



Hege, M. A., Veit, R., Krumsiek, J., Kullmann, S., Heni, M., Rogers, P. J., Brunstrom, J. M., Fritsche, A., & Preissl, H. (2018). Eating less or more – Mindset induced changes in neural correlates of pre-meal planning. *Appetite*, 125, 492-501.
<https://doi.org/10.1016/j.appet.2018.03.006>

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[10.1016/j.appet.2018.03.006](https://doi.org/10.1016/j.appet.2018.03.006)

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Eating less or more – Mindset induced changes in neural correlates of pre-meal planning

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Abstract

Obesity develops due to an imbalance between energy intake and expenditure. Besides the decision about what to eat, daily energy intake might be even more dependent on the decision about the portion size to be consumed. For decisions between different foods, attentional focus is considered to play a key role in the choice selection. In the current study, we investigated the attentional modulation of portion size selection during pre-meal planning. We designed a functional magnetic resonance task in which healthy participants were directed to adopt different mindsets while selecting their portion size for lunch. Compared with a free choice condition, participants reduced their portion sizes when considering eating for health or pleasure, which was accompanied by increased activity in left prefrontal cortex and left orbitofrontal cortex, respectively. When planning to be full until dinner, participants selected larger portion sizes and showed a trend for increased activity in left insula. These results provide first evidence that also the cognitive process of pre-meal planning is influenced by the attentional focus at the time of choice, which could provide an opportunity for influencing the control of meal size selection by mindset manipulation.

Keywords: dorsolateral prefrontal cortex, fMRI, food, insula, mindset, orbitofrontal cortex

1. Introduction

According to the World Health Organization, worldwide obesity has more than doubled since 1980 and in 2014 more than 1.9 billion adults were estimated to be overweight (WHO, 2016). Understanding factors that lead to obesity are of utmost importance as obesity is associated with diseases like diabetes and cardiovascular disease and thereby reduces average life expectancy (Haslam & James, 2005; Pischon, et al., 2008). Obesity develops due to an imbalance between energy intake and expenditure (Westerterp, 2010). A determining factor of our energy intake is not only the decision about what we eat, but maybe more importantly the decision about the size of the meals that we consume. In this regard, trends in obesity in the US have been associated with increasing portion sizes (Labbe, Rytz, Brunstrom, Forde, & Martin, 2017). A main focus in understanding portion size selection has been to investigate the processes that generate increasing fullness during a meal (Blundell, Rogers, & Hill, 1987; Hetherington, 1996). In the last decade, however, observations of natural eating behavior in humans highlight the importance of pre-meal planning, the decision of how much to eat before a meal begins (refer to review Brunstrom (2014)). This is supported by the observation that we tend to ‘plate clean’, to consume the total amount of food on our plate (Wilkinson, et al., 2012). Furthermore, it was shown that humans not only have particular expectations about the tastiness or healthiness of foods, but also about their satiating effects (Brunstrom & Rogers, 2009; Brunstrom, Shakeshaft, & Scott-Samuel, 2008; Wilkinson, et al., 2012). The extent to which a food is expected to deliver satiation (‘expected satiation’) is related to its energy density and will strongly influence the energy content of the selected portion size. Actually, participants seem to underestimate the caloric content of foods with higher energy density resulting in lower expected satiation and selection of larger portion sizes calorie wise of these foods (Brunstrom & Rogers, 2009; Brunstrom, et al., 2008). Wilkinson et al. (2012) even suggested that expected satiation might be a more important determinant of meal size than palatability. However, little

is known about how these factors are integrated during pre-meal planning and about the neural correlates involved in these decisions.

For decision making between complex options that depend on and differ in multiple attributes (e.g. expected satiation, healthiness or tastiness of a meal), the brain is assumed to compute subjective values for all of these options by assigning values to the individual attributes and integrating them (Bettman, Luce, & Payne, 1998). These integrated subjective values are then compared to make a choice (Glimcher & Rustichini, 2004; Rangel & Hare, 2010; Rushworth, Mars, & Summerfield, 2009). The ventromedial prefrontal cortex (vmPFC) has been shown to be highly involved in these computational processes for a wide range of qualitatively different choice conditions (Bartra, McGuire, & Kable, 2013; Clithero & Rangel, 2014).

It has been suggested that integration of the stimulus attributes depends on the attention assigned to them at the time of choice (Krajbich, Armel, & Rangel, 2010; Shimojo, Simion, Shimojo, & Scheier, 2003) and that the attentional focus likely varies within and across individuals (Roefs, Werthmann, & Houben, 2015). The individuals' so called 'mindsets' can influence the way they evaluate options and make choices. For the decision between different food items, several functional magnetic resonance imaging (fMRI) studies show that the number of healthy choices increases when the attentional focus is directed to the health aspects of the foods (Bhanji & Beer, 2012; Enax, Hu, Trautner, & Weber, 2015; Hare, Camerer, & Rangel, 2009; Hare, Malmaud, & Rangel, 2011). Variations in attentional focus between individuals (Hare, et al., 2009) and as a function of exogenous attention cues (Enax, et al., 2015; Hare, Malmaud, et al., 2011) is associated with increased activity in the dorsolateral prefrontal cortex (DLPFC), a region known to be important in the cognitive control of behavior in general (Miller & Cohen, 2001). It was further suggested that the DLPFC mediates the behavior change by modulating the subjective value signal in the vmPFC.

In the current study, we aimed to explore behavioral responses and neural processes during pre-meal planning. In particular, we investigated whether different mindsets are associated with altered activity in certain brain areas during the pre-meal selection of portion sizes and whether this effects the selected portion size due to altered integration of different stimulus attributes, namely expected satiation, healthiness and tastiness of a specific food.

In order to investigate the neural correlates associated with the selection of a portion size for lunch during different mindset instructions, we performed an fMRI study. Participants were asked to select their ideal portion size in a free-choice condition without further instructions (baseline), in consideration of health aspects (healthiness mindset), when they were planning to eat with pleasure (pleasure mindset) and when they were planning to be full until dinner (fullness mindset). These mindsets were selected as we consider them to be important factors that moderate portion size selection.

