Reward Processing and Inhibitory Control in Women with Bulimia Nervosa

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Submitted to the graduate degree program in Psychology and the Graduate Faculty of the University of Kansas in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

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Date Defended: 09 May 2019

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Date Approved: 09 May 2019

Abstract

Introduction: Theoretical models and empirical research support the role of negative affect in bulimia nervosa (BN). However, treatments that target negative affect in BN have not outperformed traditional, eating-disorder-focused treatments for BN. An alternative mechanism of BN is dysfunctional positive affect (i.e., reward processing). The present study aimed to understand associations among dysfunctional reward processing, affect, and eating-disorder symptom expression by testing an interactive model of reward-based processes (reward learning, effort valuation, delay discounting, inhibitory control) in women with BN. **Method:** Participants were community-recruited medication-free adult women aged 18-30 with BN (n=20) or healthy controls (HCs; n=20). Behavioral tasks and self-report measures were used to assess reward learning, effort valuation, delay discounting, inhibitory control, BN symptom frequencies, and affect. **Results:** Women with BN did not differ from HCs on effort valuation and inhibitory control; however, women with BN showed *less* delay discounting and demonstrated slower reward learning compared to HCs. Frequency of fasting and excessive exercise episodes increased as inhibitory control decreased. Slowed reward learning was associated with increased self-induced vomiting frequencies in BN. **Conclusions:** Results suggested a modified model of reward dysfunction in BN, with delay discounting, reward learning, and negative urgency as central features. Given the associations of reward learning, delay discounting, and negative urgency, clinicians working with persons with BN may introduce strategies, such as pleasant activity scheduling, as a means to promote positive affect, regulate negative affect, and potentially decrease symptom expression in BN. (Word Count: 238 words)

Acknowledgements

My dissertation would not have been possible without the support of my dissertation committee and graduate advisors, my funding sources, and my family and friends. Below, I acknowledge the ways in which each supported myself and my work throughout my dissertation and my graduate training.

First, I am immensely grateful for my graduate co-advisors, Drs. Kelsie Forbush, Ph.D., Dissertation Committee Chair, and Rick Ingram, Ph.D., Dissertation Committee Member, for their support of this project, as well as their support of and investment in my professional and intellectual development throughout my graduate training. Kelsie, thank you for engendering and facilitating my interests in eating disorders and specific research methodologies through invaluable opportunities and collaborations, and the countless hours of thoughtful feedback and productive meetings you have invested in my dissertation, in my other research endeavors, and in my professional development. Rick, thank you for your unwavering support of my academic and professional pursuits and for encouraging me to not question my potential as an academic. I also thank my dissertation committee members Drs. Tera Fazzino, Ph.D., Dave Jarmolowicz, Ph.D., and Laura Martin, Ph.D. Tera, thank you for the guidance with grantsmanship you provided for this project and for your support in general; you are an excellent role model for me. Dave, thank you for introducing me to the true fun that is behavioral economics and helping me to apply it to an eating-disorder population. Laura, thank you for your investment in this project as a committee member and co-sponsor on grant applications associated with this research, as well as your investment in me as a trainee and providing opportunities aligned with my research interests.

Finally, my family and friends have been another important source of support while I completed this dissertation and other requirements associated with the Ph.D. I thank my parents, Greg and Michelle, and two younger sisters, Kristin and Mackenzie, who have served as pillars of strength and love throughout my Ph.D. studies. I also thank my partner, Alex, for helping to keep me balanced, encouraging me to be kind to myself, and bringing levity and laughter in times of stress. I lastly thank my best friend, Caroline, who is an unending source of inspiration and validation; I feel so lucky to have completed undergraduate studies at the same institution and graduate studies (separate institutions and different doctoral programs) at the same time as you because you have a unique and empathic perspective on graduate school.

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Reward Processing and Inhibitory Control in Women with Bulimia Nervosa

Bulimia nervosa (BN) is an eating disorder characterized by recurrent binge eating, inappropriate compensatory behaviors, and overvaluation of body weight and/or shape in persons *without* an objectively low body weight (American Psychiatric Association, 2013). Binge eating is defined as eating a large amount of food in a distinct time period (e.g., two hours) and experiencing a subjective loss-of-control over eating. Inappropriate compensatory behaviors are behaviors used to counteract the effects of binge eating, influence body shape and/or weight, and/or gain a sense of control over eating. Inappropriate compensatory behaviors include fasting, severe food restriction, excessive exercise, self-induced vomiting, misuse of laxatives, diuretics, enemas, and/or syrup of ipecac, and insulin omission among persons with insulin-dependent diabetes.

BN is a public health priority. BN affects approximately 1-3% of people in their lifetime (Smink, van Hoeken, & Hoek, 2013; Stice, Marti, & Rohde, 2013; Trace et al., 2012). According to the US Burden of Disease Collaborators, the number of years lived with an eating disorder increased by 55.4% and disability-adjusted life years lost due to an eating disorder increased by 60.9% from 1990 to 2010 (Murray et al., 2013). Moreover, eating disorders rank as the 12th leading cause of death and disability among young women aged 15 to 19 in high-income countries and rank as the 16th leading cause of death and disability among women of all ages (Erskine, Whiteford, & Pike, 2016).

Despite the considerable burden-of-disease associated with BN, the best-available evidence-based psychotherapies for BN do not work for 40-60% of patients (Keel & Brown, 2010; Steinhausen & Weber, 2009). Moreover, pharmacologic treatments (namely antidepressants) have modest efficacy; although BN symptom frequencies reduce by

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approximately 50% at short-term follow-up (eight weeks), symptom reduction is negligible at long-term (one year) follow-up (Hay & Claudino, 2012). Low efficacy of current treatments for BN suggest that core mechanisms of BN are not being fully treated with currently available interventions. Thus, additional research to elucidate maintaining mechanisms of BN is critically needed so that more effective treatments can be developed.

Negative Affect in Bulimia Nervosa

Scholars in the field of BN have provided substantial theoretical and empirical support for negative affect as a core mechanism of BN (for a review see (Stice, 2016)). An important theoretical model of negative affect in BN is the Affect-Regulation Model (Polivy & Herman, 1993), which posits that negative emotions trigger binge eating and inappropriate compensatory behaviors which, in turn, provide temporary relief from aversive emotions and cognitions. Thus, the Affect-Regulation Model indicates that, over time, eating-disorder behaviors increase because they are negatively reinforcing (i.e., provide temporary relief from aversive emotions). Behaviorally and biologically based empirical research has supported the Affect-Regulation Model and suggested that negative affect plays an important role in the etiology, maintenance, and prognosis of BN (e.g., (Haedt-Matt & Keel, 2011; Stice, 2016; Stice & Fairburn, 2003)). A recent systematic review of prospective risk factors for the development of BN found that pre-morbid negative affect predicts the onset of BN, indicating that negative affect is an important etiological factor for BN (Stice, 2016). Other behavioral (i.e., non-biological) research has demonstrated a temporal association among negative affective states and BN symptoms through ecological momentary assessment (EMA), an assessment tool that enables real-time tracking of affective states, BN symptoms, and the temporal association of these symptoms in a person's natural environment. EMA research has shown that high levels of negative affect and stress are

significant antecedents of binge eating and inappropriate compensatory behaviors episodes in BN (Haedt-Matt & Keel, 2011; Lavender et al., 2016; Smyth et al., 2007). Although some EMA studies found that binge eating was prospectively associated with *decreased* negative affect in BN (Berg et al., 2013; Lavender et al., 2016; Smyth et al., 2007), meta-analytic results suggested that binge eating is prospectively associated with *increased* negative affect in BN (Haedt-Matt & Keel, 2011). Researchers have posited that heterogeneity of post-binge-eating affect in BN may be due to differences in statistical analysis methods (Engel et al., 2013). Engel et al. (2013) noted that results from EMA studies may differ because some researchers have used linear mixed models to assess *immediately* before and after binge eating, whereas other researchers have used growth curve models to examine the general trajectory of affect pre- and post-binge eating. Results from previous studies indicated that purging behaviors (e.g., self-induced vomiting) are prospectively associated with *decreased* negative affect (Berg et al., 2013; Haedt-Matt & Keel, 2011). Other researchers have shown that negative urgency, or the tendency to act rashly when experiencing negative affect, is significantly associated with BN psychopathology. Meta-analytic results suggested a medium-sized association among negative urgency and BN symptoms (*r*=0.40) (Fischer, Smith, & Cyders, 2008).

Finally, in addition to negative affective states, preliminary evidence suggested that affective lability may be an important contributor to BN psychopathology. A recent study examined affective instability and degree of affective change (vs. level of negative affect) using EMA in women with BN; results suggested that extreme increases in negative affect occurred *prior* to binge-eating and purging episodes, and extreme increases in positive affect occurred *after* binge-eating and purging episodes (Berner et al., 2017). Thus, previous behavioral research

supports the Affect-Regulation Model of BN and indicates that negative affect is a reliable prospective predictor of BN symptoms.

Incorporating negative affect into eating-disorder nosology also has diagnostic utility. For example, using latent class modeling, scholars have reliably classified persons with BN into subtypes based dietary restriction and high (vs. low) levels of negative affect (Chen & Le Grange, 2007; Grilo, Masheb, & Berman, 2001; Stice & Agras, 1999; Stice et al., 2001; Stice, Bohon, Marti, & Fischer, 2008; Stice & Fairburn, 2003). Persons with BN who reported high levels of both negative affect and dietary restriction (a "dietary-negative" subtype of BN) reported more frequent binge eating and inappropriate compensatory behaviors, increased psychosocial impairment, and had greater rates of treatment non-response than persons with BN who reported elevated levels of dietary restraint *only* (Stice et al., 2008; Stice & Fairburn, 2003). These findings suggest that high levels of negative affect are associated with increased illness severity and poorer prognosis of BN.

Biological research on negative affect in BN dovetails with the previously described behavioral research. Dysfunction in the serotonergic (5-HT) system – a system implicated in mood, eating, sleep, and impulse control – has been observed in adults with BN. Scholars have theorized that binge-eating episodes lead to increases in 5-HT in the brain that, in turn, decrease 5-HT receptor sensitivity in persons with BN (Jimerson, Lesem, Kaye, & Brewerton, 1992). Research has shown that persons with BN have *decreased* 5-HT receptor binding (Kaye et al., 2001; Marazziti, Macchi, Rotondo, Placidi, & Cassano, 1988) and *increased* 5-HT reuptake (Goldbloom, Hicks, & Garfinkel, 1990), suggesting that too little 5-HT is available for binding at 5-HT receptors. Based on this evidence, selective-serotonin reuptake inhibitors designed to increase 5-HT availability have been used as a pharmacological intervention for BN (Goldstein,

Wilson, Ascroft, & al-Banna, 1999; Levine, 1992). Considered together, biological research suggested that there is dysfunction of the 5-HT system in BN and, given the associations of the 5-HT system with mood, further underscores the role of negative affect in BN psychopathology.

Due to the clear importance of negative affect in BN, psychological and pharmacological treatments that directly target high negative affect in BN were developed. One of the most popular traditional psychotherapies for BN is cognitive-behavioral therapy (CBT) (Fairburn, 1981), which initially focused almost exclusively on eating-disorder-specific behaviors and not on negative affect. Given that remission rates of BN in CBT treatment studies were low and meta-analytic results showed that approximately 40-60% of patients with BN did not achieve symptom remission (Thompson-Brenner, Glass, & Westen, 2003), researchers developed Enhanced Cognitive Behavioral Therapy (CBT-E) for the trans-diagnostic treatment of eating disorders (Fairburn, 2008). CBT-E focuses on establishing regular patterns of eating and self-monitoring – which includes completing daily logs of regular eating, loss-of-control eating, and inappropriate compensatory behaviors, and tracking emotions and cognitions accompanying eating behaviors – to help clients identify factors contributing to disordered-eating behaviors and cognitions. Two varieties of CBT-E exist: (1) a *focused* version (CBT-Ef) that solely targets eating-disorder symptoms; and (2) a *broad* version (CBT-Eb) that targets eating-disorder symptoms and incorporates additional, optional modules to address issues common in eating disorders, including mood "intolerance" (negative affect and mood-related cognitive distortions) and interpersonal difficulties. Initial evidence suggested that persons with more "complex" eating-disorder cases (e.g., more co-morbid psychopathology) had greater eating-disorder symptom reductions when treated with CBT-Eb versus CBT-Ef at end-of-treatment and 60-week follow-up (Fairburn et al., 2009), suggesting that directly targeting the negative-affect system is

important for improving treatment outcome results in BN. A recent randomized-control trial showed that persons with BN and co-morbid borderline personality disorder – a psychiatric disorder characterized by marked affective instability and high levels of negative affect – show similar remission rates with CBT-Eb (vs. CBT-Ef) at end-of-treatment, with 40.0% and 44.0% achieving remission at end-of-treatment for CBT-Eb and CBT-Ef, respectively (Thompson-Brenner et al., 2016). However, persons who received CBT-Eb fared better at six-month follow-up, with 46.7% in the CBT-Eb group achieving full BN remission versus 36.8% in the CBT-Ef group. It is noteworthy that remission rates remained below 50% for both forms of CBT-E. Thus, while targeting negative affect in BN through CBT-E has shown some promise for increasing treatment efficacy, less than 50% of those with BN who receive CBT-E achieve symptom remission.

Other evidence-based therapies that specifically target negative affect in BN have been developed. Dialectical Behavior Therapy (DBT), a therapy that was initially developed for chronic suicidality and borderline personality disorder that focuses on reducing affective instability and negative affect, was modified for use in patients with BN due to the clear role of negative affect on bulimic-symptom expression (Safer, Telch, & Chen, 2009). An initial randomized-control trial showed that persons with BN who received DBT had a 28.6% remission rate versus 0% of participants in the waitlist-control group after 20 weeks (Safer, Telch, & Agras, 2001). A recent study compared DBT vs. CBT-E in persons with BN who had poor initial treatment response to a guided self-help version of CBT (<65% remission of disordered-eating behaviors) (Chen et al., 2017). Results showed that DBT and CBT-E led to similar reductions of binge-eating frequency at end-of-treatment, 6-months follow-up, and one-year follow-up. However, persons with BN who received DBT (vs. CBT-E) showed greater reductions in self-

induced vomiting (Chen et al., 2017). Another more recently developed therapy is Integrative

Cognitive-Affective Therapy (ICAT) (Wonderlich, Peterson, & Smith, 2015), which focuses on

helping clients recognize temporal associations among (negative) affective states and bulimic

symptoms. A randomized-control trial of ICAT versus CBT-E in persons with BN showed that

ICAT did not outperform CBT-E, and both therapies facilitated similar reductions in binge-

eating and purging frequencies (Wonderlich et al., 2014). Thus, despite the important role that

negative affect plays in the etiology and maintenance of eating disorders, results from the

psychological treatment literature show that, in general, targeting negative-affective processes

does not improve results of traditional eating-disorder-focused treatment for BN.

Pharmacological treatments that solely target negative affect systems in BN, such as

selective-serotonin reuptake inhibitors, do not fare better than psychotherapies in treating BN.

Pharmacological treatments have modest outcomes at short term follow-up, with patients

experiencing only 50% decrease in binge-eating and purging frequencies at the end of

randomized-control trials, and negligible outcomes at long-term (one year) follow-up (Hay &

Claudino, 2012). Approximately 30-45% of patients with BN who experienced symptom

reduction when taking a selective-serotonin reuptake inhibitor experienced symptom relapse over

four- to six-month medication maintenance phases (Bacaltchuk & Hay, 2003; Hay & Claudino,

2012; Mitchell, Roerig, & Steffen, 2013). Additionally, drop-out rates for pharmacologic

treatments of BN were approximately 40%, likely due to low tolerability of side effects (Hay &

Claudino, 2012).

In summary, research suggests that psychological and pharmacological treatments that

exclusively target negative affect in BN do not show improvements over traditional eating-

disorder psychotherapies, suggesting that while negative affect is an important mechanism of

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BN, it is not sufficient in our current understanding of BN. Thus, the identification of mechanisms that move beyond a focus on negative affect is imperative for developing a more comprehensive understanding of factors that maintain BN and can serve as future treatment targets.

Application of a Trans-Diagnostic Model of Imbalanced Reward Processing and Inhibitory Control to Bulimia Nervosa

One potential mechanism of BN that is *not* the focus of currently available treatments for eating disorders is positive affect (e.g., the reward-processing system), which is responsible for the experience of pleasurable emotions and responses to rewarding stimuli, such as palatable food. Many psychiatric disorders that frequently co-occur with BN are characterized by dysfunctional or low positive affect. For example, results from a nationally representative sample of persons with eating disorders suggested that the lifetime co-morbidity rate of BN and major depressive disorder is approximately 50.1% (Hudson, Hiripi, Pope, & Kessler, 2007), and a defining feature of major depressive disorder is low positive affect (e.g., anhedonia) (American Psychiatric Association, 2013). Substance use disorders also co-occur with BN, with lifetime co-morbidity estimates from a nationally-representative sample suggesting that up to 36.8% of persons with BN also have had a drug or alcohol use disorder (Hudson et al., 2007). In addition, results from a literature review (O'Brien & Vincent, 2003) and a meta-analysis (Calero-Elvira et al., 2009) of co-morbid conditions in treatment-seeking persons with BN suggested higher rates of substance use disorders in BN compared with the general population and other eating disorders (e.g., binge-eating disorder or anorexia nervosa). Biological research has shown robust dysfunction in the positive-affect (reward-processing) and inhibitory control systems in persons with substance abuse disorders, which has been summarized into a model of reward processing

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and inhibitory control involved in addictions (Volkow, Fowler, Wang, Baler, & Telang, 2009) (see **Figure 1**).

