

**Biological evidence for attention bias to food, emotional dysregulation, disinhibition and deficient somatosensory awareness in obesity with binge eating disorder**

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Phone: 972-52-606-6876

Abstract: 233 words

Text: 4657 words

Figures: 1, 2, 3

Tables: 1-5

Supplemental information: 0

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## Acknowledgments

The authors gratefully acknowledge Ian Ang, who provided technical help, and the grant support by the NIH: RO1DK07406 (AG) and RO1DK080153 (AG) (this funding agency did not have a role in any other aspect of the study and/or article preparation). Some of the research data were presented in an abstract at the New York City Regional Obesity Forum on September, 2016.

# Conflict of interest

Dr. Aviram-Friedman, Astbury, Ochner, Contento, and Geliebter report no financial interests or potential conflict of interest.

## Abstract

**Objectives:** To refine the biobehavioral markers of binge eating disorder (BED). **Methods:** We conducted fMRI brain scans using images of high energy processed food (HEPF), low energy unprocessed food (LEUF), or non-foods (NF) in 42 adults (obese with BED [obese -BED;  $n = 13$ ] and obese with no BED [obese non-BED;  $n = 29$ ]) selected via ads. Two blood oxygenated level dependent (BOLD) signal contrast maps were examined: food versus nonfood, and HEPF versus LEUF. In addition, score differences on the disinhibition scale were correlated with BOLD signals.

**Results:** food versus nonfood showed greater BOLD activity for BED in emotional, motivational and somatosensory brain areas: insula, anterior cingulate cortex (ACC), Brodmann areas (BA) 19 & 32, inferior parietal lobule (IPL), posterior cingulate cortex (PCC), and lingual, postcentral, middle temporal and cuneate gyri ( $p \leq 0.005$ ;  $k \geq 88$ ). HEPF versus LEUF showed greater BOLD activity for BED in inhibitory brain regions: BA 6, middle and superior frontal gyri ( $p < 0.01$ ;  $k \geq 119$ ). The groups also differed in the relationships between disinhibition and BOLD activity in the postcentral gyrus (PCG;  $p = 0.04$ ) and ACC-BA 32 ( $p = 0.02$ ). For all participants jointly, PCG BOLD amplitude predicted greater disinhibition ( $p = 0.04$ ). **Discussion:** Food images elicited neural activity indicating attention bias (cuneate & PCG), emotion dysregulation (BA 19 & 32), and disinhibition (MFG, BA6 & SFG) in obese with BED. These may help tailor a treatment for the obesity with BED phenotype.

**Keywords:** obesity, binge eating disorder (BED), fMRI, brain, disinhibition, neural activation

Obesity is associated with chronic medical conditions, such as heart disease, hypertension, diabetes, and the metabolic syndrome,<sup>1</sup> and exerts a large toll on the US healthcare budget.<sup>2</sup> A subgroup of obese individuals also has binge eating disorder (BED), which is a stand-alone mental illness in the DSM-5, and may coincide with addictive eating.<sup>3-5</sup> BED is characterized by repeated episodes of uncontrollable overeating in the absence of compensatory behaviors, such as purging, and it can result in weight gain leading to obesity.<sup>6</sup>

The biobehavioral components of obesity and BED are becoming better understood, but a clear distinction between obesity alone versus obesity with BED has not yet been adequately formulated.<sup>7</sup> In obesity with BED, emotion dysregulation, stress, and negative affect can trigger binge episodes.<sup>8-11</sup> Furthermore, BED is often characterized by cycles of rigid dietary restriction, coupled with high disinhibition in the face of the restricted food or its cues,<sup>12-15</sup> which may help cope with emotion dysregulation.<sup>16-19</sup> Moreover, anxiety and disinhibition can synergistically affect eating; overeating in the absence of hunger was noted following a stressful task and was greater in those with high disinhibition and anxiety scores.<sup>11</sup> Thus, dysregulated affect, anxiety, and dietary disinhibition are associated with binge-eating, but their neural correlates in relation to food cues are unclear.