For each of these mindsets, we expected changes in portion size selection and activity changes in mindset specific brain areas when compared to the baseline condition. More specifically, we hypothesized that participants would select smaller portion sizes and show activity changes in left DPLFC (according to Hare et al. (2009)) for the healthiness mindset. For the fullness mindset, we anticipated increased portion sizes and activity changes in the insula based on its suggested role in interoceptive and satiation processes (for review refer to Frank et al. (2013)). Finally, for the pleasure mindset we had no directed hypothesis for the portion size selection, but expected changes in activity in the orbitofrontal cortex (OFC) as the main integrative region for pleasure evaluation (for reviews refer to Kringelbach (2005); Rolls (2015)).

2. Material and Methods

2.1. Participants

23 young, healthy, and lean adults with no self-reported eating disorder, diabetes, or vegetarian/vegan diet participated in the study. One participant had to be excluded due to technical problems, one due to not finishing his meal and failing to provide answers during the feedback phase, one due to having a BDI-II (German version of the Beck depression inventory) (Hautzinger, Keller, & Kühner, 2006) score of 24 (moderate depression) and two due to selecting bigger portion sizes than available already in the baseline condition. The mean age of the remaining 18 participants (9 women / 9 men) was 24.6 (range: 18-31) years and the mean body mass index (BMI) was 21.8 (range: 19.5-24.0) kg/m². There was no significant difference in age ($t(16)=0.16$, $p=0.88$) and BMI ($t(16)=0.95$, $p=0.36$) between the genders, however, men were expectedly heavier (71.6 ± 2.1 kg vs 61.3 ± 1.1 kg; $t(16)=4.37$, $p<0.001$) and taller (1.80 ± 0.02 m vs 1.69 ± 0.02 m; $t(16)=3.25$, $p=0.005$) than women. All participants were right-handed and had normal or corrected-to-normal vision (contact lenses, MR compatible glasses). Written consent was obtained prior to the study. The study was approved by the Ethics Committee of the Medical Faculty of the University of Tübingen.

2.2. Stimuli

Stimuli were selected from a database of different food stimuli of meals photographed in systematically varying portion sizes and on a standard background as described in Brunstrom and Rogers (2009). For the fMRI task, we selected 10 meals that are also common in Germany and used 10 pictures per meal showing different portion sizes, starting with a portion size of 100 kcal and increasing portion sizes in 100 kcal steps to 1000 kcal. For all rating tasks, the meals were presented in 500-kcal portions. The type and energy density of the meals are provided in Table S1.

2.3. fMRI Task

As described above, we used 10 different meals in 10 different portion sizes for the fMRI task. Each task block consisted of 30 trials, which started with the presentation of a randomly selected meal. For each meal, there were three trials in each task block, with an initial meal size once in the lower range of portion sizes, once in the middle and once in the upper range to control for anchoring effects.

In each trial, upon the initial meal presentation, participants were required to decide whether they wanted to increase or decrease the portion size (Figure 1). They were instructed to respond with their right thumb; pressing a right button increased the portion size and pressing a left button decreased the portion. The picture was shown until the participants responded, then the next bigger or smaller portion size was shown after presentation of an inter-stimulus fixation cross for a randomized time between 1 to 2 s.

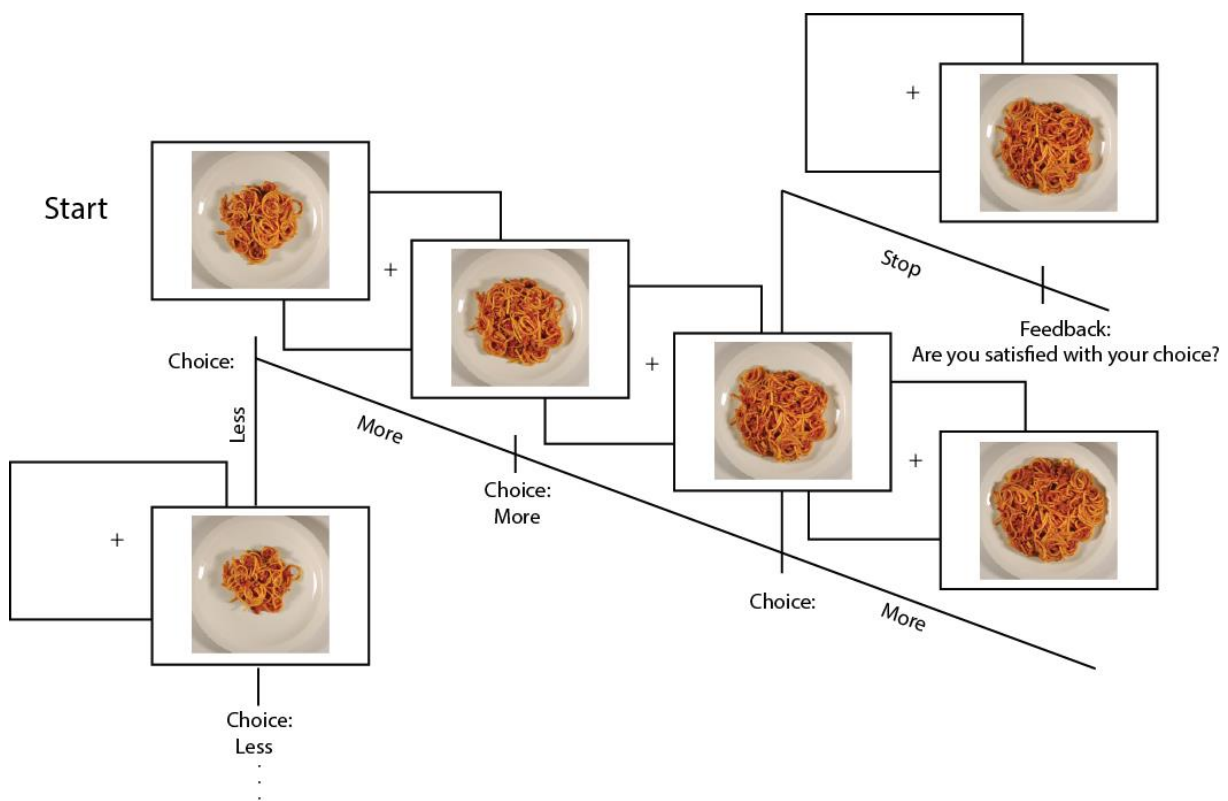


Figure 1 Illustration of the fMRI task in which participants had to select portion sizes which they wanted to consume for lunch for different meals. During the task, 10 different meals were presented.

