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RELATION BETWEEN CHANGES IN NEURAL RESPONSIVITY AND REDUCTIONS IN DESIRE TO EAT HIGH-CALORIE FOODS FOLLOWING GASTRIC BYPASS SURGERY

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Abstract—Reductions in reward-related (e.g. striatal) neural activation have been noted following obesity surgery. It has been speculated that these postoperative neural changes may be related to documented postoperative changes in food preferences; however, this relation has not been previously established. In this study, functional magnetic resonance imaging and rating scales were used to assess neural responsivity, desire to eat (i.e. wanting), and liking for high- and low-calorie food cues in 14 females one month pre- and one month post-Roux-en-Y gastric bypass (RYGB) surgery. Pre- to post-RYGB changes in all variables were assessed, and postoperative changes in neural responsivity were regressed on postoperative changes in desire to eat and liking of foods. Results revealed significant postoperative reductions in mesolimbic (e.g. striatal) neural responsivity, desire to eat (wanting), and liking for high- relative to low-calorie food cues. Postoperative reductions in mesolimbic responsivity were associated with postoperative reductions in wanting, but not liking, for high- versus low-calorie foods. Interestingly, reductions in food wanting were also related to reductions in inhibitory (e.g. dorsolateral prefrontal cortex) activation following RYGB. Results are consistent with the hypothesized delineation between wanting and liking, supporting the notion that wanting, but not liking, is processed through the dopaminergic reward pathway. Concurrent reductions in both reward-related and inhibitory activation-predicted reductions in desire to eat might suggest that less dietary inhibition was elicited to resist potential overconsumption as the anticipated reward value of high-calorie foods decreased following RYGB.

Key words: brain, striatum, bariatric, obesity, weight, diet.

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Abbreviations: BMI, body mass index; dlPFC, dorsolateral prefrontal cortex; fMRI, functional magnetic resonance imaging; MNI, Montreal Neurologic Institute; RYGB, Roux-en-Y gastric bypass.

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The mesolimbic reward pathway, particularly the striatum, processes the perceived reward value of food (Berthoud and Morrison, 2008; Volkow et al., 2008a). Striatal signaling largely mediates "hedonic eating," or eating driven by the rewarding aspects of food versus caloric deficit, which typifies food intake in most industrialized nations (Lowe and Butryn, 2007; Lenard and Berthoud, 2008; Lowe et al., 2009). This reward-related neural activation frequently overrides counter-regulatory signaling from homeostatic areas (i.e. hypothalamus) or inhibitory areas (i.e. dorsolateral prefrontal cortex [dlPFC], cingulate cortex), driving food intake despite the absence of hunger or presence of dietary inhibition (Petrovich et al., 2002, 2007; Volkow et al., 2008b). Thus, although there is increasing interest in the potential role of inhibitory dlPFC activation, the majority of research on the neural control of eating behavior and body weight continues to focus on reward-related (particularly striatal) activation, as it appears to be a major driver of food intake in the United States and other industrialized nations.

In 2011, we reported significant reductions in striatal activation in obese women from pre- to post-gastric bypass surgery (Ochner et al., 2011b), which was consistent with one (Dunn et al., 2010) of only two other pre- to post-obesity surgery imaging studies (Dunn et al., 2010; Steele et al., 2010). Dunn et al. (2010) reported postoperative decreases in striatal D2 receptor availability in five bariatric patients assessed using positron emission tomography, whereas Steele et al. (2010) reported postoperative increases in striatal D2 receptor availability in a similar sample. In our functional magnetic resonance imaging (fMRI) study, postoperative reductions in striatal responsivity to food cues were found in 10 women following Roux-en-Y gastric bypass (RYGB). Interestingly, this study also showed that postoperative reductions in striatal responsivity to high-calorie food cues were larger in magnitude than postoperative reductions in striatal responsivity to low-calorie food cues. This pattern of postoperative reduction in reward-related neural responsivity is reminiscent of the pattern of postoperative changes in preferences for high- versus low-calorie foods following RYGB. We and others have reported a postoperative reduction in desire to eat high-calorie food that is significantly larger in magnitude than the postoperative reduction in desire to eat low-calorie food (Tichansky et al., 2006; Thirlby et al., 2006; Thomas and Marcus, 2008; Ochner et al., 2011b). Importantly, it has been shown that this selective postoperative reduction in preference for high- versus low-calorie foods is not attributable to adverse postingestive effects of high-

calorie foods following surgery (Thomas and Marcus, 2008).

