ACUTE PSYCHOSOCIAL STRESS IN BINGE EATING DISORDER

THE EFFECTS OF ACUTE PSYCHOSOCIAL STRESS ON INHIBITORY CONTROL AND RELATIONSHIPS WITH TREATMENT OUTCOME IN BINGE EATING DISORDER

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Descriptive Note

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Lay Abstract

Stress is a common precursor for a binge episode in individuals with binge eating disorder (BED). This study examined the effects of acute psychosocial stress on a measure of inhibitory control, which may underlie loss of control during binge eating in individuals with BED. Participants with BED were assigned to a stress or a no stress condition, completed questionnaires about their mood, experienced a stressor, and completed a task measuring inhibitory control. Results showed that individuals in the stress condition experienced an increase in anxiety, but this rapidly decreased back to baseline levels. The experience of stress impaired individuals' inhibitory control during the task. Nevertheless, acute stress effects on inhibitory control and mood-related impulsivity did not relate to their treatment outcome. These results suggest a need to further investigate different forms of loss of control, and relationships between chronic stress and treatment outcome in BED.

Abstract

Background: Individuals with binge eating disorder (BED) experience a loss of control (i.e., poor inhibitory control) during binge eating, where stress is a common antecedent for binge episodes. However, few studies examine acute stress in BED and, to date, psychosocial stress relationships with inhibitory control are unexamined.

Purpose: The current study investigated acute psychosocial stress effects on inhibitory control in BED. Additionally, inhibitory control relationships with BED treatment outcome were explored.

Methods: Thirty-three individuals with BED were randomized to a stress (n = 17) or no stress condition (n = 16). All completed self-report measures including the Profile of Mood States and the Binge Urge Scale. Following the stressor, individuals completed the Stop-Signal Task (SST), a well-validated measure of inhibitory control. Relationships between post-stress anxiety with inhibitory control and eating pathology were explored. Furthermore, treatment outcome relationships with levels of inhibitory control, and negative urgency (an impulsive personality trait) were explored.

Results: In the stress condition, individuals reported increased state anxiety immediately following stress, but experienced a decrease back to baseline levels of anxiety by the end of the SST. Stress resulted in impaired inhibitory control performance on the SST. Binge urges increased across both conditions over time. Measures of inhibitory control and negative urgency did not relate to treatment outcome.

Conclusion: This study is novel in directly examining psychosocial stress effects on inhibitory control, which has not been studied in BED. These results show subjective stress effects in BED are short-lived; however, behaviourally, stress has a lingering effect on inhibitory control. Increasing binge urges across the experimental session in the no stress condition suggests a role

for generalized anxiety on this impulse. These findings have clinical implications for binge urges as a therapeutic target, and for informing individuals with BED about the implications of stress on their binge eating.

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List of Abbreviations

BMI: body mass index

BED: binge eating disorder

DSM-5: Diagnostic and Statistical Manual of Mental Disorders Version 5

HPA axis: Hypothalamic-Pituitary-Adrenal axis

PFC: prefrontal cortex

PNS: Parasympathetic Nervous System

CRH: corticotropin releasing hormone

ACTH: adrenocorticotropin hormone

SST: Stop Signal Task

SSRT: stop signal reaction time

OFC: orbitofrontal cortex

ACC: anterior cingulate cortex

IFG: inferior frontal gyrus

CRF: corticotropin releasing factor

ED Clinic: Eating Disorders Clinic

SJHH: St Joseph's Healthcare Hamilton

DART: The Diagnostic Assessment Research Tool

HiREB: Hamilton Integrated Research Ethics Board

CBT: Cognitive Behavioural Therapy

TSST: Trier Social Stress Test

POMS: Profile of Mood States

BUS: Binge Urge Scale

CO: carbon monoxide

MINI: International Neuropsychiatric Interview

BDI: Beck Depression Inventory

BAI: Beck Anxiety Inventory

EDE-Q: Eating Disorders Examination Questionnaire

UPPS-P: The Impulsive Behaviour Scale

MCQ: Menstrual Cycle Questionnaire

GUS: Gambling Urge Scale

Hz: hertz

ms: milliseconds

SPSS: Statistical Package for the Social Sciences

ANOVA: analysis of variance

M: mean

SD: standard deviation

SEM: standard error of the mean

RT: reaction time

Declaration of Academic Achievement

I collaborated with Dr. Balodis on the study design and execution. Dr. Balodis was responsible for the development of the main research questions with this project and study funding. Dr. Balodis and research assistants at the Peter Boris Centre for Addictions Research were responsible for obtaining ethics approval for this study. Regarding data collection, I was responsible for recruitment, screening, and conducting experimental sessions, alongside other students and research assistants, as this project is part of a larger study. I am the primary author of this thesis, and was responsible for the analysis, interpretation, and write up of the manuscript in Chapter 2.

Special Considerations

The following manuscript components (Chapter 2) will be included at a later date due to the 2019-2020 COVID-19 pandemic:

1. Salivary cortisol measures
2. Participant's medication lists
3. One participant's treatment outcome data

Chapter 1: General Introduction

Overview

As modern day humans, our reaction to stress extends beyond the physical changes accompanying it; the way in which we perceive certain events and attribute meaning to them influences our psychological response to stress. Psychosocial stress, which encompasses stressors that are psychological in nature, is the most prevalent form of stress humans experience in modern times, and influences the onset of psychiatric disorders (e.g., Enoch, 2011; Kessler, 1997). Psychosocial stress is heavily implicated in obesity, which has reached epidemic levels worldwide (Block, He, Zaslavsky, Ding, & Ayanian, 2009; Gluck, Geliebter, & Lorence, 2004; World Health Organization, 2020; Sinha & Jastreboff, 2013). Obesity is associated with multiple health risks and is measured as an individuals' body mass index (BMI) of 30 (weight kg/height m^2) or greater. In 2016, obesity was estimated to affect 1.9 billion adults, with the worldwide prevalence continuing to increase (World Health Organization, 2020). Recent evidence suggests that obesity, however, is not a homogeneous condition, and is comprised of multiple subgroups (Eldredge & Agras, 1996; Karelis, St-Pierre, Conus, Rabasa-Lhoret, & Poehlman, 2004; Klatzkin, Gaffney, Cyrus, Bigus, & Brownley, 2015). Binge eating disorder (BED) is the best-studied of these obese subgroups and is also the most prevalent eating disorder (Udo & Grilo, 2019). Psychosocial stress is implicated in the maintenance of binge eating disorder (BED), whereby negative affect resulting from stress is an antecedent for the consumption of an unusually large amount of a food within a short period of time (American Psychiatric Association [APA], 2013; Munsch, Meyer, Quartier, & Wilhelm, 2012; Wolff, Crosby, Roberts, & Wittrock, 2000). In the *Diagnostic and Statistical Manual for Mental Disorders 5th edition*

(DSM-5), this symptom is characterized as a binge episode, accompanied with a loss of sense of control. Accordingly, individuals with BED often cite stress as a major trigger for binge eating (Gluck, 2006; Gluck, Geliebter, & Lorence, 2004). Binge episodes are the prominent symptom of BED, which makes identifying the effects of the circumstances that precipitate them critical. To date, few studies systematically investigate how psychosocial stress affects control (i.e., inhibitory control) and binge urges in BED. Additionally, no research has examined whether stress-induced alterations in inhibitory control relate to an individual's treatment outcome for BED.

This first thesis chapter contains 1) an overview of stress-system reactivity, 2) a review of binge eating disorder and stress, 3) a review of inhibitory control in binge eating disorder, and concludes with 4) an introduction to the current study. Chapter 2 comprises an original manuscript in preparation for submission to the journal *Obesity*, examining the effects of acute psychosocial stress on inhibitory control and relationships with treatment outcome in BED. Finally, Chapter 3 provides a general discussion, followed by an appendix with supplementary material of measures.

Stress-System Reactivity

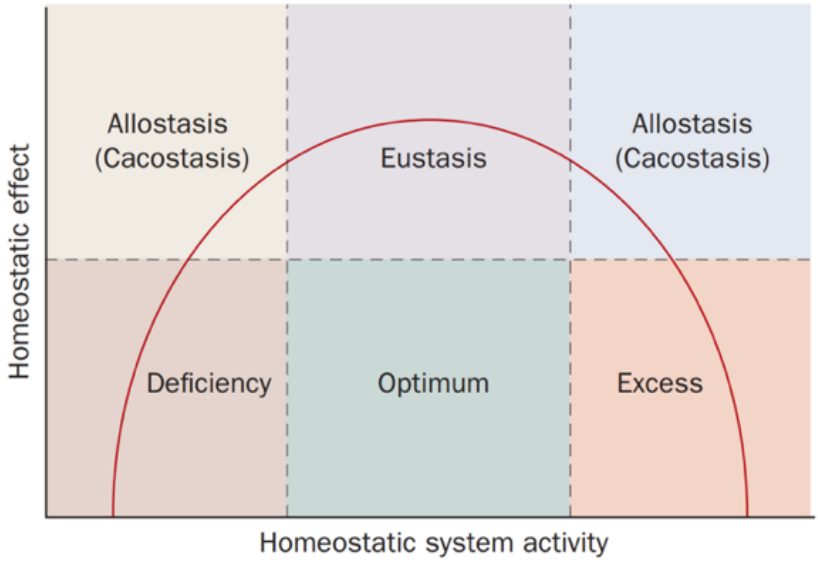
Humans have a self-protection mechanism: the ability to adapt to changes in their environment (Lovallo, 2005). Called the *fight or flight* response, individuals experience a change in emotion and physiological response in the presence of uncertainty or when unable to control a certain outcome. Psychosocial stressors are of interest in the psychiatric field because they do not cause direct bodily harm like a physical stressor (e.g., electric shock), however, the perceived threat poses psychological challenges while producing physiological changes in the body (Lovallo, 2005). Psychosocial stressors create a combination of negative affect that include: (1)

anxiety, which is a sense of apprehension when anticipating a threat, (2) fear, which is a form of arousal during the experience of stress, and (3) anger, encompassing dangerous outward impulse (Lovallo, 2005). Such psychosocial stressors range in intensity and include experiences such as a job interview, strained relationships, financial burden, to coping with the loss of a loved one (Lovallo, 2005).