After the initial decision to increase or decrease the portion size, participants were only allowed to go on in the same direction until they reached their desired portion size (pre decisions). Before selecting the final portion size, they were allowed to change directions once if needed. When they reached the desired portion size, participants confirmed their decision by pressing the middle button (final decision). The selected portion size was then shown again for 2s and participants were asked to indicate whether they were satisfied with their selection or not by using their right thumb to press an upper button for 'yes' and a lower button for 'no' (feedback). If the participants still wanted to increase or decrease when there was no bigger or smaller portion size, respectively, the last available portion size was shown again and they were also asked whether they were satisfied with it or not (feedback). For the final analysis, we only included final decisions with an active and satisfactory selection of a portion size (on average 28 out of 30 trials). Trials were separated by a fixation cross of random duration (uniform: 2-6 s; additionally we included 3 null events per task block of 12 s each).

As the task was mainly self-paced, some participants were faster than others to complete the requested 30 trials. Participants were allowed 10.5 min to complete the task. If they needed less time to complete the 30 trials, dummy trials were included until the end of the recording. These trials were not used for later behavioral analysis and only included as a regressor of no interest in the fMRI model (see fMRI data analysis). During scanning, stimuli were presented visually using Presentation® (Neurobehavioural Systems, Inc., Albany, CA.) and were displayed using a video projector that illuminates a rear projection screen at the end of the head-bore. Participants viewed the stimuli through an adjustable mirror attached to the head coil.

Each participant completed the task 4 times. Each time, they received a different instruction to induce a specific mindset. During each of the 4 task blocks, participants had to select for each meal the portion size that they wanted to eat for lunch that day. For the baseline condition, they would not receive any additional instruction. For the other three conditions, they were instructed to imagine selecting their portion sizes under certain considerations. To induce a pleasure

mindset, they were told to select a portion size that they would eat with pleasure, for the healthiness mindset if they were considering health aspects and for the fullness mindset if they were planning to be full until dinner. Except for the baseline condition, all other conditions were pseudo-randomized to avoid order effects. In addition, participants were informed that one of the trials from the baseline condition would be randomly chosen and that they would be served the meal of this trial in their selected portion size for lunch.

2.4. Study procedure

Participants were instructed to follow an overnight fast of at least 12 h and to have a normal breakfast between 7.30 and 8.00 am at home on the recording day, and then refrain from eating and drinking anything else except water until arriving in our lab at 10.30 am.

Before the fMRI scanning session, participants were familiarized with the experimental procedure and the associated stimuli. First, each meal (10 meals used for the fMRI task and 4 additional meals used for the training session) was displayed on a laptop. In order to familiarize themselves with the meals and respective portion sizes, participants were instructed to decrease and increase the portion sizes and to select the portion size that they wanted to consume right now. Secondly, they practiced the fMRI task with four additional meals not used for the task in the scanner. Finally, their weight and height was measured and they indicated their current hunger on a 10 cm visual analog scale (VAS; 0: not hungry at all, 10: very hungry).

The fMRI scanning session with the fMRI task as described above started at around 11.15 am and lasted for around 1.5 h. Participants then provided a blood sample for standard blood parameters and the determination of glucose and HbA1c levels. All of the participants had a glucose level of <100 mg/dl and a HbA1c level of <37 mmol/mol (<5,6%) indicating that they were moderately fasted and had no diabetes.

After the fMRI session, participants were asked to indicate the healthiness, tastiness, and expected satiation of each meal on a laptop, and they reported their current hunger again on the

VAS. Healthiness and tastiness were measured with a scale of 1-5 with 1 indicating very unhealthy/very bad taste and 5 indicating very healthy/very good taste for the 500 kcal portions. Expected satiation was measured according to Brunstrom and Rogers (2009). In this task, two meals, a standard and a comparison meal, were displayed in parallel on a laptop screen. The 'standard' meal was a 500 kcal portion size of Spaghetti Bolognese and was displayed on the left side of the screen. During each trial, a different 'comparison' meal was displayed on the right side and participants were asked to change the portion size of this meal by depressing the arrow keys on the keyboard. Participants were instructed to imagine having the meals for lunch and matching the meal size of the comparison to the standard meal until both meals would leave them equally satiated/would deliver equal satiation. This "method of adjustment" provides a "point of subjective equality." The point of subjective equality represents the amount of the comparison meal (i.e., energy) that is expected to be equally as satiating as the standard.

At around 1-1.15 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 baseline condition in the fMRI task. Due to organizational limitations, we chose to serve a specific meal to all participants and not as instructed a randomly picked meal. Participants were left alone to finish their meal for around 15 min (as long as they needed). They were again asked to report their current hunger and indicate whether the amount just eaten was a) too much, b) too little, c) about right, d) exactly right and whether the taste was a) very good, b) good, c) neutral, d) not good, e) not good at all.

To make the selection more realistic, participants had to stay in the lab for another hour. Over this period they completed several questionnaires. Finally, participants again indicated their current hunger and eating in the relative absence of hunger was assessed in an ad libitum snack test presented as a 'taste test' as described in Thienel et al. (Thienel, et al., 2016). This test will not be analyzed in the framework of this study. For an overview of the study procedure refer to Figure S1.

2.5. Behavioral analysis

Decision times were compared across mindsets by calculating mean reaction times for all decisions (pre and post) for each mindset and each participant separately and by entering them in a repeated measures ANOVA with the within factor mindset (4 levels: baseline, fullness, pleasure, healthiness). Post hoc tests were Bonferroni corrected.

The selected portion size of each meal for each participant was defined as the median of the responses (up to 3) of that meal per task block. As described in the participants section, two participants were excluded before analysis due to repeatedly wanting to select bigger portion sizes than available already in the baseline condition. If participants only wanted to select a bigger portion size for up to three meals in the fullness mindset (3 participants: 1x3 meals, 2x1 meal), they were included and the missing value for the portion size of that meal was replaced with the largest available amount of 1000 kcal.