Volkow's model contends that consummatory behavior is regulated by three distinct reward-based processes (delay discounting, effort valuation, reward learning) and inhibitory control, and that imbalances among these processes maintain symptom expression in persons with substance use disorders. Specifically, Volkow posits that desire to obtain a substance now versus later (delay discounting), great effort to obtain and consume a substance (effort valuation), and difficulty learning stimulus-reward associations between using the substance and consequences of using the substance (reward learning) override and weaken inhibitory control. Weakened inhibitory control is theorized to result in impulsive consumption of a substance. Although Volkow's model was developed for understanding factors that maintain substance misuse, it is relevant to understanding bulimic behaviors. For example, research has demonstrated that persons with BN show a preference for obtaining a reward now versus later (delay discounting) (Kekic et al., 2016) and increased efforts to work for and obtain food (effort valuation) (Bodell & Keel, 2015; Schebendach, Broft, Foltin, & Walsh, 2013). Moreover, persons with BN appear to have reduced reward learning, as evidenced by recurrent engagement in binge eating and compensatory behaviors despite physical consequences and psychosocial impairment (Labouliere, Terranova, Steinglass, & Marsh, 2016). Dysregulated reward-based processes in BN may work in concert to decrease inhibitory control over food intake, resulting in over-consumption of food accompanied by loss-of-control (i.e., binge eating).

Biological research has implicated alterations in reward-processing, as demonstrated by alternations in the dopaminergic system, in the maintenance of substance use disorder psychopathology. Reward-processing alterations have been characterized as *decreased* striatal

dopamine (DA) D$_2$ receptor availability (Volkow et al., 2009) and *blunted* striatal DA release to rewarding stimuli (e.g., drugs, alcohol) (Martinez et al., 2005; Martinez et al., 2007). Inhibitory control deficits in substance use disorders include reduced availability of striatal DA D$_2$, which is associated with *decreased* activity in brain regions implicated in inhibitory control, including the orbitofrontal cortex, cingulate gyrus, and prefrontal cortex (Volkow et al., 2001; Volkow et al., 1993; Volkow et al., 2007). Thus, Volkow purports that decreased availability of DA D$_2$ receptors overrides fronto-striatal circuits associated with inhibitory control, thereby decreasing ability to inhibit reward-driven behaviors. In sum, Volkow's model has been supported by neurobiological research on reward processing and inhibitory control.

There are clear and compelling parallels between substance use disorders and BN that warrant the application of Volkow's model to BN psychopathology. First, persons with substance use disorders use drugs and/or alcohol as a means to temporarily regulate their (negative) affect in the same way that persons with BN use binge eating and inappropriate compensatory behaviors to regulate their negative emotions (Gold, Frost-Pineda, & Jacobs, 2003). Second, persons with BN and persons with substance use disorders both report subjective loss-of-control over disorder-specific behaviors (e.g., subjective feelings that they cannot stop or cut down on what or how much they are eating or drinking) and continue to engage in disorder-specific behaviors despite potential negative consequences (Gold et al., 2003). Finally, lifetime co-morbidity estimates from a nationally representative sample indicated that 36.8% of persons with BN have had a substance use disorder (Hudson et al., 2007). Given the parallels between and co-morbidity of BN and substance use disorders, examination of the reward-processing system, inhibitory control system, and the interaction of these systems in BN could lead to better understanding of mechanisms that underlie BN and thereby advance treatments for BN.

Reward-Processing Dysfunction in Bulimia Nervosa

Emerging research supports reward-processing dysfunction as a candidate disease-mechanism of BN. Candidate disease-mechanisms refer to processes that have shown preliminary evidence for maintaining disease symptom expression. Neurobiological and behavioral data implicate the dopaminergic (DA) system in ingestive behavior (Small, Jones-Gotman, & Dagher, 2003; Volkow et al., 2002) and, as with substance use disorders, reduced striatal DA levels and DA D_2 receptor availability – biological markers of reward-processing dysfunction – have been observed in BN. Pre-clinical studies of bulimic-type behaviors in rodents found that binge-like consumption of palatable food (e.g., sucrose solutions) was associated with *decreased* striatal DA release in the nucleus accumbens (Rada, Avena, & Hoebel, 2005) and *decreased* striatal D_2 receptor availability (Bello, Lucas, & Hajnal, 2002; Johnson & Kenny, 2010). Early clinical work in persons with BN showed *lower* levels of cerebrospinal fluid homovanillic acid (HVA; a DA metabolite) compared to healthy controls (Jimerson et al., 1992; Kaye et al., 1990). Moreover, these studies found that lower levels of HVA correlated with increased frequency of binge-eating episodes in persons with BN.

Neuroimaging findings in persons with BN converge with early pre-clinical and clinical work. Broft et al. (2012) used positron emission tomography (PET) imaging to examine striatal response to a psychostimulant in persons with BN and found significantly *blunted* striatal DA response to a psychostimulant in the posterior and anterior putamen of persons with BN compared to healthy controls. Blunted striatal DA response was correlated with increased binge-eating and self-induced vomiting frequencies and increased caloric density of binge-eating episodes. Another study found *decreased* striatal DA transporter availability in persons with BN compared to healthy controls using single photon emission computed tomography (SPECT)

(Tauscher et al., 2001). Finally, research using functional magnetic resonance imaging (fMRI) found that persons recovered from BN do not have differential reactions to wins and losses like healthy controls, as evidenced by significantly *lower* activation of the left caudate nucleus and right anterior ventral striatum during a guessing game paradigm in which participants could win or lose money based on their guess (Wagner et al., 2010).

In addition to neurobiological work, behavioral evidence points to dysfunctional reward processing in BN. Persons with BN showed greater *effort valuation* compared to healthy controls by working harder for food reward on the Progressive Ratio Task (Bodell & Keel, 2015; Schebendach et al., 2013). Persons with BN also showed greater *delay discounting* than healthy controls because they discounted the value of a monetary reward as a function of its delay during a delay discounting task (Kekic et al., 2016). In pre-clinical rodent models, increased *delay discounting*, as measured by a delay discounting task developed for rodents, was associated with increased binge-eating frequency (Cano, Murphy, & Lupfer, 2016). Other behavioral research suggests persons with both acute and remitted BN show difficulties with *reward learning*, which is conceptualized as the ability to learn stimulus-response associations and subsequently modulate behavior to optimize chance of reward receipt (e.g., positive feedback, money, palatable food). One study found that persons with BN showed deficits on a probabilistic learning task that provided positive (smiling face) and negative feedback (frowning face) to participant responses (Labouliere et al., 2016). Specifically, persons with BN were not able to modulate behavior from feedback to improve response accuracy like healthy controls, and increased inaccuracy of responses was associated with increased binge-eating and self-induced vomiting frequency in persons with BN. Moreover, catecholamine-depleted (Grob et al., 2012) and non-catecholamine-depleted (Wagner et al., 2010) persons with recovered BN did not

distinguish between positive and negative feedback on reward-based tasks compared to healthy controls, suggesting decreased ability to form stimulus-reward associations and impaired *reward learning*. Studying catecholamine depletion in remitted BN is important because catecholamines are a parent class of neurotransmitters that include DA and are implicated in the functioning of the reward-processing system (Kaye, 2008). Catecholamine depletion results in decreased levels of DA in the central nervous system and is thought to temporarily induce lower DA levels similar to those present in persons with active BN.

Thus, across multiple samples and methods, the extant research literature suggests that there are broad deficits in reward-processing in BN and that reward dysfunction is associated with increased frequency of binge eating and purging episodes. The association of reward-processing dysfunction with increased frequency of bulimic symptoms is important because it suggests that targeting the mechanisms underlying impaired reward processing may decrease bulimic-symptom frequency.

Inhibitory Control Deficits in Bulimia Nervosa

In addition to deficits in reward processing, inhibitory control deficits are well-documented in persons with BN and represent a defining feature of BN. For example, the *DSM-5* diagnostic criteria for BN require that persons experience loss-of-control during eating episodes, and loss-of-control during binge eating could also be conceptualized as decreased inhibitory control. Empirical research supports this diagnostic criterion. For example, meta-analytic results of behavioral research suggested that persons with BN show decreased behavioral inhibitory control toward both non-disease-related (e.g., monetary) and disease-related (e.g., food, body) stimuli that they are instructed to ignore (Wu, Hartmann, Skunde, Herzog, & Friederich, 2013). Other behavioral research has shown that persons with BN exhibit difficulty in ceasing impulsive

behavior once it is already underway (e.g., feeling like one cannot stop eating a bag of chips after starting) compared to healthy controls (Wu, Giel, et al., 2013). Thus, behavioral research suggested that persons with BN have difficulties inhibiting responses to initial presentation of a rewarding stimuli as well as difficulty ceasing impulsive behavior that is already underway.

Neuroimaging evidence converges with behavioral evidence to support dysfunctional inhibitory control in persons with BN. fMRI studies of adolescents (Marsh et al., 2011) and adults (Marsh et al., 2009; Skunde et al., 2016) with BN showed decreased behavioral inhibitory control and decreased activation of fronto-striatal circuits when asked to withhold responses to both non-disease-related (e.g., neutral arrows) and disease-related (e.g., body, food) stimuli. Additionally, these studies found that binge-eating (Marsh et al., 2011; Marsh et al., 2009; Skunde et al., 2016) and self-induced vomiting (Marsh et al., 2011) frequency increased with decreased activation of fronto-striatal circuits. A recent cross-sectional fMRI study showed that persons with BN do not show expected maturation of circuits associated with inhibitory control over time compared to healthy controls (Dreyfuss et al., 2017). The finding that inhibitory control functioning was deficient in *both* adolescents and adults with BN is important because it is widely documented that fronto-striatal circuit functioning, and therefore inhibitory control, improves with age; thus, poor inhibitory control may be an important neurocognitive marker of BN. Other research used electroencephalogram (EEG) event-related potentials (ERP) and showed that women with BN showed reduced amplitude and shorter latency of N200 waveforms and greater amplitude of P300 waveforms during an oddball distractor task, suggesting decreased inhibitory control (Merlotti et al., 2013). In sum, previous evidence from behavioral and multi-modal neuroimaging studies suggested that persons with BN exhibit decreased inhibitory control, which may explain why they experience subjective loss-of-control during binge-eating episodes.

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Clinical Implications

Treatment research for substance use disorders has been guided by Volkow's model, leading to the development of novel treatments for substance use disorders. These novel treatments simultaneously target dysfunctional reward-processing and inhibitory control systems by *decreasing* limbic system (e.g., reward processing) activation and *increasing* inhibitory control activation (Cabrera et al., 2016) in response to disease-salient cues (e.g., drugs, alcohol). Such treatments include novel applications of pharmacological agents, such as modafinil and aripiprazole (Abilify ®). Modafinil is a mild stimulant indicated for use in decreasing daytime sleepiness in persons with narcolepsy through modulation of the dopaminergic system. Because modafinil modulates dopaminergic system functioning and dopaminergic dysfunction has been observed in persons with substance use disorders, researchers tested the effects of modafinil on substance use disorder symptom expression. One fMRI study found that administration of modafinil prior to a delay discounting task in persons with alcohol use disorders resulted *increased* preference for larger-later rewards, *decreased* activation of the ventromedial prefrontal cortex (reward-processing), *increased* activation of frontoparietal regions (inhibitory control), and *increased* connectivity among reward and inhibitory control regions (Schmaal et al., 2014). Another fMRI study in persons with methamphetamine dependence found that administration of modafinil prior to a reward-learning task resulted in *increased* activity in the anterior cingulate cortex and ventrolateral prefrontal cortex (inhibitory control) (Ghahremani et al., 2011). These studies suggested that modafinil may have utility as a treatment for substance use disorders. Indeed, modafinil has been effective in the treatment of persons with cocaine-dependence with and without co-morbid alcohol use disorders (Kampman et al., 2015).

In addition to modafinil, the pharmacological agent aripiprazole has been applied in persons with substance use disorders. Aripiprazole is an antipsychotic that is a partial agonist of DA D_2 receptors. Applications of aripiprazole to persons with alcohol use disorders have resulted in decreased alcohol consumption over a two-week trial, as well as *decreased* activation of the right ventral striatum, a brain region associated with reward-processing (Myrick et al., 2010). Another fMRI study found that aripiprazole *increased* activation of the anterior cingulate cortex (inhibitory control) in response to presentation of alcohol-related cues and *decreased* subjective cravings of alcohol in persons with alcohol use disorders (Han, Kim, Choi, Min, & Renshaw, 2013). These findings highlight the potential utility of aripiprazole for treatment of substance use disorders.

Finally, Volkow's model has informed neurocognitive "brain retraining" programs for substance use disorders in which patients learn to inhibit responses to disease-salient rewarding stimuli (e.g., drugs, alcohol) (Eberl et al., 2013). fMRI evidence shows that neurocognitive brain retraining programs have normalized the functioning of the mesolimbic dopaminergic system, thereby decreasing substance use disorder symptoms and increasing remission rates for persons with substance use disorders in randomized-control trials (for a review see (Cabrera et al., 2016)).

Application of Volkow's model to BN will enhance understanding of neurocognitive dysfunction in BN and will help to contribute treatment improvement and development for BN. For example, results from the present study will provide a useful starting point for development of a novel and targeted neurocognitive "brain retraining" program that normalizes reward processing and, ultimately, contributes to reductions in BN symptoms. Neurocognitive treatments have been shown to be efficacious for several mental disorders, including for anorexia

nervosa (for a meta-analysis and review see Hagan and Forbush (in preparation)), but have not been applied to BN. Previous research also suggested that reward-processing dysfunction can be improved through use of the pharmacological agents modafinil and aripiprazole (Abilify®), and this study marks a first step toward testing the effects of modafinil and/or aripiprazole on BN symptoms. Given that this project will elucidate associations among reward-processing and inhibitory control systems in BN and their effect on BN symptom expression, the results of this study will lay the groundwork for future neuroimaging and neurochemical studies on the interaction of the reward-processing, inhibitory control systems, and neurotransmitters in BN.

The Present Study

There is considerable interest in identifying reliable, mechanisms of BN to improve current treatments and inform more effective treatments. The research described above suggested that deficits in the inhibitory control and reward-processing systems, and an imbalance between these systems, may be potential mechanisms of bulimic-symptom expression. Given research showing that reduced availability of reward-based neurotransmitters and decreased activations of fronto-striatal circuits associated with inhibitory control are associated with increased binge eating and inappropriate compensatory behaviors in BN [e.g., (Labouliere et al., 2016; Marsh et al., 2011)], Volkow's model has potential utility for characterizing BN and explaining the "binge-purge cycle." In addition, one limitation of previous research is that it has not tested whether reward-based and inhibitory control deficits are disease-specific (i.e., food) or general (i.e., money) in women with BN. Research is needed to disentangle whether these processes are broad or specific to advance our understanding of the neurocognitive underpinnings of BN and to inform treatment development.

The purpose of the present study was to test Volkow's model, for the first time, in persons with BN by testing associations among components of Volkow's model with bulimic-symptom expression and self-reported affect. Toward that end, the *first aim* of this study was to identify reward-processing and inhibitory control deficits in women with BN compared to matched healthy controls. Based on Volkow's model and previous literature in substance use disorders and BN, I hypothesized that women with BN would exhibit greater reward-processing deficits (e.g., domains specified by Volkow's model) than healthy controls, as demonstrated by: (1) working harder for monetary reward (effort valuation); (2) showing reduced ability to incorporate implicit feedback to earn a reward (reward learning); and (3) selecting smaller-sooner rewards over larger-later rewards (e.g., $5 now or $10 in a week; delay discounting). I also hypothesized that women with BN would show decreased inhibitory control compared to healthy controls, as evidenced by decreased ability to inhibit response to a stimulus they are instructed to ignore. Additionally, an exploratory aim of this study was to test whether reward-based processes were disease-specific (food), general (money), or both in women with BN.

The *second aim* of this study was to apply Volkow's model to BN by testing associations among reward-processing, delay discounting, and inhibitory control tasks in women with BN. Based on Volkow's model, I hypothesized that delay discounting would positively correlate with effort valuation, and inversely correlate with reward learning and inhibitory control. Additionally, I hypothesized that inhibitory control would inversely correlate with effort valuation and reward learning.

The *third and final aim* of this study was to test associations among facets of reward processing, delay discounting, inhibitory control, eating-disorder symptoms, and affective correlates in women with BN. I hypothesized that reward-processing and inhibitory control

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dysfunction and increased delay discounting would correspond to more frequent binge eating and compensatory behaviors, based on research suggesting that decreased availability of reward-based neurotransmitters and decreased activation of fronto-striatal regions associated with inhibitory control have been associated with increased frequency of eating-disorder behaviors [e.g., (Labouliere et al., 2016; Marsh et al., 2011)]. I also hypothesized that reward-processing and inhibitory control dysfunction and increased delay discounting would be associated with higher self-reported negative affect and negative urgency, and lower self-reported positive affect.

Method

All study procedures were approved by the University of Kansas Institutional Review Board (IRB). All participants provided written, informed consent prior to engaging in any study-related procedures.

Participants

Participant demographic characteristics are presented in **Table 1**, participant clinical characteristics are presented in **Table 2**, and mean values of self-report measure constructs are presented in **Table 3**.

Women with BN. Twenty medication-free (no psychotropic medication), community recruited females with *DSM-5* BN (confirmed with a semi-structured diagnostic interview) were recruited from: 1) Dr. Forbush's existing registry of community-recruited persons with an eating disorder; 2) the Lawrence, Kansas community and University of Kansas campus using flyers and email methods; and 3) the University of Kansas Research Participant Pool system (SONA).

Matched psychiatrically healthy control women. Twenty psychiatrically healthy control women (HCs) were recruited and matched to women with BN for overall equivalence on age, education, and racial-ethnic identification. Although I had proposed to match women with

BN and HCs for overall equivalence on body mass index, there were challenges in recruitment that rendered matching for overall equivalence on body mass index difficult. Thus, women with BN and HCs differed in overall (e.g., mean) body mass index; however, body mass index was used as a covariate in statistical analyses.

For the purposes of this study, "psychiatrically healthy" was defined as no lifetime or current eating disorder, substance use disorder, major depressive disorder, generalized anxiety disorder, panic disorder, social phobia, and/or post-traumatic stress disorder. HCs were recruited using the aforementioned flyer and email methods from the Lawrence, Kansas community and from the University of Kansas campus, as well as through the University of Kansas Psychology Research Participant Pool (SONA).

