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Negative Affect and Neural Response to Palatable Food Intake in Bulimia Nervosa

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Abstract

Binge eating is often preceded by reports of negative affect, but the mechanism by which affect may lead to binge eating is unclear. This study evaluated the effect of negative affect on neural response to anticipation and receipt of palatable food in women with bulimia nervosa (BN) versus healthy controls. We also evaluated connectivity between the amygdala and reward-related brain regions. Females with and without BN (N = 26) underwent functional magnetic resonance imaging (fMRI) during receipt and anticipated receipt of chocolate milkshake and a tasteless solution. We measured negative affect just prior to the scan. Women with BN showed a positive correlation between negative affect and activity in the putamen, caudate, and pallidum during anticipated receipt of milkshake (versus tasteless solution). There were no significant relations between negative affect and receipt of milkshake. Connectivity analyses revealed a greater relation of amygdala activity to activation in the left putamen and insula during anticipated receipt of milkshake in the bulimia group relative to the control group. The opposite pattern was found for the taste of milkshake; the control group showed a greater relation of amygdala activity to activation in the left putamen and insula in response to milkshake receipt than the bulimia group. Results show that as negative affect increases, so does responsivity of reward regions to anticipated intake of palatable food, implying that negative affect may increase the reward value of food for individuals with bulimia nervosa or that negative affect has become a conditioned cue due to a history of binge eating in a negative mood.

Keywords

bulimia nervosa; negative affect; fMRI; reward

Introduction

Bulimia nervosa is a prevalent eating disorder characterized by frequent binge eating and purging that is associated with numerous negative health consequences (Devlin & Steinglass, 2010; Stice & Bohon, in press). Many individuals with bulimia nervosa do not seek treatment (Fairburn et al., 2000), and those who do often continue to suffer from

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chronic course of the disorder, as even treatments of choice result in lasting symptom remission for only 35-45% of patients (Agras et al., 2000; Grilo et al., 2011; Lock et al., 2010). Because current interventions are limited in their efficacy, it is important to understand etiologic factors that increase risk for bulimia nervosa that may inform the design of more efficacious treatments for this pernicious psychiatric disorder.

Negative Affect and Bulimia Nervosa

Research has implicated negative affect in bulimia nervosa (Bulik, 2002), although the mechanism behind this relation is not clear. A recent meta-analysis of ecological momentary assessment studies (EMA), a research method involving randomly determined ratings throughout the day that allows for improved analysis of temporal antecedents to behaviors, found that negative affect ratings tend to be higher than normal just prior to a binge episode in bulimia and binge eating disorder (Haedt-Matt & Keel, 2011). The analysis showed that binge eating does not result in a decrease in negative affect, suggesting that binge eating is not an effective means of emotion regulation. So although negative affect is often an antecedent to binge eating, it does not appear that alleviation of this affect is driving the binge behavior.

One possible explanation for frequent binge eating in response to negative affect may be a heightened sensitivity in reward-related brain regions to food cues in a negative mood state. Peciña and colleagues (2006) found that cortico-releasing factor (CRF), frequently released during stress, enhanced the salience of reward cues in rats, providing some support for this theory. The impact of negative affect on the neural response to reward in bulimia nervosa has not yet been examined.

Prior research on reward-related brain function in bulimia nervosa has revealed greater activation in the medial orbitofrontal cortex (OFC), anterior cingulate cortex (ACC), visual cortex, dorsolateral prefrontal cortex (DLPFC), and insula in response to palatable food images (vs. non-food images) relative to healthy controls (Brooks et al., 2011; Schienle et al., 2009; Uher et al., 2004), echoing effects observed in obese versus lean individuals (Martin et al., 2009; Rothenmund et al., 2007; Stice et al., 2010; Stoeckel et al., 2008). This hyper-responsivity to food cues in bulimia could reflect an overall heightened reward sensitivity to these cues that could increase risk for binge eating. However, these studies did not include a mood induction, so it could be that group differences were due to differences in negative affect between BN and healthy controls or to differential effects of negative affect on response to food cues in the two groups. This is quite possible given that up to 70% of individuals with bulimia nervosa have a lifetime history of a mood disorder (Hudson et al., 2007).

