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Weight Suppression in Bulimia Nervosa: Associations with Biology and Behavior

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Abstract

Bulimia nervosa (BN) is a serious eating disorder that can persist for years and contribute to medical complications and increased mortality, underscoring the need to better understand factors maintaining this disorder. Higher levels of weight suppression (WS) have been found to predict both the onset and maintenance of BN; however, no studies have examined mechanisms that may account for the effects of WS on BN. We hypothesized that high WS would lead to reduced leptin levels, which may increase risk of binge eating by modulating reward responses to food. The current study examined the relationship between WS, leptin levels, and the reinforcing value of food in women with BN (n=32) and non-eating disorder controls (n=30). Participants provided information on WS, completed a fasting blood draw to obtain serum leptin, and completed a progressive ratio task to measure the reinforcing value of food. Individuals with BN had greater WS ($p<.01$) and reinforcing food value ($p<.05$) compared to controls. Additionally, higher WS was associated with both lower leptin ($p<.05$) and increased reinforcing value of food ($p<.05$). Contrary to hypotheses, BN and control participants did not differ significantly on leptin levels, and leptin levels were not significantly associated with the reinforcing value of food. Findings support that efforts to conform to the thin ideal may alter drive to consume rewarding foods and leave women vulnerable to binge episodes. However, mechanisms through which WS contributes to food reward and binge eating remain unknown.

Keywords

bulimia nervosa; weight suppression; leptin; binge eating; food reward

Bulimia nervosa (BN) is a serious eating disorder characterized by binge-eating episodes and subsequent compensatory behaviors, such as self-induced vomiting. BN can persist for several years (Keel & Brown, 2010), produce severe medical complications (Mehler, 2011), and increase risk of death (Arcelus, Mitchell, Wales, & Nielsen, 2011), underscoring the need to identify risk and maintenance factors for this disorder. Weight suppression (WS), defined as the difference between one's highest previous weight at adult height and one's current weight, has emerged as a robust predictor of both the onset (Keel & Heatherton,

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2010) and maintenance of BN in independent studies (Butryn, Juarascio, & Lowe, 2011; Butryn, Lowe, Safer, & Agras, 2006; Keel & Heatherton, 2010; Lowe et al., 2011). Higher levels of WS predicted the onset and maintenance of a bulimic syndrome ten years later (Keel & Heatherton, 2010). Additionally, higher WS at baseline was associated with longer time to remission from BN over eight-year follow-up (Lowe et al., 2011). Several authors (Butryn et al., 2006; Keel & Heatherton, 2010; Lowe, Davis, Lucks, Annunziato, & Butryn, 2006; Lowe et al., 2011) have posited that biobehavioral mechanisms underlie the association between WS and illness trajectory in BN. Yet, no study has examined biological consequences of WS in BN or their behavioral correlates which could account for vulnerability for binge eating. The current study sought to address this gap in the literature.

Individuals who are weight suppressed may experience psychobiological pressures toward weight gain that may contribute to the persistence of BN (Butryn et al., 2006; Keel & Heatherton, 2010; Lowe et al., 2006). Significant weight loss (i.e., high WS) contributes to loss of adipose tissue, which is responsible for producing leptin (Considine et al., 1996; Maffei et al., 1995; Wolfe et al., 2004). Importantly, leptin modulates the effects of feeding-related neurons and energy homeostatic systems and contributes to overall decreased food intake (Coll, Farooqi, & O'Rahilly, 2007) and changes in body weight (Leibel, 2002; Rosenbaum, Kissileff, Mayer, Hirsch, & Leibel, 2010). Additionally, leptin has been implicated in hedonic or motivational aspects of eating and behaviors to obtain non-food rewards (Figlewicz, Evans, Murphy, Hoen, & Baskin, 2003; Fulton et al., 2006; Hommel et al., 2006; Krugel, Schraft, Kittner, Kiess, & Illes, 2003). For example, studies have found that central administration of leptin reduces rats' willingness to work for both food and non-food rewards (Bruijnzeel, Corrie, Rogers, & Yamada, 2011; Davis et al., 2008; Figlewicz, Bennett, Naleid, Davis, & Grimm, 2006; Shalev, Yap, & Shaham, 2001; Wellman, Nation, & Davis, 2007), supporting leptin's broad influence on the reinforcing value of rewards and its role in hedonic as well as homeostatic regulation of eating.