Psychological stressors activate the stress system and disrupt *homeostasis*, a term coined by Walter Cannon to describe a coordinated set of processes that counteract the effects of stress. Such processes are not only to overcome physiological challenges that we encounter in our environment, but also to maintain psychological stability (Cannon, 1939; Lovallo, 2005). The stress response is not exclusively a set of physical changes, as an individual's perceived level of threat, or the subjective meaning of the stressor also plays a role in the stress response. This is why individuals exhibit differential responses to stress, which are largely based on early life experience and development (McEwen, 2008). As such, acute changes in response to a stressful event, or *allostasis* occurs and provides an adaptive response for maintaining homeostasis (McEwen, 2004). When chronic stress persistently activates the stress response, the result is *allostatic overload* whereby overexertion of the stress response can predispose individuals to physical and neuropsychiatric illness (Chrousos, 2009; McEwen, 2005). See **Figure 1**.

Figure 1

Stress Response Effects on Homeostasis



Note. The stress response produces an inverted U-shaped curve, whereby baseline levels of homeostasis (i.e., eustasis) is in the optimum or middle portion of the curve. Non-adaptive responses to stress occur on the left side of the curve, in which an insufficient (i.e., deficient) response occurs which results in a decreased ability to adequately respond to a stressor. On the right-hand side of the curve, allostasis is indicative of a hyperfunctioning (i.e., excessive) stress response. Both deficient and excess responses to stress have negative outcomes. From Chrousos, 2009.

In humans, stress activates the Hypothalamic-Pituitary-Adrenal axis (HPA axis) (Dickerson & Kemeny, 2004). The HPA axis is coordinated by the sympathoadrenal medullary and parasympathetic pathways (Kyrou & Tsigos, 2007; Sinha, 2018). HPA axis activation creates a cascade of events, resulting in both central and peripheral changes, with the goal of providing an adaptive response to cope with the stressor (Black, 1994). Stressors activate

cognitive and affective components of the central nervous system, including the thalamus, which plays a role in the regulation of energy homeostasis (Cowley et al., 2003; Williams et al., 2001) and the prefrontal cortex (PFC), involved in self-regulation and goal-directed behaviour (McEwen & Morrison, 2013). The thalamus can be thought of as the central-stress information hub, where information about the stressor is first recognized (Lovallo, 2005). The PFC and thalamus assess the stressor and stimulate affective centres that make connections with emotional processing structures in the brain including the amygdala and its steroid receptors, to recognize the sensory input (LeDoux, 1994). Protracted amygdala hyperactivity has been shown to cause atrophy, which is implicated in psychiatric disorders (McEwen, 2004). These components of the brain are responsible for producing the emotional response toward stress (Lovallo, 2005). Where the limbic system and hypothalamus intersect is the pathway responsible for activating the HPA axis; the central systems enhance arousal, resulting in increased attention, alertness, and adaptive aggression, while pausing vegetative functions (e.g., growth, reproduction; Black, 1994; Chrousos, 2009). The parasympathetic nervous system (PNS), is a division of the sympathetic nervous system, and can act to both enhance and decrease sympathetic functions (Charmandari, Tsigos, & Chrousos, 2005; Chrousos, 2007). As such, simultaneous peripheral changes include acute physiological responding such as increased heart rate, blood pressure, and increased respiration allowing for increased energy to respond to stress (Black, 1994; Chrousos, 2009).

Endocrinological changes resulting from HPA axis activation include stimulation and the coordinated increase of corticotropin releasing hormone (CRH) which activates the anterior pituitary to secrete adrenocorticotropin hormone (ACTH), in turn triggering cortisol release into the bloodstream (Dickerson & Kemeny, 2004). As an output measure of the HPA axis cascade, cortisol is a valid biomarker of the stress response (Bozovic, Racic, & Ivkovic, 2013), because it

is serves as the end product of the HPA axis system, thereby providing a proxy for how active the stress system is (Nicolson, 2008). Cortisol is regulated via a negative feedback mechanism within the central nervous system, as following its secretion into the bloodstream, it travels back to the brain and binds to receptors within the limbic system, including the hippocampus, amygdala, and PFC (Dedovic, Duchesne, Andrews, Engert, & Pruessner, 2009; Feldman & Weidenfeld, 1995; Herman & Cullinan, 1997; Herman, Ostrander, Mueller, & Figueiredo, 2005). In this way, cortisol is used as a proxy to gauge stress-system reactivity in studies examining the stress response across psychiatric disorders, including BED and other eating disorders (e.g., Monteleone et al., 2011; Rosenberg et al., 2013; Young, Abelson, & Cameron, 2004; Zorn et al., 2017). Activation of the HPA axis not only generates acute physiological changes (McEwen, 2004), it also produces behavioural changes (Black, 1994; Chrousos, 2000, 2009; Koob, Heinrichs, Menzaghi, Pich, & Britton, 1994). Longer term behavioural consequences of chronic stress occur due to CRH, norepinephrine, and cortisol elevations that activate the fear system, resulting in anxiety, depression, changes in sleep (e.g., insomnia), and drastically altered eating behaviour (Chrousos, 2009). These alterations due to prolonged activation of the stress response may be distressing for the individual and result in additional psychological changes.

Binge Eating Disorder and Stress

BED was first introduced into the Eating Disorders category in the DSM-5 and is characterized by recurrent and persistent episodes of binge eating within a 2-hour period, including feelings of shame or guilt (APA, 2013). In particular, this condition is manifested by a strong sense of loss of control over eating, which includes eating more rapidly than normal, eating until uncomfortably full, and feeling disgusted with oneself or depressed/guilty after overeating (APA, 2013). Binge episodes must be accompanied by marked distress regarding

binge eating and an absence of regular compensatory behaviours (e.g., vomiting), in addition to occurring at least once a week for a 3 month period (APA, 2013). BED is the most common eating disorder, with a lifetime prevalence of up to 2% (Kessler et al., 2013; Udo & Grilo, 2019).

In the general population, stress can predispose individuals to engage in stress-induced eating (Sinha & Jastreboff, 2013; Torres & Nowson, 2007). Additionally, following psychosocial stress, healthy women with greater physiological (i.e., increased cortisol) stress reactivity consume greater calories, and stress-induced negative affect relates to greater food consumption (Epel, Lapidus, McEwen, & Brownell, 2001). Although the etiology of obesity and eating disorders is multifaceted, repeated and chronic stress states can increase adiposity vulnerability as observed in obesity subgroups (Block et al., 2009; Gluck, Geliebter, Hung, & Yahav, 2004; Sinha & Jastreboff, 2013). In BED particularly, stress plays a prominent role as individuals report experiencing a greater number of life stressors in comparison to both control and psychiatric control participants (Pike et al., 2006). These include long-term psychosocial stressors and major life events one year preceding the onset of disordered eating (Pike et al., 2006). Stress is often also cited as a common antecedent for a binge episode; individuals who binge eat report increased negative affect from daily stressors and a greater impact from these stressors, especially on binge days (Gluck, 2006; Wolff et al., 2000).

Altered stress responding in BED can therefore predispose an individual to give in to urges or demonstrate a lack of behavioural control to eating. *Inhibitory control,* broadly defined as an individual's ability to inhibit a pre-potent response (Logan, Schachar, & Tannock, 1997), is a mechanism that may underlie this loss of control experienced, when faced with the psychological consequences of stress. This makes understanding stress relationships with loss of control an important area for study in BED.

Laboratory Stress Investigations in BED

Stress and Subjective Effects. Acute laboratory psychosocial stress studies in BED demonstrate mixed findings regarding subjective stress responses. Following stress, there is evidence that BED participants report heightened negative affect, including high perceived stress, anxiety, distress, and body dissatisfaction (Hilbert, Vogele, Tuschen-Caffier, & Hartmann, 2011; Klatzkin et al., 2015; Klatzkin, Gaffney, Cyrus, Bigus, & Brownley, 2018; Laessle & Schulz, 2009). However, the majority of these studies find heightened negative affect in BED throughout the experimental session (i.e., before and after stress) in comparison to BMI-matched control participants, suggesting that stress does not alter negative affect significantly. There is some evidence that stress increases negative affect in BED relative to BMI-matched control participants (Naumann, Svaldi, Wyschka, Heinrichs, & von Dawans, 2018). However, there are some studies that demonstrate no differences in subjective stress responses between BED and non-BED groups following stress (Laessle & Schulz, 2009; Rouach et al., 2007; Schulz & Laessle, 2012). Nonetheless, there is some evidence for relationships between stress, anxiety, and desires to binge eat in individuals with BED following stress (Rosenberg et al., 2013). Ambiguous findings between studies could be attributed to small sample sizes (sometimes < 10 BED participants), different applications of the stressor, and individuals with BED from the community, who may experience less severe, or subclinical BED, and are not necessarily representative of those seeking treatment for this disorder. Taken together, these findings suggest that subjective responses to psychosocial stress in BED require more research to clarify mixed outcomes.