Indeed, there is evidence that brain regions involved in emotion regulation may also play a role in reward processing. The amygdala plays a role encoding both positive and negative affect (Hamann & Mao, 2002). The basolateral amygdala is connected to the nucleus accumbens, and this pathway is thought to modulate cue-triggered motivated behaviors (Koob & LeMoal, 2005; Stuber et al., 2011). Optical stimulation of this pathway in mice increased behavior for stimulation, and optical inhibition to this connection reduced cue-induced sucrose intake (Stuber et al., 2011).

Emotional eaters, who tend to eat in response to negative mood states, show heightened activations in the parahippocampal gyrus and ACC in response to visual cues signifying impending delivery of a pleasurable taste during a negative mood state versus a neutral mood state, as well as heightened activations in the thalamus, pallidum, and ACC in response to receipt of the pleasurable taste in the negative mood state (Bohon, Stice, & Spoor, 2009); the effects were opposite in non-emotional eaters, suggesting that negative

mood is associated with less reward response in regions implicated in reward processing in individuals who do not express a tendency to eat in a negative mood. Taken together, these findings suggest that negative affect can alter the brain's response to rewarding stimuli, such as food, and the direction of the effect may depend on individual differences.

There is evidence of decreased neural response to actual taste in bulimia nervosa shown in both PET (Frank et al., 2006) and fMRI (Bohon & Stice, 2011; Frank et al., 2011) studies. This reduced response was found in the ACC, cuneus, insula, ventral putamen, amygdala, and OFC in response to a glucose taste (Frank et al., 2006; 2011) and in the precentral gyrus, middle frontal gyrus, thalamus, and insula in response to a chocolate milkshake taste, as found in the initial analyses of the present study (Bohon & Stice, 2011). This decrease in neural response to taste, yet the identified increase in response to food cues is congruent with studies that have compared obese versus lean individuals (e.g., Stice et al., 2008; Stice et al., 2010). The hypersensitivity to food cues may increase motivation to binge eat, yet reduced reward region response to food receipt may lead to overconsumption in a compensatory fashion.

Brain Connectivity

Little is known about brain connectivity in bulimia nervosa. To date, only one study has utilized functional connectivity methods in this group, and it focused on response to negative body words rather than taste or reward processing (Miyake et al., 2010). A small number of studies have investigated brain connectivity involved in reward processing in healthy adults. Connections between the dorsal striatum, substantia nigra, insula, amygdala, hippocampus, and ventral striatum have been found during various reward-related tasks (Camara et al., 2009; Cohen et al., 2008; Kahnt et al., 2009). Roy and colleagues (2009) identified unique connectivity of subregions of the amygdala. Of particular interest for this study, activity in the basolateral amygdala was significantly related to activity in the striatum. Thus, there could be differential connectivity between the amygdala, and in particular the basolateral amygdala, and other reward regions that could lead to greater impact of affective state on reward processing.

Because no studies to date have investigated the impact of negative affect on reward processing or functional connectivity during reward processing in bulimia nervosa, this preliminary study addresses an important gap in the literature. We extended our previous study (Bohon & Stice, 2011), which focused on group differences in neural response to taste in bulimia nervosa versus controls, to examine the impact of negative affect on these processes. We measured brain activity during anticipation and receipt of chocolate milkshake, as well as state negative affect just prior to scanning. We hypothesized that women with bulimia nervosa would show a positive correlation between reward region activation and negative affect when anticipating receipt of chocolate taste, which may help explain a greater tendency to binge in a negative mood state. We predicted that there would be an inverse relation between negative affect and neural response to the receipt of the taste because prior research found overall reduced neural response to reward receipt in bulimia nervosa (Frank et al., 2006; Frank et al., 2011), and we expect negative affect to enhance effects related to bulimic pathology. Finally, we predicted an inverse relation between negative affect and neural response to both anticipation and receipt of milkshake in healthy controls, congruent with our findings from control subjects in a prior study inducing negative affect (Bohon, Stice, & Spoor, 2009). Although little background research in connectivity in bulimia nervosa exists, we predicted greater connectivity between the amygdala and reward-related regions during anticipation of milkshake receipt in the bulimia group versus controls, as this greater connectivity could help explain a tendency to binge eat in a negative mood state.