Supporting the possibility that greater WS in BN may contribute to lower leptin levels, previous studies have found leptin levels to be decreased in individuals with BN compared to healthy controls matched for body mass index (BMI) (Brewerton, Lesem, Kennedy, & Garvey, 2000; Jimerson, Mantzoros, Wolfe, & Metzger, 2000; Jimerson, Wolfe, Carroll, & Keel, 2010; Monteleone, Bortolotti, Fabrazzo, La Rocca, Fuschino, & Maj, 2000; Monteleone, Di Lieto, Tortorella, Longobardi, & Maj, 2000; Monteleone, Fabrazzo, Tortorella, Fuschino, & Maj, 2002). Furthermore, some studies have reported associations between lower leptin levels and greater frequency of binge-eating episodes (Jimerson et al., 2000; Monteleone et al., 2002) and longer duration of illness (Monteleone et al., 2002). Thus, despite the appearance of healthy weight in BN, high levels of WS may contribute to lower leptin levels, and lower leptin may increase drive to eat and subsequent binge episodes by influencing the rewarding value of food.

Although findings from several studies support satiation deficits in individuals with BN (e.g., Devlin et al., 1997; Geliebter et al., 1992; Keel, Wolfe, Liddle, De Young, & Jimerson, 2007), few have focused on behavioral measures of hedonic aspects of eating (e.g., the reinforcing value of food) (Bulik & Brinded, 1994; Schebendach, Broft, Foltin, & Walsh, 2013), and none have examined their associations with WS or leptin in BN. Schebendach et

al. (2013) completed the largest study to date examining food reinforcement in women with BN (n=10) compared to healthy controls (n=10). In order to measure the reinforcing efficacy of food, participants completed a progressive ratio (PR) task in which they pressed a computer keyboard button to earn portions (175 mL) of a strawberry shake. The amount of work required to earn 175 mL of shake increased progressively over the course of the task (50 key presses for the first 175 mL, then 250, 450, 650 etc… across trials). The number of presses in the final completed trial (breakpoint) represented the reinforcing value of food in terms of the amount of work participants were willing to do to earn food. At the end of the task, the earned reward was given to participants to consume. When instructed to work for the amount they could binge on/overeat, women with BN worked harder than the controls, supporting greater reinforcing value of food in BN. Importantly, this study was limited by a small sample size (n=10 women with BN), and the food reward was delayed until the end of the task. Thus, this task may better capture anticipation of how rewarding food will be rather than the reinforcing value of food during consumption. Measuring the reinforcing value of food during consumption would more closely reflect the nature of deficits observed in BN in which the individual feels unable to stop eating *during* the binge (Russell, 1979).

In this study, we hypothesized that higher levels of WS would be associated with lower leptin and greater reinforcing value of food and that leptin levels would be negatively associated with reinforcing value of food. Furthermore, we hypothesized that higher WS, lower leptin, and greater reinforcing value of food would be associated with greater severity of eating disorder symptoms (e.g., frequency and size of binge-eating episodes) and longer duration of illness. Finally, we posited that leptin would mediate associations between WS and reinforcing value of food and severity and duration of symptoms in BN.

Method

Participants

Participants were 32 women with DSM-5 BN (American Psychiatric Association, 2013) and 30 female control participants without a history of any eating disorder. All participants were required to be between 18–45 years of age, have a BMI between 18.5–26.5 kg/m^2 and be free of medical conditions and medications known to affect appetite or weight. Additionally, individuals allergic to food used in the study and control women who endorsed dieting in the past eight weeks to lose weight were excluded. The mean (SD) age of the sample was 21.4 (4.8) (range=18–40) years. All participants had completed high school, and 12.9% had a college degree. Approximately 66.1% of the sample was White/non-Hispanic, 16.1% Hispanic, 11.3% Black/non-Hispanic, 3.2% Asian/non-Hispanic and 3.2% Mixed/Other (Table 1). Three BN participants (9.4%) reported currently receiving treatment for eating or mental health problems, and 68.8% (n=22) endorsed a history of such treatment.

Procedure

This study consisted of three visits over the course of two days. All procedures were approved by the University's Institutional Review Board, and informed consent was obtained from participants prior to participation.

The first visit was used to determine study eligibility. Participants had their height and weight measured, were assessed by a master's level interviewer to determine presence of current and lifetime psychiatric diagnoses, and completed self-report questionnaires.