Inclusion/exclusion criteria. Inclusion criteria for all study participants were: 1) female; 2) aged 18-30 years; and 3) fluency in written and spoken English. Exclusion criteria were: 1) medical conditions that affected appetite or body weight (thyroid disorder, cancer, diabetes, current pregnancy or post-partum, etc.); 2) neurological disorder, intellectual disability, and/or current psychosis; 3) current substance use disorder (due to well-documented dysfunctional reward processing and inhibitory control system functioning in these disorders); 4) current use of medications shown to affect reward circuitry or dopamine function (e.g., modafinil, second-generation antipsychotic, amphetamine, acetylcystein, ceftriaxone, memantine, methylphenidate, etc.); and 5) current use of medication that affected reaction time (e.g., antihistamines or other sedatives in the past 24 hours).

Screening. Medication-free (no psychotropic medication) women with BN in Dr. Forbush's registry who consented to be contacted for future studies were emailed information about the study. The email to medication-free women with BN in Dr. Forbush's registry

provided a description of the study and a link to complete the eligibility screen online via Qualtrics, an online survey platform supported by the University of Kansas. HCs and women with BN not in Dr. Forbush's registry who responded to recruitment emails and flyers were sent an email with a description of the study and a link to the Qualtrics eligibility screen. Additionally, the eligibility screen was available as a single-credit online study in the University of Kansas SONA system to female students aged 18 to 30; respondents who met eligibility criteria for the study and consented to be contacted for participation in other studies were sent an email with a description of the study.

The screen for <u>both</u> groups included demographic questions regarding age, education level, racial-ethnic identification, and height and weight (to calculate body mass index) to match HCs to women with BN. The Eating Disorder Diagnostic Scale (Stice, Telch, & Rizvi, 2000) was included to assess current eating-disorder diagnosis. Portions of the M.I.N.I. International Neuropsychiatric Interview (Lecrubier et al., 1997) that screened for presence of current and past substance use disorder, major depressive disorder, generalized anxiety disorder, panic disorder, social phobia, and/or post-traumatic stress disorder diagnosis were administered, as current or past presence of these disorders was an exclusion criterion for HCs.

Procedure

Study sessions were conducted in-person at the University of Kansas Center for the Advancement of Research on Eating Behaviors (CARE Lab) in Fraser Hall. All study sessions were approximately two hours in duration. Participants first reviewed the consent form and provided informed consent for the study with a trained undergraduate research assistant and/or the principal investigator (K.H.). Second, participants completed a semi-structured eating-disorder interview, the Eating Disorder Diagnostic Interview (described below), with a trained

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undergraduate research assistant and/or the principal investigator. Undergraduate research assistants were trained in interview administration by the principal investigator. Interview administration training included practice administration of the interview with peers and the principal investigator, observing the principal investigator administer the interview to one HC and one woman with BN, and administration of the interview to one HC and one woman with BN under direct/live observation of the principal investigator. The principal investigator provided verbal feedback and collaboratively reviewed paper copies of the interview with undergraduate research assistants. Once an undergraduate research assistant was cleared to independently administer interviews, undergraduate research assistants were asked to audiotape the interview (if the participant agreed to be audiotaped, by checking the appropriate box in the consent form and initialing) and the principal investigator reviewed audiotapes along with corresponding paper copies of the interview. Ten percent of audiotapes were randomly selected to compute inter-rater reliability.

During the semi-structured eating-disorder interview, objective height and weight measurements were obtained. Next, participants completed self-report measures on a laptop via the Qualtrics platform. Within Qualtrics, the order of self-report measure completion was randomized across participants. Upon completion of self-report measures, behavioral tasks were administered to participants. The order of behavioral tasks was counter-balanced across participants. Finally, participants were debriefed and compensated. Participants recruited through Dr. Forbush's registry and from the Lawrence, Kansas community and University of Kansas campus through flyer and email methods were compensated for their time and participation with $50 in the form of a debit or gift card. Participants recruited via SONA were presented the option

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of compensation through SONA credits (up to four credits) or $50 in the form of a debit or gift card for their time and participation.

Measures

      Behavioral tasks.

      Reward learning. The Probabilistic Reward Learning Task (Pizzagalli, Jahn, & O'Shea, 2005) is a computerized task that was used to test reward learning. The Probabilistic Reward Learning Task has been used to examine reward learning in women with recovered BN (Grob et al., 2012). Participants are instructed that the goal of the Probabilistic Reward Learning Task is to earn as much money as possible; money "earned" via the Probabilistic Reward Learning Task was hypothetical (i.e., participants were not additionally compensated for performance). Prior to completing the task, participants reviewed instructions with the experimenter and engaged in two practice trials with the experimenter in the room in order to facilitate understanding. The task consisted of three blocks of 100 trials, and 30 seconds separated each block. Each trial began with presentation of a fixation cross for 500 milliseconds (ms). Next, a "mouthless" face was presented for 500 ms. Then, a face with either a short mouth (11.5 millimeters) or a long mouth (13 millimeters) was presented for 100 ms. The mouthless face was again presented while participants identified whether they saw a short mouth or a long mouth by pressing the "m" key or the "v" key on a standard computer keyboard. Mouth length associated with reward (e.g., short or long) and keys used to identify mouth length ("m" and "v" keys) were counterbalanced across participants. Participants were asymmetrically reinforced on their response; specifically, only 40 (30 rewarding mouths and 10 non-rewarding mouths) of the 100 trials in each block are reinforced with, "Correct!! You won 20 cents." An equal number of short and long mouths are presented in each block and no more than three consecutive repetitions of the same mouth length

were permitted. Reward learning measured by the Probabilistic Reward Learning Task has demonstrated evidence for test-retest reliability in a university-student sample over approximately one month (average 38.28 days between administrations), with a correlation of $r=0.57$ ($p=0.003$) between administrations, (Pizzagalli et al., 2005).

The main variable of interest for the Probabilistic Reward Learning Task was response bias, which corresponds to the participant's preference for the mouth (either short or long, depending on counterbalancing assignment) that yields the most reward. Additionally, we were interested in participant ability to correctly discriminate short and long mouths, which is termed discriminability. Discriminability was entered as a covariate in statistical analyses.

Inhibitory control. A computerized go/no-go task adapted from Batterink, Yokum, and Stice (2010) was used to assess inhibitory control toward specific (i.e., food) and generalized (i.e., "pleasant" animal images) pleasurable stimuli in order to test whether inhibitory control deficits might be a specific or general process in women with BN. "Pleasant" animal images and food images were normed for palatability, intensity, and valence. Participants were instructed to respond ("go") as quickly and accurately as possible to images framed in blue or yellow (depending on task version assigned via counterbalancing; see below) by pressing the "1" key on a computer keyboard and to withhold response ("no-go") to images framed in blue or yellow. The go/no-go task consisted of four blocks of 112 trials. "Go" cues consisted of 75% of the trials and "no-go" cues comprised 25% of the trials. Two versions of the go/no-go task were administered; one version asked participants to "go" to images framed in blue and "no-go" to images framed in yellow, whereas the other version instructed participants to "go" to images framed in yellow and "no-go" to images framed in blue. Task version was counterbalanced across participants. The outcome variable of interest was the number of commission errors (an

index of inhibitory control) – pressing a key for the "no-go" stimulus – made by a participant. Batterink et al. (2010) administered the go/no-go task to participants while they simultaneously underwent an fMRI scan, and results showed elevated activity in the superior and inferior frontal gyrus during no/go (vs. go) trials. The superior and inferior frontal gyrus activity have been linked to response inhibition (Nakata et al., 2008); thus, Batterink et al. (2010)'s go/no-go task appeared to engage the inhibitory control system. Data for two participants with BN were omitted from analyses because their responses indicated that they reversed instructions and pressed the "1" key for "no-go" trials and withheld response for "go" trials.

Self-report measures.

Demographics. A researcher-designed demographics questionnaire assessed participant age, racial-ethnic identification, education level, treatment history, current medication usage (to verify medication-free status), nicotine use, and highest and lowest lifetime body weights at current height.

Menstrual cycle phase information. I collected self-reported information regarding the start and end dates of the most recent menstrual period, typical duration of menstrual periods, use of hormonal contraceptive methods, and reproductive stage (e.g., menopause), due to evidence that menstrual cycle phase can influence reward-processing function (Dreher et al., 2007). Participants were not matched on menstrual cycle phase and use of contraceptives due to the challenges this would have created with recruitment and matching groups; however, these variables were used as covariates in statistical analyses if there were group differences.

Delay discounting. Delay discounting was tested using the 27-item Monetary Choice Questionnaire (Kirby, Petry, & Bickel, 1999), which is featured in the National Institutes of Health PhenX Toolkit, and an experimenter-designed Food Choice Questionnaire. Use of the

Monetary Choice Questionnaire and Food Choice Questionnaire enabled us to test whether delay

discounting was generalized (money) and/or specific (food) process in persons with BN. The

Monetary Choice Questionnaire asked the participant to select whether they preferred

hypothetical smaller amounts of money now or larger amounts of money later (delay). Previous

research indicated that use of hypothetical commodities yields results similar to use of real

commodities (Lawyer, Schoepflin, Green, & Jenks, 2011). The Monetary Choice Questionnaire

has demonstrated evidence for good test-retest reliability as well as temporal stability over one

year and 57 weeks (Kirby, 2009).

A 27-item experimenter-designed Food Choice Questionnaire based on the Monetary

Choice Questionnaire was used to test specific delay discounting. Participants were asked to

identify their favorite snack food and how many servings of the snack food were worth $100 to

them; thus, the commodity (favorite snack food) and equivalency amount (servings) were

individualized for each participant. The favorite snack food and amount of servings were then

input into Reed and Jarmolowicz (2013)'s Customizable Commodity Choice Excel Software to

create a unique, individualized Food Choice Questionnaire. The Customizable Commodity

Choice Software is based on the Monetary Choice Questionnaire.

The outcome variable of interest for both the Monetary Choice Questionnaire and the

Food Choice Questionnaire was k, a value that represents the degree of delay discounting.

Smaller values of k are reflective of a preference for larger-later rewards, whereas larger k values

are reflective of a preference for smaller-sooner rewards.

Effort valuation. A food-specific hypothetical purchase task was developed based on the

Alcohol Purchase Task (Murphy, MacKillop, Skidmore, & Pederson, 2009) and used to measure

effort valuation. Our food-specific hypothetical purchase task measured the relative reinforcing

efficacy of food. Participants were asked to consider how many commodities of their favorite food they would be willing to purchase for 17 different prices, ranging from $0 (free) to $20.00.

Each participant's reported food consumption is plotted as a function of price into a demand curve, which yields several outcome variables of interest. One outcome variable is the intensity of the demand, or the number of food portions "consumed" when food portions cost $0.00 (i.e., food portions are free). A second outcome variable is maximum food portion consumption, termed O_{max}. A third outcome variable is the price-point at which the food demand becomes "elastic," or when number of snack servings purchased decreases significantly faster than price increases, known as P_{max}. A final outcome variable of interest and the main variable of interest in this study is *breakpoint*, or the price at which food consumption completely ceases (i.e., no portions of food are purchased and consumed). All outcome variables (intensity, O_{max}, P_{max}, and breakpoint) were empirically derived for this study, and the main outcome variable of interest for this study is breakpoint, as it is a proxy variable for how much effort one puts forward to obtain the reward.

The psychometric properties of our food-specific purchase task are not known. However, the hypothetical purchase task has been widely used to study other commodities of interest, including alcohol (Murphy et al., 2009), indoor tanning (Reed, Kaplan, Becirevic, Roma, & Hursh, 2016), and cigarettes (MacKillop et al., 2008). Moreover, the alcohol-based hypothetical purchase task (Alcohol Purchase Task) has demonstrated good-to-excellent test-retest reliability over two-week periods (Murphy et al., 2009) as well as construct validity (i.e., high correlation; $r=.87$) between hypothetical alcohol consumption measured by the Alcohol Purchase Task and actual alcohol consumption in a laboratory setting (Amlung, Acker, Stojek, Murphy, & MacKillop, 2012).

Eating Pathology Symptoms Inventory (EPSI). The 45-item EPSI (Forbush et al., 2013) was used to assess self-reported disordered-eating symptoms over the past four weeks. The EPSI was used to address the third goal of this study, which was to examine associations among reward-processing and inhibitory control deficits and eating-disorder symptoms. The EPSI is comprised of eight subscales: *Body Dissatisfaction* (feeling badly about one's body shape and/or weight); *Binge Eating* (eating large amounts of food in a distinct period of time and experiencing a subjective loss-of-control); *Restricting* (successful caloric restriction to influence body weight and/or shape); *Cognitive Restraint* (attempts – successful or not – to restrict caloric intake to influence body weight and/or shape); *Excessive Exercise* (intensive exercise lasting two or more hours); *Purging* (forced expulsion of calories from the body, including self-inducing vomiting and use of diet pills, laxatives, and/or diuretics); *Muscle Building* (dissatisfaction with muscle size and use of substances to increase muscle mass); and *Negative Attitudes Towards Obesity* (negative beliefs about and emotional reactions to persons with overweight or obesity). In this study, only the *Binge Eating*, *Restricting*, *Excessive Exercise*, and *Purging* scales were used to assess self-reported levels of binge-eating and inappropriate compensatory behaviors.

The EPSI scales have demonstrated evidence for strong psychometric properties. The EPSI scales have demonstrated good-to-excellent internal consistency (Forbush et al., 2013) and good test-retest reliability over periods of two and four weeks (Forbush, Hilderbrand, Bohrer, & Chapa, 2017; Forbush et al., 2013); however, reliabilities for the *Muscle Building* scale were lower for women than men. The EPSI scales have shown evidence for excellent discriminant validity from mood- and anxiety-related measures and moderate-to-strong convergent validity with other eating-disorder-related measures (Forbush, Wildes, & Hunt, 2014; Forbush et al., 2013). The EPSI scales have also shown evidence for criterion-related validity, because they

have differentiated eating-disorder cases from non-eating disorder cases (Forbush et al., 2013).

Finally, the EPSI scales have shown evidence for construct validity in both men and women (Forbush et al., 2013); however, the *Muscle Building* scale did not perform as well in women as in men. Decreased psychometric performance of the *Muscle Building* scale in women versus men could be attributed to women having less desire to increase muscle mass. Due to the EPSI's strong psychometric properties, the National Institutes of Health has included the EPSI in its PhenX Toolkit of recommended measures. Internal consistency of the EPSI scales used in this study was acceptable-to-excellent, as Cronbach's alpha values ranged from 0.73 for *Purging* to 0.954, 0.907, and 0.921 for *Binge Eating*, *Excessive Exercise*, and *Restricting*, respectively.

Externalizing Spectrum Inventory – Brief Form (ESI-bf). The 160-item ESI-bf (Patrick, Kramer, Krueger, & Markon, 2013) was developed from the original 415-item ESI (Krueger, Markon, Patrick, Benning, & Kramer, 2007) and assesses three higher-order dimensions and 23 lower-order facets of externalizing symptoms (detailed below). The three factor-analytically derived higher-order dimensions of the ESI-bf include a general *Externalizing* factor comprised of two sub-factors: *Callous-Aggression* (non-empathic, deviant behaviors characteristic of psychopathy) and *Substance Abuse* (problems with use of marijuana, other drugs, and alcohol). Twenty-three factor-analytically derived sub-scales of the three higher-order factors include scales that assess aggression, destruction of property, impulsivity, sensation-seeking, empathy, and use and problems with use of drugs, marijuana, and alcohol. The ESI-bf scales have demonstrated evidence for strong psychometric properties in male and female college-student and prisoner populations. For example, the ESI-bf scales have demonstrated good-to-excellent internal consistency on all scales in college-student and prisoner populations (α's>0.85)(Patrick et al., 2013). The ESI-bf also demonstrated evidence for criterion-related validity with similar

scales on a self-report measure of positive and negative emotionality. In this study, only the *Substance Abuse* factor scale will be used to assess substance use. Internal consistency of the *Substance Abuse* factor scale in this sample was marginal, with a Cronbach's alpha value of 0.603. Poor internal consistency within the *Substance Abuse* factor may be due to the fact that presence of a substance use disorder was an exclusion criterion for this study, which may have led to range restriction and lowered correlations among items.

  Inventory of Depression and Anxiety Symptoms-II (IDAS-II). The 99-item IDAS-II (Watson et al., 2012) was used to assess symptoms associated with mood and anxiety disorders over the past two weeks on a 5-point Likert that ranges from "*not at all*" to "*extremely.*" The IDAS-II was used to test the third goal of this study. Part of the third goal of this study was to examine the associations of reward-processing and inhibitory control dysfunction with self-reported affect. The IDAS-II assesses symptoms related to depression, mania, obsessive-compulsive disorder, post-traumatic stress disorder, social phobia, specific phobia, agoraphobia, and panic disorder via 18 factor-analytically distinct scales. The IDAS-II scales have demonstrated evidence for acceptable-to-excellent internal consistency in college-student (α's=0.76-0.88), community adult (α's=0.72-0.90), and patient (α's=0.79-0.90) samples (Watson et al., 2012). In the current study, the IDAS-II scales demonstrated evidence for good-to-excellent internal consistency (α's=0.807-0.946). Additionally, the IDAS-II scales have shown good convergent validity in comparison to related mood and anxiety self-report measures and clinical interviews on obsessive-compulsive (mean convergent r's=0.72 and 0.59 for self-report and interview, respectively), trauma-related (mean convergent r's=0.73 and 0.60 for self-report and interview, respectively), social anxiety (convergent r's=0.53-0.68), claustrophobic (convergent r=0.51), and manic (r's=0.44-0.56) symptoms. The IDAS-II scales have also

demonstrated evidence for discriminant validity because convergent correlations were greater than all discriminant correlations (Watson et al., 2012). Finally, each of the IDAS-II scales demonstrated evidence for criterion-related validity with their corresponding *DSM-IV* diagnosis. In sum, the IDAS-II scales have demonstrated evidence for strong psychometric properties.