The primary goals of this study were to: (1) assess post-RYGB changes in neural activation and food preferences and (2) formally test the proposed association between postoperative changes in neural responsivity (to high- versus low-calorie food cues) and postoperative changes food preferences (for high- versus low-calorie food cues). In assessing food preferences, it was important for us to consider that reward involves two dissociable cognitive constructs with separable neural substrates (Berridge and Robinson, 2003; Berthoud and Morrison, 2008; Lenard and Berthoud, 2008). Berridge and Robinson (2003) draw clear distinctions between wanting (motivational salience) and liking (affective salience). Wanting, or the desire to pursue something perceived to be rewarding (e.g. desire to eat palatable food) is mediated primarily through dopaminergic projections within the mesolimbic pathway (Berthoud and Morrison, 2008; Lenard and Berthoud, 2008). In contrast, liking, or the hedonic impact (of food), is mediated primarily by mu-opioid transmission across a more distributed neural network (Berridge and Robinson, 2003; Cannon and Palmiter, 2003; Berridge, 2009, 2010). Thus, both self-reported desire to eat (wanting) and liking for high- and low-calorie foods were assessed. It was hypothesized that postoperative changes in neural responsivity within the mesolimbic reward pathway (particularly the striatum) would predict postoperative changes in desire to eat (wanting), but not liking, for high- versus low-calorie foods.

EXPERIMENTAL PROCEDURES

Subjects

Seventeen female RYGB candidates were recruited from the Center for Bariatric Surgery and Metabolic Diseases at St. Luke's Hospital in New York. Three participants yielded corrupt scan data, leaving 14 completers. Participants ranged in preoperative body mass index (BMI) from 40 to 54 (mean=45.4±4.4 [SD]; see Table 1) kilogram/meter^2 and age from 20 to 54 (mean=36±10) years, were weight-stable (<5% weight change in the 3 months preceding surgery), right-handed, non-smoking, premenopausal, free of major psychological or physical disorders (including diabetes) and were not taking medication that may have affected body weight. Participants in this study were not required to lose weight preoperatively or to undergo pre- or postoperative nutritional counseling, other than standard advice for postoperative eating provided by the staff nutritionist. Fifty-seven percent of the sample was Hispanic, 29% African American, and 14% Caucasian. Institutional Review Board approval was granted by Columbia University and St. Luke's Hospital, and all procedures followed were in accordance with the ethical standards of these institutions. All participants provided informed consent and met NIH Consensus Panel criteria (NIH, 1991).

Table 1. Weight and BMI of female participants (mean±SD)

	1 month presurgery	1 month postsurgery	Change[a]
Weight (kg)	121.8±16.1	106.6±13.2	−15.1±4.7*
BMI (kg/m^2)	45.5±4.4	39.8±3.7	−5.6±1.6*
% Initial body weight	100	87.8±2.9	−9.91±2.9*

[a] Change from 1 month presurgery to 1 month postsurgery.
* Significant at $P<0.0005$, paired sample t-test.

Design and procedure

A within-subjects design was used, with assessments at one month pre- and one month post-RYGB surgery. Following an overnight (12-hour) fast, participants reported to the fMRI Research Center at the Columbia University Medical Center between 11 AM and 1 PM. Assessment time was consistent across assessments for each participant. Participants ingested a 250 kilocalorie liquid meal (Glytrol; Nestlé Nutrition, Vevey, Switzerland), used to minimize between-subject differences in repletion, 60 minutes before scanning. During fMRI scans, participants were presented with visual and auditory representations (cues) of high-calorie foods (e.g. pepperoni pizza, fudge sundae), low-calorie foods (e.g. raw vegetables) and neutral non-foods (office supplies e.g. pencil, notepad). Ss were scanned in the same phase of their menstrual cycle pre- and postsurgery. Procedures were identical pre- and postsurgery, and the same surgeon performed all surgeries.