Visits two and three occurred in the morning and afternoon on the same day. These visits were scheduled during the follicular phase of the menstrual cycle in order to control for the potential influence of menstrual cycle phase on leptin levels (e.g., Ludwig, Klein, Diedrich, & Ortmann, 2000; Quinton et al., 1999), consistent with previous studies (e.g., Jimerson et al., 2000; Monteleone et al., 2002; Monteleone, Bortolotti, et al., 2000; Monteleone, Di Lieto, et al., 2000). Participants had their blood drawn at approximately 9:00am after an overnight fast to measure leptin and blood glucose concentrations, had their weight and percent body fat measured, and consumed a standardized breakfast of a yogurt parfait and juice (approximately 300 kcal). All participants had fasting blood glucose values within the expected range (91–113 mg/dL) (ReliOn® Prime). After consuming the standardized breakfast, participants were told to abstain from eating or drinking anything except water and from engaging in any compensatory behaviors until they returned to the laboratory at 1:00pm for their third visit.

During the third visit, participants completed a PR task designed to measure the reinforcing value of food. Instructions for the task (detailed below) were played on a cassette tape and printed on a card to decrease likelihood of experimenter influence. Digital video monitoring was used to confirm that participants followed instructions. Two BN participants (6%) did not follow task instructions, and their data were excluded from analyses examining reinforcing value of food. All control participants followed instructions.

Measures

Weight Suppression—Consistent with previous studies, WS was calculated as self-reported highest weight minus objectively measured current weight (e.g., Butryn et al., 2006; Herzog et al., 2010; Lowe et al., 2006). Previous research supports the validity of self-reported highest weight (Tamakoshi et al., 2003), including one study that found a strong correlation (r=0.92) between reported and documented highest weight in patients with eating disorders (Swenne, Belfrage, Thurfjell, & Engstrom, 2005).

Leptin Levels—Serum leptin levels were measured after an overnight fast. After blood collection, serum was transferred to cryotubes and stored in a −80 degree C freezer until assayed (less than 6 months). Leptin levels were determined by enzyme-linked immunosorbent assay using commercially available kits (Human Leptin ELISA kit, Linco/Millipore, St. Charles, MO). Intra-assay coefficient of variability (CV) was good (mean % CV=5.15±3.46).

Reinforcing Value of Food—The reinforcing value of food was measured using a modified version of the PR computer task used by the Columbia Center for Eating Disorders (Klein et al., 2010; Schebendach et al., 2013). During this task, participants pressed a keyboard button to earn M&M® chocolate candies (©Mars, Incorporated, Hackettstown, NJ). The task consisted of 10 trials, with the opportunity to earn 10 M&Ms® per trial. As trials progressed, more keyboard presses were required to earn 10 M&Ms® to establish the

work participants were willing to complete to earn the reward. Participants were left alone to complete the task and instructed to notify the experimenter when she had completed all 10 trials or decided to stop. Consistent with the ratio used in previous studies (Klein et al., 2010; Schebendach et al., 2013), the number of key taps required for the first trial was 50 and increased by 200 keyboard presses during each subsequent trial (i.e., 250 presses for trial two, 450 for trial three, 650 for trial four…and 1850 for trial 10). After completion of each trial, 10 M&Ms® were dispensed from a candy dispenser next to the participant. The participant was instructed to consume all 10 M&Ms® before initiating the next trial. Consistent with previous studies, the breakpoint or number of key presses in the last completed trial was used to reflect the work participants were willing to complete for the reward, or the reinforcing value of the food. Previous research supports the validity and use of operant paradigms as a measure of food reinforcement (e.g., Epstein, Leddy, Temple, & Faith, 2007).

Percent Body Fat—Percent body fat was used as a covariate in analyses with leptin and measured using foot-to-foot bioelectrical impedance analysis (BIA) (Tanita body-fat analyzer; Tanita Corporation of America, Inc., Arlington Heights, IL). Studies have found high correlations (r=.88–.94) between BIA and dual-energy X-ray absorptiometry (DXA) (Boneva-Asiova & Boyanov, 2008; Tyrrell et al., 2001).

Psychiatric Diagnoses—The Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1995) mood, substance use, and eating disorder modules were administered to assess current and lifetime diagnoses. The SCID-I questions were adjusted to evaluate DSM-5 diagnostic criteria (e.g., binging and purging frequency of once versus twice per week), and follow-up questions were used to confirm presence of binge-eating episodes and to evaluate average binge size in kcal, consistent with prior studies (e.g., Keel, Brown, Holm-Denoma, & Bodell, 2011; Keel, Mitchell, Miller, Davis, & Crow, 1999). Duration of illness for BN participants was obtained during the interview. Interrater reliability was excellent among clinical interviewers (K=1.00 for lifetime mood, eating, and substance use disorders).

