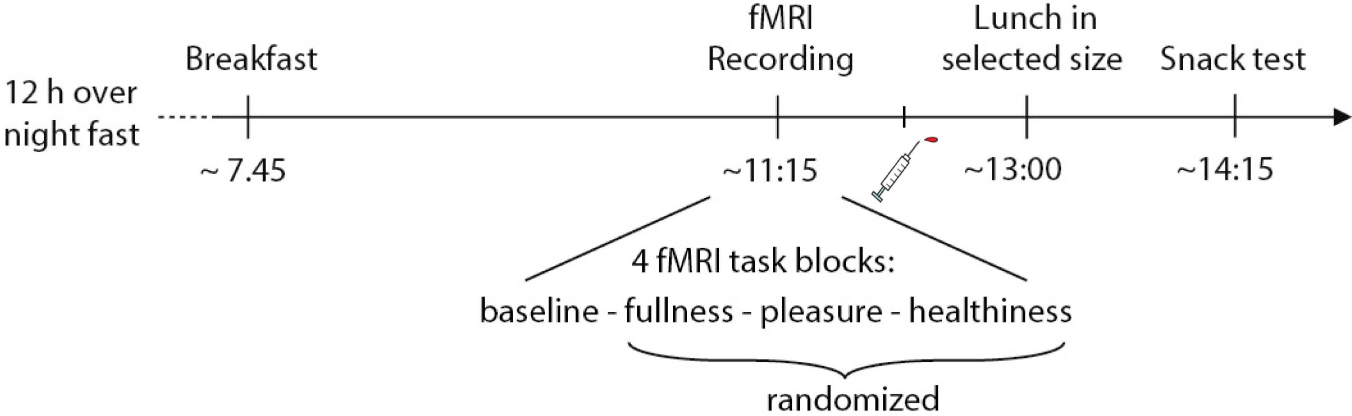
Figure 2. Portion size (kJ) selected by study participants expressed in % of individual energy requirement. Values (mean±SEM) are stratified by condition. A) Plot shows significant within group mindset induced changes in portion size selection. B) Plot shows, in relation to baseline, significant group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

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

Figure 4. Pleasure mindset induced changes in brain activity and selected portion size. Cluster shows an increase in the right inferior frontal operculum activation in the BMI ≥ 25 kg/m^2 group compared to the BMI < 25 kg/m^2 group ($P_{FWE}<0.05$,whole brain-corrected). Correlation plot shows significant relationship between the portion size under the pleasure mindset and activation of the right inferior frontal operculum (For both weight groups: r= 0.408; p= 0.01). Solid regression line for BMI≥ 25kg/m2 group; dashed regression line for BMI < 25 kg/m^2 group.