Ratings of desire to eat and liking

Following each run, participants were asked, "On a scale from 0 to 100, how much did what you just saw/heard make you want to eat, zero being 'not at all' and 100 being 'very much.'" Ratings were averaged across all four runs from each condition to obtain an overall desire to eat rating for each stimuli type (high- and low-calorie foods) for each participant, pre- and postsurgery. Following each scan session, participants viewed the written names and pictures of each stimulus presented during scanning, and rated liking from −100 (dislike intensely) to 100 (like very much). Liking ratings were averaged individually for high- and low-calorie food items for each participant, pre- and postsurgery.

Stimuli presentation paradigm

Cues were presented individually through two different modalities, visual (pictorial) stimuli transmitted through goggles and auditory (spoken name) stimuli transmitted through headphones. Cues were presented in runs of 10 consecutive 4-second epochs (total block duration 40 second), with a 52-second prerun baseline epoch and a 40-second postrun baseline epoch. Visual cues were pictures of prepared foods, presented on plates and approximately balanced for visual size. Auditory stimuli were recorded two-word names similar in content to visual stimuli (e.g. chocolate brownie), repeated twice to fill the 4-second epoch. All high-calorie cues had an energy density of >3.5 kilocalorie/gram and all low-calorie cues had an energy density of <1 kilocalorie/gram (Rolls, 2007). There were 20 different high-calorie, and 20 different low-calorie, food cues. A Latin-Square paradigm employed two different nonconsecutive runs for each type of food (high-calorie, low-calorie) in each condition (visual, auditory). During each scan session, each cue was presented exactly twice, once visually and once auditorily. Only areas activated in both visual and auditory conditions were included in image analyses, which helps eliminate spurious and sensory-specific activation (Friston et al., 2005).

fMRI data acquisition

A 1.5-Tesla twin-speed fMRI scanner (General Electric, Fairfield, CT, USA) with quadrature radio-frequency head coil and 65-centimeter bore diameter was used. Participants were positioned in the scanner with the head in a passive restraint. Three-plane localization was used to verify head position, and motion was minimized with restraint pads around the head and a tape strapped across the forehead. Total time in the scanner was about

60 minutes. In each run, 36 axial scans of the whole brain were acquired, each scan consisting of 25 contiguous slices (4-millimeters thick), with a 19×19 centimeters^2 field of view, an acquisition matrix size of 128×128 and 1.5×1.5 millimeters^2 in plane resolution. The first three scans of each run (12 seconds) were discarded to attain magnetic equilibration. The axial slices were parallel to the anterior commissure/posterior commissure line. T2*-weighted images with a gradient echo pulse sequence (echo time=60 milliseconds, repetition time=4 seconds, flip angle=60°) were acquired with matched anatomic high resolution T_1*-weighted scans. fMRI stimuli presentation and data acquisition procedures were consistent with those published previously (Ochner et al., 2011b).

Statistical analyses

Functional data were analyzed with SPM8 (Wellcome Department of Imaging Neuroscience, London, UK). Before statistical analyses, the realigned T2*-weighted volumes were slice-time corrected, spatially transformed to a standardized brain [Montreal Neurologic Institute (MNI)], and smoothed with an 8- millimeter full-width half-maximum Gaussian kernel. First level regressors were created by convolving the onset of each trial (audio and visual high-calorie, low-calorie, and non-food) with the canonical HRF with duration of 40 seconds for both pre- and postsurgery scan sessions. Both scan sessions were included in the first level model for each participant. Average beta estimates of each condition (8 per participant) were passed to a second level model from which subsequent contrasts were generated. Pre- to postoperative changes in BMI and pre-scan fullness ratings were included as nuisance regressors to control for postoperative weight loss (see Table 1) and increases in postprandial fullness.

t-values for neural responses to visual and auditory stimuli significant at $P<0.005$ uncorrected were averaged to obtain areas activated across both modalities for pre-post analyses and entered concurrently in regression analyses in SPM. Statistical maps for neural activation are displayed at $P<0.005$ uncorrected for display purposes. Significance was determined using a threshold of $P<0.005$ uncorrected tested against the global null hypothesis, combined with a cluster-extent threshold of 152 contiguous voxels, resulting in a threshold of $P<0.05$ corrected for multiple comparisons. The cluster threshold was determined by 1000 Monte Carlo simulations of whole-brain fMRI data with respective data parameters of the present study using the AlphaSim program as implemented in AFNI (version 2011, National Institutes of Mental Health, Bethesda, MD, USA) (Cox, 1996, 2011).