For the investigation of the induced mindset effects, we averaged over the meals to obtain one value per participant and condition. The meal size selection was compared to the selection in baseline for each mindset separately in a repeated measures ANOVA with the within factor condition (2 levels: baseline, respective mindset) and the between factor gender (2 levels: men, women). Gender effects were further investigated with two-way independent t-tests to clarify directionality.

Investigation of the stimulus attribute integration was performed in two separate analyses. As a first step for both analyses, we calculated expected satiation values for each meal from the expected-satiation-task in which participants matched the size (in kcal) of a ‘comparison’ to the ‘standard’ meal for delivering equal satiation as described above. Expected satiation was defined as the ‘satiation ratio’ for each meal derived by dividing the size of the ‘standard’ (500 kcal) by the size of the selected ‘comparison’ meal (in kcal) (the satiation ratio of the standard was recorded as 1).

Next, we analyzed associations between portion size selection in the baseline condition, energy density, expected satiation, tastiness and healthiness ratings on a group average level with bivariate correlations. We transformed each participant's data into a set of Z scores to control for differences in the average response between participants. For each measure and test meal, we then calculated a mean Z score. Two-sided Pearson correlations were then calculated to assess the relationship between the measures.

Finally, we used multilevel linear modeling to account for individual differences in the investigation of the influence of the meal related ratings on portion sizes during the different mindsets. Multilevel linear modeling was used as meals and ratings were nested within participants (multiple observation and non-independence between participants). We calculated two kind of models. In these models, portion sizes were the level 1 units of analysis, and participants the level 2 units of analysis. First, we were interested in the overall effect of each rating and whether there was an interaction effect between ratings and mindset conditions. We calculated one full model including all mean-centered ratings (expected satiation, tastiness and healthiness), the mindset conditions and the interactions between the ratings and the mindset conditions as level 1 factors. Secondly, for better visualization of the different rating and mindset effects, we additionally calculated separate models for each rating (healthiness, tastiness, expected satiation) and each mindset including only the ratings as level 1 factors. In all models, we allowed random intercepts to account for individual differences in mean portion size selection. Parameters were estimated using maximum likelihood criteria.

Behavioral data was analyzed with the software package SPSS 22.0 (SPSS Inc., Illinois; USA). All data are presented as unadjusted mean \pm standard error of the mean. P-values < 0.05 were considered significant.

2.6. fMRI data acquisition and preprocessing

Whole brain fMRI data were obtained by using a 3.0 T scanner (Siemens MAGNETOM Prisma, Erlangen, Germany) equipped with a 20 channel head coil. Each block consisted of 312 scans (repetition time = 2 s, echo time = 30 ms, matrix 64 x 64, flip angle 90°, voxel size 3 x 3 x 3 mm³, 30 slices), and the images were acquired in ascending order. Furthermore, a high-resolution T1-weighted anatomical image (magnetization-prepared rapid gradient echo (MPRage): 176 slices, matrix 256 x 256, 1 x 1 x 1 mm³) of the brain was obtained. In addition, we acquired a static field map to unwarp geometrically distorted functional scans. Participants were scanned while lying in a supine position with their head stabilized by foam padding around their head within the head coil. In addition, we acquired a resting state and diffusion tensor imaging (DTI) measurement, which are not analyzed in the framework of this study.

Preprocessing and statistical analysis of the fMRI data were performed using SPM12 (Wellcome Trust Centre for Neuroimaging, London, UK). Images were realigned and resliced to the first image. Unwarping in the phase-encoding direction (anterior-posterior) was performed using the pre-calculated voxel displacement map. A mean image was created and co-registered to the T1 structural image. The anatomical image was normalized to Montreal Neurological Institute (MNI) space using the segmentation approach. The resulting forward deformation fields were used to normalize the functional images (voxel size 3 x 3 x 3 mm³). Finally, the normalized images were smoothed with a 3-dimensional isotropic Gaussian kernel [full width at half maximum (FWHM): 9 mm]. fMRI data were highpass filtered (cutoff period 128s) and global AR(1) auto correlation correction was performed.

2.7. fMRI data analysis

fMRI data were analyzed in an event-related design using the general linear model (GLM) approach in a two-level procedure. On the first level in the single participant models, responses to stimuli were modeled as events and convolved with a canonical hemodynamic response

function composed of two gamma functions (Friston, et al., 1998). The temporal derivatives were used as an additional regressor to capture possible differences in the latency of the peak amplitude of the blood oxygenation level-dependent (BOLD) signal. To account for variance caused by head movement, six realignment parameters were included as additional regressors in the model.

The data from each participant were analyzed by using linear regression between the observed event-related EPI signals and 4 regressors with an indicator for the individual trial events with a duration equal to the stimulus presentation (pre decisions (increase/decrease), final decisions (final selection of portion size), feedback trials and a regressor of no interest including the dummy trials and those decisions with which the participants were not satisfied). The individual contrast images from each participants (final decision: final decision vs pre decisions of all sessions, fullness: final decisions during fullness mindset vs baseline condition, pleasure: final decisions of pleasure mindset vs baseline condition, healthiness: final decisions of healthiness mindset vs baseline condition) were then entered into separate second level analyses using one-sample t-tests. Effects were considered 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 for multiple comparisons (Woo, Krishnan, & Wager, 2014). In addition, we performed region of interest (ROI) analysis with a statistical threshold $p < 0.001$ (initial threshold) and FWE correction of $p < 0.05$ at peak level over the ROI volume (i.e., small volume correction). Results with a statistical threshold of $p < 0.1$ FWE corrected at peak level over the ROI volume will be reported as significant on trend level. ROIs were constructed with the WFU Pickatlas (v3.1) (Maldjian, Laurienti, & Burdette, 2004; Maldjian, Laurienti, Kraft, & Burdette, 2003). For the healthiness mindset, we selected a functional ROI of left DLPFC based on Hare et al. (Hare, et al., 2009) (sphere of 10 mm with MNI center coordinates: -48 15 24). One participant was identified as an outlier and excluded from the analysis for this contrast (more than 3 standard deviations apart from the mean). For the pleasure and fullness mindset, we selected anatomical

ROIs based on the aal atlas (Tzourio-Mazoyer, et al., 2002) implemented in the WFU Pickatlas. For the fullness mindset, we selected left and right insula. For the OFC in the pleasure mindset, we selected left and right inferior orbital frontal gyrus as an ROI. This was based on the description of spatially distinct subregions of the OFC and our expectation of changes in the processing of pleasure (for reviews refer to Kringelbach (2005); Rolls (2015); Rushworth, Noonan, Boorman, Walton, and Behrens (2011); Zald (2009)).