      Positive and Negative Affect Schedule (PANAS). The 20-item PANAS (Watson, Clark, & Tellegen, 1988) was used to assess current positive and negative affect and their association with reward-processing and inhibitory control dysfunction, which is the third goal of this study. The Positive and Negative Affect scales each consist of ten items each and items are rated on 5-point Likert scale, anchored in "*not at all*" to "*very much.*" The two-factor structure of the PANAS has been replicated (Crawford & Henry, 2004). Both the Negative (α's=0.86-0.89) and Positive (α's=0.85-0.87) Affect scales have demonstrated evidence for good-to-excellent internal consistency for different time instructions (e.g., ratings for that moment, today, past few days, year, in general) (Crawford & Henry, 2004; Watson et al., 1988). In this sample, the Negative (α=0.906) and Positive (α=0.881) Affect scales demonstrated evidence for good-to-excellent internal consistency. Eight-week test-retest reliabilities for both the Positive and Negative Affect scales were significantly positively correlated for all time instructions (Watson et al., 1988). In addition to evidence for strong reliability, the Negative Affect scale has demonstrated evidence for convergent validity with self-report measures of depression and anxiety, and the Positive Affect scale has demonstrated evidence of discriminant validity with self-report measures of depression and anxiety (Crawford & Henry, 2004). The PANAS is the most widely used measure of affect in eating-disorders EMA research (Berg et al., 2013; Lavender et al., 2016).

      UPPS-P Impulsive Behavior Scale. The 59-item UPPS-P (Lynam, Smith, Whiteside, & Cyders, 2006) assesses cognitive and behavioral impulsivity across five scales: (Negative)

Urgency, (lack of) Premeditation, (lack of) Perseverance, Sensation Seeking, and Positive Urgency. Only the (Negative) Urgency scale was used in this study in order to address third goal of my study, part of which was to examine the associations among negative urgency, reward processing, and inhibitory control deficits. The UPPS-P scales have demonstrated evidence for strong psychometric properties. Regarding reliability, UPPS-P scales have shown evidence for good-to-excellent test-retest reliability over a period of approximately one week (r's=0.81-0.93) (Weafer, Baggott, & de Wit, 2013). The UPPS-P scales have also provided evidence for good-to-excellent internal consistency (α's=0.82-0.94) (Cyders, 2013). In this sample, the UPPS-P scales demonstrated evidence for good-to-excellent internal consistency (α's=0.859-0.943), except for the (lack of) Perseverance scale (α=0.519), which was not used in analyses. Regarding validity, the UPPS-P scales have provided evidence for criterion-related validity in predicting antisocial, binge eating, and problematic drinking and gambling behavior (Smith et al., 2007). The UPPS-P scales have demonstrated measurement invariance across sex, suggesting that the UPPS-P scales have construct validity in both men and women (Cyders, 2013). Finally, the UPPS-P scales have demonstrated evidence for convergent and discriminant validity across assessment method (e.g., interview versus self-report) (Smith et al., 2007).

Semi-structured interview.

Eating Disorder Diagnostic Interview (EDDI). The EDDI (Presnell & Stice, 2003) is a brief interview adapted from the widely used Eating Disorders Examination (Fairburn & Cooper, 1993). The EDDI assesses frequency of eating-disorder behaviors (e.g., binge eating, inappropriate compensatory behaviors), presence of eating-disorder-related cognitions (e.g., overvaluation of weight/shape), and weight history (e.g., current, highest, and lowest weights) over the past year. In the present study, inter-rater reliability was excellent for objective binge

eating episodes (ICC=1.00), self-induced vomiting episodes (ICC=1.00), diuretic and laxative misuse episodes (ICC=1.00), fasting episodes (ICC=1.00), and compensatory exercise episodes (ICC=1.00). Collection of binge-eating and inappropriate compensatory behaviors (e.g., self-induced vomiting) episode frequencies allowed me to derive and confirm current *DSM-5* BN diagnoses. Frequency of binge-eating and inappropriate compensatory behaviors episodes were used to test the third aim of my study, part of which was to examine the association of these behaviors with reward-processing and inhibitory control.

Objective height and weight measurements. Height was assessed using a wall-mounted stadiometer and weight was measured with a digital scale. These measurements were used to compute objective body mass index (kg/m^2).

Statistical Analysis

Data were analyzed using R statistical software (R Core Team, 2018) and IBM SPSS Version 25 (IBM Corp, 2017). Participant demographic characteristics and clinical characteristics were compared using parametric or nonparametric independent samples *t*-tests and effect sizes for continuous variables and χ^2 tests for categorical variables.

Aim One. The first aim of this study was to compare distinct reward-processing components in women with BN compared to matched HCs. For inhibitory control data (go/no-go task), mean differences in commission errors were examined using general linear models and body mass index was entered as a covariate.

Delay discounting data (Monetary Choice Questionnaire; Food Choice Questionnaire) were screened for inconsistency and datasets with consistency values less than 75% were excluded from analyses. Delay discounting values (i.e., *k* values) rendered for the Monetary Choice Questionnaire and Food Choice Questionnaire were non-normally distributed. As such, *k*

values were natural-logarithm transformed, in accordance with Jarmolowicz, Lemley, Cruse, and Sofis (2015). After natural-logarithm transformation, *k*-values were normally distributed and general linear models, with body mass index entered as a covariate, were used to test mean differences in delay discounting between groups.

For reward learning (Probabilistic Reward Learning Task), general linear mixed models were used to test differences in response bias to mouth length using a group (BN, HC) by task block (1, 2, 3) model, and discriminability and body mass index were entered as covariates. In addition, a reward learning score was calculated for each participant by subtracting their response bias score in the first block from their response bias score in the third (final) block of the task; group mean differences in reward learning were examined using an independent samples *t*-test. Prior to analyses, Probabilistic Reward Learning Task data were evaluated for quality along four different criteria (detailed in the following sentences), based on procedures established by Pizzagalli et al. (2005). First, data were checked for validity, or reaction times slower than 150 ms per block; previous recommendations suggested that at least 80% of trials in each of the three blocks needed to be valid for inclusion in analyses. Second, the ratio of "rich" and "lean" trials given feedback (i.e., "Correct!! You won 20 cents.") in each block was evaluated to ensure that the rich-to-lean feedback ratio was close to 3:1. Data with rich-to-lean feedback ratios less than 2.5:1 per block were excluded, in line with Pizzagalli et al. (2005). Third, data were evaluated for "outliers" or trials with reaction times faster than 150 ms, slower than 2500 ms, or three standard deviations above or below the mean reaction time; no more than 10 outliers per block or 30 overall outliers were permitted. Finally, data were evaluated for accuracy in discriminating short and long mouths; data with >55% accuracy per block (i.e., slightly greater than chance) were included.

For effort valuation (food-specific hypothetical purchase task), data were analyzed using the R beezdemand (Kaplan, 2018) package, which was built specifically to analyze hypothetical purchase task data. In line with approaches from past hypothetical purchase task analyses, raw food purchase task data were examined for outliers (defined as > four standard deviations above or below the mean number of snack servings purchased at each price point) and outliers were replaced with the next-highest non-outlying value (Kaplan & Reed, 2018). Next, raw data were screened for non-systematic patterns of responding, based on three criteria proposed by Stein, Koffarnus, Snider, Quisenberry, and Bickel (2015): 1) bounce (i.e., increases in number of food servings purchase with increasing price; this criterion requires that ≤ 10% of a participant's servings purchased increase with increasing price and that the increases in portions purchased are < 25% greater than the amount of food servings purchased when food servings were free); 2) reversals from zero (i.e., purchase of food servings resumes at a higher price after the respondent did not purchase any food servings for two consecutive price points); and 3) trend (i.e., purchase of food servings decreases with increasing price, such that there is at least a 0.025 log-unit decrease in food purchase per long-unit change in price). Participant datasets that passed all three of Stein et al. (2015)'s criteria were used in analysis. Outcome variables of interest (breakpoint, intensity, O_{max}, and P_{max}) were then empirically derived and, consistent with previous research (Kaplan & Reed, 2018), were screened for outliers ± 3.29 standard deviations away from the mean for each outcome variable; outliers were recoded as the next highest (or lowest) non-outlying value. Next, intensity, O_{max}, P_{max}, and breakpoint were not normally distributed; as such, these variables were square-root transformed (to account for zero values) and examined for normality. Intensity, O_{max}, P_{max}, and breakpoint remained non-normally distributed after

transformation; thus, non-parametric Mann-Whitney U tests were performed to examine differences in groups across demand measures.

Aim Two. The second aim of the study was to apply Volkow's reward-processing model to women with BN. Due to non-normality of the distributions of some outcome variables, Spearman's rank-order correlations were used to test correlations among the four aspects of Volkow's model in women with BN: delay discounting (Monetary Choice Questionnaire; Food Choice Questionnaire), reward learning (Probabilistic Reward Learning Task), effort valuation (food-specific hypothetical purchase task), and inhibitory control (go/no-go task). Additionally, two mediational models were tested using non-parametric bootstrapping in the R (R Core Team, 2018) mediation package (due to relatively small sample size): (1) reward learning mediating the association between delay discounting and inhibitory control; and (2) delay discounting mediating the association between reward learning and inhibitory control.

Aim Three. The third aim of the study was to test associations among reward-processing and inhibitory control tasks, bulimic symptoms, and affect. Associations among binge eating and inappropriate compensatory behaviors frequencies (EDDI), self-reported positive and negative affect (PANAS, IDAS-II), negative urgency (UPPS-P), and the four components of Volkow's model [delay discounting (Monetary Choice Questionnaire; Food Choice Questionnaire), reward learning (Probabilistic Reward Learning Task), effort valuation (food-specific hypothetical purchase task), inhibitory control (go/no-go task)] were tested using non-parametric Spearman's rank-order correlations due to non-normally distributed variables.

Results

Aim One

The first aim of this study was to identify reward-processing deficits in women with BN compared to matched HCs. Results for each measure are presented in **Table 4**.

Inhibitory control. Data for two participants with BN were omitted from analyses because participants reversed directions and responded to no-go images and withheld response to go images. Women with BN (vs. HCs) made more commission errors toward "pleasant" animal images (medium effect size) and more commission errors toward food images (small-to-medium effect size). However, women with BN did *not* significantly differ from matched HCs on both number of commission errors toward "pleasant" animal images (e.g., general) and food images (e.g., specific). Additionally, results suggested no differences in inhibitory control between general (pleasant animal) and disease-specific (food) images in women with BN, $t(17)$=-0.954, p=0.353.

Delay discounting. Data from the Food Choice Questionnaire were excluded from analyses for three participants. One HC and one woman with BN did not fully complete the Food Choice Questionnaire and data from one HC demonstrated inconsistent responding. Thus, there were complete and usable datasets from 19 women with BN and 18 HCs. All datasets from the Monetary Choice Questionnaire were included, as there was no evidence of inconsistent responding or missing data. Contrary to my hypothesis, women with BN showed significantly *greater* preference for larger-later (vs. smaller sooner) monetary (general) and food (specific) commodities compared to HCs. The effect sizes for both monetary commodities and food commodities was large. Additionally, results suggested that women with BN showed increased discounting of delayed food versus monetary commodities, $t(18)$=-2.617, p=0.017, suggesting that delay discounting may be more pronounced toward food commodities.

Reward learning. Following data screening procedures established by Pizzagalli et al. (2005), data for five women with BN and two HCs did not pass the quality check and were excluded from analyses. Results from the Probabilistic Reward Learning Task showed a

significant task block by diagnosis interaction and women with BN demonstrated significantly

less response HCs. However, response biases did not differ between women with BN and HCs

for the second and third blocks of the task (see **Figure 2**). Women with BN and HCs

significantly differed in overall reward learning, such that women with BN showed significantly

greater reward learning over the task than HCs. The significant difference in reward learning

between groups can be attributed to the fact that HCs learned stimulus-reward associations

quickly in the first block of the task and did not show learning throughout the remaining two

blocks of the task because of relatively rapid learning in the first block. On the other hand,

women with BN did not learn stimulus-reward associations as quickly (evidenced by poor

performance in the first block of the task) but learned stimulus-reward associations over the

course of the task and "caught up" to HCs.

Effort valuation. One woman with BN did not complete the measure and her dataset was

excluded from analyses. The dataset for one woman with BN did not pass Stein et al. (2015)'s

criteria and her data were excluded from analyses; all other datasets passed criteria for systematic

responding and were included, for a total of n=18 women with BN and n=20 HCs. One woman

with BN had an extreme outlier in her raw data (2,000,000 portions of her favorite food) and this

number was recoded to the next-highest value of 100. There was one outlier for demand

measures; a HC had an extreme outlier for O_{max} of 120 and this value was replaced with the next-

highest value of 80.

The primary measure of interest was breakpoint. Compared to HCs, women with BN did

not have significantly higher breakpoints. However, women with BN (vs. HCs) consumed

significantly more food portions when the cost was $0.00 and had significantly higher maximum

food portion consumptions (O_{max}). Groups did *not* significantly differ on P_{max}, the price-point at

which the food demand becomes "elastic," or a one-unit change in cost is associated with a one-unit change in number of food portions consumed. Finally, a graphic of demand curves by group is presented in **Figure 3**.

Aim Two

The second aim of the study was to apply Volkow's reward-processing model to women with BN. Results are presented in **Table 5** and **Figure 4**. There was partial support for Volkow's model in this sample. Increased discounting of monetary values was significantly associated with elevated inhibitory control to both food and "pleasant" animal images; however, there were no significant associations between discounting of food commodities and inhibitory control. In addition, preference for smaller-sooner food commodities was associated with greater breakpoints (effort valuation) for food commodities; delay discounting of monetary commodities and breakpoint were not significantly associated. Finally, preference for larger-later commodities of food increased as reward learning increased; however, there were no associations with reward learning and discounting of monetary commodities. Inconsistent with Volkow's model, there were no significant associations among inhibitory control and reward learning, nor inhibitory control and effort valuation.

Aim Three

The third aim of the study was to test associations among reward-processing and inhibitory control tasks, bulimic symptoms, and affect in women with BN. Frequency of fasting episodes over the past three months significantly decreased with decreased inhibitory control toward "pleasant" animal images. Additionally, frequency of compensatory exercise episodes over the past three months significantly decreased with decreased inhibitory control toward food images on the go/no-go task. Finally, reduced reward learning in the first block of the

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Probabilistic Reward Learning Task was associated with increased frequency of self-induced vomiting episodes; however, overall reward learning and reward learning in the second and third blocks of the Probabilistic Reward Learning Task was *not* associated with self-induced vomiting frequencies in BN. There were no other significant relationships among reward-processing and inhibitory control measures and bulimic symptoms.

There were three significant associations among reward-processing and inhibitory control measures and affect. First, reward learning significantly increased as UPPS-P *Negative Urgency* decreased. Second, preference for smaller-sooner amounts of food (delay discounting) increased as UPPS-P *Negative Urgency* increased. Finally, preference for smaller-sooner commodities of money increased as PANAS *Positive Affect* decreased.

Discussion

The present study was the first application of Volkow's transdiagnostic model of reward processing and inhibitory control to women with BN. Volkow's model contends that imbalances among three different reward-processing components (delay discounting, reward learning, and effort valuation) and inhibitory control maintain symptom expression in persons with substance use disorders. Given certain parallels between reward-processing dysfunction in persons with substance use disorders and BN, as well as data from nationally representative samples suggesting that 36.8% of persons with BN will have a substance use disorder in their lifetime (Hudson et al., 2007), I proposed that Volkow's model might have utility for improved understanding of the neurocognitive mechanisms underlying BN. An additional aim of the present study was to determine whether reward-processing dysfunction was general or eating-disorder specific.

Reward-Processing and Inhibitory Control Functioning in Bulimia Nervosa

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The *first aim* of the present study was to identify differences in reward processing and inhibitory control (e.g., domains specified by Volkow's model) between women with BN and matched HCs. I hypothesized that women with BN would exhibit greater reward-processing deficits and poorer inhibitory control than HCs. As I describe below, support for this hypothesis was mixed.

Effort valuation. Women with BN and HCs did *not* significantly differ in effort expended (breakpoint) to consume food commodities (effort valuation) on a food-specific hypothetical purchase task. The null finding for differences in effort valuation (breakpoint) between women with BN and HCs was not consistent with results of two previous studies that found women with BN had significantly higher breakpoints for food reward than HC women on behavioral progressive ratio tasks (Bodell & Keel, 2015; Schebendach et al., 2013). Although participants from the present study had similar ages and educational statuses, the present study differed from past research by using more rigorous exclusion criteria. For example, current alcohol and substance use disorders were not exclusion criteria for Bodell and Keel (2015), whereas current alcohol and/or substance use disorder were exclusion criteria for this study. Prior research suggested that substance use disorders are associated with greater effort expenditure for reward (MacKillop et al., 2008; Murphy et al., 2009); thus, Bodell and Keel's (2015) finding that women with BN expend more effort to obtain a food reward may be due to the presence of current alcohol and substance use disorder co-morbidities in their sample. Another difference in the current effort valuation tasks and previous research is that Schebendach et al. (2013) instructed participants to overeat or "binge" while completing the progressive ratio task. In the present study, and in Bodell and Keel (2015), participants were not instructed to "binge" or overeat. Thus, the very large difference in breakpoints between women with BN versus HCs seen

in Schebendach et al. (2013) compared to the null effect in the present study may be due to differences task instructions.

In the future, it will be important to disentangle whether increased breakpoint toward food reward is associated with BN or unique to persons with co-morbid BN and alcohol/substance use disorders. Additionally, it will be useful to examine whether differences in breakpoint toward food reward vary under "binge" and non-binge instruction conditions in BN. Future research on effort valuation in BN is important because it will allow the field to understand whether effort valuation represents a dysfunctional mechanism that could be targeted in future treatments for BN.