Eating Disorder Symptoms and Impairment—The Eating Disorder Examination-Questionnaire (EDE-Q; Fairburn & Beglin, 1994) is a self-report questionnaire adapted from the EDE interview, and studies support moderate to strong correlations between these two measurements (Berg, Peterson, Fraizer, & Crow, 2011; Berg et al., 2013). Specifically, this questionnaire assesses frequency of disordered eating behaviors over the previous 28 days, including binge eating, purging, and excessive exercise. Additionally, the questionnaire assesses specific features of eating disorders that contribute to four subscales: Restraint, Eating Concern, Shape Concern, and Weight Concern. Reliability in the current study was good with alphas ranging from .91– .98 for the subscales and total score.

The Clinical Impairment Assessment (CIA; Bohn et al., 2008) is a 22-item self-report measure that evaluates interpersonal, occupational, and emotional domains of impairment attributable to the presence of an eating disorder. Internal consistency for this measure was excellent (α=.96).

Statistical Analysis

All analyses were conducted using *SPSS version 22.0*. One extreme outlier was found for WS (i.e., greater than three standard deviations above the mean); thus, this score was replaced by the next highest value (Howell, 2010). An independent samples t-test was conducted to examine group differences in WS, and an analysis of covariance (ANCOVA) was conducted with percent body fat and assay[1] included as covariates to examine group differences in leptin. Importantly, results were not altered by inclusion of covariates. A t-test was used to examine group differences in the reinforcing value of food with breakpoint entered as the dependent variable. Finally, Pearson's correlation and regression analyses were conducted in the full, BN, and Control samples to examine associations among WS, leptin levels, reinforcing food value, and clinical characteristics (e.g., frequency and size of binge episodes, compensatory behaviors, weight/shape concerns, and eating disorder impairment). Given *a priori* hypotheses and the well-established relationship between leptin and adipose tissue, one-tailed p-values were used for examining associations between leptin and WS, BMI, and percent body fat.

Results

Demographic data for the BN and control participants appear in Table 1. There were no significant differences between the groups on age, current BMI, percent body fat, race, ethnicity, or highest education (*p*s>.2). As expected, individuals with BN had significantly greater eating-related psychopathology across all measures (Table 2). In terms of comorbid disorders, three women with BN (9.4%) and no controls met criteria for current major depression (χ^2=2.96, *p*=.09). Nineteen women with BN (59.4%) and two controls (6.7%) endorsed a history of major depression (χ^2=19.21, *p*<.001). Additionally, seven women with BN (21.9%) and two controls (6.7%) met criteria for a current alcohol use disorder (χ^2=2.89, *p*=.09), and four BN (12.5%) and one control participant (3.3%) met diagnostic criteria for a current substance use disorder (χ^2=1.76, *p*=.19). In terms of compensatory behaviors, 29 BN participants (90.6%) endorsed fasting to control shape and weight, 25 (78.1%) endorsed excessive exercise, 16 (50%) endorsed self-induced vomiting, and 5 (15.6%) endorsed laxative use.

Consistent with hypotheses, individuals with BN had significantly greater WS (mean[SD]=16.6[18.0] lbs) compared to control participants (5.8[5.3] lbs) (*t*=3.27, *p*=.002, Cohen's *d*=.81), despite no significant difference in height, percent body fat, current body weight, or current BMI. Furthermore, group differences in WS remained significant while controlling for current mood, alcohol use, and substance use disorders (*F*[1,57]=9.06, *p*=.004, partial η^2=0.14). Contrary to our hypotheses, there were no group difference on leptin levels (*F*[1, 53]=0.10, *p*=.76, partial η^2=0.002), while controlling for assay and percent body fat.

[1]Given limited space in each hormonal assay kit, two separate leptin assays were required. The assays were balanced by group (control and BN participants); however, assay was associated with some key variables (i.e., weight suppression), and thus, was included as a covariate in analyses of leptin.

Although the range in number of trials completed was the same for both groups (1–10), individuals with BN worked harder for the food reinforcer as demonstrated by significantly higher breakpoint (753.5±429.9 vs. 498.3±380.4) (t[56]=2.39, p=.02, Cohen's d=0.63) compared to controls. Additionally, group differences on breakpoint (F[1,53]=5.30, p<.03) remained significant while controlling for current comorbid disorders.