Methods

Participants

The sample and procedures were previously described in a prior report of group differences (Bohon & Stice, 2011) and are summarized here. This study was approved by the Institutional Review Board of the University of Oregon. We recruited females, aged 18-26 ($M = 20.3$, $SD = 1.87$) with ($n = 13$) and without ($n = 13$) bulimia nervosa, assessed with the Eating Disorder Diagnostic Interview (Stice, Marti, Shaw, & Jaconis, 2009). The sample was 4% Hispanic, 80% Caucasian, 12% Asian, and 4% African American. Participants had a mean body mass index (BMI) of 23.6 (Range = 19.5-28.2, $SD = 2.6$). Groups did not differ significantly on BMI, or age. One participant in each group was left-handed, although the bulimia group had a significantly lower laterality index for handedness, suggesting slightly more use of the left hand across activities. Thus, laterality effects should be interpreted cautiously.

Measures

Screening Measure for Bulimic Pathology—The Eating Disorder Diagnostic Scale (Stice et al., 2000), which assesses diagnostic criteria for anorexia nervosa, bulimia nervosa, and binge eating disorder, was used to screen for bulimic pathology. The EDDS has shown high agreement ($k = .78 - .83$) with eating disorder diagnoses made with the Eating Disorder Examination (EDE; Fairburn & Cooper, 1993), internal consistency ($\alpha = .89$), 1-week test-retest reliability ($r = .87$), sensitivity to detecting intervention effects, and predictive validity for future onset of eating pathology and depression (Stice et al., 2000; Stice, Fisher, & Martinez, 2004).

Screening Measure for Axis I Disorders—The screening questions from the Structured Clinical Interview for DSM-IV Disorders was used to screen potential participants for psychiatric disorders. Specifically, the rule-out questions for major depression, bipolar disorder, substance abuse, and anxiety disorders were administered. Participants showing evidence of a psychiatric disorder on these questions were excluded from the study. The SCID shows good inter-rater reliability and test-retest reliability for major depression ($r = .80$ and $.61$ respectively), alcohol dependence/abuse ($r = 1.00$ and $.77$, respectively), and anxiety disorders ($r = .57-.88$ and $.44-.78$, respectively) (Zanarini & Frankenburg, 2001; Zanarini et al., 2000).

Handedness—Handedness was assessed with the Edinburgh Handedness Questionnaire (Oldfield, 1971), and both the laterality quotient and the laterality scale were calculated (Schachter, 1993).

Bulimic Symptoms—The Eating Disorder Diagnostic Interview (Stice, Marti, Shaw, & Jaconis, 2009), a semi-structured interview adapted from the Eating Disorder Examination (Fairburn & Cooper, 1993), was used to determine whether potential participants met criteria for bulimia nervosa or were free of an eating disorder. The diagnostic interview has shown high inter-rater agreement between independent and blinded assessors ($\kappa = .86$) and high 1-week test-retest reliability ($\kappa = .96$; Stice, Marti, Shaw, & Jaconis, 2009). Clinical interviewers for this study produced high inter-rater agreement with supervisors using recorded interviews ($\kappa = .90$ or higher) before collecting data.

Negative Affect—Participants completed the Positive and Negative Affect Schedule (PANAS; Watson, Clark, & Tellegen, 1988), which consists of ratings of 20 adjectives to describe their current mood on a 5-point scale. This scale is consistent ($\alpha = .95$) and reliable

over 3-week test-retest ($r = .78$) and shows convergent and predictive validity (Stice, Shaw, Burton, & Wade, 2006; Watson & Clark, 1992).

Procedure

Students in introductory psychology courses reporting at least 4 binge episodes and 4 compensatory behaviors in the prior month and those reporting no bulimic pathology on a screening measure (Eating Disorder Diagnostic Scale; Stice, Telch, & Rizvi, 2000) were invited for further screening with a diagnostic interview. Additional participants were recruited via flyers posted on campus and surrounding areas.