Inhibitory control. Women with BN and HC women did *not* significantly differ on a behavioral task of proactive inhibitory control (inhibition of a response that is not yet underway) in the present study. Groups showed similar ability to inhibit response to a stimulus they were instructed to ignore. Results were consistent with a meta-analysis of inhibitory control that found that persons with BN showed less proactive inhibitory control compared to HCs on the go/no-go task (g=-0.26; small effect) (Wu, Hartmann, et al., 2013). Although groups in the present study did not demonstrate statistically significant differences on an inhibitory control task, the effect sizes found in the present study were greater than effect sizes found in Wu, Hartmann et al. (2013). Specifically, in this study, women with BN (vs. HCs) showed less inhibitory control toward both disease-specific (food; d=-0.42/g=-0.41, small-to-moderate effect) and general (animal; d=-0.53/g=-0.53, moderate effect) images. In addition, results from the present study suggested that inhibitory control is a both a general and eating-disorder-specific process in women with BN, as the number of commission errors on the go/no-go task did not significantly differ between food (disease-specific) and pleasant animal (general) images.

Delay discounting. Women with BN showed a preference for larger-later rewards over smaller-sooner rewards (delay discounting) compared to HC women; thus, women with BN showed *less* discounting than HC women. This finding contradicts my hypothesis that women with BN would show *greater* (not less) preference for smaller-sooner reward than their healthy counterparts. Prior research demonstrated that participants with BN and binge-eating syndromes show increased discounting of delayed monetary reward (i.e., preference for smaller-sooner reward) compared to HCs (Kekic et al., 2016; McClelland et al., 2016). One limitation of prior research is that only one study of delay discounting (with monetary commodities) has been conducted in persons with BN compared to HCs (Kekic et al., 2016). Thus, more research is needed to understand the nature of delay discounting in BN. Past research has demonstrated that persons with anorexia nervosa, an eating disorder characterized by objectively low body weight maintained through chronic dietary restriction, is associated with *increased* preference for larger-later (vs. smaller sooner) reward compared to HCs (Decker, Figner, & Steinglass, 2015; Steinglass et al., 2012). Given the frequency of diagnostic crossover between BN and anorexia nervosa (due to fluctuations in body mass index) (Eddy et al., 2008; Schaumberg et al., 2018), an important future direction will be to further understand if past history of anorexia nervosa influences delay discounting in persons with current BN.

Reward learning. Results from the present study support differences in reward learning between women with BN and HC women. In particular, women with BN (vs. HC women) took significantly longer to learn implicit stimulus-reward associations during the Probabilistic Reward Learning Task. Specifically, in the first block of the Probabilistic Reward Learning Task, women with BN (vs. HC women) demonstrated significantly lower ability to learn stimulus-response associations between mouth length and hypothetical monetary reward.

However, reward-learning performance was similar for both groups at the end of the reward learning task, suggesting that women with BN were slower to learn associations, but eventually caught up to HCs. Findings are consistent with those of Labouliere et al. (2016), who found that adults with BN (vs. healthy controls) showed reduced ability to incorporate feedback to improve response accuracy on the first three (of five) blocks of an implicit reward-learning task and then showed reward learning performance commensurate to matched HCs in the last two blocks of the task. Taken together, findings from the present study and previous research suggest that persons with BN (vs. HCs) take longer to learn stimulus-response associations but eventually "catch up" to their healthy counterparts.

Challenges with integrating stimulus-response associations may affect ability to modulate behavior as a function of reinforcement history and, ultimately, contribute to disease maintenance in persons with BN. Results compliment Fairburn, Cooper, and Shafran (2003)'s Trans-Diagnostic Model of Eating Disorders, which suggests that persons with BN do not learn that extreme weight-control behaviors, such as fasting and excessive exercise, are associated with subsequent binge eating and become "stuck" in a vicious cycle of extreme weight-control behaviors and binge eating. Given the cross-sectional design of the present study, an important future direction will be to test whether reward learning prospectively predicts symptom maintenance in BN. Moreover, an interesting future direction might be to assess the associations among reward-learning profiles and response to treatment in women with BN, given that reward-learning profiles predicted treatment response and symptom maintenance after eight weeks in persons with major depressive disorder (Vrieze et al., 2013).

Empirical Test of Volkow's Model in Bulimia Nervosa

The *second aim* of the present study was to empirically test Volkow's model in women with BN. Results partially supported Volkow's model in women with BN. First, preference for smaller-sooner amounts of money – but not food –was associated with decreased inhibitory control toward both disease-specific (food) and general (pleasant animal) images. Second, preference for smaller-sooner amounts of food – but not money – was associated with increased effort valuation (breakpoint) for food commodities. Third, preference for larger-later food – but not monetary – commodities were associated with increased ability to learn stimulus-response associations (reward learning). Associations of inhibitory control with effort valuation, and reward learning with inhibitory control, were not significant.

Application of Volkow's model in women with BN suggested that delay discounting may be particularly important for understanding the neurocognitive underpinnings of BN. For example, greater general (money) delay discounting was associated with decreased general ("pleasant" animal) and specific (food) inhibitory control, and greater specific (food) delay discounting was associated with increased specific (food) effort valuation. On the other hand, decreased specific (food) delay discounting was associated with greater general (money) reward learning. Given the importance of delay discounting in BN, a revised version of Volkow's model with delay discounting as a central process that influences other reward-based processes may be warranted. Clinically, findings suggested that it may be important to target delay discounting as a means to modulate other reward-based processes and affect symptom expression in BN. A recent proof-of-principle study demonstrated that a single session of active (vs. sham) transcranial direct current stimulation (tDCS) – a well-tolerated form of non-invasive brain stimulation – delivered bilaterally over the dorsolateral prefrontal cortex, significantly decreased temporal discounting, eating-disorder cognitions, and urges to binge eat for 24 hours following active

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tDCS in persons with BN (Kekic et al., 2017). Kekic et al. (2017)'s findings suggested that tDCS may have therapeutic benefit targeting dysfunctional delay discounting in BN.

Correlations Among Reward-Processing Components, Affect, and Bulimic Symptoms

The _third aim_ of the present study was to test correlations among reward-processing components, affect, and bulimic symptoms in women with BN. Results provided partial support for the hypothesis that affective and bulimic symptoms would be associated with reward-processing dysfunction. Increased inhibitory control toward food stimuli was associated with increased frequency of excessive exercise episodes. Increased inhibitory control toward pleasant animal images was also associated with increased frequency of fasting episodes. Results suggested that excessive exercise episode frequency was related to food-specific inhibitory control whereas fasting frequency was related to general inhibitory control in BN. Furthermore, results of the present study suggest that compensatory behaviors frequently seen in BN were driven by increased (vs. decreased) inhibitory control, counter to the idea that compensatory behaviors in BN are associated with decreased inhibitory control (i.e., more impulsivity).

In addition, decreased ability to learn stimulus-response associations (reward learning) in the first block of the Probabilistic Reward Learning Task was significantly associated with increased frequency of self-induced vomiting episodes. The finding that reduced ability to learn stimulus-response associations in the first block of the reward-learning task was associated with frequency of self-induced vomiting is consistent with results of Labouliere et al. (2016), who also found that reduced reward learning was associated with greater self-induced vomiting frequencies. Previous research suggested that decreased reward learning was associated with low positive affect (i.e., anhedonia) in persons with depression (Pizzagalli et al., 2005; Vrieze et al., 2013). Previous ecological momentary assessment research demonstrated that positive affect

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significantly increased following purging (including self-induced vomiting) episodes in persons

with BN (Berner et al., 2017), and other research found that self-induced vomiting created

feelings of euphoria in BN (Abraham & Joseph, 1986). Thus, self-induced vomiting may be used

as a means to increase positive affect and "boost" mood in persons with BN. There were no other

significant associations among bulimic symptoms and reward-based domains.

There were several significant associations among affect and other study constructs.

Negative urgency – the tendency to act impulsively when distressed (Whiteside & Lynam, 2001)

– was significantly associated with two reward-processing components. First, negative urgency

and delay discounting of food commodities were significantly and positively associated. The

association of negative urgency and impulsive choice fits with reinforcement (Bandura, 1974)

and self-regulation (Muraven & Baumeister, 2000) theories. From a reinforcement theory

perspective, results suggested that persons with BN make impulsive choices toward food when

distressed and use food as a means to remove or reduce negative affect (i.e., negative

reinforcement). From a self-regulation perspective, stress may deplete extreme cognitive control

over eating (i.e., dietary restraint) seen in BN and result in impulsive choice toward food.

Clinicians might consider encouraging clients with BN to incorporate alternative "mood

boosting" activities for decreasing negative emotionality. For example, the addition of strategies

to help increase positive affect, such as behavioral activation or scheduling pleasant activities, to

CBT-E may be particularly helpful. Therapists might also assist clients with BN to engage in

regular eating patterns to minimize risk of lapses in strict cognitive control over eating (i.e.,

fasting or strict dieting), which may reduce risk for binge eating.

Second, negative urgency was negatively associated with reward learning, such that

reward learning decreased as negative urgency increased. Prior research has demonstrated an

association between reduced reward learning and increased stress (Porcelli, Lewis, & Delgado, 2012), and social stress in particular (Lincoln et al., 2019), which may explain the significant association between reward learning and stress in the present study, though more research is needed. Finally, decreased levels of positive affect were significantly associated with increased discounting of monetary values in women with BN, suggesting that reduced positive affect is associated with greater impulsivity toward smaller-sooner monetary choices. Taken together, results point to associations among positive and negative affective (particularly negative urgency) domains.

Limitations

There were certain limitations that may have impacted study findings. First, women with BN had significantly higher body mass indices than HC women. This limitation was important, because clinically significant body mass index classifications (i.e., overweight or obese) are associated with greater reward-processing dysfunction. Research indicates that people with BN are more likely to have overweight or obesity (Bulik, Marcus, Zerwas, Levine, & La Via, 2012) compared to people without BN. Thus, even if groups in the present study had been matched on weight status, generalizability of findings would have been limited, given that the average person with BN has overweight or obesity. To control for effects of group differences in body mass index on reward-based processes, body mass index was entered as a covariate in statistical analyses. However, it is important to note that controlling for body mass index did not change any study findings. Second, women with BN and HC women were not matched on menstrual cycle phase due to issues this would have created with recruitment. However, start and end dates of the most recent menstrual period, typical duration of menstrual periods, use of hormonal contraceptive methods, and reproductive stage (e.g., menopause) were collected, and there were

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no group differences in use of hormonal contraceptive methods, reproductive stage, and presence/absence of menstrual periods between groups. Third, the present study was cross-sectional and did not examine longitudinal associations among reward-based processes, eating-disorder symptoms, and affect in women with BN, limiting ability to infer causal directions among reward-based processes and symptom expression in BN.

Conclusions

Taken together, results from the present study provided mixed support for the utility of applying a transdiagnostic reward processing model to persons with BN. My findings suggested that a modified model that includes delay discounting as a core neurocognitive feature of BN may have greater validity than Volkow's model. Moreover, although there are certain parallels among BN and substance/alcohol use disorders, results from the present study did not suggest that BN is best conceptualized as a substance use disorder. Indeed, there was a lack of differences in reward-based processes between groups; a preference for *larger-later* (vs. smaller-sooner) rewards, which has been observed in those with high levels of trait anxiety (Steinglass et al., 2017); and decreased reward learning, which has been associated with course and outcome in major depressive disorder (Vrieze et al., 2013). Results suggest that BN may be better understood as an internalizing disorder, consistent with past behavioral research on eating disorders (Forbush et al., 2018; Forbush, Hagan, et al., 2017; Forbush et al., 2010; Forbush & Watson, 2013).

Previous research suggested that treatments targeting negative affect in BN do not outperform traditional cognitive-behavioral treatments for BN (Chen et al., 2017; Wonderlich et al., 2014). One reason why there are not outcome differences in negative-affect-specific and traditional (eating-disorder focused) treatments for persons with BN could be that previous

studies have treated all persons with BN as if they had the same affective and neurocognitive profiles. Previous research has demonstrated evidence for BN subtypes based on high (vs. low) levels of negative affect [e.g., Stice et al. (2008)]; however, no study, to my knowledge, has subtyped persons with BN based on neurocognitive domains, such as reward learning or delay discounting. Future research is needed to test whether reward learning and delay discounting are associated with treatment response in persons with BN. If certain neurocognitive domains predict treatment outcomes, this information could be leveraged to match persons with BN to treatments based on their neurocognitive profiles. Thus, an important next step for the field of eating disorders and BN, in particular, will be to test whether personalized medicine approaches, that match persons with BN to specific treatments based on affective and neurocognitive profiles, improve treatment outcomes for the disorder.

References

Abraham, H. D., & Joseph, A. B. (1986). Bulimic vomiting alters pain tolerance and mood. *Int J Psychiatry Med, 16*(4), 311-316.

American Psychiatric Association. (2013). *Diagnostic and statistical manual of mental disorders (5th ed.)*. Washington, D.C.: Author.

Amlung, M. T., Acker, J., Stojek, M. K., Murphy, J. G., & MacKillop, J. (2012). Is talk "cheap"? An initial investigation of the equivalence of alcohol purchase task performance for hypothetical and actual rewards. *Alcoholism: Clinical and Experimental Research, 36*(4), 716-724.

Bacaltchuk, J., & Hay, P. (2003). Antidepressants versus placebo for people with bulimia nervosa. *Cochrane Database Syst Rev*(4), Cd003391. doi:10.1002/14651858.cd003391

Bandura, A. (1974). Behavior theory and the models of man. *American Psychologist, 29*(12), 859.

Batterink, L., Yokum, S., & Stice, E. (2010). Body mass correlates inversely with inhibitory control in response to food among adolescent girls: an fMRI study. *Neuroimage, 52*(4), 1696-1703. doi:10.1016/j.neuroimage.2010.05.059

Bello, N. T., Lucas, L. R., & Hajnal, A. (2002). Repeated sucrose access influences dopamine D2 receptor density in the striatum. *Neuroreport, 13*(12), 1575-1578.

Berg, K. C., Crosby, R. D., Cao, L., Peterson, C. B., Engel, S. G., Mitchell, J. E., & Wonderlich, S. A. (2013). Facets of negative affect prior to and following binge-only, purge-only, and binge/purge events in women with bulimia nervosa. *J Abnorm Psychol, 122*(1), 111-118. doi:10.1037/a0029703

Berner, L. A., Crosby, R. D., Cao, L., Engel, S. G., Lavender, J. M., Mitchell, J. E., & Wonderlich, S. A. (2017). Temporal associations between affective instability and dysregulated eating behavior in bulimia nervosa. *J Psychiatr Res, 92*, 183-190. doi:10.1016/j.jpsychires.2017.04.009

Bodell, L. P., & Keel, P. K. (2015). Weight suppression in bulimia nervosa: Associations with biology and behavior. *Journal of abnormal psychology, 124*(4), 994-1002. doi:http://dx.doi.org/10.1037/abn0000077

Broft, A., Shingleton, R., Kaufman, J., Liu, F., Kumar, D., Slifstein, M., . . . Walsh, B. T. (2012). Striatal dopamine in bulimia nervosa: a PET imaging study. *Int J Eat Disord, 45*(5), 648-656. doi:10.1002/eat.20984

Bulik, C. M., Marcus, M. D., Zerwas, S., Levine, M. D., & La Via, M. (2012). The changing "weightscape" of bulimia nervosa. *Am J Psychiatry, 169*(10), 1031-1036. doi:http://dx.doi.org/10.1176/appi.ajp.2012.12010147

Cabrera, E. A., Wiers, C. E., Lindgren, E., Miller, G., Volkow, N. D., & Wang, G. J. (2016). Neuroimaging the Effectiveness of Substance Use Disorder Treatments. *J Neuroimmune Pharmacol, 11*(3), 408-433. doi:10.1007/s11481-016-9680-y

Calero-Elvira, A., Krug, I., Davis, K., López, C., Fernández-Aranda, F., & Treasure, J. (2009). Meta-analysis on drugs in people with eating disorders. *European Eating Disorders Review, 17*(4), 243-259.

Cano, A. M., Murphy, E. S., & Lupfer, G. (2016). Delay discounting predicts binge-eating in Wistar rats. *Behav Processes, 132*, 1-4. doi:10.1016/j.beproc.2016.08.011

Chen, E. Y., Cacioppo, J., Fettich, K., Gallop, R., McCloskey, M., Olino, T., & Zeffiro, T.

(2017). An adaptive randomized trial of dialectical behavior therapy and cognitive

behavior therapy for binge-eating. *Psychol Med, 47*(4), 703-717.

Chen, E. Y., & Le Grange, D. (2007). Subtyping adolescents with bulimia nervosa. *Behav Res

Ther, 45*(12), 2813-2820. doi:10.1037/a0013887.

http://dx.doi.org/10.1016/j.brat.2007.09.003

Crawford, J. R., & Henry, J. D. (2004). The Positive and Negative Affect Schedule (PANAS):

Construct validity, measurement properties and normative data in a large non-clinical

sample. *British Journal of Clinical Psychology, 43*(3), 245-265.

Cyders, M. A. (2013). Impulsivity and the sexes: measurement and structural invariance of the

UPPS-P Impulsive Behavior Scale. *Assessment, 20*(1), 86-97.

doi:10.1177/1073191111428762

Decker, J. H., Figner, B., & Steinglass, J. E. (2015). On Weight and Waiting: Delay Discounting

in Anorexia Nervosa Pretreatment and Posttreatment. *Biol Psychiatry, 78*(9), 606-614.

doi:10.1016/j.biopsych.2014.12.016

Dreher, J.-C., Schmidt, P. J., Kohn, P., Furman, D., Rubinow, D., & Berman, K. F. (2007).

Menstrual cycle phase modulates reward-related neural function in women. *Proceedings

of the National Academy of Sciences, 104*(7), 2465-2470.

Dreyfuss, M. F., Riegel, M. L., Pedersen, G. A., Cohen, A. O., Silverman, M. R., Dyke, J. P., . . .

Broft, A. I. (2017). Patients with bulimia nervosa do not show typical neurodevelopment

of cognitive control under emotional influences. *Psychiatry Research: Neuroimaging*.

