Neural Mechanisms Associated With Food Motivation in Obese and Healthy Weight Adults

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One out of three adults in the United States is clinically obese. Excess food intake is associated with food motivation, which has been found to be higher in obese compared to healthy weight (HW) individuals. Little is known, however, regarding the neural mechanisms associated with food motivation in obese compared to HW adults. The current study used functional magnetic resonance imaging (fMRI) to examine changes in the hemodynamic response in obese and HW adults while they viewed food and nonfood images in premeal and postmeal states. During the premeal condition, obese participants showed increased activation, compared to HW participants, in anterior cingulate cortex (ACC) and medial prefrontal cortex (MPFC). Moreover, in the obese group, self-report measures of disinhibition were negatively correlated with premeal ACC activations and self-report measures of hunger were positively correlated with premeal MPFC activations. During the postmeal condition, obese participants also showed greater activation than HW participants in the MPFC. These results indicate that brain function associated with food motivation differs in obese and HW adults and may have implications for understanding brain mechanisms contributing to overeating and obesity, and variability in response to diet interventions.


INTRODUCTION

One-third of the US population is clinically obese (BMI ≥30 kg/m²) (1), a condition associated with increased morbidity and health-care costs (2). Although the origins of this problem are complex, caloric intake in excess of expenditure is the primary cause of weight gain. Food intake is influenced by a convergence of processes in the brain, including homeostatic mechanisms, motivation, cognitive control, and decision making (3). Research has shown that obese individuals find food more reinforcing compared to healthy weight (HW) individuals (4,5). The motivational value of food can be measured by determining the extent to which an individual will work to obtain food (3) and is influenced by a variety of factors including food composition (6,7) and hunger (3).

In experimental settings, obese individuals show increased food motivation, compared to HW individuals, by working more for food rewards than nonfood rewards (4) and by consuming more food in laboratory settings than individuals who demonstrate lower levels of food motivation (4,8). In addition, obese individuals, compared to overweight and HW individuals, report higher levels of eating disinhibition (release of control under emotional or situational triggers), and hunger (feeling hunger and its relationship to eating) (10).

Functional neuroimaging studies are beginning to examine brain mechanisms underlying food motivation. Positron emission tomography studies in HW adults, examining brain activations during food consumption, show changes in regional cerebral blood flow (rCBF) in prefrontal regions, including ventromedial prefrontal cortex (PFC), as well as insular cortical regions (11–15). In these studies, researchers manipulated food motivation by increasing participant hunger through fasting (4.5–36 h) and measuring responses to a liquid meal (11–13,15) or chocolate (14). rCBF increased during hungry states in the hypothalamus, insula, and the orbitofrontal cortex (11,14,15). Meal consumption was associated with increased rCBF in prefrontal regions such as the ventromedial PFC (11,13,15). It should be noted that re-analysis of rCBF results (11,13,15) using a random effects as oppose to fixed effects analysis revealed decreases rather than increases in dorsolateral prefrontal regions (16,17).

Functional magnetic resonance imaging (fMRI) studies show that viewing photographs of food when hungry elicits activation of food motivation brain regions such as the PFC, eating disinhibition (release of control under emotional or situational triggers), and hunger (feeling hunger and its relationship to eating) (10).
orbitofrontal cortex (OFC), amygdala, and paralimbic regions (6,7,18–23) and manipulating food motivation by varying calorie content of food images is associated with fMRI activations in regions of the medial and dorsolateral PFC to high-calorie foods and activations in the OFC to low-calorie food (6). Similarly, manipulating food motivation by examining responses in premeal and postmeal states is associated with increased fMRI activations in the amygdala, insula, and OFC, particularly when participants are hungry (20,21,23).

Findings in HW adults imply that abnormal activity in these networks may be associated with overeating and obesity. Initial structural MRI studies in obese and HW groups show anatomical differences, including lower gray matter density in brain regions associated with cognitive control and motivation among obese participants (24). Obesity has also been associated with lower levels of striatal dopamine receptor availability, which modulates neural systems of motivation (25). As in HW adults, obese individuals show increases in rCBF in PFC regions in response to liquid meals following a 36-h fast; however, these changes are greater in obese individuals compared to HW individuals (12,13). Moreover, obese men show less activation in the left dorsolateral PFC following a liquid meal regardless of meal size (16) and obese women show less activation in the left dorsolateral PFC postmeal compared to formerly obese and lean women (17).