Non-fMRI data were analyzed using SPSS versus18 (IBM, Chicago, IL, USA), with two-tailed tests, $\alpha=0.05$. Mixed-model analyses of variance were used to assess postoperative changes in desire to eat and liking. Relative measures were calculated as high-calorie–low-calorie for desire to eat, liking, and brain activation. Postoperative changes in desire to eat and liking were regressed on postoperative activation changes to determine changes in neural responsivity that significantly predicted changes in these outcomes.

RESULTS

Postoperative changes in neural responsivity

Post-RYGB changes in neural responsivity found in this study are consistent with previously reported findings from a portion (10/14) of the current sample (Ochner et al., 2011b). Significant postoperative reductions in neural responsivity to food cues were found and were most pronounced in the mesolimbic pathway, particularly in the lentiform nucleus and putamen (dorsal striatum; reward), as well as the middle and superior frontal gyri (dlPFC; inhibition) (Fig. 1). Postoperative reductions in neural responsivity were significantly greater in response to high- versus low-calorie food cues (Table 2). No postoperative increases in neural responsivity were found.

Postoperative changes in desire to eat (wanting) and liking

Preoperatively, desire to eat was associated with liking for both high- and low-calorie foods. Postoperatively, however, desire to eat was associated with liking of low-calorie foods only (Table 3). Preoperatively, both desire to eat and liking were greater for high- versus low-calorie foods ($P=0.001$ and $P=0.011$, respectively). Postoperatively, however, neither desire to eat nor liking differed between high- and low-calorie foods. The postoperative reduction in desire to eat was greater for high-calorie versus low-calorie foods ($P=0.001$), indicating a preferential reduction in desire to eat for high- versus low-calorie foods (Fig. 2). Changes in liking of high- and low-calorie foods independently failed to reach significance; however, as with desire to eat, there was a preferential postoperative reduction in liking of high- versus low-calorie foods ($P=0.032$). See Table 3.

Neural prediction of changes in desire to eat (wanting) pre-to post-RYGB

Decreases in relative neural responsivity (to high- versus low-calorie food cues) in the lentiform nucleus and caudate (dorsal striatum; reward), middle and superior frontal gyri (dlPFC; inhibition), anterior cingulate (attention/inhibition), thalamus (homeostasis), and inferior parietal lobule (sensory) significantly predicted reductions in desire to eat for high- versus low-calorie foods (Fig. 3, Table 4).

Neural prediction of changes in food liking pre-to post-RYGB

Decreases in relative neural responsivity (to high- versus low-calorie food cues) in the precuneus (contextual association) significantly predicted reductions in liking of high- versus low-calorie foods (Table 4).

DISCUSSION

Results from this study show reductions in striatal activation from pre- to post-RYGB, consistent with some (Dunn et al., 2010; Ochner et al., 2011b) but not all (Steele et al., 2010) relevant previous literature. These postoperative reductions in striatal activation were greater in response to high- relative to low-calorie foods. Although the low level of preoperative striatal responsivity to low-calorie food cues may have limited postoperative reductions, results suggest a selective postoperative reduction in anticipated reward (i.e. significantly greater reduction in reward-related responsivity to high-calorie cues as compared with low-calorie cues). Only standard nutritional counseling for postoperative eating (e.g. avoid simultaneous eating and drinking, be wary of meats and sugars) is offered at our surgical center. Therefore, it is unlikely that dietary counseling accounted for the present results, particularly as large differences in neural changes resulting