There is evidence for brain system dysfunctionality in obesity with BED. The ventromedial prefrontal cortex was activated in obese adults with BED in response to high energy processed food (HEPF) cues, and the activation was positively correlated with scores on the Behavioral Activation Scale, suggesting heightened attraction toward the food stimuli, despite undesirable long-term consequences (i.e. weight gain).<sup>20,21</sup> Diminished cognitive performance in neuropsychological tasks in obese adults with BED was also reported.<sup>21-24</sup> Additionally, greater frontal beta-wave brain activity during rest, as well as during an attentional task, positively correlated with disinhibition scores.<sup>15</sup> Other evidence also supports dysfunctional frontal brain

1 systems associated with the neurobehavioral traits of disinhibition and reduced executive  
2 functioning in adult binge-eaters.<sup>19,25</sup>

3  
4 In obese adults with BED, impulsive tendencies appear to be associated with increased  
5 emotion and sensory-motor processing in response to food cues. Heightened BOLD signal in  
6 binge-eaters in Brodmann area #6 and the lingual and cuneate gyri, may indicate planning to  
7 approach food in response to appetitive stimuli.<sup>8,13,26</sup> Furthermore, a psycho-physiological  
8 interaction (PPI) analysis revealed a link between BOLD signal in the dorsal anterior cingulate  
9 cortex (ACC) and increased signal in the insula, cerebellum, and the supramarginal gyrus in  
10 response to food cues in lean and obese women with binge eating.<sup>20</sup> Together, this may indicate a  
11 link between emotional, sensory, and motor processing in response to binge-triggers, but it  
12 remains unclear why some obese develop binge-eating and others do not.

13  
14 The evidence in obese adults with BED suggests dysfunctional frontal brain systems, which  
15 may be associated with disinhibition, poor emotion regulation, and deficient executive functioning.  
16 However, a comprehensive profile of brain regions associated with these neurobehavioral findings  
17 has not yet been described. The present study focused on differences in biobehavioral traits, i.e.  
18 scores on disinhibition, behavioral activation to approach, and anxiety, between adults with obesity  
19 alone versus obesity with BED, and on correlating those scores with neural activity in response to  
20 common binge food cues.<sup>27</sup>

## Methods

We enrolled 42 right-handed obese participants, BMI of 30-40, ages of 18-65, recruited by local newspaper advertising. Fourteen obese participants (M:F; 6:8) met the diagnosis of BED, according to the DSM-5 criteria,<sup>28</sup> and 28 were non-binge eaters (M/F: 15/13; Obese group), with no differences in BMI (**Table 1**). Participants were interviewed by phone with the Questionnaire on Eating and Weight Patterns – Revised (QEWP-R),<sup>29</sup> to screen for BED. Those who appeared to meet criteria for obesity with BED were scheduled for an interview with the diagnostic Eating Disorder Examination (EDE) by a trained doctoral clinical psychology researcher to confirm BED status. To be included in the BED group, candidates had to meet the DSM-5 criteria for BED.<sup>6</sup> Otherwise they were assigned to the obese non-BED group. Candidates with significant health problems, current and past three months use of certain prescribed medications, especially those that could affect body weight, such as antidepressants, stimulants, and oral contraceptives, as well as individuals who smoked or used excess alcohol (> 3 drinks/day), or who vigorously exercised for more than 5 hours per week, were excluded. Also excluded were those with contraindications for MRI scanning (e.g. metal implants). Women needed to have regular menstrual cycles (28 days +/- 5 d), not be pregnant or lactating, and be at least 1 year postpartum. Those who met criteria for substance abuse or dependence within the past 6 months, or with current suicidal ideation, were excluded, as well as those with a history of psychotic disorder or hospitalization for psychiatric illness within the past year. Eligible candidates could not be in treatment for obesity or currently receiving psychotherapy.

**Table 1: Participant characteristics**

Groups (DSM-V)	age (years)	BMI [kg/m <sup>2</sup> ]	Percent Fat (Body Impedance Analysis)	Males (%)	Females (%)
Obese BED	38.3 (±11.1)	(±6.4) 36.3	40.0 (±6.6)	6 (43%)	8 (57%)
Obese non-BED	35.0 (±7.7)	(±5.4) 35.8	39.0 (±8.3)	15 (54%)	13 (46%)

Each participant visited the hospital for an initial consultation, signed a consent form approved by the Institutional Review Boards at Columbia University and St Luke's Hospital in New York, in accordance with the code of ethics of the World Medical Association, and had height, weight, and body composition measured using bioelectrical impedance analysis (BIA) with a Tanita scale (Arlington Heights, IL). Participants also underwent a physical exam, had the EDE clinical interview, and filled out a battery of psychobehavioral questionnaires for 30 min.

On another day, participants came into the hospital following an overnight fast at 9 am, for the experimental procedures. Participants drank a 16 fl. oz Boost liquid meal (Nestlé, Vevey, Switzerland; chocolate, vanilla, or strawberry, according to preference), over a 15-minute period, and blood samples were drawn for a different protocol not presented here. At 10:30 am, an fMRI brain scan took place, lasting 45 minutes.