Few studies have investigated the neural systems associated with food motivation in otherwise healthy obese individuals, and most of these studies have only examined food motivation in obese women (not men). Rothemund et al. (7) studied brain systems associated with food motivation in obese women by examining fMRI activations associated with viewing high- and low-calorie food images. All participants were scanned ~1.5 h after eating to control hunger levels, which could influence the motivational value of food. Women viewed images of high- and low-calorie foods, and the obese group showed enhanced activation to high-calorie food images in dorsal striatal regions compared to HW women. Furthermore, BMI predicted activation of OFC and insula regions. Similarly, Stoeckel et al. (26) found greater activation in limbic and paralimbic cortex, including OFC, amygdala, ventral striatum, MPFC, and anterior cingulate cortex (ACC), when comparing fMRI signal in obese and HW women as they viewed high- and low-calorie food images following an 8–9-h fast. Moreover, Geliebter et al. (27) found that obese binge eaters showed activation in premotor areas possibly due to motor planning when looking at binge foods. Together these studies demonstrate unique patterns of brain activation in obese compared to HW individuals when food motivation is manipulated by varying food content.

The current study extends previous fMRI studies of food motivation in obesity by examining brain responses while participants view food images before and after eating a meal. Although previous positron emission tomography studies examined food motivation by measuring changes in rCBF following a 36-h fast and after consuming a liquid meal, the current study used an ecologically valid feeding schedule in which participants fasted for 4 h and then ate a 500-kcal meal. Due to increased levels of food motivation in obesity, we hypothesized that obese participants would show greater activations compared to HW participants in prefrontal, limbic, and paralimbic regions, in both pre- and postmeal states.

**METHODS AND PROCEDURES**

**Participants**
The University of Kansas Medical Center Human Subjects Committee approved the current study and informed consent was obtained for 10 obese adults (mean BMI = 34.0, range = 30.2–38.1 kg/m²) and 10 HW adults (mean BMI = 22.1, range = 19.5–24.7 kg/m²). Each group was comprised of five female and five male participants and all participants were right-handed. Groups were matched for age (P = 0.51) and years of education (P = 0.83). Exclusion criteria for both groups included: current or recent efforts to lose weight, serious medical illness unsuitable for the magnetic resonance scanner based on best clinical judgment, any neurologic or psychiatric disorder (including animal phobia), diabetes, known heart disease, high blood pressure, any thyroid condition, significant visual impairment, current psychotropic or cardiovascular medication use, and any history of alcohol or other substance dependence or current abuse. Due to the physical dimensions of the MRI scanner, obese participants with a BMI >40 were excluded.

**Self-report scales**
All participants completed part II of the EI (10). Stunkard’s EI is the most commonly used measure of eating behavior and assesses dietary restraint (conscious effort to restrict food intake), disinhibition (degree of interference with controlled eating from emotional and situational influences), and hunger (perceptions of hunger and its relationship to overeating).

**Experimental paradigm**
The experimental paradigm has been previously published (19,20,28) and was based closely on LaBar et al. (21). Participants viewed pictures of food, animals, and Gaussian-blurred low-level baseline images during two scanning sessions: (i) after fasting for 4 h (premeal) and (ii) immediately after eating a small uniform meal (postmeal) that was standardized for energy (kcal = 500) and micronutrient content (e.g., a weighed turkey or ham sandwich, carrot sticks, a piece of fruit, and skim milk). Previous neuroimaging studies examining food motivation have included a longer fasting period (typically 8h) and utilized meals designed to fully satiate participants (21,22). Our goal was to design a paradigm that reflects typical daily hunger and eating cycles. Accordingly, our paradigm implemented a 4-h fast and a meal standardized to provide ~500 kcal. The current design has shown significant differences in brain responses between premeal and postmeal conditions (19,20,28). In order to minimize confounds associated with novelty during the first scan, the order of sessions was counterbalanced across subjects so that half the group started with the premeal condition and half started with the postmeal condition. The paradigm was designed to reflect typical daily hunger and eating cycles. All participants were scanned during lunch hours. Breakfasts on the day of scanning were not standardized for macro- and micronutrient content; however, participants were instructed to consume a typical breakfast on the day of scanning 4h before the scanning session and to eat nothing after that time.

Stimuli from two categories (food and blurred baseline images) were obtained from LaBar et al. (21). Our paradigm used animals as control stimuli, rather than tools as used by LaBar et al., in order to control for general interest and visual richness. All images for the animal category were obtained from professional stock CD-ROMs and matched to food and blurred baseline images on brightness, resolution, and size. In addition, by applying a Gaussian kernel to a subset of the animal images (so that the objects were not identifiable) –150 blurred baseline images
were obtained. To the greatest degree possible, animals that were reminiscent of food (i.e., fish) were removed from the stimuli pool to prevent the possible confusion between animal/food categorizations. Each image was presented once to subjects.