Stress and Binge Urges. There is also some evidence linking stress with heightened binge urges and faster eating behaviour in BED (Laessle & Schulz, 2009; Rosenberg et al., 2013)

in comparison to BMI-matched control participants. Additionally, post-stress self-reported stress and anxiety levels positively correlate with sweet cravings and desires to binge eat in BED (Rosenberg et al., 2013). Increased binge urges in BED remain even after watching a body-image-related stressful video clip, whereas healthy controls demonstrate decreased desires (Svaldi, Caffier, Blechert, & Tuschen-Caffier, 2009). Nevertheless, some studies show no differences in the amount of food consumed following stress between BMI-matched control participants and individuals with BED (Klatzkin et al., 2018; Schulz & Laessle, 2012). Furthermore, eating behaviour shows a positive relationship with negative affect following stress in BED (Klatzkin et al., 2018), with one study demonstrating greater consumption of food in BED following acute stress in comparison to healthy control participants (Lyu & Jackson, 2016). Interestingly, individuals with BED report higher baseline (i.e., pre-stress) binge urges, but also high desires post-stress, suggesting that acute stress may actually not have an effect on individual's desires to binge eat (Rouach et al., 2007). These inconsistent findings in BED suggest a need to clarify acute psychosocial stress impacts on binge urges, and whether they increase post-stress, or remain consistently high over time.

Physiological Changes and Stress. Physiologically, BED participants show higher blood pressure following acute stress in comparison to BMI-matched control participants (Klatzkin et al., 2015). Specifically, higher systolic blood pressure is observed in BED (Klatzkin et al., 2015), although heightened blood pressure in BED is present before stress (i.e., at baseline), and therefore may not be a stress-induced effect (Klatzkin et al., 2018). Nonetheless, greater blood pressure changes in BED are associated with greater stress-induced changes in hunger in BED (Klatzkin et al., 2015). Another common physiological stress response measure is increases in the hormone cortisol, where BED participants with greater stress reactivity (i.e.,

"cortisol responders"), show relationships between stress-induced cortisol increases with heightened desires to binge (Rosenberg et al., 2013). Individuals with BED however do not show heightened cortisol responses relative to controls, with one study actually showing blunted cortisol in BED in response to stress (Klatzkin et al., 2018; Naumann et al., 2018; Rosenberg et al., 2013; Rouach et al., 2007). Therefore, relationships between subjective stress responses, urges to binge eat, and physiological stress responses appear mixed in BED and require clarification.

Trait Characteristics and Stress. Given the differences reviewed in subjective stress responses and inhibitory control, there is also a need to consider trait characteristics. One personality trait that may underlie stress-inhibitory control relationships is negative urgency. Negative urgency is a form of impulsivity defined as an individual's tendency to act spontaneously or rashly in response to negative affect (Whiteside & Lynam, 2001). Impulsivity is heightened in BED and combined with distressing emotion around binge eating (APA, 2013; Kenny, Singleton, & Carter, 2019; Racine et al., 2015; Steward et al., 2017). Individuals with BED also demonstrate heightened impulsivity, difficulties with emotion regulation, and generally worse inhibitory control in comparison to BMI-matched and normal weight control participants under negative mood (Leehr et al., 2018). Therefore, considering the role of affect on inhibitory control in BED is of importance. Affect-related impulsivity (i.e., negative urgency) may be particularly relevant when examining stress–binge eating relationships in BED populations and also allows for an affect component when examining loss of control in BED in addition to a motor component (inhibitory control).

The *acquired preparedness model of binge eating* proposes that those high in negative urgency expect that eating will mitigate negative affect (Racine & Martin, 2017). Additionally,

this model posits that dietary restraint, a facet of eating pathology encompassing food restriction and dietary rule adherence, moderates the relationship between negative urgency and dysregulated eating (Racine & Martin, 2017). Early evidence suggests that mood-specific impulsivity, particularly high negative urgency, and poor inhibition towards food cues may serve as a predictor of treatment outcome in BED (Manasse, Espel, et al., 2016). Individuals with higher levels of negative urgency demonstrate lower reductions in binge episode frequency during treatment, whereas those with poor food-specific inhibitory control show greater overall eating pathology throughout treatment (Manasse, Espel, et al., 2016). In fact, individuals with high negative urgency who binge eat report greater negative affect in response to psychosocial stress (Owens, Amlung, Stojek, & MacKillop, 2018). These findings outline the importance of considering trait influences (i.e., negative urgency) and restraint eating pathology when examining stress-induced alterations in inhibitory control, and for predicting treatment success in BED.

Inhibitory Control in Binge Eating Disorder

Inhibitory control represents an important facet of eating pathology in BED with potential for understanding mechanisms underlying the loss of control occurring during binge episodes. There is evidence that deficits in inhibitory control are both food-specific and non-food specific in BED (e.g., Manasse, Goldstein, et al., 2016; Mobbs, Iglesias, Golay, & Van der Linden, 2011; Schag et al., 2013). Specifically, individuals with BED show worse inhibitory control when presented with both neutral and food-related stimuli in comparison to BMI-matched control participants (Grant & Chamberlain, 2020; Manasse, Goldstein, et al., 2016; Mobbs et al., 2011; Svaldi, Naumann, Trentowska, & Schmitz, 2014). Worse general inhibitory control deficits in comparison to non-binge eaters are evident even when hedonic hunger is low (Manasse et al.,

2015). While some previous BED studies examine lab-based eating behaviours and stress, no studies to date have examined the effect of psychosocial stress on inhibitory control. In healthy participants, acute stress can decrease general (i.e., non-food related) inhibitory control with greater PNS reactivity (as indicated by high heart rate variability) serving as a protective effect of stress-induced alterations in inhibitory control (Roos et al., 2017). Stress reactivity may be an important target for therapies that focus on aspects of inhibitory control - a critical area for study in BED, given this group's high stress levels and poor inhibitory control (Roos et al., 2017). Examining general inhibitory control impairments, and specifically this loss of sense of control that occurs before a binge episode allows for an understanding of how this cognitive control mechanism may be altered in BED.

Stop-Signal Task

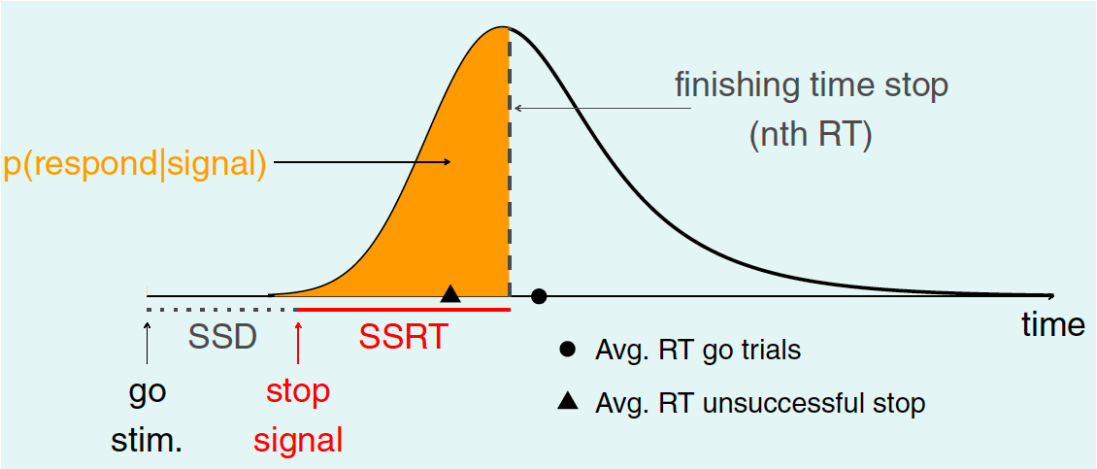
The Stop Signal Task (SST) is a validated, well-established paradigm for measuring response inhibition and has been used to study inhibitory control across a variety of psychiatric disorders (Lipszyc & Schachar, 2010; Logan, Cowan, & Davis, 1984; Logan et al., 1997; Verbruggen et al., 2019). The SST provides a unique measure of response inhibition comprising the ability to inhibit a pre-potent response once it has already been initiated. This measure of inhibition is particularly relevant in BED, as binge episodes, once initiated, are difficult to stop due to lost control. The SST paradigm captures two competing processes—the "go process" which is initiated by the presence of a go signal, and the "stop process" which is initiated by the presence of a stop signal (Logan et al., 1984; Verbruggen & Logan, 2008b). Go trials require participants to respond to a certain stimulus, whereas on a random selection of trials, stop trials present a stop signal following the presentation of the go stimulus, indicating that the participant is not to produce a response (Verbruggen & Logan, 2008a, 2008b). The competition between the 'go' and

'stop' processes follows the *independent-race model*, whereby successful inhibition occurs when the stop process finishes before the go process (Verbruggen & Logan, 2008b; See **Figure 2**). As such, the latency of one's "stop process" provides a measure of inhibitory control, as it measures how fast an individual's stop response/ability to inhibit a response is, which is calculated by subtracting the mean stop signal delay from the mean "go" reaction time. The greater the stop signal reaction time (SSRT), the poorer the inhibitory control (i.e., the stop process is slower and is unable to inhibit the go process) and the more impulsive the participant (Verbruggen et al., 2019; Verbruggen & Logan, 2008b).