As hypothesized, higher WS was significantly associated with decreased leptin levels in the full sample (β=−.24, t=−1.78, p<.05, partial r=−.24) and BN sample (β=−.34, t=−1.86, p<.04, partial r=−.34), and marginally significant in the control sample (β=−.30, t=−1.51, p=.07, partial r=−.29) while controlling for assay. There was a significant association between WS and reinforcing value of food in the full sample such that higher WS was correlated with increased breakpoint (r=.35, p<.01) (Table 3). A similar moderate effect size also was observed in the BN group for associations between WS and breakpoint (r=.37, p=.05), but there was no association between WS and breakpoint in the controls (r=−.01, p=.94). Furthermore, contrary to hypotheses, leptin levels were not significantly associated with breakpoint in any sample (Table 3). Thus, mediation analyses were not completed.

Finally, higher WS was significantly associated with higher frequency of compensatory behaviors, larger binge-episode size, and longer duration of illness in BN (Table 4). Furthermore, the relationship between WS and binge size remained significant while controlling for BMI (β=.46, t=2.79, p<.01, partial r=.46). Aside from their associations with WS, reinforcing value of food and leptin levels were not significantly associated with any clinical characteristics in the BN sample (Table 4).

Discussion

The purpose of the current study was to better understand factors driving associations between WS and BN. Consistent with hypotheses, women with BN were significantly more weight suppressed and had greater reinforcing value of food compared to control women. Furthermore, higher levels of WS were associated with lower leptin levels and higher breakpoint. However, we did not find significant group differences in leptin, and leptin was not significantly associated with the reinforcing value of food.

In addition to group differences in WS, higher levels of WS in BN were associated with greater binge size and longer duration of illness. Although not statistically significant, WS was moderately associated with greater frequency of binge eating (r=.29), which may have been significant with a larger sample. Indeed, highest BMI for individuals with BN was in the upper range of normal (25.4±3.9) and significantly higher than that of controls (22.9±2.7). Weighing more than ones' peers may increase the likelihood of body dissatisfaction, dieting and/or fasting, which may contribute to both weight loss (i.e., WS), and bulimic symptoms, given that extreme dietary restriction predicts onset of binge eating (Stice, Davis, Miller, & Marti, 2008). Furthermore, associations between WS and binge-episode size suggest that decreasing one's body weight potentially below a previous set point may impair satiety and increase propensity to overeat (Larder & O'Rahilly, 2012). Individuals with higher WS may fear returning to their premorbid weight, which may contribute to the maintenance of bulimic symptoms. For individuals with high WS, evidence

indicates that weight gain concerns may be realistic (e.g., Stice, Durant, Burger, & Schoeller, 2011); increased WS has been found to predict increased weight gain during short-term inpatient (Lowe et al., 2006) and outpatient treatment (Carter, McIntosh, Joyce, & Bulik, 2008) as well as over five-year follow-up (Herzog et al., 2010). Importantly, several studies have documented changes in energy expenditure resulting from reduced weight (i.e., weight suppression) (e.g., Leibel, Rosenbaum, & Hirsch, 1995; Stice et al., 2011) and the role of leptin in influencing resting metabolic rate, energy expenditure, and subsequent body weight (e.g., Leibel, 2002; Rosenbaum, Kissileff, Mayer, Hirsh, & Leibel, 2010). Thus, biological consequences of WS (e.g., reduced leptin) may increase vulnerability to weight gain and both the fear of weight gain and the behaviors used to prevent this outcome may contribute to illness maintenance among those with greater WS.

Consistent with Schebendach et al. (2013), we found that individuals with BN had a higher breakpoint and total number of responses than controls on the PR task for M&Ms®. This finding supports that individuals with BN find palatable food more reinforcing than controls, which may contribute to overeating. This is important because much prior work on factors contributing to binge-eating episodes in BN has focused on the use of binge episodes to regulate negative affect (Haedt-Matt & Keel, 2011) rather than rewarding aspects of food intake. Importantly, the task used in the current study found group differences even in the absence of needing to instruct participants to binge. Additionally, our task more closely resembles those used in animal studies and maps on to the Research Domain Criteria construct of approach motivation (Sanislow et al., 2010), making it well-suited to examine in relation to biological responses to food during consumption. Although breakpoint was not significantly associated with binge-episode size or frequency, it demonstrated a moderate association with longer duration of illness, suggesting that a greater reinforcing value of palatable food may indirectly contribute to eating disorder maintenance.

The association between greater WS and higher breakpoint suggests that being at a lower weight than in the past may increase “wanting” of palatable foods. This association may help explain, in part, why individuals who have lost weight often find it hard to maintain weight loss (Elfhag & Rossner, 2005), and, in turn, may help inform treatments for BN and obesity. For individuals with BN, this information may be used to educate patients on how WS may actually contribute to increased appetitive drive. Additionally, it may be particularly important to address fear of weight gain during treatment in individuals with high WS, as gaining some weight and reducing the level of WS may reduce food reward and facilitate remission. Given that BN participants were in the upper end of a healthy weight range at their lifetime highest weight, patients may be reassured that gaining some weight to reduce drive to eat does not necessarily require that they become overweight.