Participants completed two assessments. During the first, after providing informed consent, participants completed a diagnostic interview to confirm a diagnosis of bulimia nervosa or no eating disorder symptoms. Bulimia nervosa was defined as engaging in binge eating and compensatory behaviors at least once per week for a 3-month period, consistent with the proposed frequency and duration criteria for full threshold bulimia nervosa in the DSM-5 (APA, 2010). Participants who did not meet criteria for the eating disordered or non-eating disordered group (e.g., reported partial symptoms or symptoms of anorexia nervosa) were excluded.

On the second appointment, participants completed a series of written self-report measures that may be related to eating behaviors, including current negative affect, and the fMRI paradigm. This appointment was scheduled during each participant's midfollicular menstrual phase to control for effects of menstrual phase. They ate a standardized snack, consisting of a Nutri-Grain bar and fruit (e.g., apple, banana, or pear) to control for effects of acute food deprivation.

The paradigm consisted of the presentation of 2 visual cues: a picture of a glass of chocolate milkshake labeled "milkshake" and a glass of water labeled "water," and delivery of the corresponding tastes. We delivered a tasteless solution for the water condition to control for the effects of receiving and swallowing a liquid. Following 60% of the picture cues, a 3 second delivery of 0.5cc of the milkshake/tasteless solution was delivered following the jitter; for the remaining 40% of the pictures cues, no milkshake/tasteless solution was delivered (invalid presentations). The invalid presentations were utilized to separate the neural response to the picture cue from the neural response to the taste delivery. This ensures that the response to the picture cue is not confounded with response to subsequent taste. Thus, the invalid presentations are used for the anticipation condition. Additional details (e.g., duration of runs, numbers of trials) regarding this paradigm are presented in Bohon & Stice, 2011.

fMRI Scanner and Data Acquisition

We used a Siemens Allegra 3T scanner at the Lewis Center for Neuroimaging at the University of Oregon to collect functional and anatomical imaging data. Echo planar imaging was used to measure the blood oxygen level dependent (BOLD) signal as an indication of cerebral brain activation. The OFC and amygdala, areas subject to signal distortions in fMRI (Parrish et al., 2000), were of particular interest in this study. To improve BOLD signal detection and minimize susceptibility-based distortion effects, we used a protocol that utilized a high readout bandwidth, a shorter echo time, and localized shimming in the region of the OFC and amygdala to reduce the magnetic field distortion. A susceptibility weighted single shot echo planar sequence was used to image the regional distribution of the BOLD signal with TR = 2100 ms, TE = 20ms, flip angle = 80°, with an in plane resolution of $3.0 \times 3.0 \text{ mm}^2$ (64×64 matrix; $192 \times 192 \text{ mm}^2$ field of view). To cover the whole brain, 32 4mm slices (interleaved acquisition, no skip) were acquired along the

AC-PC transverse, oblique plane as determined by the midsagittal section. This procedure has consistently measured signal in the amygdala and OFC (e.g., Veldhuizen et al., 2007). In addition to functional images, a high resolution, T1 weighted 3D volume was acquired (MP-RAGE with a TR/TE of 2100ms/2.4ms, flip angle of 15°, TI of 1100ms, matrix size of 256×256, FOV of 22cm, slice thickness of 1mm).

We monitored head movement in vivo using Prospective Acquisition CorrEction (PACE) during the scan. If head movement exceeded 1 mm during a scan, the operator was notified so that the scan could be re-run. In addition, for smaller movements, PACE adjusts slice position, orientation and regrid the residual volume-to-volume motion during data acquisition.

Data Analysis

Data were analyzed using FEAT software (FMRI Expert Analysis Tool), part of the Oxford Centre for Functional Magnetic Resonance Imaging of the Brain Software Library (FSL; www.fmrib.ox.ac.uk/fsl). Images were motion corrected, skull stripped, and spatially smoothed with a 5-mm full-width half-maximum Gaussian kernel. Image processing also included mean-based intensity normalization of all volumes by the same factor and high-pass temporal filtering. Functional images were coregistered with structural images in native space and registered structural images to standard structural images (MNI-152).