In addition, we performed a psychophysiological interaction (PPI) analysis to examine whether the left DLPFC, OFC and insula showed an increase in functional connectivity with other brain regions and in particular the vmPFC during final decisions in the respective mindset compared to the baseline condition. A detailed description of the analysis is provided in the Supplementary.

Additional exploratory analyses of parametric modulation of brain activity by behavioral ratings and correlations between mindset specific brain activity and changes in portion size selection are described in the Supplementary only.

3. Results

3.1. Behavioral Results

Participants spent on average 1.13 ± 0.08 s on a decision with final decisions taking longer than pre decisions (1.37 ± 0.11 s vs 1.05 ± 0.07 s; $t(17)=5.45$, $p<0.001$). Furthermore, decision times were significantly different between mindset conditions $F(3,51)=5.68$, $p=0.002$ (baseline: 1.29 ± 0.09 s, fullness: 1.05 ± 0.10 s, pleasure: 1.11 ± 0.09 s, healthiness: 1.10 ± 0.07 s). Planned Post hoc tests revealed that this was due to significantly longer reaction times in the baseline condition only.

Mindset induced changes on portion size selection

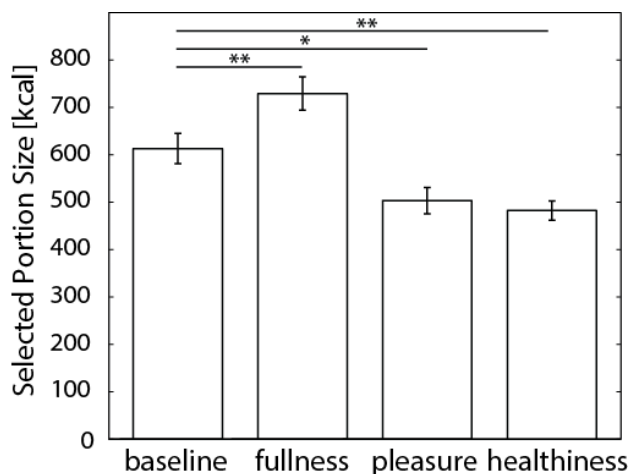


Figure 2 Selected portion size in kcal as a function of the different experimental manipulations. Shown is the mean (averaged over meals and participants) with standard error. Comparison against the baseline condition revealed significant mindset effects in portion size selection; * $p<0.01$, ** $p<0.001$.

We observed a significant main effect of condition for all three induced mindsets (fullness: $F(1,16)=35.18$, $p<0.001$; pleasure: $F(1,16)=11.31$, $p=0.004$; healthiness: $F(1,16)=71.06$, $p<0.001$). Whereas participants selected significant larger portion sizes during the fullness mindset, they reduced their portion sizes in the pleasure and healthiness mindset in comparison to the baseline condition (Figure 2). Furthermore, we observed a significant main effect of gender for all three mindsets (fullness: $F(1,16)=16.33$, $p=0.001$; pleasure: $F(1,16)=7.60$,

$p=0.014$; healthiness: $F(1,16)=12.09$, $p=0.003$) and a significant interaction between condition and gender for the pleasure ($F(1,16)=6.05$, $p=0.026$) and the healthiness mindset ($F(1,16)=13.20$, $p=0.002$). Figure S2 shows that male participants selected significantly larger portion sizes in the baseline ($t(16)=4.17$, $p=0.001$) and the fullness mindset ($t(16)=3.40$, $p=0.004$) compared with the female participants and on trend level in the healthiness ($t(16)=2.11$, $p=0.051$), but not in the pleasure mindset ($t(16)=0.53$, $p=0.61$). More specifically, Figure S2 shows that the decrease in portion size selection between baseline and respective mindset condition was stronger in male participants in the pleasure ($t(16)=-2.46$, $p=0.026$) and in the healthiness mindset ($t(16)=-3.63$, $p=0.002$), but not in the fullness mindset ($t(16)=-0.06$, $p=0.96$).

Average expected satiation, energy density and ideal portion size selection during baseline condition on group average level using bivariate correlations

As expected and reported previously (Brunstrom & Rogers, 2009), higher energy density of a meal was associated with lower expected satiation (Figure S3; $r=-0.821$, $p=0.004$). In addition, expected satiation was also related to the portion sizes of the meals selected in the baseline condition (Figure S3; $r=-0.812$, $p=0.004$). Finally, portion size selection during baseline condition was neither significantly related to tastiness ratings ($r=0.554$, $p=0.097$), nor healthiness ratings ($r=-0.297$, $p=0.405$).

Multilevel linear modeling to account for individual variability

The multilevel linear model including the mindset condition, all three ratings and the interactions between the ratings and the mindset condition showed a main effect of condition on portion size selection ($F(3,701.96)=132.12$, $p<0.001$). In addition, expected satiation rating ($F(1,710.02)=121.54$, $p<0.001$) and tastiness rating ($F(1,709.93)=51.08$, $p<0.001$) showed a main effect of rating, whereas healthiness rating did not ($F(1,708.57)=2.10$, $p=0.148$). Main effects of mindset condition and ratings were modulated by the interaction between these two

factors for the healthiness rating ($F(3,701.96)=6.93$, $p<0.001$) and the tastiness rating ($F(3,701.96)=3.54$, $p=0.014$), but not the expected satiation rating ($F(3,701.96)=1.51$, $p=0.211$). Details of the interaction effects are summarized in Table S2. The interaction effect for the tastiness ratings seemed to be modulated by a reduced influence on portion size selection in the fullness and healthiness mindset and an increased influence in the tastiness mindset, although not significant, in comparison to the baseline condition. Finally, healthiness ratings showed a significantly increased modulation in the healthiness, but not in the other mindsets.