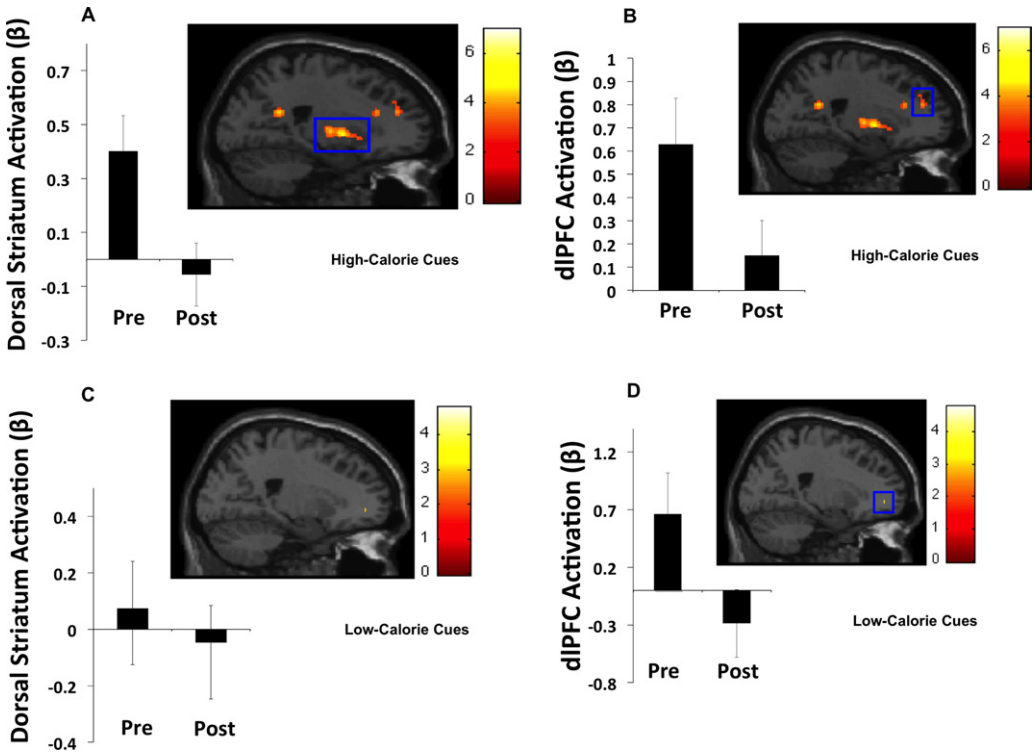

Fig. 1. Presurgery>Postsurgery Contrast. Slices depicting postoperative decreases in neural responsivity to high-calorie (top) and low-calorie (bottom) food cues. All slices are derived from MNI coordinates 22, −2, 2 (x, y, z). Bar graphs display β values depicting blood oxygen level dependent signaling, with error bars showing 90% confidence intervals. The color bar represents t values. For display purposes, activation maps are shown without a cluster extent threshold. Significant clusters are presented in Table 2. Highlighted in blue are postoperative decreases in neural responsivity in the dorsal striatum (lentiform nucleus/putamen; Fig. 1A, C) and dlPFC (middle/superior frontal gyrus; Fig. 1B, D).

from surgical versus nonsurgical weight loss treatment have been noted (Ochner et al., 2011b).

Postoperative changes in self-reported desire to eat were also consistent with prior studies (Tichansky et al., 2006; Thirlby et al., 2006; Thomas and Marcus, 2008), indicating that postoperative reductions in desire to eat and intake are reduced to a significantly greater extent for high- versus low-calorie foods. Thus, RYGB appears to reduce

Table 2. Areas showing postoperative reductions in neural responsivity

Coordinates (x, y, z)	Area(s)	Hemisphere	k	Minimal t value	Effect size (d)
High-calorie foods					
−6, −36, −18	Posterior cingulate*,[a]	L	528	5.2913	2.94
	Culmen*,[a]	L			
22, −2, 2	Lentiform nucleus*,[b]	R	341	5.1174	2.84
	Putamen*,[b]	R			
−30, −66, 26	Precuneus*	L	216	4.5061	2.5
42, 12, 20	Middle frontal gyrus*	R	206	3.9274	2.18
0, −26, 74	Medial frontal gyrus*	R	192	4.2018	2.33
−48, −2, 28	Precentral gyrus*,[c]	L	157	4.1561	2.31
	Inferior frontal gyrus*,[c]	L			
−32, −40, 50	Inferior parietal lobule*,[d]	L	153	6.9896	3.88
	Postcentral gyrus*,[d]	L			
Low-calorie foods					
6, 18, 66	Superior frontal gyrus	L, R	146	4.154	2.3
18, 46, −2	Anterior cingulate[e]	R	134	3.909	2.17
	Medial frontal gyrus[e]	L, R			
0, 22, 46	Cingulate gyrus[f]	L, R	120	4.42	2.45
	Medial frontal gyrus[f]	L			

k=number of voxels within each cluster.
[a-f] Part of same cluster.
* Significant at $P<0.05$ corrected.