We utilized the general linear model in analyses, with a convolution of the hemodynamic response function (HRF), its temporal derivative, and the timing of events of interest. Our paradigm had two contrasts of interest: the picture of a glass of milkshake vs. the picture of a glass of water that signal impending receipt of the solutions and receipt of milkshake vs. receipt of tasteless solution. We analyzed the data with multiple regression, including scores of negative affect as a regressor.

Within and between-group comparisons were performed using a mixed-effects model to account for inter-subject variability. We thresholded Z statistic images using clusters determined by $Z > 2.0$ and a corrected cluster significance threshold of $p < .05$. We utilized pre-threshold masking using regions of interest (ROI) mask created by adding the Harvard-Oxford Atlas 50 percent probability masks for the anterior cingulate cortex (ACC), amygdala, insula, accumbens, caudate, pallidum, putamen, thalamus, and orbitofrontal cortex (OFC).

For connectivity analyses, we conducted psychophysiological interaction analyses (PPI; Friston et al., 1997). We created individual seed masks for each participant by segmenting the amygdala in their structural scan using FMRIB's Integrated Registration and Segmentation Tool (FIRST) and then hand-checking the segmentation. In some instances, voxels had to be added within the mask by hand to ensure that all voxels of the amygdala were included. This individual seed was used for the PPI analyses at the individual level, and individual statistical maps were then used in higher-level group analyses. We utilized a pre-threshold ROI mask for PPI analyses consisting of the Harvard-Oxford Atlas 5 percent probability masks for the ACC, insula, accumbens, caudate, pallidum, putamen, thalamus, and OFC. We used a lower percent probability (larger region) so that we did not overly constrict our findings, as PPI analyses have lower power than general between-group analyses.

Results

Descriptive and group differences

Descriptive and group differences in this sample were reported previously (Bohon & Stice, 2011). Not included in that report were group comparisons of negative affect. Women with bulimia nervosa reported higher levels of negative affect ($M = 2.61$, $SD = .78$) than healthy control women ($M = 1.86$, $SD = .44$; $t(24) = 3.01$, $p < .01$, $R^2 = .27$).

Anticipation of Taste

We investigated the relation between brain activation in response to anticipating receipt of chocolate milkshake (> anticipating receipt of the tasteless control solution) and negative affect scores, and whether this relation differed between diagnostic groups. This contrast utilized invalid trials (e.g., when the cue signaled subsequent delivery of chocolate milkshake, but no taste was delivered), to ensure that neural response to receipt of milkshake did not influence the BOLD response. Women with bulimia nervosa showed a significant positive correlation between brain activation in the putamen, caudate, and pallidum in response to anticipated receipt of milkshake and negative affect, but there was no significant relation between brain activity and negative affect in healthy controls (see Table 1). Figure 1 shows the activation location and a graph of percentage signal change vs. negative affect score for each group. The relation between negative affect and neural response in bulimia was not significantly different from that of healthy controls, however.

Taste Receipt

We conducted similar analyses investigating the relation between negative affect and neural response to milkshake receipt (> tasteless solution receipt). There were no significant correlations between negative affect and neural response to receipt of tastes in either group or across groups within the regions of interest.

Psychophysiological Interaction

PPI analyses revealed that activation in the amygdala showed a stronger association with activation in the left putamen and left insula during anticipation of milkshake receipt in women with bulimia nervosa than healthy controls (Table 2; Figure 2). A similar finding emerged for the analysis with regard to consummatory reward, however it was in the opposite direction. Analyses revealed that activation in the amygdala showed a stronger association with activation in the left putamen and left insula during receipt of milkshake for healthy controls relative to women with bulimia nervosa. The PPI analyses did not change when negative affect was included as a regressor. Further, the connectivity between regions did not relate to negative affect.