For better visualization of the different rating and mindset effects, , we additionally calculated separate models for all four mindset conditions and ratings, which are summarized in Table S3. Expected satiation showed a significant negative and tastiness ratings a significant positive effect on meal size selection in all four mindsets. Similar to the interaction effects in the full model as reported above, tastiness ratings seemed to show an increased influence on portion size selection in the tastiness mindset and a reduced influence in the fullness and healthiness mindset in comparison to the baseline condition. Finally, also in accordance with the full model, healthiness ratings only showed a significant positive effect on portion size selection in the healthiness, but not in the other mindsets.

3.2. Imaging Results

Final Decision

When participants decided to finally select a portion size in comparison to decisions to further increase or decrease a portion size, we observed an increased response in clusters including the anterior cingulate cortex (ACC) and the left pre- and postcentral gyri (Table 1, Figure 3a).

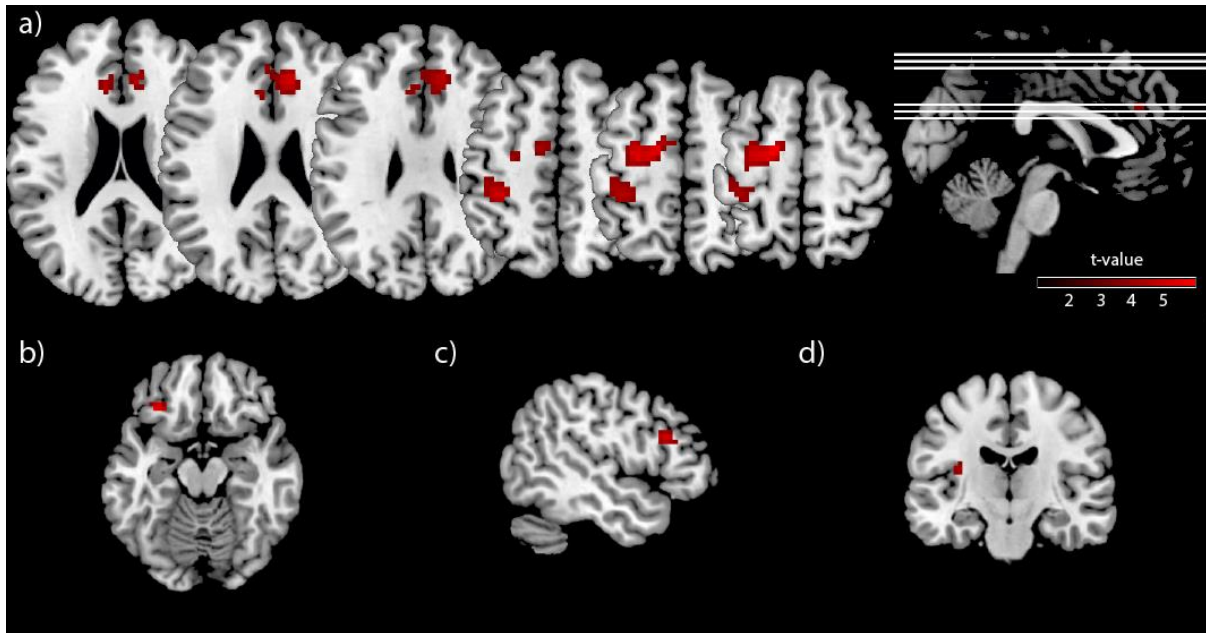


Figure 3 Brain areas associated with the final selection of a portion size and mindset induced changes in brain activity in comparison to baseline. (a) Shown are significant clusters with increased activity for the final decision to select a portion size in comparison to pre decisions to increase or decrease a portion size combined for all conditions;, (b) Selecting a portion size if eating with pleasure was associated with an increased response in left OFC, (c) if eating in consideration of health aspects with left DLPFC and (d) if eating to be full until dinner with left insula. (a: $p < 0.05$ FWE corrected, b,c,d: a moderate threshold of $p < 0.001$ uncorrected was chosen for display).

Table 1 Clusters of significant activations for final portion size selection and mindsets

Brain Region	Side	Coordinates			Cluster size (in voxels)	Z	P value (FWE corr.)
		x	y	z			
Final selection of Portion Size							
Precentral							
gyrus/Supplementary motor area	L	-15	-7	62	183	4.38	0.002
Postcentral gyrus	L	-36	-34	50	107	3.95	0.019
Anterior cingulate cortex	R	9	35	26	124	3.94	0.010
Healthiness Mindset							
Inferior frontal gyrus	L	-51	20	23	27	3.89	0.004*
Pleasure Mindset							
Inferior orbital frontal gyrus	L	-33	29	-16	14	4.05	0.013*
Fullness Mindset							
Insula	L	-33	-16	17	5	3.49	0.089*

*ROI analysis

To test for the different mindsets in comparison to the baseline condition, we focused the analysis on these final decisions and contrasted these between the different mindsets and the baseline condition. For all of the mindset contrasts we did not observe any activation significant on whole brain level corrected for multiple comparisons. Results of the ROI analysis are reported below.

Pleasure mindset

When the participants were instructed to select a portion size if planning to eat with pleasure, increased activity in left OFC was observed (Table 1, Figure 3b).

Healthiness mindset

Implementing self-control during the healthiness mindset was associated with increased activity in left DLPFC (Table 1, Figure 3c).

Fullness mindset

Finally, when the participants were planning to eat to be full until dinner, they showed on trend level an increased response in a cluster in left posterior insula (Table 1, Figure 3d).

In order to evaluate the mindset specificity of the ROIs, we also report all ROI masked activations above a significance threshold of $p < 0.001$ uncorrected in all three mindsets in Table S3. At this statistical threshold, only the left posterior insula also showed significant activations not only in the fullness, but also for the pleasure and healthiness mindset. Left DLPFC and OFC were only significant in the healthiness and pleasure mindset, respectively.