#### Brain imaging scan

For the brain scan, a 1.5-Tesla twin-speed fMRI scanner (General Electric, Global) with quadrature RF head coil and 65 cm bore diameter was used. Participants wore a head-set and goggles, with their head placed in a passive restraint (pads and tape around the head) to minimize motion. Three-plane localization (x, y, z) was used to verify head position. A head coil (MRI devices corporation, Gainesville, FL) was used to improve the signal to noise ratio. Total time in the scanner



was about 60 minutes. During the brain scan, participants were shown via the goggles visual images of high energy processed food (HEPF;  $\geq 3.5$  kcal/g; e.g. chocolate cake or French fries), selected to mimic binge type foods,<sup>27</sup> low energy unprocessed food (LEUF;  $< 1$  kcal/g; e.g. fruits and vegetables, or broiled fish), and neutral nonfood items (nonfood; office supplies, e.g. stapler). Food images consisted of 60 high-quality color photographs taken from magazines with a digital camera. All images were converted to the same resolution (800 x 600) and luminance matched. The 60 pictures were divided into three sets of 20 pictures: HEPF, LEUF, and nonfood items. Over each of the six stimulation runs, 10 items were presented in a block design, each for 4 seconds, for a total of 40 seconds per run. The stimulation epoch was preceded by a 52 seconds pre-stimulus baseline, and followed by a 40 seconds post-stimulus baseline, both with a crosshair centered on a black background. For each image category, i.e. HEPF, LEUF, and nonfood, there were two nonconsecutive runs of 10 stimuli of the same category. The two runs each had novel stimuli to reduce habituation. The order of presentation varied across participants in a pseudorandomized block design.

In each run, 36 axial scans of the whole brain were acquired, consisting of 25 contiguous slices (4mm thick), with a 19 cm x 19 cm field of view, an acquisition matrix size of 128 x 128, and 1.5 mm x 1.5 mm in plane resolution. The first three scans of each run (12 sec) were discarded to attain magnetic equilibrium. The axial slices were parallel to the AC/PC line. T2\*-weighted images with a gradient echo pulse sequence (echo time = 60 ms, repetition time = 4sec, flip angle = 60°) were acquired with matched anatomic high resolution T1-weighted scans.

Data analysis was conducted with SPSS and Excel for biobehavioral data and with Statistical Parametric Mapping version 8 (SPM8; Wellcome Department of Imaging Neuroscience, London, UK) for brain imaging data. Questionnaire scores were compared between obese BED versus obese non-BED, using an independent sample t-test ( $\alpha = .05$ ). In a first level analysis, brain imaging data was computed for the contrasts: food (HEPF + LEUF) versus nonfood, and HEPF versus LEUF. In a second level analysis, obese BED versus obese were compared using each contrast separately, to find differences in BOLD signal between the groups. A whole-brain

exploratory analysis was used, and once results indicated brain areas significantly different between the groups, parameter estimates of BOLD signal amplitudes were extracted and averaged for each group. The behavioral measures found to be significantly different between obese BED versus obese were correlated with parameter estimates of the brain imaging results to find the relationships between the behavioral measures and BOLD signal in response to the food stimuli. Lastly, we tested the strength of these relationships using a regression model, with BOLD signal as the independent variable and biobehavioral data as the dependent variable (two tailed  $\alpha = .05$ ).

Brain imaging data were analyzed in two steps (i.e. 1st and 2nd level analyses). Prior to these analyses, the realigned T2\*-weighted volumes were preprocessed, including slice-time correction, spatial transformation to a standard brain (using the Montreal Neurological Institute, MNI), and smoothing with an 8-mm full-width half-maximum Gaussian kernel. The six runs for each participant were concatenated to create a single run (i.e.  $33 * 6 = 198$  total time points). Block regressors were included in each participant's 1st level model to account for the mean of each run. In this model, additional covariates for motion, as well as global signal and spikes, were included to account for potential sources of noise. First level regressors of interest were created by convolving the onsets of each block (HEPF, LEUF, or nonfood) with the canonical Hemodynamic Response Function (HRF), with a 40 seconds duration block. Given the specific hypotheses of this project, BOLD signal in response to 'food' versus 'nonfood', and 'HEPF' versus 'LEUF', were examined. Thus, the specific contrasts submitted for a 2nd level analysis included: 1) 'food' versus 'nonfood', 2) 'HEPF' versus 'LEUF'. Also submitted for a 2nd-level analysis were the effect magnitude maps, i.e. the effect of each stimulus type on BOLD signal response: 1) 'HEPF' positive effect, 2) 'HEPF' negative effect, 3) 'LEUF' positive effect, 4) 'LEUF' negative effect, 5) 'nonfood' positive effect, and 6) 'nonfood' negative effect .