An important distinction must be made between the SST and the Go/No-Go Task (another widely used task measuring response inhibition), because they demand different forms of cognitive control (Verbruggen & Logan, 2008a). The Go/No-Go Task contains Go-stimuli that on every trial, are always associated with going, and No-Go stimuli which are always associated with stopping. This phenomenon is known as *consistent mapping*, which allows automatic inhibition to develop over the course of the trials because the No-Go signal automatically activates a response inhibition over time. The SST however, does not allow for automatic inhibition due to each stimulus being associated with both stopping and going, and therefore requires a greater level of cognitive control for successful inhibition to occur (Logan et al., 1984; Verbruggen & Logan, 2008a). Therefore, it is the SST that more accurately captures an individual's ability to withhold a behaviour once it is initiated – a cognitive distinction directly relevant to binge eating.

Figure 2

The Independent-Race Model



Note. When successful response inhibition occurs, the stop response is initiated and completed prior to the go response. However, when the go response is completed before the stop response, inhibition is unsuccessful. Verbruggen et al. (2019) state that this theory relates to: (A) The latency of the response toward unsuccessful stop trials (B) Reaction time (RT) to go trials and (C) the probably of responding on stop trials p(respond | stop-signal) as a function of stop signal delay (SSD). The delay of an individual's inhibitory control (i.e., stop) process is estimated via stop signal reaction time (SSRT). The greater the SSRT, the poorer the response inhibition. From Verbruggen et al., 2019.

The neurobiological substrates underlying inhibitory control and the specific areas activated during the SST are well-studied (e.g., Munakata et al., 2011; Tabibnia et al., 2011). Specifically, PFC areas contain the inhibitory control network and are also implicated in coping with stressors, response inhibition, and memory retrieval (Munakata et al., 2011). These PFC regions are also highly engaged in top-down control and serve as feedback mechanisms to the HPA axis (Kern et al., 2008). Stress and inhibitory control networks overlap, as the orbitofrontal cortex

(OFC) and anterior cingulate cortex (ACC) are recruited during inhibitory control, but decreased activity is observed in these regions when a significant stress response is produced (Dedovic et al., 2009; Pruessner et al., 2008). In healthy individuals, successful inhibitory control performance, and shorter response times on response inhibition tasks, including the SST, are associated with greater activity of the inferior frontal gyrus (IFG; Li, Huang, Constable, & Sinha, 2006; Tabibnia et al., 2011).

The few BED studies that have used the SST to examine response inhibition demonstrate higher SSRTs and more commission errors to food stimuli, however these extend to neutral stimuli, suggesting general inhibitory control deficits in comparison to BMI-matched control participants (Manasse, Goldstein, et al., 2016; Svaldi et al., 2014; Wu et al., 2013). Additionally, greater SSRT is negatively correlated with dietary restraint, a facet of eating pathology associated with strict dietary rules and the avoidance of eating (Wu et al., 2013). Although the neurobiological correlates of SST performance in BED have yet to be studied, other studies examining facets of cognitive inhibition show diminished activity in the IFG and ventromedial PFC in BED in comparison to control participants (Balodis et al., 2013). Additionally, BED participants also demonstrate higher self-reported impulsivity than BMI-matched controls, which negatively correlates with response inhibition accuracy (Hege et al., 2015). Greater attentional impulsivity is specifically associated with decreased activity in the right PFC (Hege et al., 2015). These neurobiological findings demonstrate overlapping brain regions involved in stress, and response inhibition, including an association between self-reported impulsivity and inhibitory control performance. These findings provide insight into the neural correlates of inhibitory control as a key cognitive mechanism that may act as a target for successful BED treatment (Balodis et al., 2014; Wilson, Grilo, & Vitousek, 2007).

Introduction to the Current Study

Studies in BED have examined acute psychosocial stress and response inhibition separately, but to date, no investigations have directly researched the two together. Given the prominent role of stress in BED eating pathology and the inhibitory control impairments in this population, understanding psychosocial stress relationships with inhibitory control is critical. Generalized impairments in inhibitory control may make it difficult for individuals with BED to suppress actions or resist interference from irrelevant stimuli, which may impact successful treatment outcome. No studies have examined how acute psychosocial stress affects inhibitory control in individuals with BED. The current study had four main aims and hypotheses:

1. To examine relationships between stress and inhibitory control in BED. It was hypothesized that individuals in the stress condition would demonstrate general inhibitory control impairments relative to the no stress condition.
2. To evaluate the effect of stress on urges to binge. Relative to the no stress condition, it was hypothesized that the stress condition would report increased binge urges following stress.
3. To explore relationships between self-report measures of anxiety post-stress with inhibitory control (i.e., SSRT), binge urges, eating pathology, and negative urgency. It was hypothesized that high post-stress anxiety would relate to binge urges, negative urgency and greater SSRTs.
4. To investigate relationships with treatment outcome in those undergoing treatment. It was hypothesized that those with high levels of negative urgency, poor inhibitory control, and greater stress reactivity would show less reductions in binge episodes throughout treatment.

Chapter 2

ACUTE PSYCHOSOCIAL STRESS EFFECTS ON INHIBITORY CONTROL AND RELATIONSHIPS WITH TREATMENT OUTCOME IN BINGE EATING DISORDER

Punia, K[1]., Laliberte, M[2]., Liu, H[1]., Lucibello, K[2]., Potter, S[2]., & Balodis, I.M[1]. (in preparation for submission). Acute psychosocial stress effects on inhibitory control and relationships with treatment outcome in binge eating disorder

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TITLE: Acute psychosocial stress effects on inhibitory control and relationships with treatment outcome in binge eating disorder

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KEYWORDS: binge eating disorder, negative urgency, stress, inhibitory control

RUNNING TITLE: Psychosocial stress in binge eating disorder

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Study Importance Questions

1) What is already known about this subject?

- Stress is a common precursor to binge eating experienced in individuals with binge eating disorder (BED)
- Individuals with BED demonstrate both general and food-specific impairments in inhibitory control, however no studies have examined psychosocial stress effects on inhibitory control in BED

2) What are the new findings in your manuscript?

- Individuals with BED exhibit rapid anxiety increases, followed by rapid decreases; urges to binge increased across both conditions over time
- Negative urgency, stress-induced alterations in inhibitory control, or stress reactivity do not relate to treatment outcome in BED

3) How might your results change the direction of research or the focus of clinical practice?

- This study has clinical implications for cognitive restructuring and coping strategies around stress-induced anxiety, high levels of binge urges, and for managing binge episodes triggered by stress
- This study identifies future research to consider restraint eating pathology, different forms of inhibitory control, and chronic stress effects on treatment

Abstract

Objective: Binge episodes are often precipitated by stress, and are accompanied with diminished control (i.e., poor inhibitory control) in individuals with binge eating disorder (BED). However, there is little research examining how stress affects inhibitory control in this population. This study examined acute psychosocial stress effects on inhibitory control, mood, and binge urges. Additionally, it explored relationships between negative urgency and stress-induced alterations in inhibitory control with treatment outcome in BED.

Methods: Thirty-three individuals with BED were randomized to a stress condition (n = 17) or a no stress condition (n = 16). Participants completed anxiety and binge urge questionnaires. Following stress, individuals completed the Stop-Signal Task (SST), as a measure of inhibitory control.

Results: In the stress condition, individuals with BED reported increased state anxiety immediately following the stressor but experienced a significant decrease back to baseline anxiety levels by the end of the SST. Stress resulted in impaired inhibitory control performance in the stress condition. Binge urges increased across conditions over time. Measures of inhibitory control, negative urgency, or stress reactivity did not relate to treatment outcome.

Conclusion: This study is novel in directly examining psychosocial stress effects on inhibitory control, which has not been studied in BED. These results show subjective stress effects in BED are short-lived; however, behaviourally, stress has a lingering effect on inhibitory control. Increasing binge urges across the experimental session in the no stress group suggests a role for generalized anxiety on this impulse. These findings have clinical implications for binge urges as a therapeutic target, and for informing individuals with BED about the implications of stress on their binge eating.

1. Introduction

Obesity is a global pandemic, affecting 1.9 billion adults worldwide (1). Growing evidence demonstrates that obesity is not a homogeneous condition and is comprised of multiple subgroups (2, 3). One subgroup is individuals with binge eating disorder (BED), a condition with a lifetime prevalence of up to 2% (4, 5). BED was introduced into the *Diagnostic and Statistical Manual for Mental Disorders 5th edition* (DSM-5) in 2013, and is characterized by the consumption of an objectively large amount of food within a short period, coupled with a loss of sense of control and negative affect (6).

