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Research report

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.

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, Cooper, Doll, Norman, & O'Connor, 2000), and those who do often continue to suffer from 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, Masheb, Wilson, Gueorguieva, & White, 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.

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Prior research on reward-related brain function in bulimia nervosa has revealed greater activation in the medial orbitrofrontal cortex (OFC), anterior cingulate cortex (ACC), visual cortex, dorsolateral prefrontal cortex (DLPFC), and insula in response to palatable food images (versus non-food images) relative to healthy controls (Brooks et al., 2011; Schienle, Schäfer, Hermann, & Vaitl, 2009; Uher et al., 2004), echoing effects observed in obese versus lean individuals (Martin et al., 2009; Rothemund et al., 2007; Stice, Yokum, Bohon, Marti, & Smolen, 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, Hiripi, Pope, & Kessler, 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 & Le Moal, 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, Reynolds, Shott, & O'Reilly, 2011) studies. This reduced response was found in the ACC, cuneous, 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, Spoor, Bohon, & Small, 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, 2008; Cohen, Elger, & Weber, 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, 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 et al., 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, Telch, & Rizvi, 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