Changes in brain activation to food pictures after adjustable gastric banding

Jared M. Bruce, Ph.D. a,b, Laura Hancock, M.A. a, Amanda Bruce, Ph.D. a, Rebecca J. Lepping, M.A. b, Laura Martin, Ph.D. c, Jennifer D. Lundgren, Ph.D. a, Steven Malley, M.D. d, Laura M. Holsen, Ph.D. e, Cary R. Savage, Ph.D. b

Department of Psychology, University of Missouri-Kansas City, Kansas City, Missouri
bCenter for Health Behavior Neuroscience, University of Kansas Medical Center, Kansas City, Kansas
Hoglund Brain Imaging Center, University of Kansas Medical Center, Kansas City, Kansas
Malley Surgical Weight Loss Center, Mission, Kansas
Department of Psychiatry and Medicine, Harvard Medical School and Brigham and Women’s Hospital, Boston, Massachusetts

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Abstract

Background: Adjustable gastric banding is an effective weight-loss treatment, but little is known about the neural mechanisms underlying weight loss. The purpose of the present study was to determine whether gastric banding affects brain function in regions previously implicated in food motivation, reward, and cognitive control. The setting for the study was the University of Missouri-Kansas City, Department of Psychology; Hoglund Brain Imaging Center, University of Kansas Medical Center; and private practice in the United States.

Methods: Ten obese participants were recruited before adjustable gastric banding surgery (mean body mass index before surgery 40.6 ± 1.96 kg/m²). Their mean body mass index at 12 weeks after surgery was 36.1 ± 3.22 kg/m², with a mean percentage of excess weight loss of 25.21% ± 8.41%.

Functional magnetic resonance imaging scans were conducted before and 12 weeks after adjustable gastric banding surgery. At each assessment point, the participants completed questionnaires assessing food motivation and were scanned while hungry (before eating) and immediately after a standardized meal (after eating). During the functional magnetic resonance imaging scans, the participants viewed food pictures, nonfood pictures (animals), and blurred baseline control pictures. The functional magnetic resonance imaging data were analyzed using BrainVoyager QX.

Results: After surgery, the participants reported significantly less food motivation and more cognitive restraint. The participants also showed decreased brain activation to food versus nonfood pictures in regions implicated in food motivation and reward, including the parahippocampus, medial prefrontal cortex, insula, and inferior frontal gyrus. In contrast, they demonstrated increased activation to food versus nonfood pictures in anterior prefrontal cortex, a region implicated in cognitive control and inhibition.

Conclusion: This is the first study to examine the functional brain changes after gastric banding surgery and the first study to longitudinally examine neural changes associated with weight loss. These results have provided preliminary evidence that adjustable gastric banding alters brain function in regions known to regulate reward and cognitive control. (Surg Obes Relat Dis 2011;xx:xxx.) © 2011 Published by Elsevier Inc. on behalf of American Society for Metabolic and Bariatric Surgery.

Keywords: Functional magnetic resonance imaging; Bariatric surgery; Neural mechanisms; Weight loss; Neuroimaging

Laparoscopic adjustable gastric banding (LAGB) is commonly used to treat obesity [1]. Although research has confirmed that LAGB is an effective long-term treatment of obesity [2], the physiologic mechanisms associated with successful LAGB surgery are unknown. Researchers have hypothesized that after food consumption, a banded stomach pouch sets into motion a series of hormonal and neural...
signals that trigger feelings of satiety in the brain [3]. The band adjustments that reduce stomach volume are associated with patient reports of reduced hunger and increased satiety [4,5]. Despite these theories, no study has been published that has directly examined how LAGB influences subcortical and cortical function.

The brain plays a fundamental role in modulating appetite and controlling motivation-driven behaviors, such as eating. The hypothalamus and caudal brainstem help control homeostasis, detecting internal cues and adjusting appetite/hunger accordingly [6]. Areas in the limbic and paralimbic regions are also involved, playing an important role in the reward, motivation, decision-making, inhibition, and cognitive control [7]. The brain regions most commonly associated with food motivation in healthy weight adults are areas involved in taste (insula), motivation (inferior frontal cortex, hippocampal formation, orbitofrontal cortex), reward (amygdala, striatum), and behavioral control (prefrontal cortex, anterior cingulate cortex) [8–12].