1.1. Relationships Between Stress and Eating

Recent theories suggest that the Hypothalamic-Pituitary-Adrenal (HPA) axis stress system prominently influences the rewarding properties of food (7). Psychosocial stress, the most prevalent type of stress in society today, enhances the reinforcing value of food (8, 9). Specifically, modulators of the stress response, including corticotropin releasing factor (CRF), adrenocorticotropic hormone (ACTH), and cortisol alter dopaminergic signaling, activating regions of the prefrontal cortex (PFC) involved in the reward system, and hypothalamic and mid-brain regions involved in self-control and decision-making (8). This promotes increased motivation to consume highly palatable foods (8). Modulators of the stress response may reinforce the consumption of palatable foods, which are common constituents of binge episodes for individuals with BED (10). In the general population, stress can lead to overeating (7, 11), which is a risk factor for obesity (7, 12, 13). Accordingly, individuals with BED often cite psychosocial stress, as a major trigger for binge eating (14). Following psychosocial stress, individuals with BED report increased negative affect as well as binge urges (e.g., 15, 16, 17, 18). They also report a stronger liking for caloric-dense foods in comparison to healthy control

participants following stress (19). In this way, acute stress may act as an antecedent for loss of control binge episodes in BED (9). Previous BED studies examining psychosocial stress effects on mood report greater negative affect and anxiety post-stress relative to BMI-matched control and normal weight control participants (3, 15, 18). In comparison to BMI-matched control participants, individuals with BED report higher psychological distress when anticipating a stressor, and greater body dissatisfaction post-stress (17). Following stress, individuals with BED report increased desire to binge eat and heightened sweet cravings, both of which positively correlate with subjective stress and anxiety (16). Behaviourally, individuals with BED increase their eating rate in comparison to BMI-matched control participants (20), and also consume a larger amount of food than healthy control participants (19) following acute stress.

1.2. Stress and Inhibitory Control

Stress may induce binge eating by altering inhibitory control mechanisms. Inhibitory control is defined as the ability to inhibit a prepotent response (21). In healthy individuals, acute psychosocial stress can result in general inhibitory control impairments (22). Specifically, a key component of inhibitory control is the ability to stop an already-initiated response; in BED, this facet relates to disinhibition during a binge episode. Although inhibitory control impairments to both neutral and food-specific stimuli are demonstrated in BED (e.g., 23, 24, 25), studies have yet to directly examine how psychosocial stress affects general inhibitory control and how it relates to binge urges.

1.3. Negative Urgency

Personality factors may also represent an important consideration in inhibitory control; the *acquired preparedness model of binge eating* proposes that negative urgency (a trait of poor inhibitory control in response to negative affect) predisposes an individual to binge eat in an

attempt to alleviate this aversive state (26). In female college students, higher levels of negative urgency, combined with unhealthy eating expectancies, is associated with a higher dysregulated eating risk (27). A pilot study in BED found that increased negative urgency in BED is linked with less reductions in binge episodes throughout treatment (28). Additionally, poor inhibition toward food-related cues is indicative of greater eating disorder pathology throughout treatment (28). Therefore, there is a need to understand how impulsive personality traits in BED populations relate to binge eating, including restraint and overall eating pathology (e.g., 26, 28).

To date, research findings suggest an important role of stress-induced negative affect on binge urges and deficits in inhibitory control. Characterizing psychosocial stress-induced alterations in inhibitory control is a novel investigation direction in BED, with potential for providing insights into binge susceptibilities and other impulsive behaviours. Additionally, stress-induced general inhibitory control impairments in this clinical group may have implications for identifying critical treatment and relapse prevention targets in BED.

1.4. Introduction to the Present Study

Previous BED studies demonstrate deficits in inhibitory control and show stress effects on multiple components of eating pathology and behaviour. No studies to date, however, have directly examined psychosocial stress effects on inhibitory control in BED.

The purpose of the current study was to examine the effects of acute psychosocial stress on inhibitory control, mood, and binge urges in individuals with BED. Additionally, the current investigation explored if negative urgency and stress-induced alterations in inhibitory control predicted treatment outcome. Participants underwent an acute stress-induction paradigm, followed by the Stop Signal Task (SST), a well-validated measure of inhibitory control (29, 30). Measures of mood and binge urges were collected throughout the experimental paradigm.

Based on previous studies implementing acute stress paradigms to study stress in BED, the aims and hypotheses of this study were:

1. To examine the effects of stress on inhibitory control in BED. It was hypothesized that stress would increase inhibitory control impairments in BED, measured through increased stop signal reaction time (SSRT) on the SST.
2. To replicate and extend findings of acute stress on mood and binge urges in BED. Consistent with prior studies, it was hypothesized that individuals in the stress condition would report heightened anxiety and binge urges following the stress procedure, and that these heightened levels would be sustained throughout the study.
3. To explore relationships between self-report measures of anxiety with inhibitory control (i.e., SSRT), binge urges, eating pathology, and personality measures (i.e., negative urgency). It was hypothesized that greater SSRTs would be related to higher negative urgency, post-stress anxiety, and post-stress binge urges.
4. To evaluate relationships between negative urgency and inhibitory control with treatment outcome in those undergoing BED treatment. It was hypothesized that those with greater negative urgency, and poorer inhibitory control would demonstrate lower reductions in binge episodes throughout treatment.

2. Methods

2.1. Participants

Participants consisted of a total of N = 33 individuals; 28 were treatment-seeking with BED recruited from the Eating Disorders (ED) clinic at St. Joseph's Healthcare Hamilton (SJHH), in Hamilton Ontario between 2017-2019, and 5 individuals reporting binge eating from the community. Participants were comprised of 33 females, and 2 males who underwent 2

research sessions. The BED diagnosis was determined by certified clinicians at the ED clinic using the *Diagnostic Assessment Research Tool* (DART; 31), which was developed based on criteria from the DSM-5. Community participants were assessed according to DSM-5 criteria for BED (APA; 6). Exclusion criteria included the presence of acute psychosis, a history of traumatic brain injury, or severe cognitive impairments.

This protocol is part of a larger study approved by the Hamilton Integrated Research Ethics Board (HiREB Project #1600). Data collection occurred at the Peter Boris Centre for Addictions Research at SJHH. All participants provided informed consent and individuals undergoing treatment gave permission to access their clinical data. Each participant from the ED clinic was in the early stages (approximately within one month of treatment) of completing a simultaneous 20-week cognitive behavioural therapy (CBT) treatment program (For detailed manual see 32).

2.2. Protocol

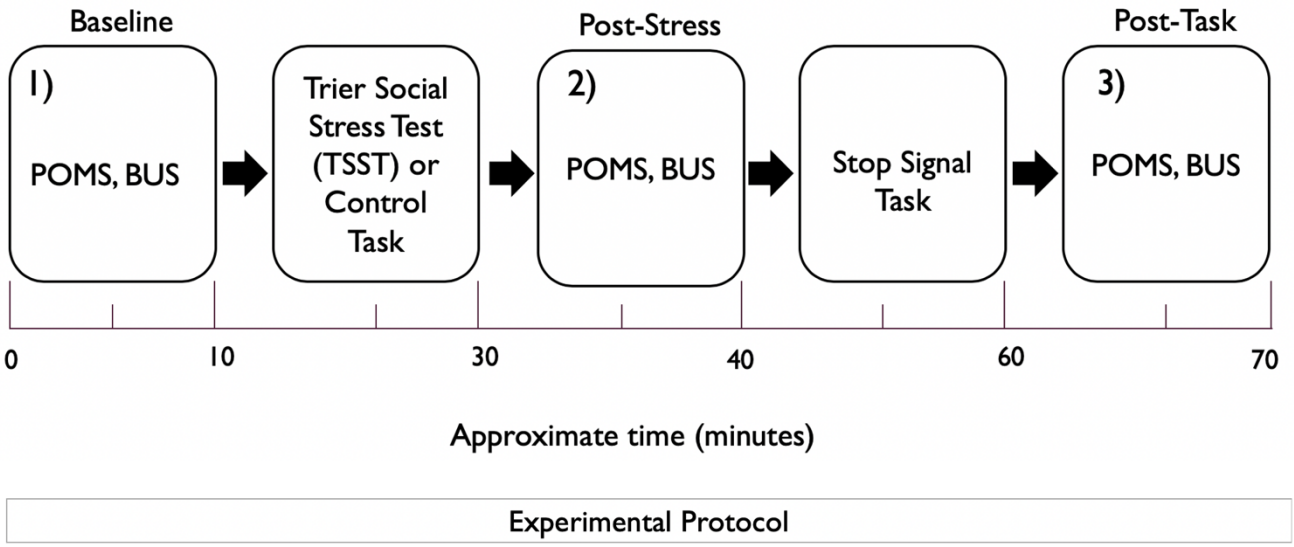
This study consisted of two visits on two separate days. Individuals were randomized to a stress (n = 17) or no stress (n = 16) condition. All participants completed self-report measures, including baseline questionnaires on day 1. On day 2 participants underwent the experimental protocol, including the psychosocial stressor, SST, and completed self-report mood and binge urge questionnaires.

Participants in the stress condition completed the Trier Social Stress Test (TSST; 33), whereas individuals in the no stress condition completed crossword puzzles. Following the stress manipulation, all participants completed the Stop-Signal Task (SST), a validated measure of inhibitory control (29). Participants also completed the Profile of Mood States (POMS; 34), and the Binge Urge Scale (BUS; based on 35). These measures of mood and binge urges were

collected at Baseline, Post-Stress, and Post-Task (See **Figure 1**). Following task completion, participants were debriefed and compensated in the form of gift cards. Additional clinical measures obtained from the ED clinic included BMI, and weekly symptom checklists to assess treatment outcome.

Figure 1

Experimental Protocol



Note. The study includes three timepoints: Baseline, Post-Stress, and Post-Task where all individuals completed the POMS and BUS questionnaires. POMS = Profile of Mood States; BUS = Binge Urge Scale; TSST= Trier Social Stress Task; Control Task = Crossword puzzles completed by the no stress condition.