The above two contrast maps were submitted to a group random effects model using multiple regression analysis with binge-eating category as a covariate of interest. First, a statistical map of binge-eating category (independent variable) and BOLD signal in response to visual images of food versus nonfood (dependent variable) was generated to find significant differences between the groups. A whole-brain analysis was conducted, with a threshold of  $p \leq 0.005$ , uncorrected, combined with a cluster-size threshold of  $k \geq 50$  contiguous voxels. We corrected for multiple comparisons, using the

Monte Carlo multiple testing correction system (URL: <http://afni.nimh.nih.gov/sscc/gangc/mcc.html>) which yielded a  $p \leq 0.005$  combined with a cluster size of 88 contiguous voxel clusters or above (i.e.  $k \geq 88$ ).

In another second level analysis, the groups were compared using the contrast HEPF versus LEUF. A statistical map of binge-eating category as the independent variable and BOLD signal as the dependent variable was generated in a whole-brain analysis, with a threshold of  $p < 0.05$ , uncorrected, combined with a cluster-size threshold of  $k \geq 10$  contiguous voxels. Compared with the first contrast map (i.e. food versus nonfood), a larger  $p$  value and a smaller cluster size were used in this analysis, since a highly specific distinction within the food category was expected to generate a weaker BOLD signal, which could have been missed with a smaller threshold and/or a larger cluster size, leading to a Type II error. To conduct this analysis, we also used the Monte Carlo multiple testing correction system, which yielded a  $p < 0.01$  and a cluster size threshold of  $\geq 119$ .

We used the MNI atlas to identify brain areas with significant differences in BOLD signals between the groups.<sup>8</sup> Spatial normalization was done by a linear scaling to the x, y, and z axes to identify brain MNI coordinates for group analyses and brain regions with significant differences in BOLD signals between the groups. A 5 mm sphere was built around each of the eight MNI coordinates identified. Some of the coordinates identified were junctions between multiple brain areas, thus some of the spheres included more than one brain area.

Parameter estimates of peak BOLD signal in each MNI tested were extracted for each participant. The parameter estimates were calculated using average BOLD signal in response to each stimulus category (i.e. 'food versus nonfood', and 'HEPF versus LEUF'), and participant responses were separately plotted to understand neuronal activity fluctuations in response to each stimulus category. Thus, parameter estimates were extracted, averaged, and plotted for each group separately in response to each stimulus type. The food category consisted of the average parameter estimates in response to (HEPF+LEUF)/2.

## Results

The contrast 'food versus nonfood' generated 17 clusters of BOLD signal, of which 11 were significant at a  $p \leq 0.005$ , combined with a cluster size of 88 or above (i.e.  $k \geq 88$ ; Monte Carlo multiple correction) [Table 2]. In addition, analysis of the contrast 'HEPF versus LEUF' generated 33 significant clusters, of which three were significant at a  $p < 0.01$ , combined with a cluster size of 119 or above ( $k \geq 119$ ; Monte Carlo correction) [Table 3].

**Table 2: Brain areas with significant differences in BOLD signal in response to visual cues of food versus nonfood (obese BED > obese;  $p \leq 0.005$  and  $k \geq 88$ )**

Region	Hemisphere	Cluster size	X	Y	Z	Peak Intensity
Insula	Right	100	34	-4	12	4.11
Cingulate cortex	Right	312	8	8	44	4.75
Posterior cingulate	Left	130	-38	-64	18	4.63
Posterior cingulate	Right	313	24	-60	8	3.94
Middle temporal gyrus	Left	97	-38	-64	18	4.63
Cuneate gyrus	Left	90	-38	-64	18	4.63
Cuneate gyrus	Right	214	16	-84	26	4.01
Lingual gyrus	Right	126	24	-60	8	3.94
Postcentral gyrus	Left	138	-66	-22	22	4.2
Brodmann area 19	Right	89	16	-84	26	4.01
Inferior parietal lobule	Right	97	54	-38	24	3.91
Brodmann area 32	Right	118	8	8	44	4.75

**Table 3: BOLD signal in response to visual cues of HEPF versus LEUF (obese BED > obese;  $p \leq 0.01$  and  $k \geq 119$ )**