Table 3. Desire to eat and liking

	Pre	Post	Change
High-calorie foods			
Desire to eat (M±SD)	31.4±29.5	11.4±26.2	−20.0±23.7**
Liking (M±SD)	46.9±29.9	32.1±37.4	−14.8±45.7
Correlation (*r*)	0.79***	0.39	0.29
Low-calorie foods			
Desire to eat (M±SD)	17.7±21.4	10.9±26.3	−6.7±22.3
Liking (M±SD)	19.5±30.4	29.0±27.8	9.5±32.2
Correlation (*r*)	0.67**	0.63*	0.19
High-cal−low-cal			
Desire to eat (M±SD)	13.7±12.0	0.4±3.5	−13.3±12.1**
Liking (M±SD)	27.4±34.8	−9.5±32.2	36.9±54.1*
Correlation (*r*)	0.43	0.21	0.38

* $P<0.05$.
** $P<0.01$.

the preoperative preference for high- versus low- calorie foods (Lowe et al., 2009; Ochner et al., 2011b). This effect has been proposed as a potentially significant mechanism of post-RYGB weight loss (Miras and le Roux, 2010), as a reduction in the consumption of high- versus low-calorie foods has been shown to reduce overall caloric intake and body weight (Yao and Roberts, 2001; Rolls, 2009). Findings from this study show that this effect is associated with changes in neural activation following RYGB, as postoperative reductions in mesolimbic activation significantly predicted reductions in desire to eat for high- versus low-calorie foods.

Postoperative reductions in reward-related signaling, particularly as they relate to postoperative reductions in desire to eat, are consistent with the reward-surfeit hypothesis (Stice et al., 2011), which suggests that obese individuals may overeat due to hyperactive reward signaling associated with food. This is in contrast to the reward-deficit hypothesis (Wang et al., 2001), which posits that obese individuals may overeat in an attempt to compensate for a deficit in reward signaling associated with food. Results introduce the possibility that RYGB surgery may help reduce this hypothesized hyperactivity in reward-related regions (e.g. striatum). It is important to note, however, that differences between neural responsivity to food cues (i.e. anticipatory reward) versus actual food intake (i.e. consummatory reward) have been reported (Stice et al., 2008, 2009, 2011), suggesting that this anticipatory versus consummatory factor may modulate the relation between reward-related activation and overconsumption in obese individuals (Stice et al., 2009).

The fact that activation reductions in both reward-related (e.g. striatum) and inhibitory (e.g. dlPFC) regions were associated with reductions in relative desire to eat is particularly noteworthy. Conscious attempts to inhibit (eating) behavior are processed primarily in the dlPFC (Tataranni et al., 1999; Braver, 2001; Del Parigi et al., 2007), and the dlPFC appears to be reciprocally activated with reward-related regions in response to palatable food cues (Stice et al., 2008, Burger and Stice, 2011), suggesting that dietary inhibition may be elicited in an attempt to limit overconsumption of calorically dense foods. The concurrent postoperative reductions in reward-related and inhibitory activation found in the present study (Table 2) suggest that less dietary inhibition was required postoperatively, as high-calorie foods were perceived of as less rewarding and desire to eat decreased.

Consistent with the established delineation between wanting and liking (Berridge and Robinson, 2003), post-RYGB changes in these variables differed substantially and changes in desire to eat were unrelated to changes in food liking (Table 3). As anticipated, the neural prediction of post-RYGB changes in desire to eat and liking also differed. Changes in mesolimbic activation predicted changes in desire to eat for high- versus low-calorie foods, particularly within the dorsal striatum and dlPFC (Table 4, Fig. 3). In contrast, neural prediction analyses of liking of high- versus low-calorie foods yielded smaller nonsignificant clusters outside the mesolimbic pathway (Table 4). These differences in the neural prediction of changes in desire to eat (wanting) versus liking are consistent with evidence from drug and animal literature, demonstrating dopaminergic mediation of wanting concentrated in the mesolimbic pathway (Berthoud and Morrison, 2008; Lenard and Berthoud, 2008) versus primarily opioidergic mediation of liking through a more diffuse neural system outside the mesolimbic pathway (Cannon and Palmiter, 2003; Berridge, 2009, 2010). These differences may relate to the aforementioned distinction between anticipatory and consummatory reward (Berridge and Robinson, 2003; Lenard and Berthoud, 2008; Stice et al., 2008), as associations have been drawn between wanting and anticipatory reward, as well as liking and consummatory reward (Berridge, 2009; Stice et al., 2009). This distinction may prove to be critical in the eventual application of this research in identifying targets for neural manipulation (e.g. pharmacology, neurofeedback); consummatory reward (~liking) may be pertinent only insofar as it affects subsequent anticipatory reward (~wanting), which will likely represent the preferred