The purpose of the present study was to determine whether gastric banding surgery affects the brain regions involved in food motivation and eating behaviors. Compared with successful dieters and healthy weight individuals, obese adults demonstrate increased activity to food cues in the brain’s reward centers and decreased activity in brain areas known to be associated with cognitive control [10,13]. From these previous studies, we hypothesized that bariatric patients would exhibit diminished responses to visual food cues in the paralimbic and limbic reward centers from before to after surgery and increased responses to visual food cues in the frontal and limbic areas known to be associated with cognitive and emotional control. In addition, we hypothesized that these brain activation changes would be significantly associated with reports of less food craving, food motivation, and unrestrained eating.

Methods

Procedure

We scanned the obese participants at 2 points: once before surgery and once 12 weeks after having undergone LAGB weight loss surgery. At each point, the participants were scanned while hungry (after at least a 12-hr fast) and after eating a small meal. Before scanning, the participants were weighed, and their height was recorded. The participants also completed self-report measures at each visit.

Participants/Recruitment

We recruited obese right-handed participants (body mass index [BMI] 35–45 kg/m²; age 25–60 yr) who had elected to undergo adjustable gastric banding weight loss surgery (LAP-BAND). We did not recruit those with a BMI of ≥46 kg/m² because of the limitations associated with the size of the scanner. Individuals were ineligible if they reported current use of insulin, appetite suppressants, or stimulants. In contrast, given the prevalence of subclinical depressive symptoms among patients seeking bariatric surgery, we included participants taking psychotropic medications not directly targeting the mesolimbic dopamine system (selective serotonin reuptake inhibitors). All potential participants were asked screening questions regarding their mood and eating habits. If they reported symptoms, a licensed master-level therapist asked follow-up diagnostic questions consistent with the criteria found in the “Diagnostic and Statistical Manual of Mental Disorders, 4th edition.” Patients with a current eating disorder or a current major depressive episode were excluded. Because most participants seeking bariatric surgery in the recruited BMI range have diabetes, we included patients who had well-controlled diabetes and were not taking insulin (most recent hemoglobin A1c <7). We did not include patients with more severe forms of diabetes or poorly controlled diabetes because this might alter the hemodynamic response as measured by functional magnetic resonance imaging (fMRI). Additional exclusion criteria included a history of central nervous system disease, pregnancy, current cancer, a recent cardiac event, and internal metal objects that are risky in magnetic fields. A total of 20 participants who met the BMI criteria were excluded from the study. Of these participants, the common reasons for exclusion included major depression (n = 5), central nervous system disorder (n = 5), the use of psychotropic medications that could affect central nervous system function (n = 4), poorly controlled diabetes (n = 3), left-handedness (n = 3), and contraindicated metallic implants (n = 2). The University of Missouri-Kansas City and the University of Kansas Medical Center institutional review boards approved the present study.

fMRI cognitive activation paradigm

The experimental paradigm has been published previously and has been previously described in detail [10,14–17]. Participants viewed pictures of food, animals, and low-level baseline control images during 2 scanning sessions: first, after fasting for ≥4 hours (premeal); and second, immediately after eating a small uniform meal (postmeal) standardized for energy (500 kcal) and micronutrient content (e.g., a weighed lean meat [turkey or ham] wrap, carrot sticks, a piece of fruit, and skim milk). The order of the sessions (premeal, postmeal) was counterbalanced across subjects. In total, each participant underwent scanning 4 times, pre- and postmeal both before and after surgery. Images were obtained from professional stock photography on-line databases (available from http://stockexpert.com). The food and animal images were selected to be matched for valence and arousal, as defined by the methods of Lang et al. [18] and maximally different in the ratings of appetite stimulation. In an image validation pilot study, the food and animal images were rated according to the extent...
to which they were appetizing, exciting, and pleasant. The selected food images were significantly more appetizing than the selected animal images ($P < .001$). No significant differences existed between the food and animal image groups with regard to valence or arousal. Low-level baseline control images were created from a set of food and animal images by applying the 2-dimensional Fourier transform to each image to generate an image with the same physical properties (i.e., hue, contrast, and spatial frequencies) of the original image but with random phases. These blurred images were used as the baseline visual comparison stimuli to control for visual cortex activation during the paradigm. All images were presented 1 time only to each subject.