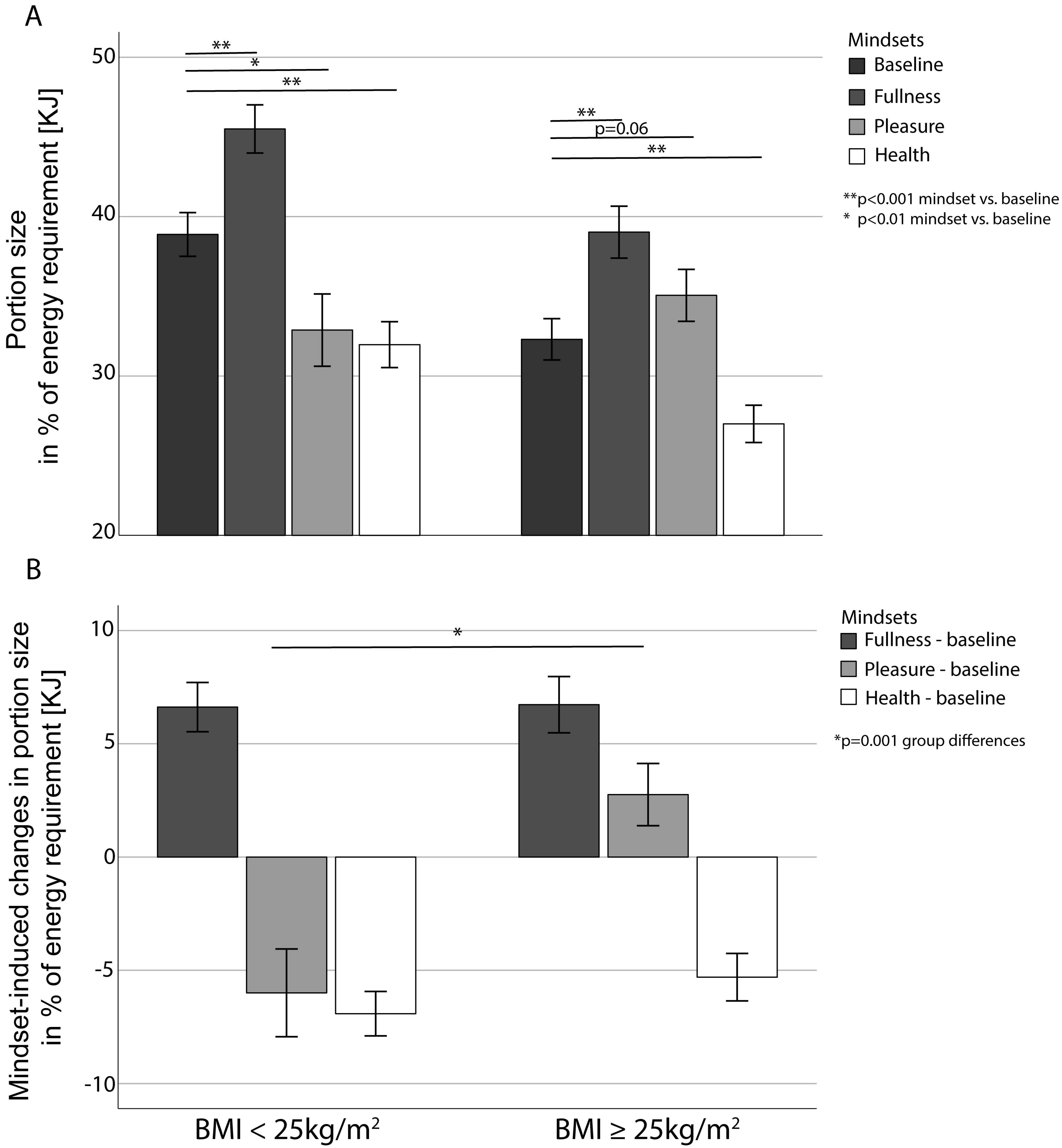
Figure 5. Fullness mindset induced changes in brain activity compared to baseline. Image on the right shows cluster in the left ventral striatum revealing a significant interaction between group and condition (fullness mindset vs. baseline) ($P_{FWE}<0.05$ small volume corrected).Bar plot, on the left,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

Figure 1



12 h over night fast
Breakfast
~ 7.45
fMRI Recording
~11:15
Lunch in selected size
~13:00
Snack test
~14:15
4 fMRI task blocks:
baseline - fullness - pleasure - healthiness
randomized

Figure 2



A
Portion size
in % of energy requirement [KJ]
50
40
30
20
**
*
**
**
p=0.06
**
Mindsets
Baseline
Fullness
Pleasure
Health
**p<0.001 mindset vs. baseline
* p<0.01 mindset vs. baseline
B
Mindset-induced changes in portion size
in % of energy requirement [KJ]
10
5
0
-5
-10
*
Mindsets
Fullness - baseline
Pleasure - baseline
Health - baseline
*p=0.001 group differences
BMI < 25kg/m2
BMI ≥ 25kg/m2