Discussion

This study found that activity in the putamen, caudate, and pallidum in response to anticipation of a pleasurable taste was greater in women with bulimia nervosa whose negative affect was higher. Results also show evidence of greater functional coupling of activity in the amygdala with activation in the left putamen and left insula in the bulimia nervosa group compared to the controls during anticipation of pleasurable taste. Functional coupling of these areas during receipt of the milkshake taste, however, was weaker in women with versus without bulimia nervosa echoing prior evidence of opposite activation of reward regions in response to anticipated palatable food receipt and actual food receipt in obese women (Stice et al., 2008). These findings represent the first test of the impact of negative affect on reward processing in bulimia nervosa and provide support for the

hypothesis that negative affect influences responsivity of reward circuitry to anticipated palatable food receipt.

The putamen, caudate, and pallidum are frequently implicated in reward-based learning and habit formation (Yin & Knowlton, 2006). Greater activation of these regions in response to anticipated palatable food receipt in those with greater negative affect and bulimia nervosa could suggest greater encoding of reward-related information. This may render these individuals more likely to consume palatable foods. Specifically, negative affect may serve as a conditioned cue for reward response. For instance, if individuals have frequently engaged in binge episodes during negative mood states, the connection between a food cue and the neural response may become stronger in that state. In this way, negative affect may become a cue that triggers cravings for binge eating.

The finding of differential connectivity between the amygdala and activity in the putamen and insula during anticipation and receipt of chocolate taste is novel. Taken together with the relation between negative affect and activity in the putamen, pallidum, and caudate in bulimia nervosa, it may be that the connectivity during anticipation of a pleasurable taste in bulimia nervosa helps explain the effect of negative affect in this group. Specifically, cross-talk between the amygdala and the putamen, for example, may be the path by which negative affect, activating the amygdala, may impact reward processing. Such cross-talk may have the effect of increasing the reward value of palatable food during periods of negative affect. Additionally, the connectivity findings were different for anticipation of the pleasurable taste and receipt of the taste. Thus, if an individual with bulimia nervosa and high negative affect comes across a cue for pleasurable food (perhaps a sign for an ice cream shop, for example), the increased connectivity between the amygdala (with enhanced activity already due to the affective state) and putamen could result in greater craving for a binge. The decreased connectivity between these regions, relative to controls, for the receipt of the pleasurable taste could reflect the lack of impact of affective processes, or amygdalar function, on reward processing of actual taste, particularly given that negative affect was not related to reward region response to taste in bulimia. The amygdala, however, has been implicated in both emotion processing and reward processing, so alternatively, the amygdala could be functioning independently of affective state and simply reflect further reward processing. This would be better tested under direct manipulations of mood, utilizing methods that allow for better analysis of the time-course of brain activation to determine whether the amygdala activity does in fact precede the putamen activity. The combined use of EEG and fMRI may help to elucidate this issue.

Although this study is the first to explore the relation between negative affect and neural response to taste in bulimia nervosa, there are a number of limitations. First, the small sample may have limited our ability to detect effects in a number of brain regions. Second, we did not manipulate negative affect, so it is unclear whether the relation between negative affect and brain activity in bulimia is due to a third variable or whether negative affect leads to different neural response or vice versa. Finally, a taste of milkshake is not equivalent to the experience of a full binge episode. Although there were no significant relations between negative affect and neural response to taste in this study, it could be that a relation would be present for the neural response to a full binge episode.

It is noteworthy that these connectivity findings are from a seed region of the entire amygdala. Despite evidence that the basolateral nuclei of the amygdala may be particularly connected to the striatum (Roy et al., 2009) and that the pathway from the basolateral nuclei to the nucleus accumbens is implicated in sucrose intake in mice (Stuber et al., 2011), we did not limit our seed region to this subcortical area. The methods used to segment this region rely on normalizing atlas-based masks to individual scans. While this method is

sufficient in many ways, the seed regions from our FIRST segmentation of the entire amygdala provided smaller, more focused seeds than the ones generated from the atlas-based masks. Indeed, when we utilized the basolateral amygdala mask from the Juelich Histological Atlas, as reported in Roy et al. (2009), we obtained a much larger seed than when we used FIRST to segment the amygdala. Larger seed regions that include other structures may result in less consistent patterns of activation to compare to other regions. Thus, we had more confidence in our findings for the entire amygdala than we did if we had conducted the analyses with a basolateral amygdala seed generated from the atlas. Future research may benefit from the use of combined methodologies (e.g., automated segmentation, atlas-masking, hand-editing) to ensure the creation of precise seed regions when conducting connectivity analyses with anatomical regions.