Each functional scan involved 3 repetitions of each block of each stimulus condition type (i.e., food, animal, baseline), alternated between blocks of blurred images. The visual stimuli were projected from the stimuli-generating computer program (Presentation, Neurobehavioral Systems, Albany, CA) onto a back-projection screen outside the magnet bore. The stimulus presentation time was 2.5 seconds, with an interstimulus interval of .5 second. Each of the 2 functional scans contained a total of 13 blocks of stimuli presentation; within each block, 10 images were presented. The order of category presentation was counterbalanced across the subjects. To ensure that the participants were attending to the images presented in the scanner, memory testing occurred after each scanning session.

Image acquisition

Scanning was performed on a 3 Tesla head-only Siemens Allegra scanner (Siemens, Erlangen, Germany) fitted with a quadrature head coil. The participants’ heads were immobilized with head cushions. After automated scout image acquisition and shimming procedures performed to optimize field homogeneity, a structural scan was completed. $T_1$-weighted anatomic images were acquired with a 3-dimensional spoiled gradient recalled sequence (repetition time/echo time 23/4 ms, flip angle 8°, field of view 256 mm, matrix 256 × 192, and slice thickness 1 mm) used for slice localization for the functional scans, Talairach transformation, and co-registration with fMRI data. After the structural scans, 2 gradient-echo BOLD scans were acquired in 43 contiguous oblique axial slices at a 40° angle (repetition time/echo time 3000/30 ms, flip angle 90°, field of view 220 mm, matrix 64 × 64, slice thickness 3 mm, 5 skip, in-plane resolution 3 × 3 mm, 130 data points).

Data analysis

The fMRI data were analyzed using the BrainVoyager QX statistical package (Brain Innovation, Maastricht, The Netherlands, 2004). The preprocessing steps included linear 3-dimensional motion correction, sinc-interpolated slice scan time correction, 3-dimensional spatial smoothing with a 4-mm gaussian filter, and high-pass filter temporal smoothing. Functional images were realigned to the anatomic images obtained within each session and normalized to Talairach and Tournoux’s stereotaxic atlas [19]. Motion in any run of >4 mm along any axis (x, y, or z) resulted in the discarding of that run.

Statistical analysis

One run from 1 participant was excluded because of motion >4 mm. The activation maps were analyzed using statistical parametric methods [20] contained within the BrainVoyager QX software. Statistical contrasts were conducted using multiple regression analysis with the general linear model. Regressors representing the conditions of interest were modeled with a hemodynamic response filter and entered into the multiple regression analysis using a random-effects model. Separate analyses were performed for the premeal and postmeal conditions. Analyses were conducted premeal and postmeal using a condition (preoperative, postoperative) × stimulus (food, nonfood) repeated-measures analysis of variance model. Statistical parametric maps were overlaid on 3-dimensional renderings of an averaged-group brain. Based on a priori regions of interest, voxel values in the amygdala, hippocampal formation hippocampus and parahippocampal cortex, prefrontal cortex, orbitofrontal cortex, medial prefrontal cortex, anterior cingulate cortex, and insular cortex were considered significant if the activation survived a statistical threshold of $P < .001$ (uncorrected) and had a minimal cluster size of 3 contiguous voxels. Other areas were considered significant if they exceeded a threshold of $P < .05$ (false discovery rate corrected for whole brain). This approach was designed to ensure maximal statistical power for a priori regions with strong evidence of activation from previous studies, while not missing other, potentially important, yet unanticipated, activations.

Exploratory data analyses

Follow-up analyses of an a priori region of interest were conducted in the regions noted that achieved statistical significance in the group analyses. The mean change in brain activation between the food and nonfood conditions (before and after surgery) in the maximal voxel within each region for each participant was exported to Predictive Analytics Software, version 18. These data were used to examine potential correlations between the changes in activation and scores on the behavioral and self-report measures.