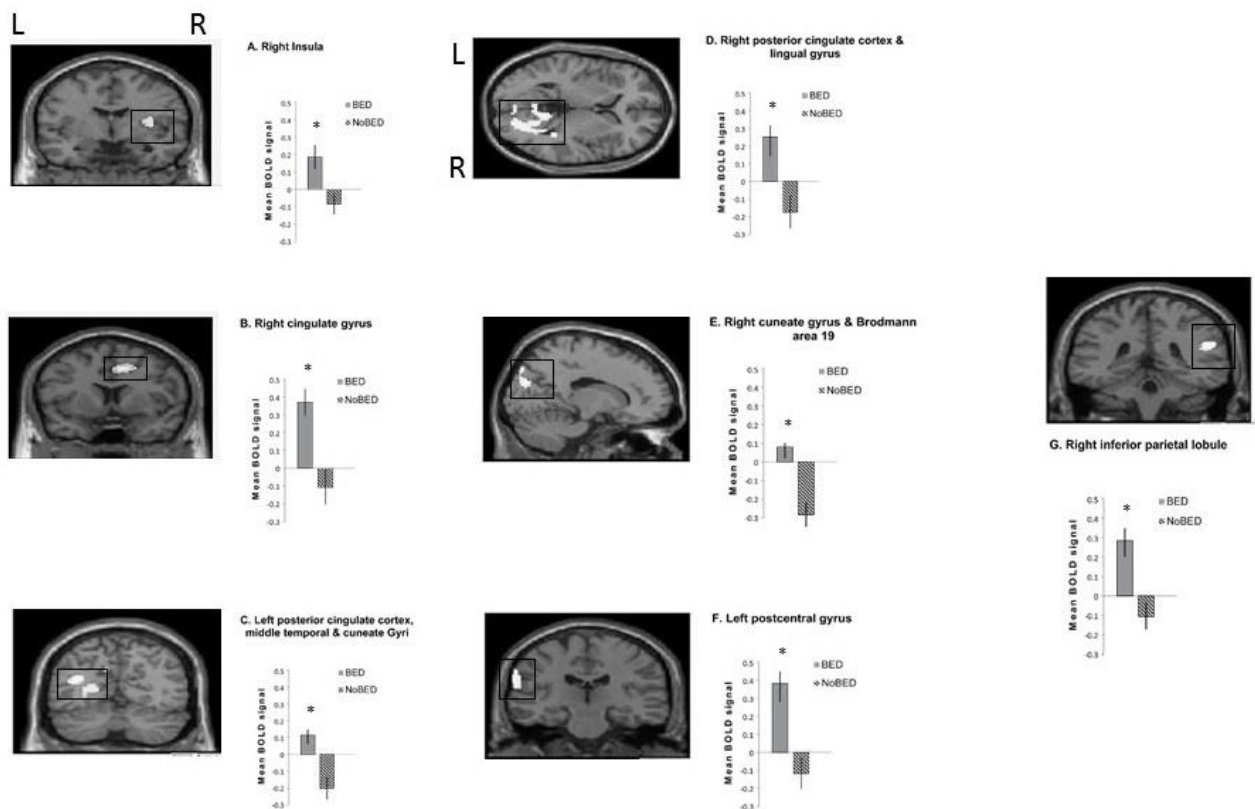
Region	Hemisphere	Cluster size	X	Y	Z	Peak Intensity
Middle frontal gyrus	Left	427	16-	8-	50	3.57
Brodmann area 6	Left	198	16-	8-	50	3.57
Superior frontal gyrus	Left	152	16-	8-	50	3.57

Thus, eight different groups of clusters were found to be significantly different between the groups, obese BED versus obese. For the contrast food versus nonfood, seven brain coordinates significantly differed between the groups: 1) right insula, 2) right anterior cingulate cortex (ACC) and Brodmann area #32 (1 & 2: salience-limbic), 3) left posterior cingulate cortex (PCC), middle temporal gyrus (MTG) and cuneate gyrus, 4) right PCC and lingual gyrus, 5) right cuneate gyrus and Brodmann area #19, 6) left postcentral gyrus (PCG); (3-6: visuospatial and somatosensory), and 7) right inferior parietal lobule (IPL) (7: attention control). For the contrast HEPF versus LEUF, one significant MNI with three brain areas was found: 8) left middle frontal gyrus (MFG), Brodmann area #6, and superior frontal gyrus (SFG) (8: cognitive control and movement planning)