The lack of a significant difference in leptin levels between the BN and control groups is somewhat surprising given that several studies have found lower leptin in individuals with BN (Brewerton et al., 2000; Jimerson et al., 2000; Jimerson et al., 2010; Monteleone et al., 2002; Monteleone, Bortolotti, et al., 2000; Monteleone, Di Lieto, et al., 2000; Monteleone et al., 2002). Although none of these previous studies on leptin reported on WS, our BN sample had relatively low WS levels (16.6 lbs) compared to other studies on WS in BN (15.6–26.5 lbs) (e.g., Butryn et al., 2011; Carter, McIntosh, Joyce, & Bulik, 2008; Dawkins,

Watson, Egan, & Kane, 2013; Lowe et al., 2006; Lowe et al., 2007; Lowe et al., 2011). Thus, it is possible that group differences in leptin found in previous studies resulted from higher WS in their BN samples or that lower WS in our BN group made it more difficult to detect differences. However, we still found significant associations between WS and leptin in our sample, and leptin levels in the current BN sample appear similar to those found in other studies (range 2.2–10 ng/mL; Brewerton et al., 2000; Jimerson et al., 2000; Jimerson et al., 2010; Monteleone et al., 2002; Monteleone, Bortolotti, et al., 2000; Monteleone, Di Lieto, et al., 2000; Monteleone et al., elih). In contrast, the control participants exhibited relatively low leptin levels compared to previous control samples. Control participants in the current study were excluded if they were attempting to diet to lose weight but were not excluded for attempting to *maintain* weight through diet and exercise or for the presence of comorbid disorders. This recruitment strategy may have led to some biases in our sample (e.g., increased exercise frequency); however, the former criterion is not dissimilar to that used in other studies that have supported lower leptin in BN (e.g., Jimerson et al., 2000; Jimerson et al., 2010).

An alternative explanation for the null leptin result is that differences between BN and control participants from prior studies may reflect differences in percentage of body fat that were not found between BN and control participants in our study. If BN was associated with lower percentage of body fat in prior studies, this could easily produce differences in leptin. However, most previous studies have controlled for BMI, which is generally highly correlated with body fat (e.g., Ablove, Binkley, Leadley, Shelton, & Ablove, 2015; Heymsfield et al., 2014) and was in the current sample (r=.79–.86). Thus, this explanation of non-replication seems unlikely.

Finally, the current study used DSM-5 criteria to define BN as compared to other studies which used DSM-III or DSM-IV criteria. DSM-5 criteria do not distinguish between purging and non-purging subtypes, and all published studies of leptin in BN have only examined BN purging subtype. In the current study, there was a trend toward BN participants who purged (n=15) to have lower leptin levels compared to those who used other forms of compensatory behaviors (n=15) (5.5±.8 vs. 7.6±.8 ng/mL) (F[1, 26]=3.39, p<.08, partial η^2=0.12). Prior work has established low leptin levels in those with purging disorder compared to controls (Jimerson et al., 2010), suggesting that purging rather than binge-eating may be linked to this biological disruption in BN. Furthermore, DSM-5 criteria only require a minimum of one versus two episodes of binge-eating/compensatory behaviors, and the average weekly frequency of binge eating in the current study (2.3±1.6) appears lower than in other studies (range 4–14 episodes/week). Given associations between lower leptin and greater frequency of bulimic symptoms in prior studies (Jimerson et al., 2000; Monteleone et al., 2002), it is possible that the women with BN in the current sample were less severe than those in other samples, which may account for the null finding. However, as noted above, leptin levels in our BN participants resembled levels reported in other samples of BN patients.