Behavioral measures

The Eating Inventory is a 51-item self-report scale with a 3-factor structure and good internal consistency [21]. The first scale assesses cognitive restraint or the ability to successfully restrict food intake and consequently control body weight. The second scale assesses disinhibition in relation to uncontrolled overeating, and the final scale assesses per-
ceived hunger. For the present study, we examined the
total percentage of change in the patients’ scores from before to
after surgery.

The Center for Epidemiological Studies Depression
Scale is a 20-item questionnaire that asks participants to rate
how frequently they have experienced various symptoms of
depression [22]. Higher scores indicate more depression.

Results

Preliminary results

Twelve participants met the inclusion criteria for the
study and were assessed before bariatric surgery. Two partici-
pants were lost to follow-up (one because of pregnancy).
For the present study, we included 10 participants who had
undergone both the preoperative and the postoperative scan-
ing sessions. Consistent with the gender prevalence of
bariatric surgery patients [23], 9 of the 10 participants were
women. The mean age of the participants was 40.10 ±
10.27 years (range 21–54). On average, the baseline evalu-
ation was conducted 10.30 ± 5.46 days (range 1–19) before
surgery, and the follow-up evaluation was conducted 105.80 ±
23.37 days (range 79–158) after surgery. After the scanning
sessions and consistent with adequate attention in the scan-
er, the participants correctly identified significantly more
food and nonfood pictures than would be expected by
chance at each of the 4 scanning sessions (all P < .001).

Behavioral results

The paired sample t tests revealed that participants ex-
perienced significant weight loss after surgery (Table 1). At
the follow-up evaluation, the mean percentage of excess
weight loss was 25.21% ± 8.41%. On average, the partici-
pants lost 13.39 ± 5.40 kg. The participants also reported
significantly less hunger, decreased disinhibition, and in-
creased cognitive restraint. No significant differences
emerged between the patients’ pre- and postoperative de-
pression scores.

Pre- and postoperative fMRI changes premeal

In the condition (pre-, postoperatively) × stimulus type
(food, nonfood) interaction premeal, the participants showed in-
creased activation to food versus nonfood pictures after
surgery in the right middle frontal gyrus and the right
superior frontal gyrus. Whole-brain statistical analyses with
false discovery rate correction (P < .05) and random effects
revealed significantly increased activation in the right mid-
dle frontal gyrus (Fig. 1). In contrast, patients showed de-
creased activation to food versus nonfood pictures after
surgery in the right medial frontal gyrus. The Brodmann
areas and Talairach coordinates for significant fMRI find-
ings are listed in Table 2.

Pre- and postoperative fMRI changes postmeal

In the condition (pre- and postoperative) × stimulus
(food, nonfood) interaction postmeal, patients showed de-
creased activation to food versus nonfood pictures after
bariatric surgery in the right middle frontal gyrus, right
insula/operculum, right and left inferior frontal gyri, and
the left parahippocampal gyrus (Fig. 1). Whole brain statistical
analyses with false discovery rate correction (P < .05) and
random effects revealed no additional significant changes
preoperatively to postoperatively in the postmeal condition.

Explanatory region of interest analyses

BMI and fMRI. We examined the association between
the BMI and brain regions that demonstrated significant pre-
to postoperative changes in activation to pictures of food.
Before surgery, a greater BMI was significantly associated
with less food versus nonfood activation in the right middle
frontal gyrus (Brodmann 10) at the premeal scan (r = .76,
P < .05). No regions of interest were significantly associated
with the percentage of excess weight loss from before to
after surgery.

Predicting behavior change using preoperative fMRI. Less
activation to food versus nonfood pictures in right inferior
frontal gyrus (Brodmann 45) at postmeal was associated
with a larger decline in disinhibited eating behaviors from
before to after surgery (r = .67, P < .05). The preoperative
fMRI results were not associated with pre- to postoperative
reductions in restraint or self-reported hunger.