Each functional scan involved three blocks of each stimulus condition type (i.e., food, animal), alternated between blocks of blurred images. Two functional scans were completed during each scanning session (premeal, postmeal). Within each functional scan there were 13 blocks of stimuli presentation; each block contained 10 images. The order of category presentation was counterbalanced across subjects. Visual stimuli were projected through two-dimensional limited view goggles (Resonance Technology, Northridge, CA) by the stimuli-generating computer program (NeuroSTIM; Neuroscan, El Paso, TX). Stimulus presentation time was 2.5 s, with an interstimulus interval of 0.5 s.

Recognition memory for the presented images was tested following the scanning sessions. All of the food and animal images used in the scanning session (60 images) were presented for recall (old) and interspersed with 15 novel distractor images from the same category (new). Participants completed the recognition memory task outside the scanner immediately following each scanning session. Participants were instructed to press one key if they had seen the image in the scanner (old), and another key if they had not seen the image (new).

**fMRI methods**

*Image acquisition.* Scanning was performed on a 3 T head-only Siemens Allegra scanner (Siemens, Erlangen, Germany) fitted with a quadrature head coil. Participants’ heads were immobilized with head cushions. Following automated scout image acquisition and shimming procedures performed to optimize field homogeneity, a structural scan was completed. T1-weighted anatomic images were acquired with a three-dimensional MP-RAGE sequence (TR/TE = 23/4 ms, flip angle = 8°, field of view = 256 mm, matrix = 256 × 192, slice thickness = 1 mm). This scan was used for slice localization for the functional scans, Talairach transformation, and co-registration with fMRI data. Following structural scans, two gradient echo blood oxygen level–dependent scans were acquired in 43 contiguous coronal slices, perpendicular to the AC-PC line (TR/TE = 3,000/30 ms, flip angle = 90°, field of view = 192 mm, matrix = 64 × 64, slice thickness = 3 mm, 0.5 skip, in-plane resolution = 3 × 3 mm, 130 data points).

*Data analysis.* fMRI data were analyzed using the BrainVoyager QX statistical package and random effects (Brain Innovation, Maastricht, the Netherlands, 2004). Preprocessing steps include trilinear three-dimensional motion correction, sinc-interpolated slice scan time correction, three-dimensional spatial smoothing with 4-mm Gaussian filter, and high-pass filter temporal smoothing. Functional images were realigned to the anatomic images obtained within each session and standardized using BrainVoyager Talairach transformation, which conforms to the space defined by the Talairach and Tournoux’s (1988) stereotaxic atlas. Functional scans were discarded if participants moved >3 mm along any axis (x, y, or z).

Activation maps were analyzed using statistical parametric methods (Friston et al. 1995) contained within the BrainVoyager QX software. Statistical contrasts were conducted using multiple regression analysis with the general linear model, allowing for multiple predictors to be built into the model. Predictors used in the general linear model represented the following experimental conditions: food, nonfood, and baseline. Regressors representing the experimental conditions of interest were modeled with a hemodynamic response filter and entered into the multiple regression analysis using a random-effects model. Contrasts between conditions of interest were assessed with t statistics using random effects. A priori regions of interest (ROIs) included the anterior hippocampus (hippocampus and parahippocampal cortex), OFC, MPFC, ACC, and insular cortex. Activations were considered significant at a statistical threshold of P < 0.001 (uncorrected) and minimum cluster size of three contiguous voxels.

**ROI data analyses.** Follow-up analyses of a priori ROIs were conducted in regions noted above that achieved statistical significance in the group analyses in order to examine potential correlations with the three factor scores of the EI. Correlation analyses were strictly limited to these a priori regions that showed significant group effects in the food vs. nonfood contrasts. Mean percent signal change (food vs. nonfood and food vs. baseline) in the maximum voxel within each ROI for each individual was exported to SPSS 16.0 for Macintosh (Statistical Package for the Social Sciences, Chicago, IL) for correlation analyses.

**RESULTS**

**Behavioral**

On the EI total score, the obese group scored higher overall than HW controls, t(18) = 2.55, P = 0.02. They also scored higher on two of the three individual factors, including disinhibition, t(18) = 2.48, P = 0.02, and hunger, t(18) = 2.64, P = 0.02, but not restraint. Thus, obese participants reported more uncontrolled eating and feelings of hunger, but did not report greater efforts to restrain eating, than did the HW control group.