Despite significant associations found between WS and leptin and between WS and reinforcing value of food, we did not find an association between leptin and reinforcing value of food, suggesting that other factors may be driving the WS/food reward association. Importantly, given the cross-sectional nature of the current study, we were only able to

examine absolute leptin levels across participants. In contrast, animal studies, which can infer that changes in leptin levels cause changes in behavior, have demonstrated robust associations between leptin and food reward (e.g., Figlewicz et al., 2006). Thus, it is possible that greater decreases in leptin levels (what could be termed "leptin suppression") drive associations between WS and food reward. Given that individuals with BN had significantly greater lifetime BMIs compared to controls, it is likely that they also had higher leptin levels previously. Thus, although current leptin levels in the BN group did not differ from those in controls, the function of that level on drive to eat may be different. This explanation is consistent with the "threshold" model, positing that leptin's main function is to alert the brain when fat stores decrease past a set point for a given individual (Rosenbaum et al., 2010). As such, examination of absolute leptin levels provides no information on an individual's potential threshold. Future studies should test hypotheses using a longitudinal design to examine potential "leptin suppression" and determine whether the *relative* concentration of leptin in one's body drives associations between WS and reinforcing value of food and contributes to bulimic symptom severity and maintenance. Such a design could also empirically identify whether these associations reside on a continuum or demonstrate discontinuity at a threshold.

Overall, the current study had several strengths to acknowledge. First, it included measures with good psychometric properties, including a semi-structured clinical interview to confirm eating disorder diagnoses. We followed rigorous procedures for leptin analyses including monitoring blood glucose levels to confirm participants were fasted, controlling for menstrual cycle phase, and measuring percent body fat. Additionally, we adapted validated operant paradigms used in previous studies to directly measure the reinforcing value of food during food consumption, which more closely resembles the nature of binge-eating episodes in BN and increases translational value of findings. The M&M® dispenser was automated so participants only had access to the candy when they completed the required number of responses. Finally PR task instructions were played on an audio recorder to minimize experimenter influence and performance was monitored, which enabled us to confirm compliance with task instructions.

Despite these strengths, the current study also had important limitations that warrant attention. Although this was the largest study to date examining reinforcing value of food in BN, the sample size was too small to detect small to medium effect sizes. Furthermore, although the intention of the PR task was to specifically measure the reinforcing value of food in BN, we cannot fully disentangle pure motivation to eat from potential deficits in self-regulatory mechanisms (Marsh et al., 2009) in response to food. For example, it is possible that the requirement to earn and eat some "forbidden food" may have undermined BN participants' ability to subsequently limit their efforts to keep earning (and thus eating) the M&Ms®, resulting in potential consumption of more M&Ms® than they actually wanted, and contribute to group differences on task performance. The current study was also cross-sectional, so we were unable to make temporal inferences regarding the direction of associations between WS and breakpoint. For example, it is possible that some individuals who experience elevated reward from palatable food overeat and gain excess weight (e.g., Carr, Lin, Fletcher, & Epstein, 2014; Epstein, Yokum, Feda, & Stice 2014). This weight

gain may then increase body dissatisfaction and lead to subsequent WS; however, prior overeating and weight gain is not necessary for elevated WS to occur. Importantly, the absence of a cross-sectional association between leptin and reinforcing value of food indicates the importance of examining other possible factors as well as changes in those factors to identify mechanisms underlying associations between WS and reinforcing value of food. Future studies may also benefit from inclusion of a high-WS non-eating disorder control group to explore potential moderators of associations between WS and bulimic symptoms.

In summary, results from the current study add to the growing literature on the role of WS in bulimic syndrome maintenance and further support that WS may be an important factor for understanding why BN often follows a chronic course. In particular, WS may contribute to increased rewarding value of palatable food and subsequent bulimic symptoms; however, the mechanisms of these associations remain unknown. Future studies examining the reinforcing value of food in BN and potential biological correlates of food reward and of weight suppression could provide critical information on the extent and nature of reward deficits in BN and how these factors may contribute to illness maintenance. Overall, improved understanding of factors maintaining bulimic symptoms is crucial to inform and refine treatments and reduce suffering from this often chronic disorder.

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General Scientific Summary

This study suggests that currently weighing less than one had in the past ("weight suppression") may contribute to the maintenance of bulimia nervosa through reducing leptin levels and increasing rewarding value of food.