2.3. Stress Induction Procedure

Trier Social Stress Test (TSST)

The TSST is a widely-used protocol for effectively inducing moderate forms of psychosocial stress (33) and has previously been used in studies including individuals with BED

(e.g., 18, 20, 36). The TSST comprises two phases: the anticipation phase and the testing phase, which includes a speech followed by a mental arithmetic task. The TSST demonstrates reliable 2-4 fold increases in the physiological stress response, and is effective in inducing negative affect (e.g., 33, 37, 38).

2.4. Physiological Measures

All participants underwent a Rapid Tox Cup II© urine screen (American Bio Media Corporation) to determine cannabis and illicit drug use. Individuals also underwent a carbon monoxide (CO) monitor to assess recency of smoking, and a breathalyzer (Intoximeters) to confirm sobriety during the experimental sessions.

2.5. Interview

International Neuropsychiatric Interview (MINI)

The International Neuropsychiatric Interview provides researchers with a short diagnostic interview to identify axis I and axis II psychiatric conditions (39). In the present study, the MINI was included to assess current co-morbid conditions and was administered by trained research assistants on day 1 of the study.

2.6. Self-Report Measures

Day 1

Demographics

All participants completed a basic demographic questionnaire including age, education, and ethnicity during day 1 of the study.

Beck Depression Inventory (BDI)

The BDI-II is a 21-item self-report tool that assesses the presence and severity of depressive symptoms, with higher scores indicating more severe depression (40). The BDI

demonstrates high internal consistency with an average Cronbach's alpha coefficient of 0.9, stable test re-test reliability, and construct validity (41).

Beck Anxiety Inventory (BAI)

The BAI is a 21-item self-report tool that assesses the presence and severity of anxiety symptoms, with higher scores indicating more severe anxiety (42). The BAI demonstrates good reliability and validity (43).

Eating Disorders Examination Questionnaire (EDE-Q)

The EDE-Q is a shorter, self-report version of the original Eating Disorders Examination Interview (EDE) developed by Cooper and Fairburn (1987), which is considered to be the "gold standard" interview technique to diagnose eating disorders (44, 45, 46). The EDE-Q has the advantage of minimal time and resources required to administer in comparison to the full interview version, and demonstrates good reliability in patients with BED (47). The EDE-Q asks individuals to retrospectively report symptomology that occurred in the past 28 days and is comprised of four distinct subscales: Restraint (5 items), Eating Concerns (5 items), Shape Concerns (8 items), and Weight Concerns (5 items), along with a total EDE-Q score. Higher scores are indicative of greater eating pathology.

The Impulsive Behaviour Scale (UPPS-P)

The Impulsive Behaviour scale (UPPS-P) is a 59-item self-report questionnaire that assesses different facets of impulsivity. The negative urgency subscale was included in the current study, which refers to an individual's tendency to engage in spontaneous/rash behaviour in response to negative affect (48). The UPPS-P shows good reliability for measuring different facets of impulsivity (49).

Menstrual Cycle Questionnaire (MCQ)

The MCQ provides a measure of an individual's menstrual cycle, including its regularity/irregularity, date of last period, contraceptive use, and gynecological issues.

Day 2

Profile of Mood States (POMS)

The POMS provides a measure of current subjective mood (34). The POMS has been used to examine subjective stress effects following acute psychosocial stress (e.g., 50, 51, 52), and shows good validity (53). The *Tension-Anxiety* subscale from the questionnaire was used to assess anxiety at baseline and following the TSST and again after the SST (See **Figure 1**). Participants rated how much they felt "tense", "shaky", "on edge", "panicky", "relaxed" (reverse-coded), "uneasy", "restless", "nervous" and "anxious" on a 5-point Likert scale ranging from not at all (0) to extremely (4). The average *Tension-Anxiety* subscale scores were used to assess subjective stress effects throughout each of the study timepoints.

Binge Urge Scale (BUS)

Participants completed the BUS, which provides information about acute binge urges, and was developed based on the 6-item Gambling Urge Scale (GUS; 35). An example item includes "nothing would be better than binging right now". Participants answer on a 7-point Likert scale ranging from completely disagree (1) to completely agree (7), with higher scores corresponding to higher levels of binge urges. Total BUS scores were used to assess binge urges throughout each of the study timepoints.

Stop-Signal Task (SST)

The SST was included as a measure of response inhibition, following guidelines outlined by Verbruggen, Aron, et al. (2019; 54). The SST provides a specific measure of the ability to

inhibit a pre-potent response once it has already been initiated (55, 56). This version of the task outlined by Verbruggen, Logan, et al. (2008;29), included 3 blocks of 64 trials, with a practice phase of 32 trials to familiarize the participant with the task. Participants were instructed to press two different response keys ("Z" and "/") in response to two different stimuli ("Z" for circles or "/" for squares), which comprised the "go" trials. On a subset of the trials, an auditory stop signal (750 Hz, 75ms) was presented after the stimulus in a random fashion, with a signal to no-signal ratio of 25:75. The stop signal was presented with a stop signal delay, which was dependent on whether the participant successfully inhibited their response on the previous trial. For instance, if the participant was successful on a previous inhibition trial, the stop signal delay increases by 50ms. If they were unsuccessful, the stop signal delay decreases by 50ms. This controls for individuals withholding responses toward go stimuli for successful performance, as participants are told not to wait for a stop signal (29). The stop signal reaction time (SSRT) is used as an indication of inhibitory control such that the longer the SSRT, the poorer the inhibitory control. SSRT is calculated using the formula: SSRT = (mean go reaction time) – (mean stop signal delay) and measures how fast one's stop, or inhibitory control process is. The SST is well-established and widely used task to measure response inhibition across multiple disciplines (54).

Clinical Data

Weekly Symptom Checklist

Throughout treatment, participants completed self-report weekly symptom checklists outlining the number of binge episodes they experienced in the last week, which was used to measure treatment outcome. BMI from dietician assessments were also included for individuals from the ED clinic. Treatment modules included: (1) Psychoeducation (weeks 2-6), (2) Nutrition and Self-Monitoring (weeks 7-11), and (3) Fine Tuning and Triggers (weeks 12-20), based on

content for treatment outcome analyses (See 32) . Data for missing weekly checklists were imputed based on the patient's average for that module from the completed weeks of treatment.

2.7. Statistical Analyses

All analyses were conducted using the Statistical Package for the Social Sciences (SPSS) Version 24. Non-parametric tests were used for non-normally distributed data, whereas parametric tests were conducted for normally distributed data. Normality was tested using the Shapiro-Wilk test for normality, and visual inspection of histograms and Q-Q plots. Homogeneity of variance was assessed using Levene's test. Between condition (stress and no stress) and within condition analyses examined differences and changes between subjective stress responses (mood and binge urges). The POMS *Tension-Anxiety* subscale scores and BUS scores were log transformed, which produced a normal distribution of the data. However, since this did not alter the results, the original, untransformed values are included. A median split of negative urgency was used to examine treatment outcome differences between high/low negative urgency in the whole sample. Similarly, a median split of SSRTs in the stress condition examined differences in treatment between high/low inhibitory control groups. According to the guidelines proposed by Girden (1992), to correct for violations of sphericity, Greenhouse-Geisser corrections were included for the mixed ANOVA analyses examining changes in anxiety and binge urges between conditions over time (57). Additionally, correlations between post-stress anxiety with inhibitory control (i.e., SSRT), binge urges, eating pathology measures (i.e., EDE-Q subscales), and negative urgency were explored using Spearman's Rho.

3. Results

3.1. Demographics

Of the total N = 33 (randomized into n = 17 stress, n = 16 no stress) participants, 28 were recruited from the ED clinic, and 5 from the community. Participant demographic variables across stress and no stress conditions are summarized in **Table 1**. There were only 2 male participants (in the no stress condition), and participants' age ranged from 20-63 years across conditions. Participants' BMI ranged from 23.7 to 68, however BMI was missing for one community individual. The majority of participants identified as European, and most individuals (n = 26) reported completion of post-secondary education. At baseline, participants in the stress and no stress conditions did not significantly differ on measures of mood (BDI, BAI) or eating pathology measures (EDE-Q subscales; $ps > 0.05$). Most participants were confirmed to be sober by a 0% breath alcohol level on the breathalyzer on day 2 of testing (missing for 6 participants: 4 no stress, 1 stress). In the stress condition, the average CO level was 9.52ppm, and in the no stress condition, the average was 2.58ppm. CO levels were not available for 5 participants (1 stress, 4 no stress). Conditions did not differ on smoking status. Menstrual status was not available for one female in the no stress condition.

To be cautious of effects due to physiological hunger, participant's last mealtime was recorded relative to the start of the experimental (day 2) session. Across conditions, the majority of individuals (n = 20) had their last meal within 2 hours of the session, 8 between 2 to 5 hours, and 5 greater than 5 hours (i.e., the day before). Conditions did not significantly differ with respect to their last mealtime ($p > 0.05$).

3.1.1. Urine Screen Results

Results from the urine screen demonstrated the following positive results: 4 individuals for benzodiazepines, 1 for methadone, 1 for methamphetamine, 1 for amphetamines, 4 for opioids, 1 for oxycodone, and 16 for THC. Urine screen results were not available for 4 participants (1 stress, 3 no stress).