On memory testing of food and nonfood images, no significant differences or interactions of group were found. There was a main effect for picture type, F(1, 18) = 25.84, P < 0.0001, with participants from both groups showing better identification of previously viewed animal pictures than food pictures. This is not surprising: the animal pictures were generally more distinctive (more variety in types of animals) than food pictures. More importantly, there was a significant session (premeal, postmeal) × stimulus type (food, animals) interaction, F(1, 18) = 4.69, P < 0.05, which showed greater memory for food pictures in the premeal compared to the postmeal condition. Memory for animal pictures did not vary between the premeal and postmeal conditions. This interaction reflects a significant effect of motivational state for food pictures but not animal pictures. This result was also documented in the three previously published studies using this paradigm (19,20,28).

**fMRI**

*Premeal response: group × stimulus interaction.* To examine group differences in premeal responses to food vs. nonfood stimuli, we examined the following statistical interactions: (i) obese > HW, food > nonfood, (ii) HW > obese, food > nonfood, (iii) obese > HW, food > baseline, and (iv) HW > obese, food > baseline.

In the premeal condition, the obese group showed greater responses to food vs. nonfood stimuli than the HW group (P < 0.001) in a priori regions including the ACC (x, y, z = −6, 44, 4; 9, 26, 25; −3, 26, 19) and MPFC (x, y, z = −9, 50, 25; −12, 47, 34; −3, 50, 28) (see Table 1). The obese group also exhibited greater responses in the medial frontal gyrus (x, y, z = 12, −1, 61), middle frontal gyrus (x, y, z = −18, 20, 40; −28, 2, 52), and the inferior frontal gyrus (x, y, z = −33, 35, 10). The HW group, however, did not show greater responses than the obese group to food vs. nonfood stimuli in any of the a priori regions. All regions that reached significance, including post hoc findings, are listed in Table 1.

For the food vs. baseline contrast, the obese group showed greater activation than the HW group in a priori regions
INTEGRATIVE PHYSIOLOGY

including the ACC \((x, y, z = -3, 32, 13)\), amygdala \((x, y, z = -21, -4, -20)\), and parahippocampal gyrus \((x, y, z = 30, -25, -11)\). Additional regions of greater activation in the obese group included the middle frontal gyrus \((x, y, z = -21, 20, 40)\) and the globus pallidus \((x, y, z = 21, -10, 1)\). In addition, the HW group showed greater activation than the obese group for the food vs. baseline contrast in MPFC \((x, y, z = 9, 26, 25; 9, 26, 28)\), middle frontal gyrus \((x, y, z = -39, 12, 31; -42, 14, 49; -48, 17, 41)\), inferior frontal gyrus \((x, y, z = -48, -28, 10; -51, -22, 10)\), and insula \((x, y, z = -39, 17, 10; 33, 20, 13)\), and the thalamus \((x, y, z = -6, -7, 7; -6, -19, 4)\).

Postmeal response: obese vs. HW group interaction. To examine group differences in postmeal responses to food vs. non-food stimuli, we examined the following statistical interactions: (i) obese > HW, food > nonfood, (ii) obese > HW, food > baseline, and (iv) HW > obese, food > baseline.

Postmeal responses were greater in obese compared to HW in the MPFC \((x, y, z = -8, 50, 22)\), superior frontal gyrus \((x, y, z = 18, 29, 58)\), caudate \((x, y, z = 27, -36, 13)\), and hippocampus \((x, y, z = -31, -31, -5)\) (see Table 2). No regions showed greater responses for the HW compared to obese for the food vs. baseline contrast. All regions that reached significance, including post hoc findings, are listed in Table 2.

No a priori ROIs showed greater responses in the obese compared to HW group for the food vs. baseline contrast. However, a parahippocampal region \((x, y, z = -24, -31, -14)\) and insular region \((x, y, z = -39, -16, 10)\) showed greater responses in the HW group compared to the obese group for the food vs. baseline contrast.