Psychophysiological Interactions

We did not observe an increase/decrease in functional connectivity between left DLPFC, OFC and insula activity during the final decision when comparing the respective mindsets and the baseline conditions in any brain region significant on whole brain level corrected for multiple comparisons, nor for the ROI analysis in vmPFC.

4. Discussion

When we make decisions about food, different attributes like tastiness or healthiness have to be integrated to select an action. In the current study, we showed that not only choices between food items, but also portion size selection during pre-meal planning was dependent on the mindset of the individual at the time of choice, which was associated with specific neural processes. For the investigated mindsets pleasure, healthiness, and fullness we observed increased activity in OFC, DLPFC, and on trend level in insula, respectively. We further observed that, although expected satiation was an important predictor for selected portion sizes, in consideration of individual variability and mindset condition also tastiness and healthiness ratings had a significant impact on portion size selection. Finally, we observed that the mindset effects might be gender specific.

When testing for bivariate correlations on group average level, expected satiation was related to the energy density of a meal and it was a strong predictor of portion size selection in the baseline condition, whereas tastiness and healthiness ratings were not. In line with the findings of Brunstrom and Rogers (2009), participants underestimated the caloric content of meals with higher energy density resulting in lower expected satiation and selection of larger portion sizes calorie wise of these meals. To better account for inter-individual variability, we further investigated the influence of expected satiation, tastiness and healthiness ratings on portion size selection in the different mindsets (baseline, fullness, pleasure, healthiness) using multilevel linear modeling. Expected satiation was again a strong predictor for meal size selection in all four mindsets. However, now also tastiness ratings showed a significant contribution to portion size selection. Furthermore, results indicated that the strength of the tastiness ratings as a portion size predictor was mindset dependent. Finally, for healthiness ratings this effect was significant due to healthiness ratings only showing a significant contribution to portion size selection in the healthiness mindset. These results suggest that during pre-meal planning,

different attributes of the meals were integrated to form a decision and that the integration might be mindset dependent and thus, be associated with the observed mindset induced changes in portion size selection.

First and foremost, meal size selection is, however, still determined by individual energy requirements and energy intakes vary with body size. Consequently, we observed that taller/heavier men selected larger portion sizes than smaller women in the baseline and fullness condition. Satiating signals arise from multiple sites in the gastro-intestinal system to prevent overconsumption during individual meals and thus, to achieve efficient nutrient digestion and absorption (Cummings & Overduin, 2007; Woods, 1991). Although one of the key satiation mechanisms is gastric distension, meal sizes are usually considerably smaller than the maximal gastric capacity (Cummings & Overduin, 2007). In our study, participants selected significantly smaller portion sizes in the baseline condition compared to the fullness condition in which the time until the next meal was fixed to dinner time. Thus, when expecting freedom to choose the time interval until the next meal, it seemed that participants might have chosen to be comfortably satiated rather than to eat as much as possible. Furthermore, during baseline decisions they might have considered additional factors like palatability and chose to eat meals that are less liked in smaller portion sizes, whereas in the fullness condition the main goal was to be full for a long predefined time. This was supported by the observation that tastiness ratings had a slightly although only significant on trend level reduced influence on portion size selection in the fullness mindset.

From a neural perspective, eating to be full until dinner was associated with increased activity in left posterior insula on trend level. Among various other functions, the insula is a key area for the integration of various internal (interoceptive) and external (exteroceptive) stimuli. In particular, the more posterior regions process somatic and visceral sensations of the body (Avery, et al., 2017; Craig, 2003), which suggests a role in the perception of fullness (produced

by gastric distention). Activity in posterior insula has been reported to be increased during satiation in response to food images (Thomas, et al., 2015) and during gastric distention without food intake (Wang, et al., 2008). Therefore, the increased activity in left posterior insula during the fullness mindset might be related to interoceptive processes. At first thought, participants might have tried to estimate their ideal portion size to reach long-term satiety without overstraining their gastric distention capability. Then again, we also observed increased left posterior insula activity in comparison to baseline in the healthiness and pleasure mindset in nearby clusters. Baseline and mindset conditions were not only different in the respective mindset, but also in the sense that it was ‘real’, highly practiced decisions versus ‘hypothetical’ decisions in an imagined context. Considering this, increased activity in left posterior insula might be related to a more general process of interoceptive estimation of satisfying meal sizes given specific hypothetical requirements.

During the healthiness mindset, participants selected significantly smaller portion sizes in comparison to the baseline condition. In addition, portion size selection was associated with the healthiness rating of a meal. This suggests that participants were considering the health aspects of the meals more strongly and trying to adjust their portion sizes accordingly. Considering and basing food decisions on health aspects is often referred to as choosing an option that reduces immediate reward outcome in favor of more advantageous long-term consequences. The associated concept of self-control has been reported previously to be important for making healthy food choices and to be negatively associated with body weight (Gunstad, et al., 2007; Weller, Cook, Avsar, & Cox, 2008). A crucial brain area for the implementation of cognitive control in general is the prefrontal cortex (Jurado & Rosselli, 2007; Miller & Cohen, 2001) with the DLPFC being particularly important for exerting self-control (Hare, et al., 2009; Hollmann, et al., 2012; Spetter, et al., 2017). Importantly, disruptions of the activity in left DLPFC by repetitive transcranial magnetic stimulation during intertemporal choice leads to increased

choices of immediate rewards over larger delayed ones (Figner, et al., 2010). In agreement with this finding, we observed increased activity in left DLPFC when participants were instructed to particularly consider health aspects, which generally have a delayed impact. These results suggest that increased self-control reflected in increased left DLPFC activity might have led to the increased integration of health aspects into the decision and the selection of smaller portion sizes.

Finally, participants also selected significantly smaller portion sizes when they were planning to eat with pleasure in comparison to the baseline choice. However, in this context it should be considered that the baseline condition is not mindset free, but is dependent on the general eating behavior of the participants. Thus, a reduction in the portion size might be specific to our normal-weight study population and might actually be in the opposite direction in a dieting overweight population, whose eating behavior is characterized by trying to restrict their food intake.