3.1.2. Co-morbidities

Results from the MINI demonstrated that the following co-morbidities were currently present among participants: 4 with depression, 6 with panic disorder (with agoraphobia), 5 with panic disorder (without agoraphobia), 7 with social phobia, 3 with obsessive compulsive disorder, 8 with post-traumatic stress disorder, and 8 with generalized anxiety disorder.

Table 1

Demographic Information Presented by Condition

Variable M ± SD	**Stress Condition** (*n* = 17)	**No Stress Condition** (*n* = 16)	**Statistic** *t* or U	*p*
Age	47.76 ± 10.72	41.50 ± 12.55	-1.5	> .05
Gender: Female/Male (%)	100/0	87.5/12.5	Fisher's Test	> .05
Ethnicity: European/South Asian/ Native North American/Other (%)	82.4/0/ 0/17.6	75/6/ 6/13	Fisher's Test	> .05
Highest Level of Education: Partial or complete high school/College or university (%)	5.9/94.1	37/63	Fisher's Test	< .05*
BMI	39.76 ± 6.87	45.07 ± 13.17	1.43	> .05
Number of binge episodes in the last month	11.47 (9.61)	10.00 (9.52)	115.5	> .05
EDE-Q Restraint/ EDE-Q Total	1.32 ± 1.33/ 3.14 ± 1.29	1.21 ± 1.47/ 2.58 ± 1.32	128/ -1.2	> .05
The Impulsive Behaviour Scale (UPPS-P) Negative Urgency	2.50 ± 0.48	2.60 ± 0.53	0.56	> .05
Beck Depression Inventory (BDI)	18.29 ± 12.56	15.12 ± 8.48	-0.84	> .05
Beck Anxiety Inventory (BAI)	19.35 ± 13.23	17.00 ± 12.65	123.5	> .05
Menstrual status: Regular periods/Irregular periods/ Peri-Menopausal/Post-menopausal/ Partial Hysterectomy/Total Hysterectomy (%)	17.6/29.4/ 11.8/17.6/ 5.9/17.6	31/39/ 15/15/ 0/0	3.87	> .05
Oral contraceptive use (%)	5.88	6.25	Fisher's Test	> .05

Note. M = mean, SD = standard deviation. BMI = body mass index (kg/m^2).

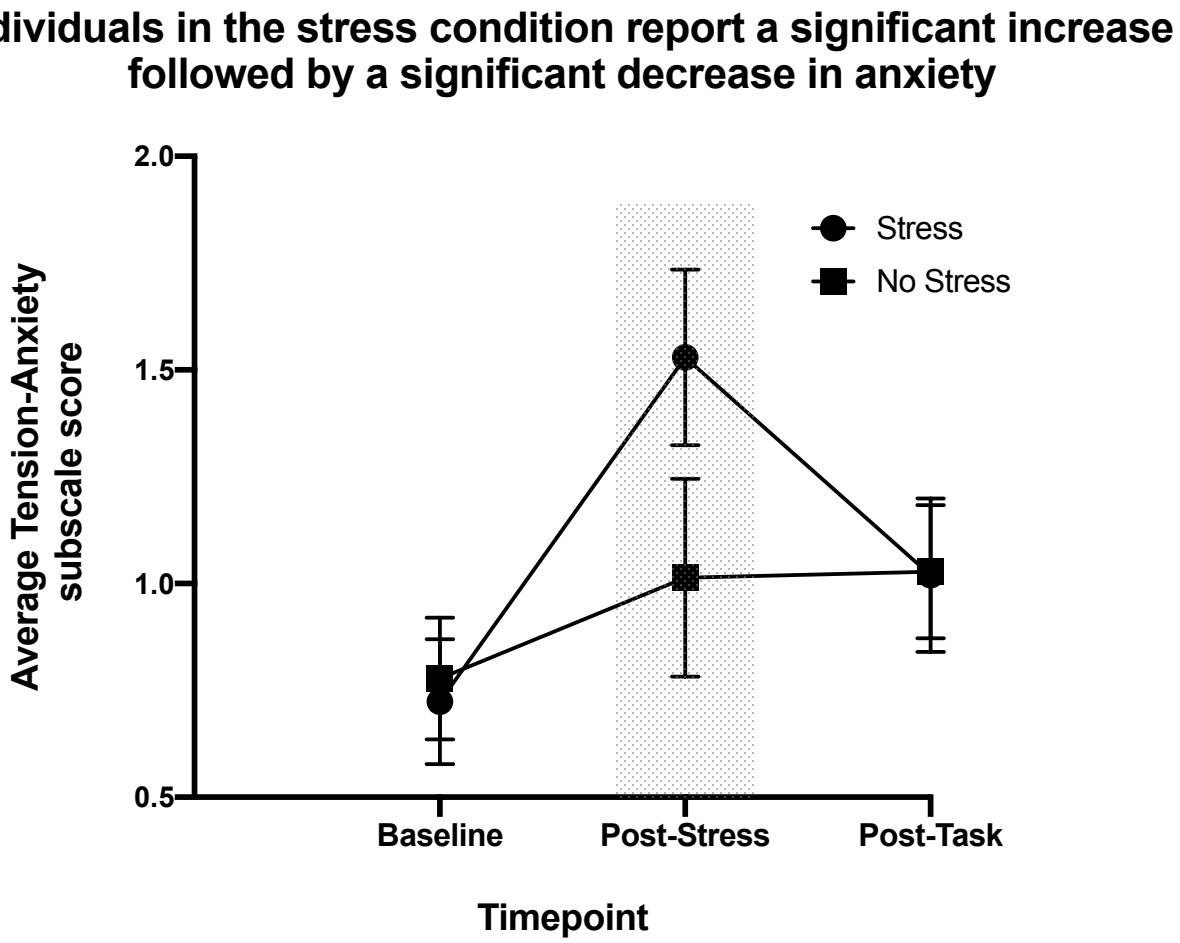
3.2. Subjective Stress Effects

Profile of Mood States (POMS) Tension-Anxiety Subscale

To examine the effects of the stress manipulation on anxiety, a 2 Condition (Stress, No Stress) by 3 Timepoint (Baseline, Post-Stress, Post-Task) mixed ANOVA (Greenhouse-Geisser corrected values) on the POMS *Tension-Anxiety* subscale was conducted. Results showed a significant main effect of Timepoint on anxiety scores ($F(1.409, 43.66) = 11.23$, $p < 0.05$, $\eta p^2 = 0.26$), and a significant Timepoint by Condition interaction ($F(1.409, 43.66) = 4.14$, $p < 0.05$, $\eta p^2 = 0.11$), however no main effect of Condition ($F(1, 31) = 0.47$, $p > 0.05$); See **Figure 2**. Post-hoc Bonferroni-corrected pairwise comparisons revealed a significant increase in anxiety between Baseline and Post-Stress ($M \pm SEM_{Baseline} = 0.72 \pm 0.147$, $M \pm SEM_{Post\text{-}Stress} = 1.53 \pm 0.215$, $p < 0.05$) and a significant decrease in anxiety from Post-Stress to Post-Task ($M \pm SEM_{Post\text{-}Stress} = 1.529 \pm 0.205$, $M \pm SEM_{Post\text{-}Task} = 1.02 \pm 0.166$, $p < 0.05$) in the stress condition only. The conditions did not differ in anxiety Post-Stress or Post-Task ($ps > 0.05$). In the stress condition, one datapoint for a Baseline "tense" rating was missing; it was imputed using the participant's average for the other *Tension-Anxiety* subscale rated items at Baseline.

Figure 2

Acute Stress Increases Anxiety Post-Stress in the Stress Condition



Note. Individuals in the stress condition reported a significant increase in anxiety Post-Stress, followed a significant decrease by the Post-Task timepoint. Error bars are ± standard error of the mean (SEM).