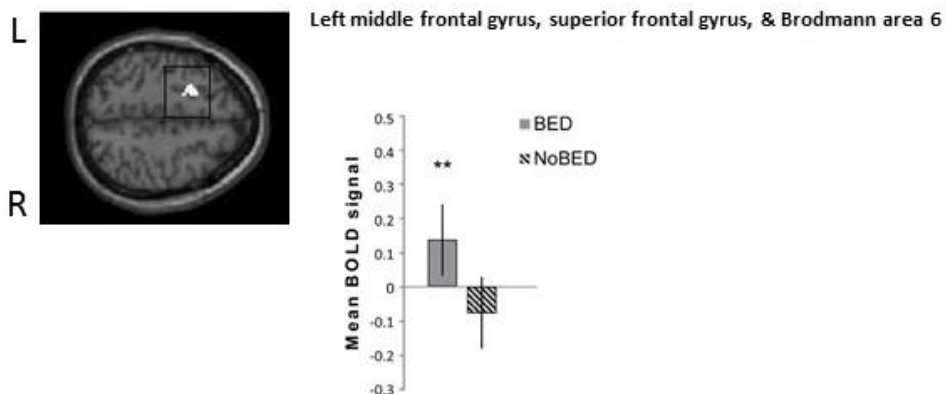
Results of the brain imaging analysis are shown in **Figures 1 and 2**. The parameter estimates of all participants in each group were averaged and plotted on a bar graph. These show differences in neuronal activity between the groups in response to the contrasts: food versus nonfood [**Figure 1(A-G)**] and HEPF versus LEUF [**Figure 2**]. The obese BED group experienced a heightened BOLD signal compared with the obese in the right insula [0.19 versus -0.09, respectively;  $t = 3.53$ ,  $p \leq 0.001$ ; **Figure 1(A)**], in the right ACC and Brodmann area #32 [0.37 versus -0.11, respectively;  $t = 4.06$ ,  $p = 0.003$ ; **Figure 1(B)**], in the left PCC, middle temporal and cuneate gyri [0.12 versus -0.23, respectively;  $t = 3.92$ ,  $p \leq 0.001$ ; **Figure 1(C)**], in the right PCC and lingual gyrus [0.25 versus -0.17, respectively;  $t = 3.5$ ,  $p \leq 0.001$ ; **Figure 1(D)**], in the right cuneate gyrus and Brodmann area #19

[0.09 versus -0.31, respectively;  $t = 3.45$ ,  $p \leq 0.001$ ; **Figure 1(E)**], in the left PCG [0.38 versus -0.12, respectively;  $t = 3.42$ ,  $p \leq 0.002$ ; **Figure 1(F)**], and in the right IPL [0.28 versus -0.11, respectively;  $t = 3.54$ ,  $p \leq 0.001$ ; **Figure 1(G)**].

For the contrast: HEPF versus LEUF (**Figure 2**), there was a significant difference between the groups in one MNI coordinate: x,y z: -16, -8, 50, pertaining to the left MFG, Brodmann area #6, and the SFG, with a  $p \leq 0.01$  and a  $k \geq 119$ , adjusted for multiple comparisons. In these brain regions, obese BED showed an increase in BOLD signal, but the obese showed a decrease [0.14 versus -0.075, respectively;  $t = 3.17$ ,  $p \leq 0.003$ ; **Figure 2**].



**Figure 1:** Differences between obese BED in comparison with the obese on BOLD signal amplitudes for the contrast map: food vs. nonfood [A-G;  $p \leq 0.005$ ,  $k \geq 88$ ].



**Figure 2:** Differences between obese BED in comparison with the obese on BOLD signal amplitudes for the contrast map: high energy processed food (HEPF) versus low energy unprocessed food (LEUF) [ $p \leq 0.01$ ,  $k \geq 119$ ].

### Psychobehavioral assessment

The comparison between obese BED versus obese on psychobehavioral assessment scores [disinhibition, anxiety and Behavioral Activation System (BAS)] is shown in **Table 4**. Differences between the groups were significant ( $p < 0.05$ ) on all three measures: the obese BED scored higher than the obese on anxiety (39 vs. 29.9,  $t = 2.4$ ,  $p < 0.02$ ) and disinhibition (10.6 vs. 7,  $t = 3.3$ ,  $p < 0.002$ ), and lower on the reward responsiveness subscale of the BAS 18.4 vs. 15.9,  $t = -3.0$ ,  $p < 0.005$ ). Following Bonferroni correction for multiple comparisons, significance level changed to a  $p \leq 0.017$ , leaving disinhibition and BAS (reward), but not anxiety, significantly different between the groups. Both measures were then correlated with the brain imaging data (see below).