Eberl, C., Wiers, R. W., Pawelczack, S., Rinck, M., Becker, E. S., & Lindenmeyer, J. (2013). Approach bias modification in alcohol dependence: do clinical effects replicate and for whom does it work best? *Dev Cogn Neurosci, 4*, 38-51. doi:10.1016/j.dcn.2012.11.002

Eddy, K. T., Dorer, D. J., Franko, D. L., Tahilani, K., Thompson-Brenner, H., & Herzog, D. B. (2008). Diagnostic crossover in anorexia nervosa and bulimia nervosa: implications for DSM-V. *Am J Psychiatry, 165*(2), 245-250. doi:10.1176/appi.ajp.2007.07060951

Engel, S. G., Wonderlich, S. A., Crosby, R. D., Mitchell, J. E., Crow, S., Peterson, C. B., . . . Lavender, J. M. (2013). The role of affect in the maintenance of anorexia nervosa: evidence from a naturalistic assessment of momentary behaviors and emotion. *Journal of abnormal psychology, 122*(3), 709.

Erskine, H. E., Whiteford, H. A., & Pike, K. M. (2016). The global burden of eating disorders. *Curr Opin Psychiatry, 29*(6), 346-353.

Fairburn, C. G. (1981). A cognitive behavioural approach to the treatment of bulimia. *Psychol Med, 11*(04), 707-711.

Fairburn, C. G. (2008). *Cognitive Behavior Therapy and Eating Disorders*. New York, NY: The Guilford Press.

Fairburn, C. G., & Cooper, I. (1993). The Eating Disorder Examination. In C. G. Fairburn & G. T. Wilson (Eds.), *Binge Eating: Nature, Assessment, and Treatment* (12th ed. ed.). New York: Guilford Press.

Fairburn, C. G., Cooper, Z., Doll, H. A., O'Connor, M. E., Bohn, K., Hawker, D. M., . . . Palmer, R. L. (2009). Transdiagnostic cognitive-behavioral therapy for patients with eating disorders: a two-site trial with 60-week follow-up. *American Journal of Psychiatry, 166*(3), 311-319.

Fairburn, C. G., Cooper, Z., & Shafran, R. (2003). Cognitive behaviour therapy for eating

    disorders: A "transdiagnostic" theory and treatment. *Behav Res Ther, 41*(5), 509-528.

Fischer, S., Smith, G. T., & Cyders, M. A. (2008). Another look at impulsivity: a meta-analytic

    review comparing specific dispositions to rash action in their relationship to bulimic

    symptoms. *Clin Psychol Rev, 28*(8), 1413-1425. doi:10.1016/j.cpr.2008.09.001

Forbush, K. T., Chen, P. Y., Hagan, K. E., Chapa, D. A. N., Gould, S. R., Eaton, N. R., &

    Krueger, R. F. (2018). A new approach to eating-disorder classification: Using empirical

    methods to delineate diagnostic dimensions and inform care. *Int J Eat Disord, 51*(7), 710-

    721. doi:10.1002/eat.22891

Forbush, K. T., Hagan, K. E., Kite, B. A., Chapa, D. A. N., Bohrer, B. K., & Gould, S. R. (2017).

    Understanding eating disorders within internalizing psychopathology: A novel

    transdiagnostic, hierarchical-dimensional model. *Compr Psychiatry, 79*, 40-52.

Forbush, K. T., Hilderbrand, L. A., Bohrer, B. K., & Chapa, D. A. (2017). Test-Retest Reliability

    of Common Measures of Eating Disorder Symptoms in Men Versus Women. *Assessment*,

    1073191117700267. doi:10.1177/1073191117700267

Forbush, K. T., South, S. C., Krueger, R. F., Iacono, W. G., Clark, L. A., Keel, P. K., . . .

    Watson, D. (2010). Locating eating pathology within an empirical diagnostic taxonomy:

    evidence from a community-based sample. *J Abnorm Psychol, 119*(2), 282-292.

    doi:10.1037/a0019189

Forbush, K. T., & Watson, D. (2013). The structure of common and uncommon mental

    disorders. *Psychol Med, 43*(1), 97-108. doi:10.1017/s0033291712001092

Forbush, K. T., Wildes, J. E., & Hunt, T. K. (2014). Gender norms, psychometric properties, and validity for the Eating Pathology Symptoms Inventory. *International Journal of Eating Disorders, 47*(1), 85-91. doi:http://dx.doi.org/10.1002/eat.22180

Forbush, K. T., Wildes, J. E., Pollack, L. O., Dunbar, D., Luo, J., Patterson, K., . . . Stone, A. (2013). Development and validation of the Eating Pathology Symptoms Inventory (EPSI). *Psychol Assess, 25*(3), 859.

Ghahremani, D. G., Tabibnia, G., Monterosso, J., Hellemann, G., Poldrack, R. A., & London, E. D. (2011). Effect of modafinil on learning and task-related brain activity in methamphetamine-dependent and healthy individuals. *Neuropsychopharmacology, 36*(5), 950-959.

Gold, M. S., Frost-Pineda, K., & Jacobs, W. S. (2003). Overeating, binge eating, and eating disorders as addictions. *Psychiatric Annals, 33*(2), 117-122.

Goldbloom, D. S., Hicks, L. K., & Garfinkel, P. E. (1990). Platelet serotonin uptake in bulimia nervosa. *Biol Psychiatry, 28*(7), 644-647.

Goldstein, D. J., Wilson, M. G., Ascroft, R. C., & al-Banna, M. (1999). Effectiveness of fluoxetine therapy in bulimia nervosa regardless of comorbid depression. *Int J Eat Disord, 25*(1), 19-27.

Grilo, C. M., Masheb, R. M., & Berman, R. M. (2001). Subtyping women with bulimia nervosa along dietary and negative affect dimensions: a replication in a treatment-seeking sample. *Eat Weight Disord, 6*(1), 53-58.

Grob, S., Pizzagalli, D. A., Dutra, S. J., Stern, J., Morgeli, H., Milos, G., . . . Hasler, G. (2012). Dopamine-related deficit in reward learning after catecholamine depletion in

unmedicated, remitted subjects with bulimia nervosa. *Neuropsychopharmacology, 37*(8), 1945-1952. doi:10.1038/npp.2012.41

Haedt-Matt, A. A., & Keel, P. K. (2011). Revisiting the affect regulation model of binge eating: a meta-analysis of studies using ecological momentary assessment. *Psychol Bull, 137*(4), 660-681. doi:10.1037/a0023660

Hagan, K. E., & Forbush, K. T. (in preparation). A Systematic Review and Meta-Analysis of Cognitive Remediation Therapy for Anorexia Nervosa.

Han, D. H., Kim, S. M., Choi, J. E., Min, K. J., & Renshaw, P. F. (2013). Adjunctive aripiprazole therapy with escitalopram in patients with co-morbid major depressive disorder and alcohol dependence: clinical and neuroimaging evidence. *Journal of Psychopharmacology, 27*(3), 282-291.

Hay, P. J., & Claudino, A. M. (2012). Clinical psychopharmacology of eating disorders: a research update. *Int J Neuropsychopharmacol, 15*(2), 209-222. doi:10.1017/s1461145711000460

Hudson, J. I., Hiripi, E., Pope, H. G., Jr., & Kessler, R. C. (2007). The prevalence and correlates of eating disorders in the National Comorbidity Survey Replication. *Biol Psychiatry, 61*(3), 348-358. doi:10.1016/j.biopsych.2006.03.040

IBM Corp. (2017). *IBM SPSS Statistics for Windows, Version 25.0.* Armonk, NY.

Jarmolowicz, D. P., Lemley, S. M., Cruse, D., & Sofis, M. J. (2015). A cup today or a pot later: on the discounting of delayed caffeinated beverages. *Journal of agricultural & food industrial organization, 13*(1), 101-111.

Jimerson, D. C., Lesem, M. D., Kaye, W. H., & Brewerton, T. D. (1992). Low serotonin and

    dopamine metabolite concentrations in cerebrospinal fluid from bulimic patients with

    frequent binge episodes. *Arch Gen Psychiatry, 49*(2), 132-138.

Johnson, P. M., & Kenny, P. J. (2010). Dopamine D2 receptors in addiction-like reward

    dysfunction and compulsive eating in obese rats. *Nat Neurosci, 13*(5), 635-641.

    doi:10.1038/nn.2519

Kampman, K. M., Lynch, K. G., Pettinati, H. M., Spratt, K., Wierzbicki, M. R., Dackis, C., &

    O'Brien, C. P. (2015). A double blind, placebo controlled trial of modafinil for the

    treatment of cocaine dependence without co-morbid alcohol dependence. *Drug Alcohol*

    Depend, 155, 105-110. doi:10.1016/j.drugalcdep.2015.08.005

Kaplan, B. A. (2018). *beezdemand: Behavioral Economic Easy Demand*.

Kaplan, B. A., & Reed, D. D. (2018). Happy hour drink specials in the Alcohol Purchase Task.

Kaye, W. H. (2008). Neurobiology of anorexia and bulimia nervosa. *Physiol Behav, 94*(1), 121-

    135.

Kaye, W. H., Ballenger, J. C., Lydiard, R. B., Stuart, G. W., Laraia, M. T., O'Neil, P., . . . Hsu,

    G. (1990). CSF monoamine levels in normal-weight bulimia: evidence for abnormal

    noradrenergic activity. *Am J Psychiatry, 147*(2), 225-229. doi:10.1176/ajp.147.2.225

Kaye, W. H., Frank, G. K., Meltzer, C. C., Price, J. C., McConaha, C. W., Crossan, P. J., . . .

    Rhodes, L. (2001). Altered serotonin 2A receptor activity in women who have recovered

    from bulimia nervosa. *Am J Psychiatry, 158*(7), 1152-1155.

    doi:10.1176/appi.ajp.158.7.1152

Keel, P. K., & Brown, T. A. (2010). Update on course and outcome in eating disorders. *Int J Eat*

    Disord, 43(3), 195-204. doi:10.1002/eat.20810

Kekic, M., Bartholdy, S., Cheng, J., McClelland, J., Boysen, E., Musiat, P., . . . Schmidt, U. (2016). Increased temporal discounting in bulimia nervosa. *Int J Eat Disord*. doi:10.1002/eat.22571

Kekic, M., McClelland, J., Bartholdy, S., Boysen, E., Musiat, P., Dalton, B., . . . Schmidt, U. (2017). Single-Session Transcranial Direct Current Stimulation Temporarily Improves Symptoms, Mood, and Self-Regulatory Control in Bulimia Nervosa: A Randomised Controlled Trial. *PLoS One, 12*(1), e0167606. doi:10.1371/journal.pone.0167606

Kirby, K. N. (2009). One-year temporal stability of delay-discount rates. *Psychonomic bulletin & review, 16*(3), 457-462.

Kirby, K. N., Petry, N. M., & Bickel, W. K. (1999). Heroin addicts have higher discount rates for delayed rewards than non-drug-using controls. *Journal of Experimental Psychology: General, 128*(1), 78.

Krueger, R. F., Markon, K. E., Patrick, C. J., Benning, S. D., & Kramer, M. D. (2007). Linking antisocial behavior, substance use, and personality: An integrative quantitative model of the adult externalizing spectrum. *Journal of abnormal psychology, 116*(4), 645.

Labouliere, C. D., Terranova, K., Steinglass, J., & Marsh, R. (2016). Implicit learning on a probabilistic classification task in adults and adolescents with Bulimia Nervosa. *J Psychiatr Res, 77*, 35-41. doi:10.1016/j.jpsychires.2016.02.004

Lavender, J. M., Utzinger, L. M., Cao, L., Wonderlich, S. A., Engel, S. G., Mitchell, J. E., & Crosby, R. D. (2016). Reciprocal associations between negative affect, binge eating, and purging in the natural environment in women with bulimia nervosa. *Journal of abnormal psychology, 125*(3), 381.

Lawyer, S. R., Schoepflin, F., Green, R., & Jenks, C. (2011). Discounting of hypothetical and potentially real outcomes in nicotine-dependent and nondependent samples. *Exp Clin Psychopharmacol, 19*(4), 263-274. doi:10.1037/a0024141

Lecrubier, Y., Sheehan, D. V., Weiller, E., Amorim, P., Bonora, I., Sheehan, K. H., . . . Dunbar, G. C. (1997). The Mini International Neuropsychiatric Interview (MINI). A short diagnostic structured interview: reliability and validity according to the CIDI. *European psychiatry, 12*(5), 224-231.

Levine, L. R. (1992). Fluoxetine in the treatment of bulimia nervosa. *Arch Gen Psychiatry, 49*, 139-147.

Lincoln, S. H., Pisoni, A., Bondy, E., Kumar, P., Singleton, P., Hajcak, G., . . . Auerbach, R. P. (2019). Altered reward processing following an acute social stressor in adolescents. *PLoS One, 14*(1), e0209361. doi:10.1371/journal.pone.0209361

Lynam, D. R., Smith, G. T., Whiteside, S. P., & Cyders, M. A. (2006). The UPPS-P: Assessing five personality pathways to impulsive behavior. *West Lafayette, IN: Purdue University*.

MacKillop, J., Murphy, J. G., Ray, L. A., Eisenberg, D. T., Lisman, S. A., Lum, J. K., & Wilson, D. S. (2008). Further validation of a cigarette purchase task for assessing the relative reinforcing efficacy of nicotine in college smokers. *Experimental and clinical psychopharmacology, 16*(1), 57.

Marazziti, D., Macchi, E., Rotondo, A., Placidi, G. F., & Cassano, G. B. (1988). Involvement of serotonin system in bulimia. *Life Sci, 43*(25), 2123-2126.

Marsh, R., Horga, G., Wang, Z., Wang, P., Klahr, K. W., Berner, L. A., . . . Peterson, B. S. (2011). An FMRI study of self-regulatory control and conflict resolution in adolescents

with bulimia nervosa. *Am J Psychiatry, 168*(11), 1210-1220.
doi:10.1176/appi.ajp.2011.11010094

Marsh, R., Steinglass, J. E., Gerber, A. J., Graziano O'Leary, K., Wang, Z., Murphy, D., . . .
Peterson, B. S. (2009). Deficient activity in the neural systems that mediate self-regulatory control in bulimia nervosa. *Arch Gen Psychiatry, 66*(1), 51-63.
doi:10.1001/archgenpsychiatry.2008.504

Martinez, D., Gil, R., Slifstein, M., Hwang, D. R., Huang, Y., Perez, A., . . . Abi-Dargham, A.
(2005). Alcohol dependence is associated with blunted dopamine transmission in the
ventral striatum. *Biol Psychiatry, 58*(10), 779-786. doi:10.1016/j.biopsych.2005.04.044

Martinez, D., Narendran, R., Foltin, R. W., Slifstein, M., Hwang, D. R., Broft, A., . . . Laruelle,
M. (2007). Amphetamine-induced dopamine release: markedly blunted in cocaine
dependence and predictive of the choice to self-administer cocaine. *Am J Psychiatry,
164*(4), 622-629. doi:10.1176/ajp.2007.164.4.622

McClelland, J., Dalton, B., Kekic, M., Bartholdy, S., Campbell, I. C., & Schmidt, U. (2016). A
systematic review of temporal discounting in eating disorders and obesity: behavioural
and neuroimaging findings. *Neurosci Biobehav Rev*.
doi:10.1016/j.neubiorev.2016.09.024

Merlotti, E., Mucci, A., Volpe, U., Montefusco, V., Monteleone, P., Bucci, P., & Galderisi, S.
(2013). Impulsiveness in patients with bulimia nervosa: electrophysiological evidence of
reduced inhibitory control. *Neuropsychobiology, 68*(2), 116-123. doi:10.1159/000352016

Mitchell, J. E., Roerig, J., & Steffen, K. (2013). Biological therapies for eating disorders. *Int J
Eat Disord, 46*(5), 470-477. doi:10.1002/eat.22104

Muraven, M., & Baumeister, R. F. (2000). Self-regulation and depletion of limited resources: Does self-control resemble a muscle? *Psychol Bull, 126*(2), 247-259. doi:http://dx.doi.org/10.1037/0033-2909.126.2.247

Murphy, J. G., MacKillop, J., Skidmore, J. R., & Pederson, A. A. (2009). Reliability and validity of a demand curve measure of alcohol reinforcement. *Experimental and clinical psychopharmacology, 17*(6), 396.

Murray, C. J., Atkinson, C., Bhalla, K., Birbeck, G., Burstein, R., Chou, D., . . . Murray. (2013). The state of US health, 1990-2010: burden of diseases, injuries, and risk factors. *Jama, 310*(6), 591-608. doi:10.1001/jama.2013.13805

Myrick, H., Li, X., Randall, P. K., Henderson, S., Voronin, K., & Anton, R. F. (2010). The effect of aripiprazole on cue-induced brain activation and drinking parameters in alcoholics. *J Clin Psychopharmacol, 30*(4), 365.

Nakata, H., Sakamoto, K., Ferretti, A., Gianni Perrucci, M., Del Gratta, C., Kakigi, R., & Luca Romani, G. (2008). Somato-motor inhibitory processing in humans: an event-related functional MRI study. *Neuroimage, 39*(4), 1858-1866. doi:10.1016/j.neuroimage.2007.10.041

O'Brien, K. M., & Vincent, N. K. (2003). Psychiatric comorbidity in anorexia and bulimia nervosa: Nature, prevalence and causal relationships. *Clin Psychol Rev, 23*(1), 57-74. doi:http://dx.doi.org/10.1016/S0272-7358(02)00201-5

Patrick, C. J., Kramer, M. D., Krueger, R. F., & Markon, K. E. (2013). Optimizing efficiency of psychopathology assessment through quantitative modeling: Development of a brief form of the Externalizing Spectrum Inventory. *Psychol Assess, 25*(4), 1332.

Pizzagalli, D. A., Jahn, A. L., & O'Shea, J. P. (2005). Toward an objective characterization of an anhedonic phenotype: a signal-detection approach. *Biol Psychiatry, 57*(4), 319-327. doi:10.1016/j.biopsych.2004.11.026

Polivy, J., & Herman, C. P. (1993). Etiology of binge eating: Psychological mechanisms.

Porcelli, A. J., Lewis, A. H., & Delgado, M. R. (2012). Acute stress influences neural circuits of reward processing. *Front Neurosci, 6*, 157. doi:10.3389/fnins.2012.00157

Presnell, K., & Stice, E. (2003). An experimental test of the effect of weight-loss dieting on bulimic pathology: tipping the scales in a different direction. *J Abnorm Psychol, 112*(1), 166-170.