Behavior change and postoperative fMRI. Less activation to
food versus nonfood pictures at postmeal in the right infe-

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before surgery</th>
<th>After surgery</th>
<th>t Value</th>
<th>df</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg/m²)</td>
<td>40.61 ± 1.96</td>
<td>36.14 ± 2.32</td>
<td>7.90</td>
<td>9</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Eating Inventory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive restraint</td>
<td>7.20 ± 3.05</td>
<td>14.60 ± 3.71</td>
<td>−6.74</td>
<td>9</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Disinhibition</td>
<td>11.40 ± 3.24</td>
<td>5.10 ± 2.60</td>
<td>5.37</td>
<td>9</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Hunger</td>
<td>10.10 ± 2.18</td>
<td>4.30 ± 2.67</td>
<td>4.15</td>
<td>9</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>CES-D</td>
<td>17.40 ± 10.44</td>
<td>11.90 ± 5.88</td>
<td>1.43</td>
<td>9</td>
<td>NS</td>
</tr>
</tbody>
</table>

BMI = body mass index; CES-D = Center for Epidemiological Studies Depression scale; NS = not significant.

Data presented as mean ± standard deviation.
ior frontal gyrus (Brodmann 45) was associated with increased cognitive restraint and reduced hunger from before to after surgery ($r = -0.71$, $P < .05$; and $r = 0.78$, $P < .01$, respectively). Similarly, less activation to food versus nonfood pictures at postmeal in the right middle frontal gyrus (Brodmann 47) was associated with a larger reduction in disinhibited eating from before to after surgery ($r = 0.67$, $P < .05$).

Discussion

The present study has extended the obesity and food motivation data by providing preliminary evidence of functional brain changes that occur before to after adjustable gastric banding surgery. We hypothesized that bariatric patients would exhibit diminished responses to visual food cues in paralimbic reward centers from before to after surgery. The results supported this, because in both premeal and postmeal conditions, brain activations decreased from before to after surgery in insula/frontal operculum, inferior frontal gyrus, medial prefrontal cortex, and parahippocampus. These observed reductions in activation after surgery are consistent with lower levels of food motivation [12]. Previous studies have also demonstrated that healthy weight adults experience less activation to visual food stimuli than obese adults in similar brain regions [9–11]. Moreover, a recent study found similar reductions in areas associated with food motivation after Roux-en-gastric bypass surgery [24].

We also hypothesized that participants would show increased responses to visual food cues in frontal areas known to be associated with cognitive and emotional control. As predicted, the participants showed significantly increased activation in the anterior prefrontal cortex, even when using

<table>
<thead>
<tr>
<th>Variable</th>
<th>Brodmann</th>
<th>x Axis</th>
<th>y Axis</th>
<th>z Axis</th>
<th>Voxels (n)</th>
<th>t Value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premeal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right middle frontal gyrus</td>
<td>10</td>
<td>27</td>
<td>59</td>
<td>13</td>
<td>48</td>
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<tr>
<td>Right superior frontal gyrus</td>
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<td>56</td>
<td>19</td>
<td>9</td>
<td>5.60</td>
<td>0.00034</td>
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<tr>
<td>Right medial frontal gyrus</td>
<td>9</td>
<td>6</td>
<td>50</td>
<td>19</td>
<td>4</td>
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<td>0.00177</td>
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<td>Postmeal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Right middle frontal gyrus</td>
<td>47</td>
<td>45</td>
<td>44</td>
<td>-5</td>
<td>21</td>
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<td>0.00010</td>
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<tr>
<td>Right inferior frontal gyrus</td>
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<td>42</td>
<td>14</td>
<td>19</td>
<td>4</td>
<td>-4.99</td>
<td>0.00849</td>
</tr>
<tr>
<td>Right insula/operculum</td>
<td>47</td>
<td>30</td>
<td>14</td>
<td>-8</td>
<td>18</td>
<td>-6.55</td>
<td>0.00105</td>
</tr>
<tr>
<td>Left parahippocampal gyrus</td>
<td>28</td>
<td>-24</td>
<td>5</td>
<td>-20</td>
<td>3</td>
<td>-5.48</td>
<td>0.00389</td>
</tr>
<tr>
<td>Left inferior frontal gyrus</td>
<td>10</td>
<td>-45</td>
<td>44</td>
<td>-2</td>
<td>8</td>
<td>-5.37</td>
<td>0.00153</td>
</tr>
</tbody>
</table>

Positive maximal voxel t values indicate increased activity to food versus nonfood pictures from before to after surgery; negative t values indicated reduced activity to food versus nonfood pictures from before to after surgery.
strict statistical thresholds. These increases in activation could be facilitating the self-regulation necessary to maintain a more restrictive postoperative diet. Supporting this assertion, increased activation to food versus nonfood images in anterior prefrontal cortex before surgery was associated with a lower BMI.