**Table 4: Psychobehavioral scores in the two groups**

	Behavioral Activation Scale (reward)	Anxiety	Disinhibition
Obese BED	.159 ±3.5	39 ±13.8	10.6 ±3.1
Obese non-BED	18.4 ±2.00	29.9 ±9.5	7 ±3.4
P value	0.005 <sup>4</sup>	0.02 <sup>5</sup>	0.002 <sup>4</sup>

#### Differences between the groups in the relationships between brain imaging and psychobehavioral measures

For each of the eight significant MNI coordinates detailed above (seven for the contrast food versus nonfood, and one for the contrast HEPF versus LEUF) parameter estimates of each MNI were correlated with disinhibition and BAS scores of each group (**Table 5**). Pearson correlation coefficients were calculated and converted into a z distribution scores using an online calculator (<http://vassarstats.net/rdiff.html>) to assess the significance of the difference between the two independent samples in the relationships between BOLD signal and psychobehavioral measures. **Table 5** shows significant differences between the groups in the correlation between BOLD signal in the right ACC - Brodmann area #32 and disinhibition scores [(-.5) in the obese BED group, versus (0.3) in the obese,  $p < .018$ ]. Similarly, the correlation between BOLD signal in the left PCG and disinhibition scores was significantly different between the groups [(-0.5) in the obese BED group, versus (0.4) in the obese,  $p < 0.008$ ]. The correlation between BAS reward scores and BOLD signal amplitudes was not significantly different between the groups in any of the MNIs tested.

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<sup>4</sup> Significant also at  $p \leq 0.017$  (Bonferroni correction for multiple comparisons)

<sup>5</sup> Significant at  $p \leq 0.05$



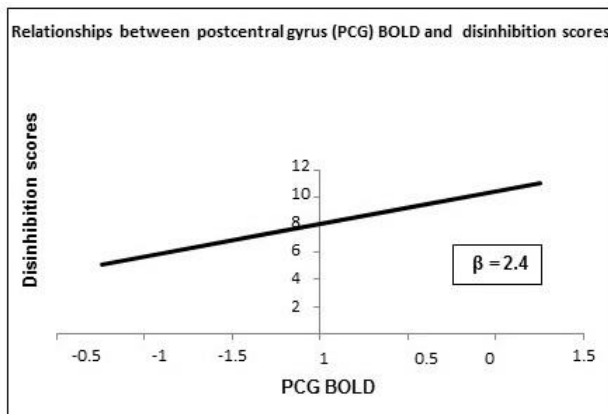
To examine the interaction between psychobehavioral measures and BOLD signal in response to food cues, we plotted a regression line for one MNI (66- 22- 22) (left PCG) found to be significantly different for obese BED versus obese in response to food vs. nonfood ( $r^2 = 0.105$ ,  $F = 4.69$ ,  $p = 0.04$ ). **Figure 2** shows the regression line for the significant relationships between BOLD signal in the left PCG to food versus nonfood, and disinhibition scores for all participants combined. About 10% of the variability in disinhibition scores can be explained by differences in BOLD signal in the left PCG in response to images of food, corresponding to the regression equation: disinhibition score =  $8.05 + 2.4 \times [\text{left PCG BOLD}]$  ( $p = 0.04$ ).

**Table 5: Correlation (Pearson's r) between brain BOLD signal in response to food cues and disinhibition scores**

Brain area	Obese BED	Obese non-BED	Difference between groups <sup>*</sup>
Right anterior cingulate cortex, Brodmann area 32	-0.5	+0.3	$z = -2.4$ $p = 0.018^a$
Left postcentral gyrus	-0.5	+0.4	$z = -2.7$ $p = 0.008^*$

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<sup>\*</sup>Significant difference between the groups in the correlation of 'Disinhibition' and BOLD signal



**Figure 3: Relationships between left postcentral gyrus BOLD signal and disinhibition scores ( $p = 0.04$ )**

## Discussion

The study aim was to identify biobehavioral differences between obese BED versus obese with no BED. There were four main findings: the obese BED group responded to images of food distinctly from the obese group in areas responsible for top-down control of visual attention and its integration with memory and evaluation of salience (i.e. the PCC, PCG, IPL and cuneate gyrus), possibly reflecting attentional bias toward visual targets that are of high motivational value.<sup>30</sup> Furthermore, in the obese BED group, greater disinhibition scores were associated with lower BOLD signal in brain areas functionally regulating affect, drives and arousal (i.e. anterior cingulate cortex, and Brodmann area #32). This is relevant to obese BED, as negative emotions may be a motivator to engage in binge eating behavior to lessen emotional states.<sup>31</sup> The anterior cingulate cortex is involved in translating intentions into action, by integrating motor control, motivational drives/arousal state, and cognitive messages.<sup>32</sup> These results may reflect a biobehavioral process in obese BED, who exhibit impaired executive functions when facing an emotionally laden stimulus, such as a binge-type food cue, often resulting in a self-regulatory failure.

The obese BED group responded to HEPF, more so than the obese non-BED group, in areas responsible for cognitive planning of motor movements, driven by emotions and drives (i.e.