Table 1  Regions reaching significance for the group interaction analysis in the premeal condition

<table>
<thead>
<tr>
<th>Contrast and region</th>
<th>Brodmann’s area</th>
<th>Coordinates</th>
<th>t</th>
<th>No. of voxels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premeal: obese &gt; HW, food vs. nonfood</td>
<td>MPFC</td>
<td>9</td>
<td>-9</td>
<td>50</td>
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<td></td>
<td></td>
<td>9</td>
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<td>47</td>
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<td>9</td>
<td>-3</td>
<td>50</td>
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<td></td>
<td>Medial frontal gyrus</td>
<td>6</td>
<td>12</td>
<td>-1</td>
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<td></td>
<td>Middle frontal gyrus</td>
<td>8</td>
<td>-18</td>
<td>20</td>
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<td>6</td>
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<td></td>
<td>ACC</td>
<td>32</td>
<td>-6</td>
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<td>32</td>
<td>9</td>
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<td></td>
<td>24</td>
<td>-3</td>
<td>26</td>
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<td></td>
<td>Inferior frontal gyrus</td>
<td>46</td>
<td>-33</td>
<td>35</td>
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<tr>
<td></td>
<td>Cingulate</td>
<td>24</td>
<td>-9</td>
<td>5</td>
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<td></td>
<td></td>
<td>32</td>
<td>12</td>
<td>17</td>
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<tr>
<td></td>
<td>Fusiform gyrus</td>
<td>36</td>
<td>33</td>
<td>-28</td>
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<tr>
<td></td>
<td>Cuneus</td>
<td>18</td>
<td>15</td>
<td>-61</td>
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<tr>
<td></td>
<td>Superior temporal gyrus</td>
<td>38</td>
<td>-51</td>
<td>5</td>
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<td></td>
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<td>38</td>
<td>-36</td>
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<td></td>
<td>Middle temporal gyrus</td>
<td>37</td>
<td>30</td>
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<tr>
<td></td>
<td>Occipital gyrus</td>
<td>19</td>
<td>25</td>
<td>-52</td>
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<tr>
<td></td>
<td>Cerebellum</td>
<td>—</td>
<td>9</td>
<td>-61</td>
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<td>-6</td>
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<td>Brainstem</td>
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<td>3</td>
<td>-31</td>
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<tr>
<td>Premeal: HW &gt; obese, food vs. nonfood</td>
<td>Superior temporal gyrus</td>
<td>22</td>
<td>-61</td>
<td>-52</td>
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<td></td>
<td>Planum temporale</td>
<td>40</td>
<td>-60</td>
<td>-34</td>
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ACC, anterior cingulate cortex; HW, healthy weight; MPFC, medial prefrontal cortex.
Correlations between ROIs and EI scores

Correlations were examined between obese participants’ EI factor scores and brain activations (% signal change from the maximum voxel) in a priori regions differentially activated by obese compared to the HW participants. Premeal activations in the ACC showed negative correlations with obese participants’ scores on the disinhibition factor of the EI. Greater activation premeal in the obese group in the middle frontal gyrus that was positively correlated with obese participants’ scores on the hunger factor of the EI. MPFC, medial prefrontal cortex.

DISCUSSION

Previous fMRI studies in HW adults (21) and children (20) reported differential activation of neural reward systems when manipulating food motivation by examining pre- and postmeal states. However, this approach has not been utilized in otherwise healthy obese individuals. The current results revealed increased activations in prefrontal and limbic regions, for obese compared to HW participants, in both premeal and postmeal conditions.
states. During the premeal condition, obese participants activated ACC and MPFC regions to a greater extent than HW participants. ACC activations were negatively correlated with self-report ratings of disinhibition and MPFC activations were positively correlated with self-report ratings of hunger among obese participants. No a priori regions showed greater activation for HW compared to obese participants in the food vs. nonfood contrast. Postmeal responses revealed greater activations for obese compared to HW participants in the MPFC. Similar to the premeal condition, no a priori regions showed greater activations for HW compared to obese participants.

Overall, these results are consistent with previous fMRI studies in obese compared to HW individuals, showing enhanced activations in limbic and paralimbic regions when viewing pictures of high-calorie foods (7, 26). Unlike previous positron emission tomography studies documenting less activation in dorsolateral prefrontal regions during meal consumption in obese compared to HW individuals (16,17), the PFC activation increases found in the current study were in medial prefrontal territories. Considered together, findings indicate that obesity may be associated with increases in medial PFC activation during food anticipation or craving, and decreases in lateral PFC activity during consumption. There is also evidence from the behavioral literature that obese individuals work more for food rewards compared to nonfood rewards than HW individuals (4). Current results indicate that food motivation in obese individuals is associated with increased self-reported disinhibition and hunger, and increased activation in the ACC and MPFC—regions strongly implicated in motivational processing. The MPFC is particularly interesting because it has also been implicated in processing other forms of self-referent activations which may lead to the development of personalized and more effective weight management programs.

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DISCLOSURE
The authors declared no conflict of interest.

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