In sum, these findings support an affective model of binge eating, with greater negative affect related to greater responsivity of reward regions in response to anticipation of pleasurable taste in women with bulimia. This may explain a greater propensity to engage in binge eating in a negative mood state. This effect may be due to a unique function of negative mood on reward processing in bulimia wherein negative affect increases the reward value of food. Alternatively, this finding may reflect a conditioned response during that mood state. Taken together with prior findings of overall reduced reward response to taste of milkshake in bulimia (Bohon & Stice, 2011), it may be that individuals with bulimia find it more difficult to resist tempting food cues when in a negative mood due to heightened neural response, but do not experience satisfaction from just a taste and end up engaging in a binge episode in attempt to match their expected level of reward. If neural response to anticipation of the taste were attenuated, perhaps by decreased negative affect, the mismatch of reward expectation and receipt may also be reduced, allowing for greater control over eating episodes. Further research should address both components of this potential explanation: (1) that reductions in negative affect would result in reduced neural response to anticipated taste reward and (2) that the mismatch between response to anticipated and actual taste receipt puts people at particular risk for binge eating.

It is important for future research to manipulate mood to rule out the possibility of a third variable affecting both neural response to food cues/tastes and negative affect. Further, there may be differences in impact of negative affect on response to food cues and tastes in bulimia nervosa dependent on whether or not an individual has the negative affect-dietary restraint subtype or the pure restraint subtype. Future research should explore this question by adequately sampling each of these subtypes in order to detect group differences. These findings could have implications for treatment development, particularly the inclusion and emphasis of emotion regulation skills for helping patients handle tempting food cues.

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Highlights

- Brain response to a visual food cue is related to negative affect in bulimia nervosa.
- Connectivity between amygdala and putamen and insula was investigated.
- Connectivity during visual food cue greater in bulimia nervosa.
- Connectivity during receipt of taste greater in healthy controls.

Figure 1.

Positive correlations between negative affect and signal change in the left caudate, putamen, and pallidum in the bulimia nervosa group. Images are in radiological view on the MNI- 152 standard brain, with the left hemisphere displayed on the right in axial and coronal slices. Scatterplot reveals percentage signal change in this region as function of negative affect. Bulimia nervosa in blue and healthy controls in red.

Figure 2.

Left putamen and insula show stronger positive correlations with amygdala activity in the BN group compared to the healthy controls as a function of seeing the visual cue associated with the milkshake taste versus the cue associated with the tasteless control taste. The same regions showed stronger positive correlations with amygdala activity in healthy controls compared to the BN group as a function of receiving the milkshake taste versus the tasteless control taste. Images are in radiological view on the MNI-152 standard brain, with the left hemisphere displayed on the right in axial and coronal slices.

Table 1

Brain regions related to negative affect in bulimia nervosa group (MNI coordinates of cluster centers) and cluster Z-score for each contrast

x	y	z	Max Z	Brain Region
-26	-6	12	3.00	Left Putamen
-18	4	-2	2.79	Left Pallidum
-8	8	6	2.71	Left Caudate
-28	0	-4	2.63	Left Putamen
-24	8	6	2.6	Left Putamen
-32	-14	-4	2.47	Left Putamen

Table 2

Brain regions related to amygdala activity (MNI coordinates of cluster centers) and cluster Z-score for each contrast

Contrast	x	y	z	Max Z	Brain Region
Anticipation Bulimia > Control					
	-26	-4	2	4.29	Left Putamen
	-18	4	-10	3.11	Left Putamen
	-38	0	4	3.01	Left Insula
	-42	2	-4	2.92	Left Insula
	-40	12	-4	2.88	Left Insula
	-44	6	-4	2.78	Left Insula
Receipt Control > Bulimia					
	-24	-2	2	4.46	Left Putamen
	-18	4	-10	3.03	Left Putamen
	-40	12	-4	2.89	Left Insula
	-44	2	-6	2.89	Left Insula
	-38	-2	4	2.88	Left Insula