R Core Team. (2018). R: A Language and Environment for Statistical Computing, R Foundation for Statistical Computing, Austria, 2015. In: ISBN 3-900051-07-0: URL http://www. R-project. org.

Rada, P., Avena, N. M., & Hoebel, B. G. (2005). Daily bingeing on sugar repeatedly releases dopamine in the accumbens shell. *Neuroscience, 134*(3), 737-744. doi:10.1016/j.neuroscience.2005.04.043

Reed, D. D., & Jarmolowicz, D. P. (2013). Questionnaire Development Tool: 27-Item Monetary Choice and Customizable

Commodity Choice Questionnaires [software].

Reed, D. D., Kaplan, B. A., Becirevic, A., Roma, P. G., & Hursh, S. R. (2016). Toward quantifying the abuse liability of ultraviolet tanning: A behavioral economic approach to tanning addiction. *Journal of the Experimental Analysis of Behavior, 106*(1), 93-106.

Safer, D. L., Telch, C. F., & Agras, W. S. (2001). Dialectical behavior therapy for bulimia nervosa. *American Journal of Psychiatry, 158*(4), 632-634.

Safer, D. L., Telch, C. F., & Chen, E. Y. (2009). *Dialectical behavior therapy for binge eating and bulimia*: Guilford Press.

Schaumberg, K., Jangmo, A., Thornton, L. M., Birgegard, A., Almqvist, C., Norring, C., . . . Bulik, C. M. (2018). Patterns of diagnostic transition in eating disorders: a longitudinal population study in Sweden. *Psychol Med*, 1-9. doi:10.1017/s0033291718001472

Schebendach, J., Broft, A., Foltin, R. W., & Walsh, B. T. (2013). Can the reinforcing value of food be measured in bulimia nervosa? *Appetite, 62*, 70-75.

Schmaal, L., Goudriaan, A., Joos, L., Dom, G., Pattij, T., van den Brink, W., & Veltman, D. (2014). Neural substrates of impulsive decision making modulated by modafinil in alcohol-dependent patients. *Psychol Med, 44*(13), 2787-2798.

Skunde, M., Walther, S., Simon, J. J., Wu, M., Bendszus, M., Herzog, W., & Friederich, H. C. (2016). Neural signature of behavioural inhibition in women with bulimia nervosa. *J Psychiatry Neurosci, 41*(5), E69-78.

Small, D. M., Jones-Gotman, M., & Dagher, A. (2003). Feeding-induced dopamine release in dorsal striatum correlates with meal pleasantness ratings in healthy human volunteers. *Neuroimage, 19*(4), 1709-1715.

Smink, F. R. E., van Hoeken, D., & Hoek, H. W. (2013). Epidemiology, course, and outcome of eating disorders. *Curr Opin Psychiatry, 26*(6), 543-548. doi:http://dx.doi.org/10.1097/YCO.0b013e328365a24f

Smith, G. T., Fischer, S., Cyders, M. A., Annus, A. M., Spillane, N. S., & McCarthy, D. M. (2007). On the validity and utility of discriminating among impulsivity-like traits. *Assessment, 14*(2), 155-170.

Smyth, J. M., Wonderlich, S. A., Heron, K. E., Sliwinski, M. J., Crosby, R. D., Mitchell, J. E., & Engel, S. G. (2007). Daily and momentary mood and stress are associated with binge eating and vomiting in bulimia nervosa patients in the natural environment. *J Consult Clin Psychol, 75*(4), 629-638. doi:10.1037/0022-006x.75.4.629

Stein, J. S., Koffarnus, M. N., Snider, S. E., Quisenberry, A. J., & Bickel, W. K. (2015). Identification and management of nonsystematic purchase task data: Toward best practice. *Experimental and clinical psychopharmacology, 23*(5), 377.

Steinglass, J. E., Figner, B., Berkowitz, S., Simpson, H. B., Weber, E. U., & Walsh, B. T. (2012). Increased capacity to delay reward in anorexia nervosa. *J Int Neuropsychol Soc, 18*(4), 773-780. doi:10.1017/s1355617712000446

Steinglass, J. E., Lempert, K. M., Choo, T. H., Kimeldorf, M. B., Wall, M., Walsh, B. T., . . . Simpson, H. B. (2017). Temporal discounting across three psychiatric disorders: Anorexia nervosa, obsessive compulsive disorder, and social anxiety disorder. *Depression and anxiety, 34*(5), 463-470.

Steinhausen, H.-C., & Weber, S. (2009). The outcome of bulimia nervosa: findings from one-quarter century of research. *American Journal of Psychiatry, 166*(12), 1331-1341.

Stice, E. (2016). Interactive and mediational etiologic models of eating disorder onset: Evidence from prospective studies. *Annual Review of Clinical Psychology, 12*, 359-381. doi:http://dx.doi.org/10.1146/annurev-clinpsy-021815-093317

Stice, E., & Agras, W. S. (1999). Subtyping bulimic women along dietary restraint and negative affect dimensions. *J Consult Clin Psychol, 67*(4), 460-469.

Stice, E., Agras, W. S., Telch, C. F., Halmi, K. A., Mitchell, J. E., & Wilson, T. (2001). Subtyping binge eating-disordered women along dieting and negative affect dimensions.

International Journal of Eating Disorders, 30(1), 11-27.

doi:http://dx.doi.org/10.1002/eat.1050

Stice, E., Bohon, C., Marti, C. N., & Fischer, K. (2008). Subtyping women with bulimia nervosa

along dietary and negative affect dimensions: Further evidence of reliability and validity.

J Consult Clin Psychol, 76(6), 1022-1033. doi:10.1037/a0013887.

http://dx.doi.org/10.1037/a0013887

Stice, E., & Fairburn, C. G. (2003). Dietary and dietary-depressive subtypes of bulimia nervosa

show differential symptom presentation, social impairment, comorbidity, and course of

illness. *J Consult Clin Psychol, 71*(6), 1090-1094. doi:10.1037/0022-006x.71.6.1090

Stice, E., Marti, C. N., & Rohde, P. (2013). Prevalence, incidence, impairment, and course of the

proposed DSM-5 eating disorder diagnoses in an 8-year prospective community study of

young women. *Journal of abnormal psychology, 122*(2), 445.

Stice, E., Telch, C. F., & Rizvi, S. L. (2000). Development and validation of the Eating Disorder

Diagnostic Scale: A brief self-report measure of anorexia, bulimia, and binge-eating

disorder. *Psychol Assess, 12*(2), 123-131. doi:http://dx.doi.org/10.1037/1040-

3590.12.2.123

Tauscher, J., Pirker, W., Willeit, M., de Zwaan, M., Bailer, U., Neumeister, A., . . . Brücke, T.

(2001). [123 I] β-CIT and single photon emission computed tomography reveal reduced

brain serotonin transporter availability in bulimia nervosa. *Biol Psychiatry, 49*(4), 326-

332.

Thompson-Brenner, H., Shingleton, R. M., Thompson, D. R., Satir, D. A., Richards, L. K., Pratt,

E. M., & Barlow, D. H. (2016). Focused vs. Broad enhanced cognitive behavioral therapy

for bulimia nervosa with comorbid borderline personality: A randomized controlled trial. *Int J Eat Disord, 49*(1), 36-49. doi:10.1002/eat.22468

Thompson-Brenner, H., Glass, S., & Westen, D. (2003). A Multidimensional Meta-Analysis of Psychotherapy for Bulimia Nervosa. *Clinical Psychology: Science and Practice, 10*(3), 269-287.

Trace, S. E., Thornton, L. M., Root, T. L., Mazzeo, S. E., Lichtenstein, P., Pedersen, N. L., & Bulik, C. M. (2012). Effects of reducing the frequency and duration criteria for binge eating on lifetime prevalence of bulimia nervosa and binge eating disorder: Implications for DSM-5. *International Journal of Eating Disorders, 45*(4), 531-536. doi:http://dx.doi.org/10.1002/eat.20955

Volkow, N. D., Chang, L., Wang, G. J., Fowler, J. S., Ding, Y. S., Sedler, M., . . . Pappas, N. (2001). Low level of brain dopamine D2 receptors in methamphetamine abusers: association with metabolism in the orbitofrontal cortex. *Am J Psychiatry, 158*(12), 2015-2021. doi:10.1176/appi.ajp.158.12.2015

Volkow, N. D., Fowler, J. S., Wang, G. J., Baler, R., & Telang, F. (2009). Imaging dopamine's role in drug abuse and addiction. *Neuropharmacology, 56 Suppl 1*, 3-8. doi:10.1016/j.neuropharm.2008.05.022

Volkow, N. D., Fowler, J. S., Wang, G. J., Hitzemann, R., Logan, J., Schlyer, D. J., . . . Wolf, A. P. (1993). Decreased dopamine D2 receptor availability is associated with reduced frontal metabolism in cocaine abusers. *Synapse, 14*(2), 169-177. doi:10.1002/syn.890140210

Volkow, N. D., Wang, G. J., Fowler, J. S., Logan, J., Jayne, M., Franceschi, D., . . . Pappas, N. (2002). "Nonhedonic" food motivation in humans involves dopamine in the dorsal

striatum and methylphenidate amplifies this effect. *Synapse, 44*(3), 175-180. doi:10.1002/syn.10075

Volkow, N. D., Wang, G. J., Telang, F., Fowler, J. S., Logan, J., Jayne, M., . . . Wong, C. (2007). Profound decreases in dopamine release in striatum in detoxified alcoholics: possible orbitofrontal involvement. *J Neurosci, 27*(46), 12700-12706. doi:10.1523/jneurosci.3371-07.2007

Vrieze, E., Pizzagalli, D. A., Demyttenaere, K., Hompes, T., Sienaert, P., de Boer, P., . . . Claes, S. (2013). Reduced reward learning predicts outcome in major depressive disorder. *Biol Psychiatry, 73*(7), 639-645.

Wagner, A., Aizenstein, H., Venkatraman, V. K., Bischoff-Grethe, A., Fudge, J., May, J. C., . . . Kaye, W. H. (2010). Altered striatal response to reward in bulimia nervosa after recovery. *Int J Eat Disord, 43*(4), 289-294. doi:10.1002/eat.20699

Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063.

Watson, D., O'Hara, M. W., Naragon-Gainey, K., Koffel, E., Chmielewski, M., Kotov, R., . . . Ruggero, C. J. (2012). Development and validation of new anxiety and bipolar symptom scales for an expanded version of the IDAS (the IDAS-II). *Assessment, 19*(4), 399-420.

Weafer, J., Baggott, M. J., & de Wit, H. (2013). Test–retest reliability of behavioral measures of impulsive choice, impulsive action, and inattention. *Experimental and clinical psychopharmacology, 21*(6), 475.

Whiteside, S. P., & Lynam, D. R. (2001). The five factor model and impulsivity: Using a structural model of personality to understand impulsivity. *Pers Individ Dif, 30*(4), 669-689.

Wonderlich, S. A., Peterson, C., Crosby, R., Smith, T., Klein, M., Mitchell, J., & Crow, S. (2014). A randomized controlled comparison of integrative cognitive-affective therapy (ICAT) and enhanced cognitive-behavioral therapy (CBT-E) for bulimia nervosa. *Psychol Med, 44*(03), 543-553.

Wonderlich, S. A., Peterson, C. B., & Smith, T. L. (2015). *Integrative cognitive-affective therapy for bulimia nervosa: a treatment manual*: Guilford Publications.

Wu, M., Giel, K. E., Skunde, M., Schag, K., Rudofsky, G., de Zwaan, M., . . . Friederich, H. C. (2013). Inhibitory control and decision making under risk in bulimia nervosa and binge-eating disorder. *Int J Eat Disord, 46*(7), 721-728. doi:10.1002/eat.22143

Wu, M., Hartmann, M., Skunde, M., Herzog, W., & Friederich, H. C. (2013). Inhibitory control in bulimic-type eating disorders: a systematic review and meta-analysis. *PLoS One, 8*(12), e83412. doi:10.1371/journal.pone.0083412

Table 1

Demographic Characteristics by Group

Characteristic	BN (*n*=20)	HC (*n*=20)			
	Mean (SD)	*Mean (SD)*	*t*	*p*	Cohen's *d*
Age (years)	20.00 (2.36)	20.40 (2.93)	-0.479	0.635	0.150
Body mass index (BMI)	27.72 (7.98)	23.40 (4.27)	2.137	0.039	0.675
					Fisher's Exact Test
			χ^2	*p*	*p*
Ethnicity and Race			3.034	0.695	-
Caucasian	14	15			
African American	0	1			
Asian	2	1			
Native-American/Alaskan Native	1	0			
Multi-racial	2	1			
Other	1	2			
Hispanic/Latinx	4	1	2.057	0.151	0.171
Education			1.667	0.797	-
Some College	17	14			
Associate's Degree	1	1			
Bachelor's Degree	1	2			
Master's Degree	1	3			
Employment			1.026	0.311	0.501
Yes	12	15			
No	8	5			

Table 2

Clinical Characteristics by Group

Clinical Characteristic	BN (*n*=20)	HC (*n*=20)	χ^2	*p*	Fisher's Exact Test *p*
	Mean (SD)	*Mean (SD)*			
Eating-Disorder Symptoms					
Objective Binge Eating Episodes	26.10 (27.97)	-			
Restricting Episodes	21.35 (23.81)	-			
Compensatory/Excessive Exercise Episodes	24.45 (23.09)	-			
Self-Induced Vomiting Episodes	6.10 (16.25)	-			
Diuretic and/or Laxative Misuse Episodes	4.70 (13.46)	-			
	n (%)				
Treatment-Seeking: Psychotherapy			-	-	-
Yes	4 (20%)	-			
No	16 (80%)	-			
Treatment-Seeking: Medications			-	-	-
Yes	0	-			
No	20	-			
Current *DSM-5* Disorders			-	-	-
Major Depressive Disorder	8 (40%)	-			
Generalized Anxiety Disorder	4 (20%)	-			
Panic Disorder	3 (15%)	-			
Post-Traumatic Stress Disorder	2 (10%)	-			
Social Anxiety Disorder (Social Phobia)	5 (25%)	-			
Current Menstrual Periods			2.057	.151	.171
Yes	16	19			
No	4	1			
Hormonal Contraceptive Use			2.506	.113	0.205
Yes	13	8			
No	7	12			
Cigarette/Nicotine Use			-	-	-
Yes	0	0			
No	20	20			

Note. Eating-disorder symptom frequencies (derived from the *Eating Disorder Diagnostic Interview*) were assessed over the past three months, in line with *DSM*-5 diagnostic criteria for BN.

Table 3

Self-Report Measures by Group

Self-Report Measure	BN (*n*=20) Mean (SD)	HC (*n*=20) Mean (SD)	t	p	Cohen's d
EPSI					
Binge Eating	21.25 (6.59)	5.80 (4.90)	8.408	0.000	2.661
Excessive Exercise	9.00 (5.73)	3.70 (4.39)	3.283	0.001	1.038
Purging	2.90 (3.24)	0.55 (2.23)	2.668	0.006	0.850
Restricting	7.70 (7.13)	2.30 (2.51)	3.191	0.002	1.010
ESI-bf					
Substance Abuse Factor	17.70 (11.39)	11.90 (8.48)	1.826	0.038	0.578
IDAS-II					
General Depression	57.10 (11.19)	30.55 (6.97)	9.008	0.000	2.848
Dysphoria	32.05 (7.18)	15.05 (4.37)	9.040	0.000	2.680
Lassitude	18.60 (5.22)	10.05 (3.38)	6.145	0.000	1.944
Insomnia	16.85 (5.24)	10.80 (3.16)	4.421	0.000	1.398
Appetite Loss	7.75 (3.24)	4.45 (1.50)	4.129	0.000	1.307
Appetite Gain	11.15 (2.87)	5.25 (2.55)	6.870	0.000	2.173
Well-Being	16.75 (5.11)	24.00 (4.86)	-4.600	0.000	-1.454
Ill Temper	9.00 (3.20)	5.95 (1.43)	3.895	0.000	1.231
Mania	11.50 (4.74)	7.85 (2.25)	3.110	0.002	0.984
Euphoria	8.75 (3.85)	7.90 (2.95)	0.783	0.219	0.248
Panic	18.45 (7.24)	8.95 (1.36)	5.771	0.000	1.824
Social Anxiety	16.95 (6.26)	8.45 (3.59)	5.226	0.000	1.666
Claustrophobia	8.90 (4.45)	5.35 (1.57)	3.367	0.002	1.064
Traumatic Intrusions	9.95 (4.35)	5.55 (2.33)	3.991	0.000	1.261
Traumatic Avoidance	10.50 (4.10)	6.50 (2.54)	3.709	0.001	1.173
Checking	9.10 (3.37)	4.80 (2.12)	4.831	0.000	0.871
Ordering	10.65 (5.33)	7.40 (3.00)	2.375	0.012	0.751
Cleaning	11.85 (7.43)	8.25 (1.77)	2.108	0.023	0.667
PANAS					
Positive Affect	21.30 (5.82)	28.60 (1.52)	-3.646	0.000	-1.716
Negative Affect	21.95 (7.52)	11.45 (1.82)	6.608	0.000	1.919
UPPS-P					
Negative Urgency	2.77 (0.57)	1.81 (0.47)	5.829	0.000	1.838

Table 4

Reward Processing and Inhibitory Control Measures by Group

	BN	HC			
	Mean (SD)	*Mean (SD)*	*Test*	*p*	Effect Size
Inhibitory Control			$F(2, 34) = 1.294$	0.287	
Animal Commission Errors	16.833 (13.725)	11.150 (6.612)	$F(1, 35) = 2.603$	0.116	0.528
Food Commission Errors	17.833 (14.122)	13.050 (8.108)	$F(1, 35) = 2.396$	0.131	0.415
Delay Discounting			$F(2, 33) = 5.893$	0.006	
MCQ k-value[a]	-5.617 (1.326)	-4.533 (1.194)	$F(1, 34) = 9.367$	0.004	0.859
FCQ k-value[a]	-4.544 (1.468)	-3.364 (1.492)	$F(1, 34) = 6.799$	0.013	0.797
Reward Learning			$F(2, 20) = 3.620$	0.046	
Response Bias: Block 1	0.055 (0.145)	0.131 (0.115)		0.043	0.581
Response Bias: Block 2	0.128 (0.204)	0.161 (0.236)		0.263	0.150
Response Bias: Block 3	0.175 (0.145)	0.108 (0.169)		0.115	0.425
Reward Learning	0.120 (0.166)	-0.023 (0.165)	$F(1, 21) = 6.856$	0.016	0.864
Effort Valuation					
Breakpoint	16.4722 (5.791)	12.675 (7.270)	$U=130, Z=-1.605$	0.149	-0.261
Intensity	19.72 (24.571)	20.75 (35.139)	$U=118, Z=-1.821$	0.072	-0.295
O_{max}	30.889 (20.230)	18.225 (12.046)	$U=92.5, Z=-2.579$	0.009	-0.418
P_{max}	10.111 (7.586)	9.625 (6.836)	$U=176, Z=-0.119$	0.919	-0.019
Elasticity			$F(1, 642)=1.097$	0.295	

[a]k-values presented were natural-logarithm-transformed.