Table 1

Demographic Data for Bulimia Nervosa and Control Participants

	Full Sample (n=62)		BN (n=32)		Controls (n=30)				
Variable	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**t**	**df**	**p**
Age	21.39	4.83	21.22	4.24	21.57	5.46	0.28	60	.78
BMI (kg/m^2)	22.29	2.00	22.47	1.79	22.09	2.22	−0.75	60	.46
Highest BMI	24.20	3.55	25.38	3.91	22.94	2.65	−2.86	60	.006
Percent Body Fat	26.35	5.62	26.71	4.90	25.98	6.37	−0.51	60	.62
WS (lbs)	11.37	14.43	16.63	18.00	5.75	5.32	−3.27	36.71*	.002
Leptin (ng/ml) †	6.56	3.53	6.56	3.64	6.56	3.48	0.004	55	.997
	n (%)		**n (%)**		**n (%)**		**Chi-Square**	**df**	**p**
Ethnicity							0.27	1	.60
Hispanic	10 (16.1%)		6 (18.8%)		4 (13.3%)				
Non-Hispanic	52 (83.9%)		26 (81.2%)		26 (86.7%)				
Race							3.17	4	.53
Asian	4 (6.5%)		2 (6.3%)		2 (6.7%)				
Black	7 (11.3%)		4 (12.5%)		3 (10%)				
White	46 (74.2%)		22 (68.8%)		24 (80%)				
Mixed/Other	5 (8.1%)		4 (12.5%)		1 (3.3%)				
Highest Education							3.27	2	.20
High School	54 (87.1%)		30 (93.7%)		24 (80%)				
College	6 (9.7%)		2 (6.3%)		4 (13.3%)				
Graduate	2 (3.2%)		0 (0%)		2 (6.7%)				

Note. BN=bulimia nervosa; BMI=body mass index; WS=weight suppression.

† n=30 BN and n=27 controls due to inability to obtain blood samples on five participants.

* Degrees of freedom for tests when equal variance not assumed due to violation of assumption.

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Table 2

Group Differences in Eating Disorder Psychopathology

	BN (n=32)		Controls (n=30)				
Variable	**Mean**	**SD**	**Mean**	**SD**	**t**	**df**	**p**
EDE-Q	3.98	0.95	0.53	0.46	−18.43	45.2*	<.001
Restraint	3.80	1.29	0.43	0.77	−12.62	51.1*	<.001
Eating Concerns	2.79	1.21	0.06	0.13	−12.65	31.8*	<.001
Shape Concerns	4.64	1.00	0.85	0.77	−16.70	60	<.001
Weight Concerns	4.08	1.00	0.50	0.56	−17.56	49.1*	<.001
OBEs per Week	2.02	1.57	--	--	--	--	--
Compensatory Behaviors per Week	6.44	5.06	--	--	--	--	--
Binge Size (kcal)	2291.9	1059.1	--	--	--	--	--
CIA-Distress/Impairment	26.94	12.24	1.73	2.32	−11.44	33.4*	<.001
Duration of Illness (years)	4.59	4.13	--	--	--	--	--

Note. BN=bulimia nervosa; CIA=Clinical Impairment Assessment; EDE-Q=Eating Disorder Examination Questionnaire; OBEs=Objective binge episodes.

*Degrees of freedom for tests when equal variance not assumed due to violation of assumption.

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Table 3

Correlations among Weight Suppression, Leptin Levels, and Progressive Ratio Task Performance in the Full Sample (a), BN Participants (b), and Control Participants (c)

a.

Variable	1	2	3	4	5
1. Weight Suppression	--				
2. Leptin‡	−.24*	--			
3. Breakpoint	.35**	−.13	--		
4. BMI	.15	.33**	−.18	--	
5. Percent Body Fat	.03	.47***	−.21	.83***	--

b.

Variable	1	2	3	4	5
1. Weight Suppression	--				
2. Leptin‡	−.34*	--			
3. Breakpoint	.37*	−.11	--		
4. BMI	.11	.24	−.20	--	
5. Percent Body Fat	−.06	.47***	−.26	.79***	--

c.

Variable	1	2	3	4	5
1. Weight Suppression	--				
2. Leptin‡	−.30	--			
3. Breakpoint	−.01	−.18	--		
4. BMI	.25	.39*	−.23	--	
5. Percent Body Fat	.20	.43*	−.25	.86***	--

Note. BN=bulimia nervosa; BMI=body mass index. One-tailed p-value was used for associations between leptin and weight suppression, BMI, and percent body fat.

* p<.05,

** p<.01,

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***p<.001.

‡Estimates represent standardized beta coefficients controlling for assay.

Table 4

Correlations between Clinical Characteristics and Weight Suppression, Progressive Ratio Task Performance, and Leptin in the BN Sample

Variable	Weight Suppression	Breakpoint	Leptin‡
OBEs/week	.29	−.16	.02
Comp Behaviors/week	.54***	.03	−.10
Binge Size (kcal)	.47***	.12	.24
CIA -Distress/Impairment	.32*	.29	.13
Duration of Illness (years)	.44**	.34*	−.10

Note. CIA= Clinical Impairment Assessment; Comp=Compensatory; OBE=Objective binge episode.

‡Estimates represent standardized beta coefficients controlling for assay.

* p<.10,

** p<.05,

*** p<.01.