Figure 3

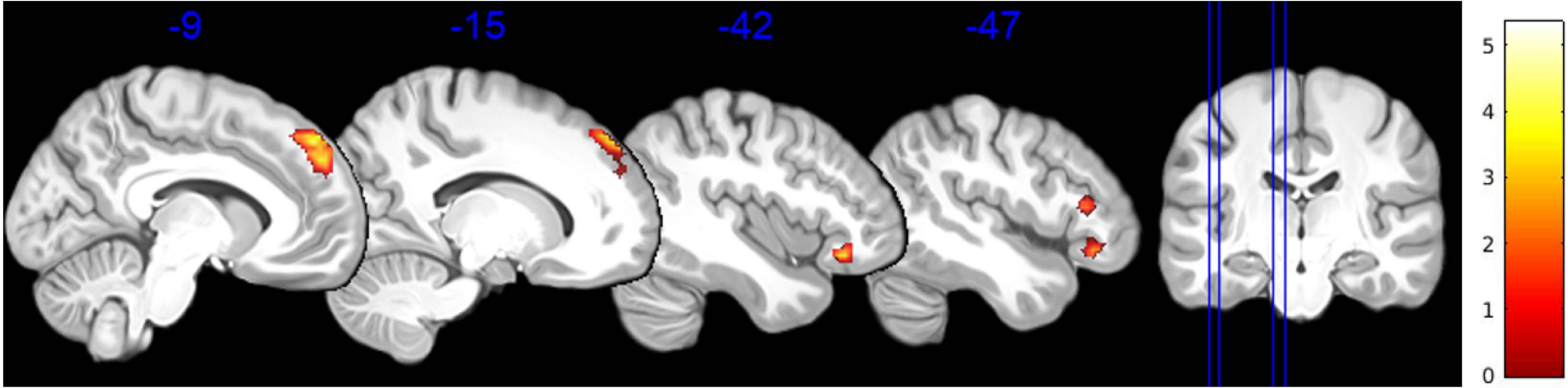
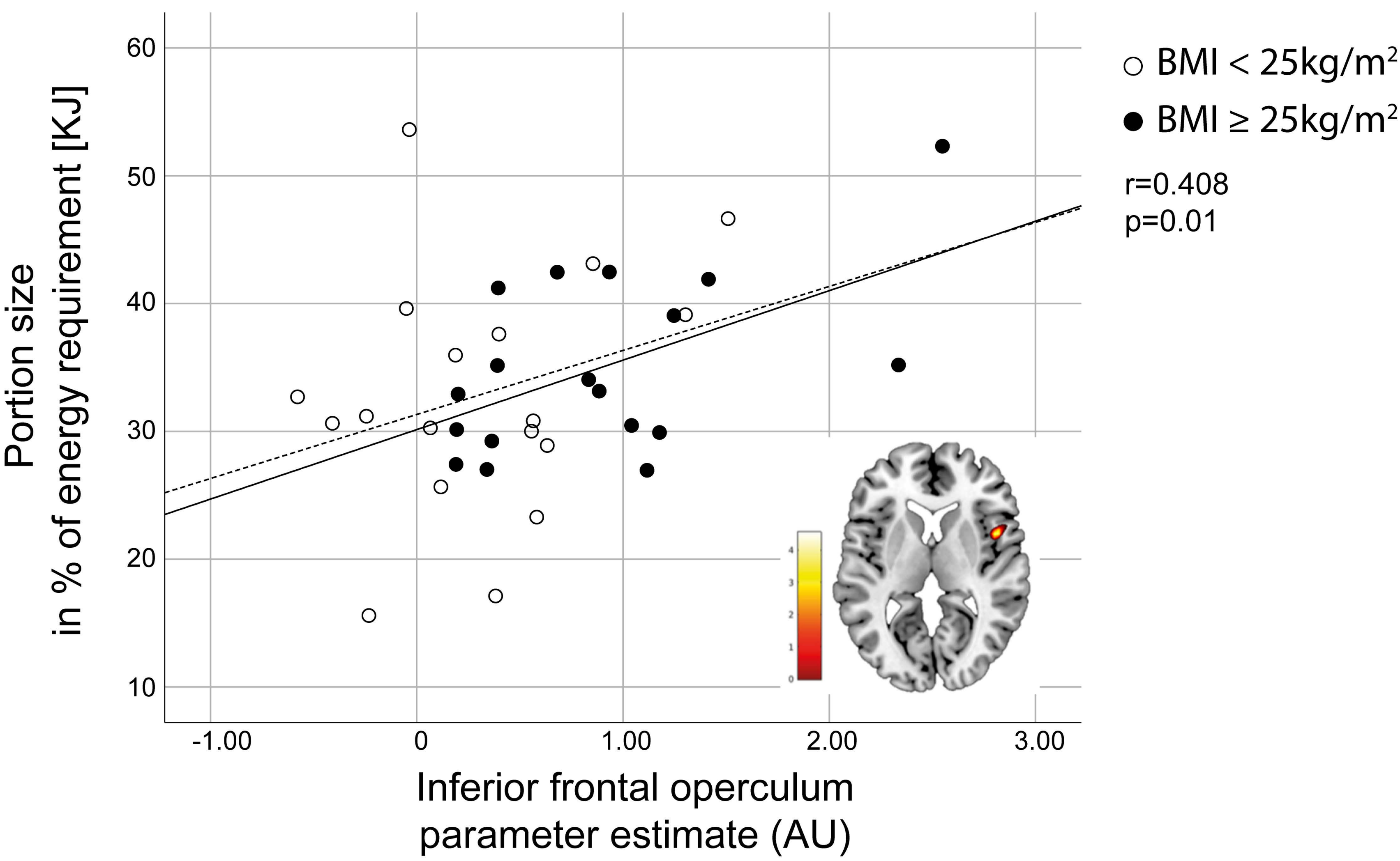
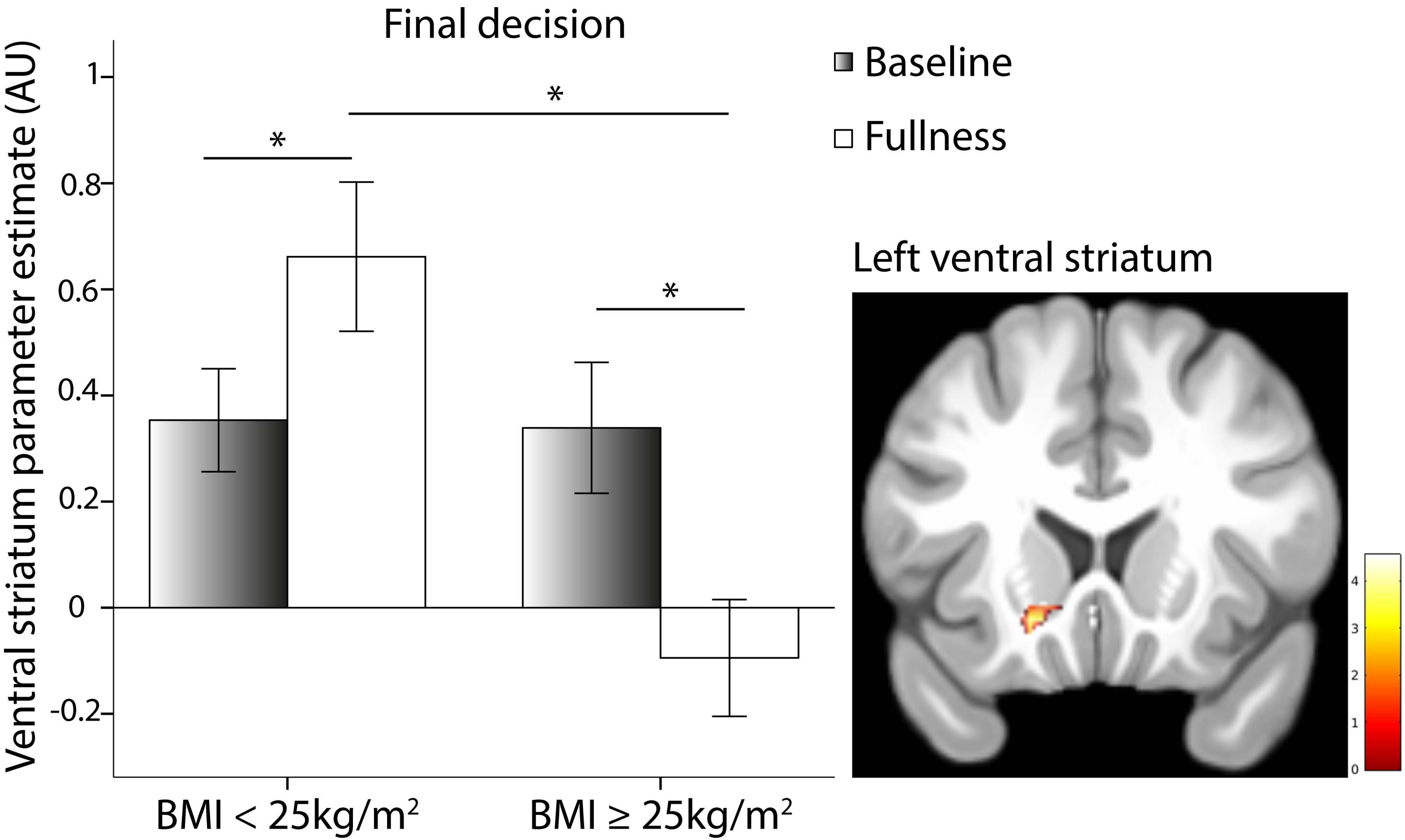


Figure 4



Portion size
in % of energy requirement [KJ]
60
50
40
30
20
10
-1.00
0
1.00
2.00
3.00
Inferior frontal operculum
parameter estimate (AU)
○ BMI < 25kg/m2
● BMI ≥ 25kg/m2
r=0.408
p=0.01

Figure 5



Final decision
Baseline
Fullness
Ventral striatum parameter estimate (AU)
1
0.8
0.6
0.4
0.2
0
-0.2
*
*
*
BMI < 25kg/m²
BMI ≥ 25kg/m²
Left ventral striatum
4
3
2
1
0