Table 5

Empirical Test of Volkow's Model in Women with Bulimia Nervosa

	Inhibitory Control		Delay Discounting		Reward Learning	Effort Valuation (Breakpoint)
	Animal	Food	Money	Food		
Inhibitory Control						
Animal	-					
Food	**.920****	-				
Delay Discounting						
Money	**.513***	**.437***	-			
Food	.245	.131	**.393***	-		
Reward Learning	.141	.123	-.256	**-.550***	-	
Effort Valuation (Breakpoint)	.118	.104	-.130	**.607****	-.064	-

Note. Correlations are non-parametric Spearman's rho (r_s) values.

*$p < 0.05$ (one-tailed)
**$p < 0.01$ (one-tailed)

Table 6

Associations Among Reward-Processing and Inhibitory Control Measures, Disordered-Eating Behaviors, and Affect in Women with Bulimia Nervosa

	IC-A	IC-F	DD-M	DD-F	RL	EV	BE	SIV	DiLax	FAST	CE	PA	NA	DYS	NURG
IC-A	-	.920**	.513*	.245	.141	.118	.010	-.275	-.248	-.483*	-.368	.079	.186	.144	-.060
IC-F	.920**	-	.437*	.131	.123	.104	.106	-.144	-.127	-.370	-.412*	.191	.289	.163	-.071
DD-M	.513*	.437*	-	.393*	-.256	-.130	-.183	-.165	-.127	-.412*	-.260	-.442*	-.033	.194	-.016
DD-F	.245	.131	.393*	-	-.550*	-.085	-.183	-.202	-.186	-.260	-.197	-.235	.122	.168	-.667**
RL	.141	.123	-.256	-.550*	-	.607**	-.070	.404	.071	-.152	-.263	.351	.028	.250	-.027
EV	.118	.104	-.130	-.085	.607**	-	.068	-.135	.140	-.109	-.135	-.138	.345	.035	-.194
BE	.010	.106	-.183	-.183	-.070	.068	-	.093	.022	.240	-.040	.151	.540**	.405*	-.339
SIV	-.275	-.144	-.165	-.202	.404	-.135	.093	-	.229	.096	-.030	.159	.470*	-.074	.003
DiLax	-.248	-.127	-.127	-.186	.071	.140	.022	.229	-	.224	.115	-.096	.104	-.253	.166
FAST	-.483*	-.370	-.412*	-.260	-.152	-.109	.240	.096	.224	-	-.285	.063	.195	.273	-.059
CE	-.368	-.412*	-.260	-.197	-.263	-.135	-.040	-.030	.115	-.285	-	.037	-.249	-.556**	.317
PA	.079	.191	-.442*	-.235	.351	-.138	.151	.159	-.096	.063	.037	-	-.221	-.370	-.121
NA	.186	.289	-.033	.122	.028	.345	.540**	.470*	.104	.195	-.249	-.221	-	.472*	-.187
DYS	.144	.163	.194	.168	.250	.035	.405*	-.074	-.253	.273	-.556**	-.370	.472*	-	-.121
NURG	-.060	-.071	-.016	-.667**	-.027	-.194	-.339	.003	.166	-.059	.317	-.121	-.187	-.121	-

Note. Correlations are non-parametric Spearman's rho (r_s) values. BE=EDDI Binge Eating Episodes over past three months; CE=EDDI Compensatory Exercise Episodes over past three months; DD-F=delay discounting of food commodities (k-values); DD-M=delay discounting of monetary commodities (k-values); DiLax=EDDI Laxative/Diuretic Misuse Episodes over past three months; DYS=IDAS-II Dysphoria; EV=Effort Valuation (breakpoint on food-specific hypothetical purchase task); FAST=EDDI Fasting Episodes over past three months; IC-A=commission errors toward animal images on go/no-go task (inhibitory control); IC-F=commission errors toward food images on go/no-go task (inhibitory control); NA=PANAS Negative Affect; NURG=UPPS-P Negative Urgency; PA=PANAS Positive Affect; RL=Reward Learning derived from Probabilistic Reward Learning Task; SIV=EDDI Self-Induced Vomiting Episodes over past three months.
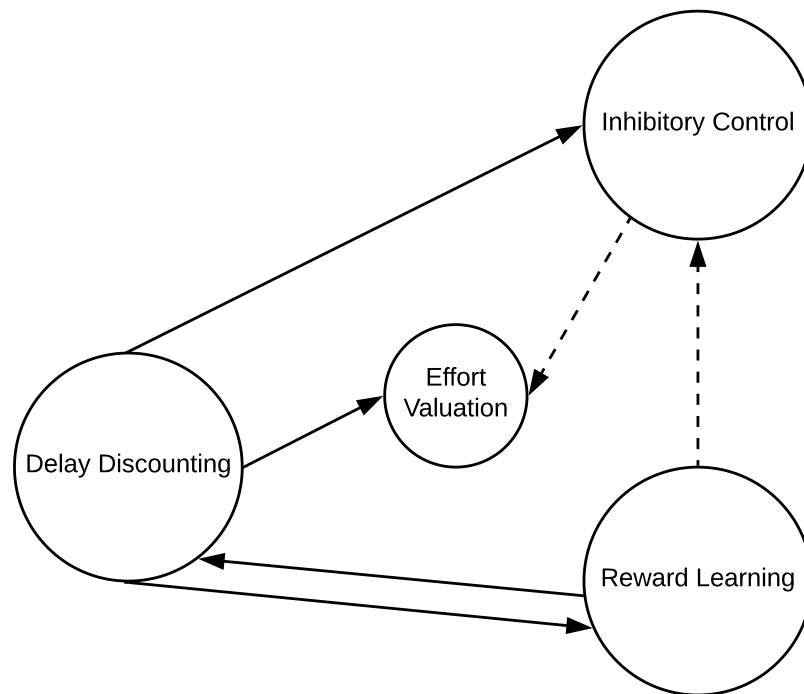
*p < 0.05 (one-tailed)
**p<0.01 (one-tailed)

Figure 1. Volkow's Model of Imbalanced Reward-Processing and Inhibitory Control

Systems. Note that this model posits that three distinct facets of reward processing override

inhibitory control over reward-driven behaviors (e.g., binge eating) and maintain behaviors.

First, increased wanting (delay discounting) of a substance (e.g., alcohol, food) may decrease

inhibitory control over substance use, resulting in over-consumption accompanied by loss-of-

control (e.g., binge eating). Next, repetitive use of a substance, despite negative consequences

(e.g., weight gain, psychosocial impairment), suggests that learning alternative stimulus-reward

associations (reward learning) may be challenging. Impaired reward learning may override

inhibitory control and facilitate disinhibition. Decreased inhibitory control, in turn, increases

efforts (effort valuation) to obtain substances. Finally, reward learning and delay discounting

may mutually reinforce and strengthen one another.

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Probabilistic Reward Learning Task
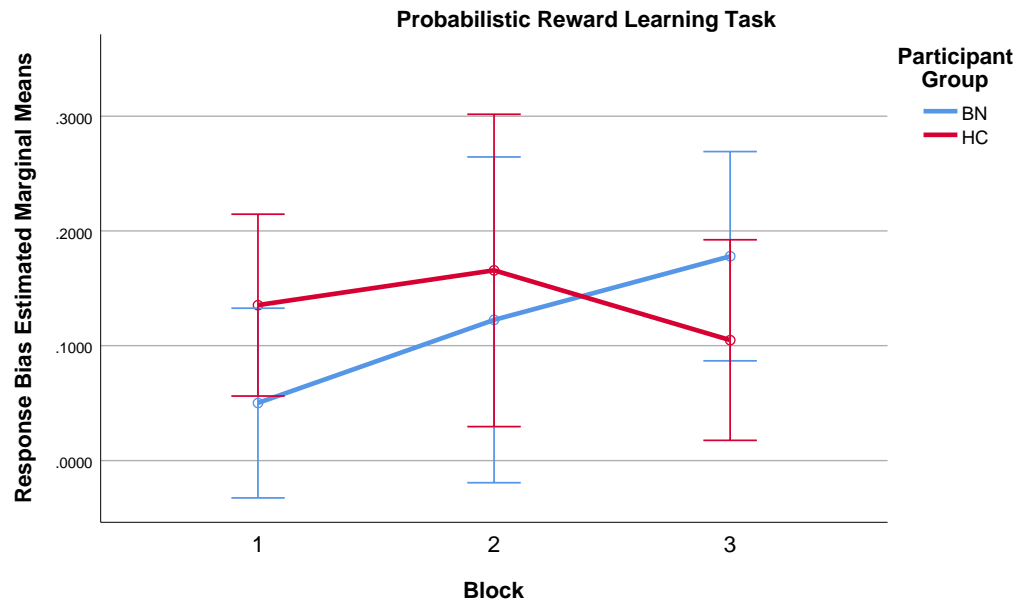
Covariates appearing in the model are evaluated at the following values: BMI Computed in Lab = 25.2636, discriminability = .3177

Error bars: 95% CI

Figure 2. Group Differences in Response Bias by Block on the Probabilistic Reward

Learning Task. BN=women with bulimia nervosa; HC=healthy control women.
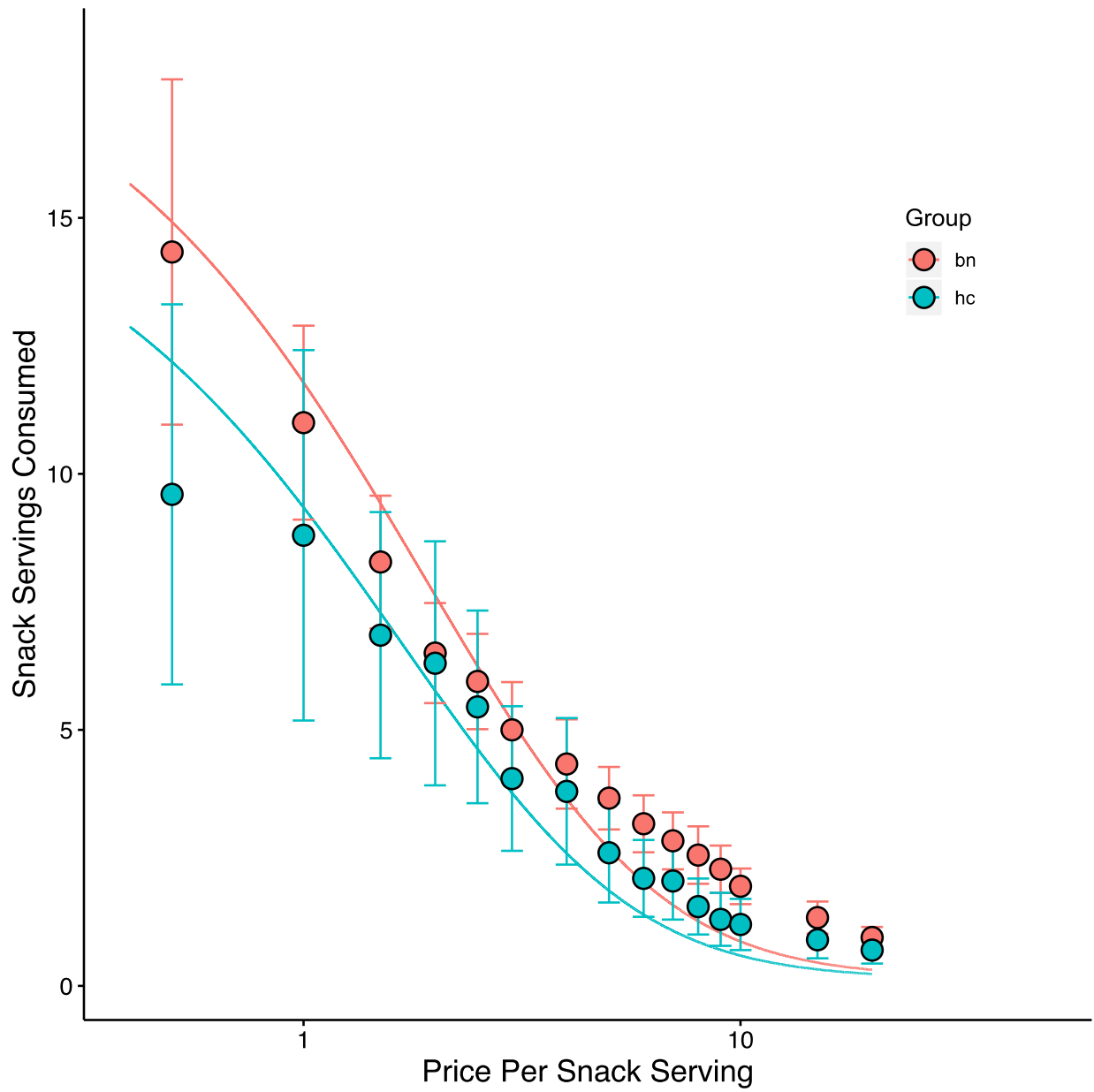
Figure 3. Demand Curves by Group for the Food-Specific Hypothetical Purchase Task.

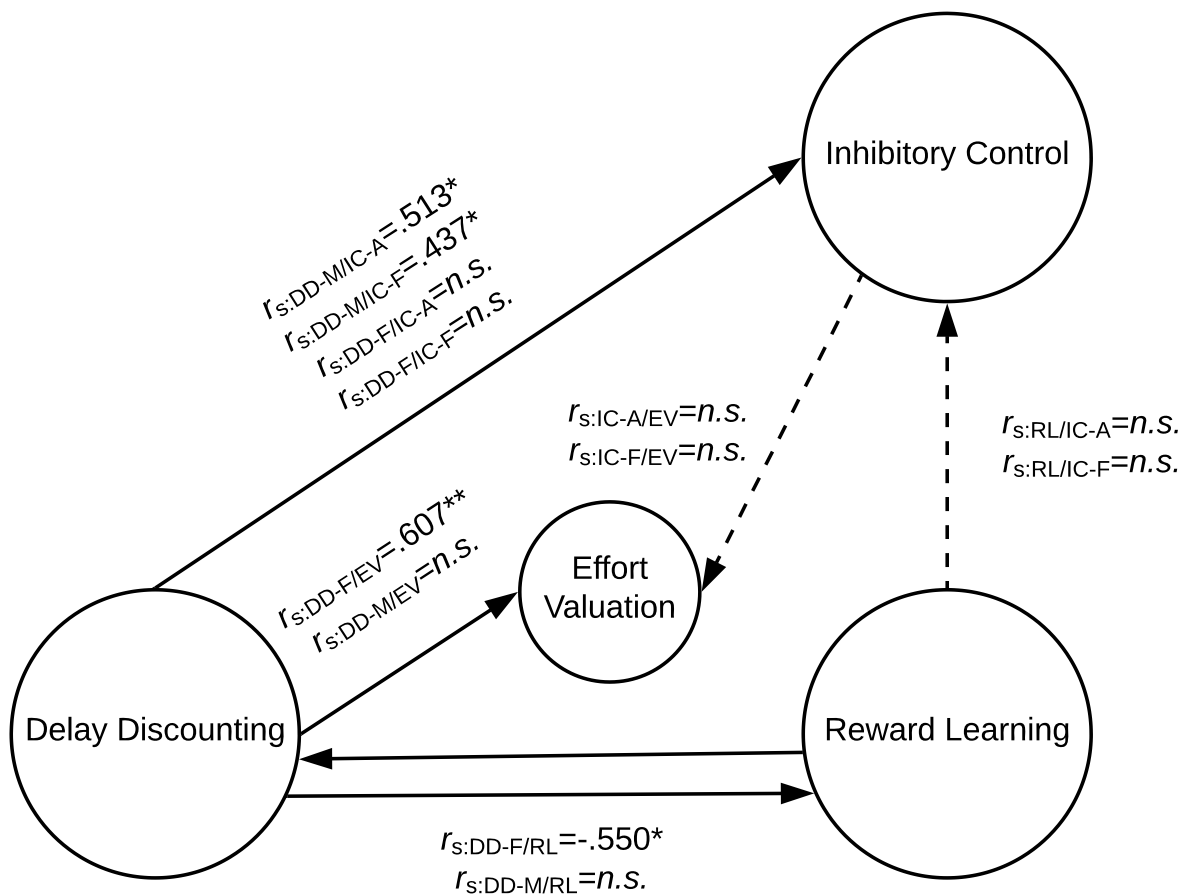BN=women with bulimia nervosa; HC=healthy control women.

Figure 4. Empirical Test of Volkow's Model of Imbalanced Reward-Processing and

Inhibitory Control Systems in Women with Bulimia Nervosa. Correlations are non-parametric

Spearman's rho (r_s) values. DD-F=delay discounting of food commodities (*k*-values); DD-

M=delay discounting of monetary commodities (*k*-values); EV=Effort Valuation (breakpoint on

food-specific hypothetical purchase task); IC-A=commission errors toward animal images on

go/no-go task (inhibitory control); IC-F=commission errors toward food images on go/no-go task

(inhibitory control); RL=Reward Learning derived from Probabilistic Reward Learning Task.

p < 0.05 (one-tailed)

**p<0.01 (one-tailed)