When making decisions for pleasure, one would assume activity changes in brain areas associated with the processing of the pleasurable aspects of eating. Consequently, we observed increased activity in left OFC during the pleasure mindset compared with baseline decisions. In several studies it was shown that activations in OFC, close to the observed cluster in our study, were correlated with the subjective pleasantness of food and decreased to a particular food when it was eaten to satiety (sensory-specific satiety) (Gottfried, O'Doherty, & Dolan, 2003; Grabenhorst, Rolls, Parris, & d'Souza, 2010; Kringelbach, O'Doherty, Rolls, & Andrews, 2003; Small, Zatorre, Dagher, Evans, & Jones-Gotman, 2001).

Interestingly, mostly men (8 out of 9) showed a reduction in portion size during the pleasure mindset, whereas 5 out of 9 women showed an increase instead. We also observed a gender specific effect for the healthiness mindset, men showed a stronger reduction in portion size than women. Several studies report that women are generally more concerned with weight control

and health aspects during their food decisions (Wardle, et al., 2004; Westenhoefer, 2005). Our results might suggest that women making baseline decisions already put more weight on pleasure and health aspects, and restricted their food intake, whereas young men prioritized satiation.

Changes in behavior indicated that mindsets are important for stimulus attribute integration and option selection during pre-meal planning. From a neural perspective, the vmPFC is a major area involved in the decision related computation of reward values by integrating different attributes (Bartra, et al., 2013; Clithero & Rangel, 2014). Changes in subjective value computation have been suggested to be related to increased modulation of vmPFC activity by left DLPFC during self-control when making decisions between different foods (Hare, et al., 2009; Hare, Malmaud, et al., 2011). Consequently, we hypothesized increased coupling between observed mindset specific brain areas and the vmPFC in the respective mindset in comparison to baseline. In the current study, PPI failed to reveal any significant mindset specific increase in coupling with vmPFC, which might, however, be due to several reasons. From a methodological point of view, PPI analyses tend to lack power and hence a high proportion of false negatives should be expected particularly in an event-related design (O'Reilly, Woolrich, Behrens, Smith, & Johansen-Berg, 2012). Furthermore, modulation might not be by direct connectivity but by one or several intermediate brain regions. Finally, it might be due to the nature of the task itself. Instead of one single decision per food item, our task design included sequential decisions possibly diluting decision related activity. Thus, investigation of connectivity during pre-meal planning should be postponed to future more specifically designed studies.

Decision making processes in general do not end with the selection of an option. Rather, choices also have to be implemented by activating the necessary motor response and then taking an action. Thus, the computed stimulus values have to be compared to make a choice, which has

to be transmitted to the motor system. It has been suggested that the medial PFC/ACC plays an important role in this action-stimulus association (Hare, Schultz, Camerer, O'Doherty, & Rangel, 2011; Rudebeck, et al., 2008); for review: Rushworth, et al. (2011);Zald (2009)). This hypothesis is supported by the described anatomical connections of the rostral cingulate motor area to primary motor cortex, several premotor areas and to the ventral horn of the spinal cord (Morecraft & Tanji, 2009; Van Hoesen, Morecraft, & Vogt, 1993). Among others, ACC is considered to be particularly involved in behavioral change and update (reviews: Alexander and Brown (2011); Kolling, et al. (2016)). This fits with our results, which show increased ACC activity when a change in response is requested for the final selection of a portion size in comparison to portion size increases or decreases. Increased activity in left motor and somatosensory cortices were probably also related to the implementation of the changed motor response as participants responded with their right hand.

A possible limitation of our study design is that mindsets were not completely randomized. Always executing the baseline condition first resulted in an order effect as indicated by slower reaction times in this condition. However, this limitation was necessary to exclude possible mindset induced effects on the baseline condition. As we observed expected mindset specific changes in brain activity (except for the insula, reported ROIs only showed a significant effect in their respective mindset contrast and not in the other contrasts), we assume that our results are not just due to an order effect. Furthermore, we would like to point out that baseline and mindset conditions not only differed in order and in mindset instruction itself, but also in their setting of 'real' versus 'hypothetical'. We chose this setup to boost the mindset effects, however, it might be different from pre-meal planning in a real world setting. In addition, it is the case that our study design has limited power to decipher whether the observed effects, in particular related to gender, are due to baseline differences or due to differences in their susceptibility to the mindset inductions. Investigation of larger cohorts in future studies that

also include overweight and obese people will contribute additional information to the understanding of pre-meal planning.

In conclusion, we provide evidence that not only choices between food items, but also portion size selection during pre-meal planning is dependent on the mindset of the individual at the time of choice. Changing the focus during pre-meal planning was associated with activity changes in certain brain areas and changes in attribute integration resulting in an increase or decrease of selected portion sizes. Given the observed influence of attentional focus on meal size selection, the *per se* cognitive process of pre-meal planning would appear to provide a key opportunity to influence the control of portion size selection by mindset manipulation.

5. Conflict of interest

Conflicts of interest: none.

6. Acknowledgments

We thank Maïke Borutta for her assistance during the measurements. This work was supported by the European Union Seventh Framework Programme (FP7/2007-2013) under Grant Agreement 607310 (Nudge-it), a grant (01GI0925) from the Federal Ministry of Education and Research (BMBF) to the German Center for Diabetes Research (DZD e.V.) and the Helmholtz Alliance ICEMED-Imaging and Curing Environmental Metabolic Diseases.

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Figure captions

Figure 1 Illustration of the fMRI task in which participants had to select portion sizes which they wanted to consume for lunch for different meals.

Figure 2 Selected portion size in kcal as a function of the different experimental manipulations. Shown is the mean (averaged over meals and participants) with standard error. Comparison against the baseline condition revealed significant mindset effects in portion size selection; * $p < 0.01$, ** $p < 0.001$.

Figure 3 Brain areas associated with the final selection of a portion size and mindset induced changes in brain activity in comparison to baseline. (a) Shown are significant clusters with increased activity for the final decision to select a portion size in comparison to pre decisions to increase or decrease a portion size combined for all conditions. (b) Selecting a portion size if eating with pleasure was associated with an increased response in left OFC, (c) if eating in consideration of health aspects with left DLPFC and (d) if eating to be full until dinner with left insula. (a: $p < 0.05$ FWE corrected, b,c,d: a moderate threshold of $p < 0.001$ uncorrected was chosen for display).