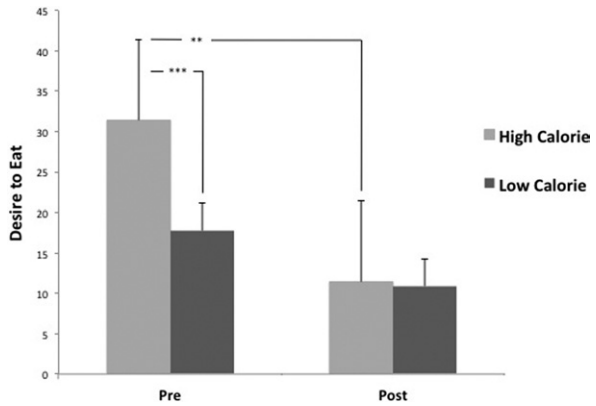

Fig. 2. Desire to eat in response to high- and low-calorie food cues. Preoperatively, the difference (13.7±12) between the desire to eat for high- versus low-calorie foods (high-calorie–low-calorie) was greater than the nonsignificant postoperative difference (0.4±3.5) in desire to eat for high- versus low-calorie foods, $F(1,13)=16.7$, $P=0.001$. The postoperative reduction in desire to eat was greater for high- versus low-calorie cues ($P=0.001$), indicating a preferential reduction in desire to eat for high-, relative to low-, calorie foods. ** $P<0.01$, *** $P<0.001$.

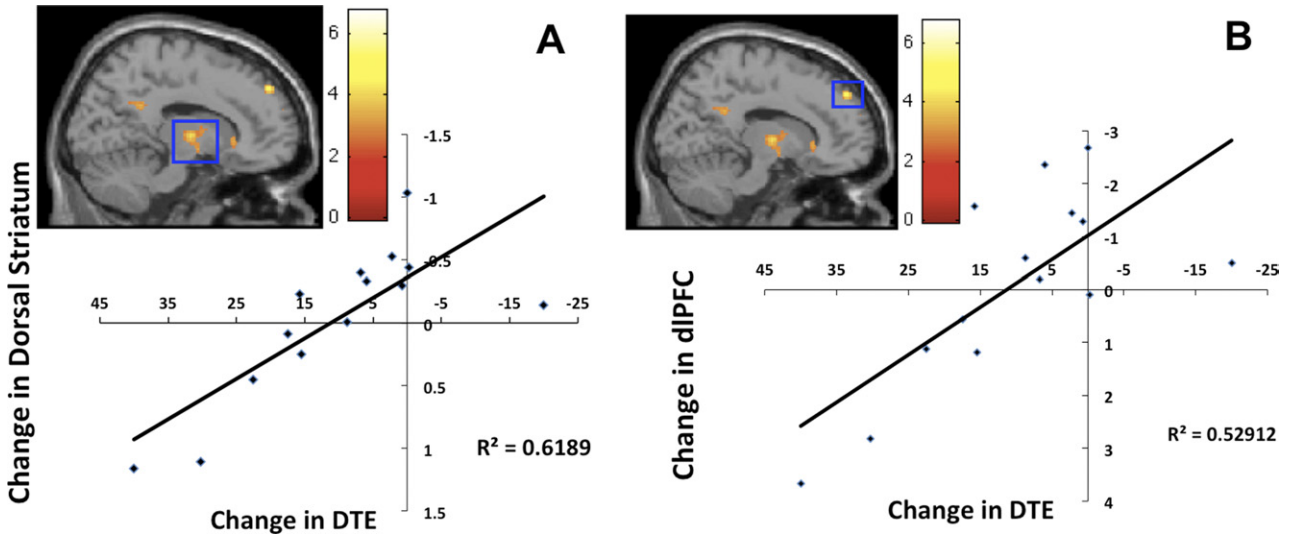

Fig. 3. Postoperative changes in relative desire to eat (DTE) regressed on postoperative reductions in relative neural responsivity. Slices depicting areas in which significant postoperative reductions in neural responsivity to high- versus low-calorie food cues predicted reductions in desire to eat for high- versus low-calorie foods. All slices are derived from MNI coordinates 14, −10, 2 (x, y, z). The color bar represents *t* values. Results shown at $P<0.005$ are uncorrected for display purposes. Significant clusters are presented in Table 4. Highlighted in blue are associations in the dorsal striatum (caudate and lentiform nucleus; Fig. 3A) and dlPFC (superior frontal gyrus; Fig. 3B).