Behavioral changes that occur after surgery can help to further characterize the nature of our findings. Consistent with previous research [25], after surgery, patients reported significant increases in cognitive restraint and reductions in hunger and disinhibited eating. Furthermore, several differential brain activations to food versus nonfood images were significantly associated with postoperative behavioral changes. For instance, after surgery, less activation to food versus nonfood pictures at postmeal in the right middle frontal gyrus was associated with a larger reduction in disinhibited eating. This finding is consistent with the conceptualization that activation in this area of the cortex is associated with food motivation and drive [12].

These findings also suggest that preoperative fMRI might be useful in identifying changes in eating behavior after surgery. Before surgery, more activation to food versus nonfood images in the right inferior frontal gyrus postmeal was associated with a lower decline in disinhibited eating. Given the strict eating regimen required after surgery, disinhibited eating might be associated with postoperative complications. Future studies that follow-up a large number of patients for an extended period might investigate whether preoperative measures of food motivation and reward can predict complications and outcomes associated with adjustable gastric banding.

One of the limitations of the present study was the relatively small sample size. Despite this, both our behavioral and fMRI findings were highly statistically significant. An additional limitation was the lack of behavioral weight loss controls. Thus, we cannot completely extricate the changes associated with weight loss from those specific to surgery. To our knowledge, only 1 other study has used fMRI to longitudinally examine weight loss, and no longitudinal study has included a matched control group [24].

Although our research was able to show neural changes in the areas associated with food motivation and reward, we are unable to fully dissect the mechanism of this change. It might be that gastric banding alters the consequences of eating behaviors. For instance, over time, previously rewarding foods and portion sizes might become associated with discomfort and punishment. This in turn could change how the brain responds to food cues. Alternatively, banding the stomach might directly or indirectly alter the neural and hormonal pathways that connect the brain and gut [26,27]. Additional longitudinal research that includes matched obese controls and measures of behavior and hormonal change might better elucidate the mechanisms associated with brain changes after gastric banding.

Overall, the preliminary results from the present study suggest that, in response to appetizing pictures of food after surgery, decreased activation was present to pictures of food in the areas known to be associated with the motivational, rewarding aspects of food. In addition, after surgery, activity is increased in the brain regions known to be associated with cognitive control and inhibition. Therefore, in addition to food cues being less salient to the patients after they have undergone surgery, they also have the added benefit of increased cognitive control/self-control. This finding is strengthened by corroborations in the significant correlations with BMI and fMRI results and behavioral measures and fMRI results.

Conclusion
To our knowledge, this is the first study to use fMRI to examine the effects of gastric banding weight loss surgery on brain function. Moreover, although some studies have compared obese patients and weight loss controls [13,28], only 1 other study has longitudinally examined the association between weight loss and neural responses to food cues [24]. The results of our longitudinal study have demonstrated an association between bariatric surgery and changes in brain functioning, specifically in areas known to be related to food motivation. These findings have potential clinical implications, including obesity interventions that manipulate brain activation. Future studies should consider scanning patients undergoing different types of bariatric surgery to compare the brain activation between groups (gastric banding surgery versus gastric bypass surgery). Such studies will increase our understanding of how weight loss interventions affect the brain. Ultimately, this knowledge could be used to determine which type of weight loss intervention has the greatest potential for success for a given patient.

Disclosures
Dr. Malley has served as a consultant to Allergan and is on their advisory board.

Uncited references

This section consists of references that are included in the reference list but are not cited in the article text. Please either cite each of these references in the text or, alternatively, delete it from the reference list. If you do not provide further instruction for this reference, we will retain it in its current form and publish it as an "un-cited reference" with your article [29–31].
References