1 MFG, BA #6, and the SFG). This may reflect impulsive tendencies when facing a binge-trigger, seen  
 2 in patients with BED or bulimia nervosa.<sup>33–35</sup> The HEPF images appear to have elicited an emotional  
 3 reaction driving a motor movement to approach. Impulsive behavior has been associated with the  
 4 construct of disinhibition in eating behavior,<sup>36</sup> as found in the present study. Across participants,  
 5 BOLD signal in the left PCG in response to food vs. nonfood cues predicted 10% of the variability in  
 6 disinhibition scores. Furthermore, BOLD signal in the left PCG in the obese BED group was inversely  
 7 related to their disinhibition scores, while in the obese group it was positively related. The postcentral  
 8 gyrus is the primary somatosensory cortical area, involved in mechanosensation and cognitive  
 9 integration of sensory stimulation with emotions, memory, and the body's internal state.<sup>23,37</sup> Our  
 10 results may reflect a propensity for dietary disinhibition in obesity with BED, possibly in a state of  
 11 negative affect, coupled with a weak attentiveness to somatosensory feedback, which may lead to  
 12 overeating. Lastly, the greater left-sided BOLD in the PCG in the obese BED group may reflect  
 13 asymmetry in brain laterality, favoring approach tendencies, as suggested by Spielberg, Heller, &  
 14 Miller (2013).<sup>24</sup>

15         Only one previous study from our group used functional brain imaging in fed obese BED  
 16 adults and found neural activation in the ventral premotor area in response to binge-type foods.<sup>38</sup>  
 17 Using different methodology, several studies have found BOLD signals in the right insula,<sup>29,39–41</sup> the  
 18 anterior cingulate cortex,<sup>24,39</sup> the precentral gyrus, BA #6, BA #19, and the lingual gyrus, in response  
 19 to food cues in binge eaters.<sup>38</sup> Our findings indicate heightened neural response to food cues in  
 20 sensorimotor, emotional and association areas (BA #6, BA #19, cuneate and lingual gyri, PCC and  
 21 ACC), similarly to previous reports. We extend those reports by showing heightened neural activity in  
 22 the multimodal association area network (i.e. insula, cingulate cortex, inferior parietal lobule, cuneate  
 23 gyrus, lingual gyrus, and the postcentral gyrus)<sup>3,42</sup> in obesity with BED, possibly indicating involuntary  
 24 attention to binge-food stimuli and preparation for a motor action.<sup>3,43</sup> We also demonstrate a link  
 25 between disinhibitory tendencies and functional integrity of the left PCG, implying a role of the left

1 PCG in somatosensory processing, memory and emotions related to eating. This may be associated  
2 with self-regulatory failure and binge-eating in obesity with BED.

3 Our findings may contribute to characterizing the obesity with BED phenotype, whereby a  
4 binge-eating episode occurs in a state of emotional challenge, plus the availability of binge-type  
5 foods, sensed through sight and/or olfaction. In this state, disinhibition and impulsiveness may lead to  
6 a binge. Moreover, a binge-eating episode may occur regardless of hunger or satiety level, for  
7 example despite stomach distention. Thus, a psycho-behavioral intervention working on increasing  
8 awareness to each component in this chain of events leading to a binge, and identifying  
9 psychophysiological states leading to automatic overeating, may offer a therapeutic approach to  
10 binge-eating in this population.

11 The present study had several strengths: the participants were scanned 1.5 hours after  
12 drinking a liquid meal, which is a shorter period compared with Geliebter et al. (2006),<sup>38</sup> who studied  
13 BOLD signal of obese BED adults three hours post-meal. The shorter postprandial time period in the  
14 present study was intended to imitate the condition of eating in the absence of hunger, which is  
15 common in BED.<sup>11,37</sup> There were also some study limitations in that there was no lean with BED  
16 group included, and the questionnaires were administered on a different day than the brain scan.

#### 17 In conclusion

18 The present study found evidence for a biobehavioral model of BED in obese adults in  
19 response to visual food cues, characterized by a heightened BOLD signal in the PCC and cuneate  
20 gyri (bilaterally), suggesting attentional bias to relevant food stimuli, and in the BA #6, MFG, and the  
21 SFG, implying cognitive planning of a motor behavior to act on a motivational drive to approach food.  
22 Moreover, reduced BOLD signal in the right ACC and BA #32, and in the left postcentral gyrus, were  
23 inversely related to disinhibition scores in the obese BED group. This suggests emotion dysregulation  
24 and reduced mechanosensory processing when faced with binge-triggers. Lastly, across both obese  
25 groups, disinhibition was positively associated with BOLD signal in the left postcentral gyrus,  
26 providing evidence of a link between somatosensory processing when faced with food cues and

1 dietary disinhibition tendencies in obese. These novel findings may have clinical implications for the  
2 treatment of obesity and BED.

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