intervention point (i.e. before food choices being made and food consumed). Thus, the mesolimbic pathway, including inhibitory areas, may represent a promising target for future brain-based obesity interventions.

Subsequent research should address several limitations of the current study. All participants were female, which limits generalizability. The sample size of 14 is small, though the longitudinal within-subjects design did provide sufficient power to detect significant effects in rating scale and neural measures, as well as in neural regression analyses. Social desirability may have affected desire to eat, liking, and neural responsivity. However, postoperative increases in socially desirable responding would suggest increased inhibitory neural responsivity, which was not found. The fact that postoperative scans necessarily followed preoperative scans may have introduced an order effect, which may have contributed to reductions in neural responsivity. A control group was not included; however, this did not hinder the establishment of a statistical association between postoperative changes in neural responsivity and postoperative changes in food preferences. Finally, consummatory reward was not directly assessed in response to food intake in this study. Future work may seek to assess postoperative changes in the neural prediction of wanting in response to food cues versus liking of actual food ingestion to further tease apart these constructs.

CONCLUSIONS

Results indicate that reward-related (e.g. striatal) responsivity to palatable food cues decreased from pre-to post-

Table 4. Brain areas in which postoperative reductions in neural responsivity to high- versus low-calorie food cues predicted postoperative changes in desire to eat and liking for high- versus low-calorie foods

Coordinates (x, y, z)	Area(s)	Hemisphere	k	Maximum *t* value	Effect size (d)
Desire to eat					
−24, 28, 58	Middle frontal gyrus (dlPFC)*,[a] Superior frontal gyrus (dlPFC)*,[a]	L	349	6.039	3.35
−6, −4, 0	Thalamus*	L	275	3.664	2.03
44, −30, 26	Inferior parietal lobule*	R	260	7.018	3.89
14, −10, 2	Lentiform nucleus (dorsal striatum)*,[b] Thalamus*,[b]	R	216	4.493	2.49
−8, 28, −6	Anterior cingulate*,[c] Caudate (dorsal striatum)*,[c]	L	197	4.570	2.53
Liking					
10, −70, 40	Precuneus*	R	157	4.039	2.24
58, −64, 20	Superior temporal gyrus[d] Middle temporal gyrus[d]	R	31	4.384	2.43

k=number of voxels within each cluster.
[a-d] Part of same cluster.
* Significant at $P<0.05$ corrected.

RYGB, consistent with the hypothesis that obese individuals show hyperactive reward responsivity to food cues, which may be partially corrected following RYGB surgery. It is unclear what may be driving these postoperative changes in neural responsivity. Well-documented increases in postprandial satiety peptides (i.e. Glucagon-like peptide-1, Peptide $YY_{3–36}$) could contribute to postoperative reductions in reward-related neural responsivity (Bose et al., 2010; Ochner et al., 2011a). However, this remains speculative; further research is necessary to test whether postoperative changes in neural responsivity are related to postoperative changes in gut peptide concentrations. Greater relative reductions in reward-related activation, desire to eat, and liking were found in response to high- versus low-calorie food cues, suggesting a preferential reduction in expected reward value, wanting and liking of high- versus low-calorie foods following RYGB. Reductions in reward-related neural responsivity predicted decreases in desire to eat, but not liking, for high- versus low-calorie foods. This finding is consistent with evidence that wanting, but not liking, of food is mediated by dopaminergic signaling within the mesolimbic pathway. Finally, inhibitory activation was found to be elicited and altered in conjunction with reward-related activation, suggesting that inhibitory activation may be produced in response to palatable food cues perceived to be rewarding, and decrease as reward-related activation and desire to eat decrease following RYGB surgery.

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