3.3. Binge Urges

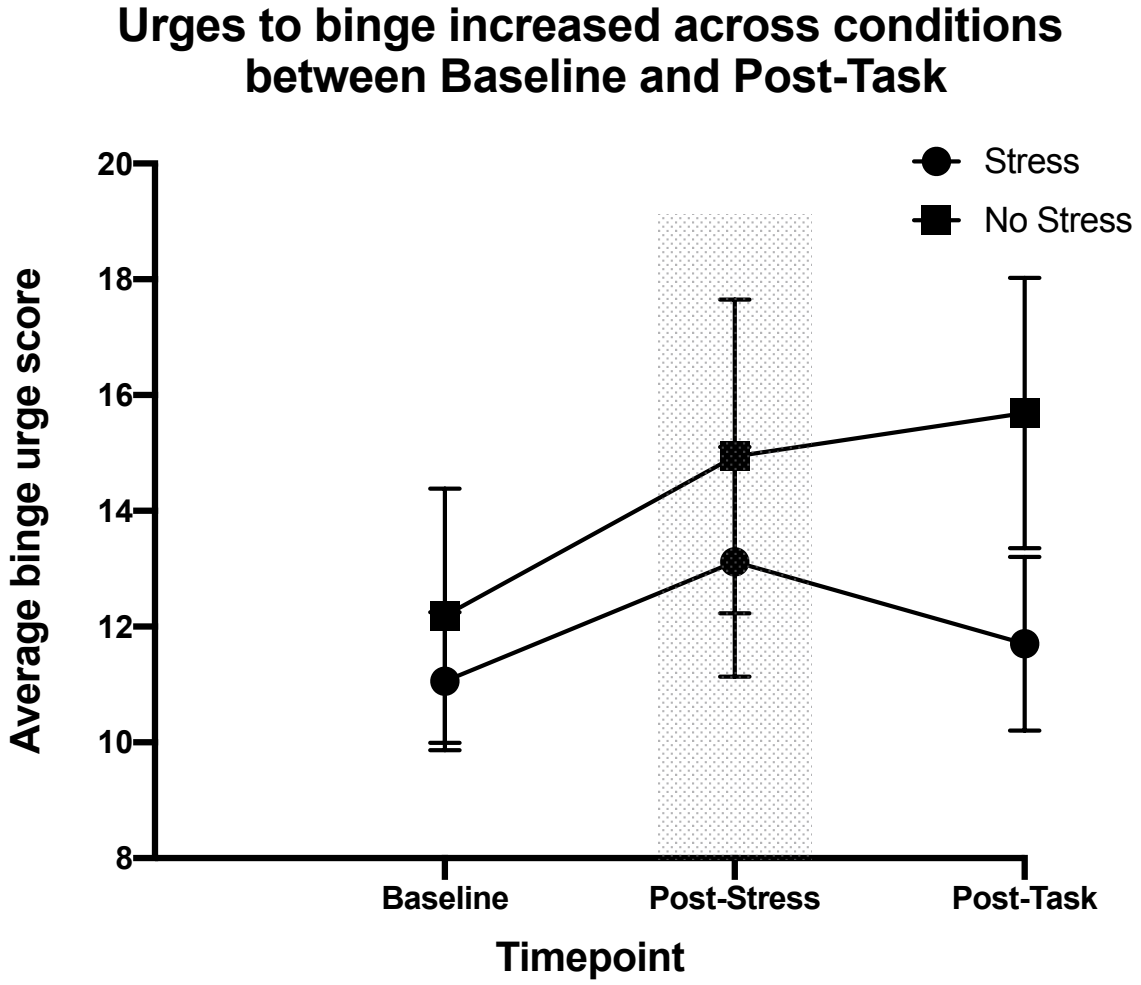
Binge Urge Scale (BUS) Scores

To examine the effect of stress on binge urges, a 2 Condition (Stress, No stress) by 3 Timepoint (Baseline, Post-Stress, Post-Task) mixed ANOVA (Greenhouse-Geisser corrected values) on BUS scores across the study timepoints revealed a significant main effect of

Timepoint on binge urge scores ($F(1.488, 46.138) = 3.848, p < 0.05, \eta p^2 = 0.11$). Across conditions, post-hoc Bonferroni-corrected pairwise comparisons showed that binge urge scores significantly increased between the Baseline ($M \pm SEM_{Baseline} = 11.623 \pm 1.230$) and Post-Task ($M \pm SEM_{Post\text{-}Task} = 13.697 \pm 1.372$) timepoints ($p < 0.05$), but not between the other timepoints and Post-Stress ($M \pm SEM_{Post\text{-}Stress} = 14.028 \pm 1.667$, $ps > 0.05$). There was no Timepoint by Condition interaction ($F(1.48, 46.13) = 1.25, p > 0.05$) or main effect of Condition ($F(1, 31) = 0.756, p > 0.05$), although a between-condition post-hoc Bonferroni-corrected comparison looks as though this effect was driven by the no stress condition, such that they experienced a significant increase between Baseline and Post-Task ($M \pm SEM_{Baseline} = 12.187 \pm 2.197$), $M \pm SEM_{Post\text{-}Task} = 15.687 \pm 2.335, p < 0.05$; See **Figure 3)**.

Figure 3

Across Conditions, Individuals Report Significant Increases in Binge Urges From Baseline to Post-Task



Note. Error bars are ± SEM.

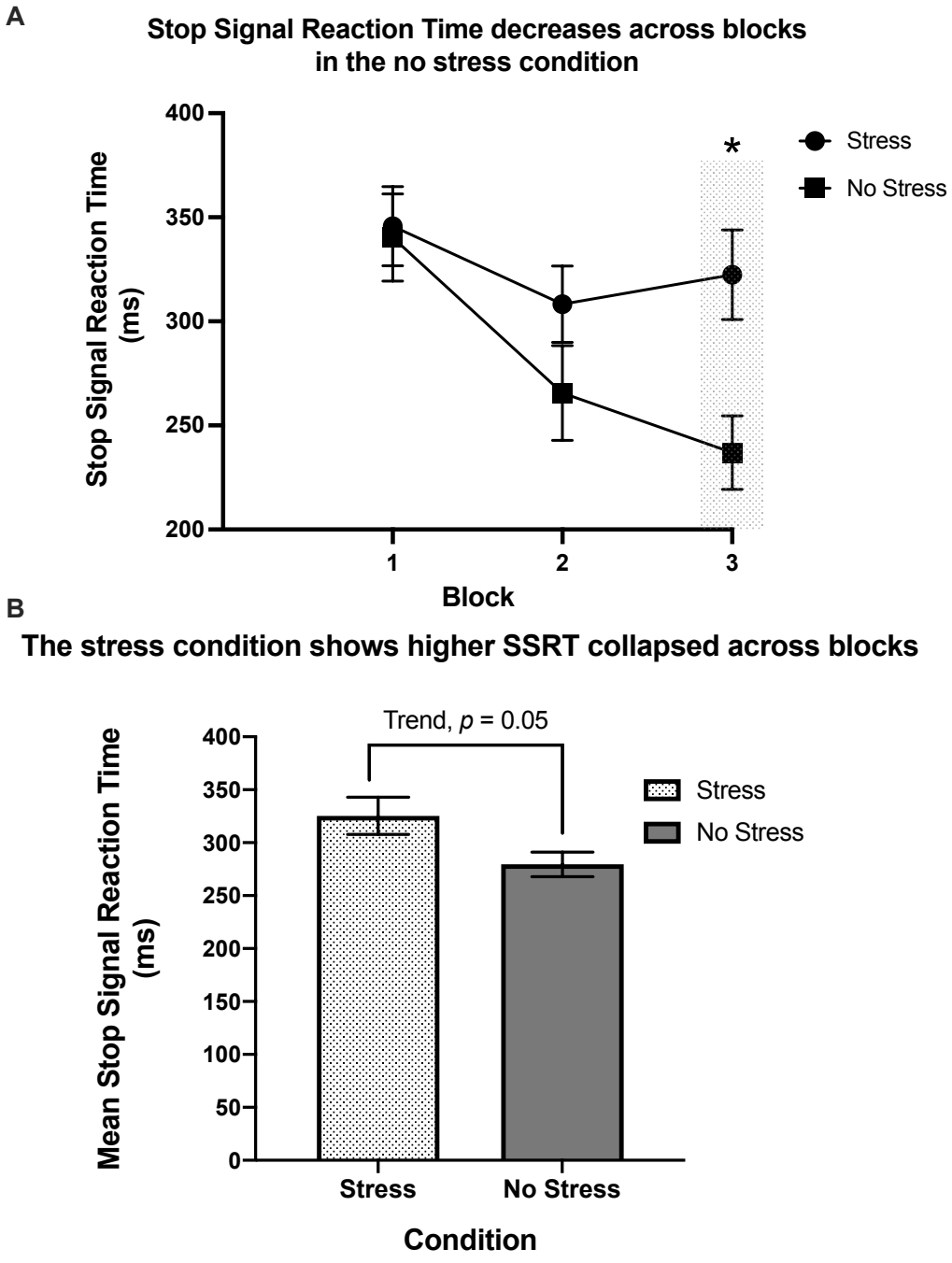
3.4. SSRT Performance by Condition

Due to a technological error, two participant's SST data were not retrievable in the no stress condition. Additionally, two outliers (one in each condition) were determined based on values greater and less than 3x the interquartile range, and individual inspection of their SST data. These were removed from the SST analyses. To test the hypothesis that acute stress would

impair inhibitory control, the SST was first examined by block to examine immediate stress effects. A 2 Condition (Stress, No Stress) by 3 (Block) mixed ANOVA demonstrated a main effect of Block on SSRT scores ($F(2, 54) = 9.584$ $p < 0.05$, $\eta p^2 = 0.26$), a trend for a main effect of Condition ($F(1, 27) = 4.061$ $p = 0.054$, $\eta p^2 = 0.13$), and a significant Block by Condition interaction ($F(2, 54) = 3.190$ $p < 0.05$, $\eta p^2 = 0.10$). Post-hoc Bonferroni-corrected pairwise comparisons revealed a significant decrease in SSRTs in the no stress condition between Blocks 1 and 2 ($M \pm SEM_{Block\ 1} = 340.315 \pm 20.965$, $M \pm SEM_{Block\ 2} = 265.554 \pm 22.812$) and Blocks 1 and 3 ($M \pm SEM_{Block\ 1} = 340.315 \pm 20.965$, $M \pm SEM_{Block\ 3} = 236.992 \pm 17.695$) (*ps* < 0.05). There were no significant decreases or changes in SSRT across blocks in the stress condition (*ps* > 0.05). A post-hoc one-way ANOVA demonstrated that conditions differed at Block 3 ($F(1, 27) = 8.810$, $p < 0.05$), such that the stress condition had a significantly greater SSRT during the last block of the task in comparison to the no stress condition ($M \pm SEM_{Stress} = 322.356 \pm 21.537$ vs. $M \pm SEM_{No\ Stress} = 236.992 \pm 17.695$, $p < 0.05$); See **Figure 4A**. Additionally, to assess overall differences (i.e., collapsed across blocks) in SST performance by condition, a Mann-Whitney U test demonstrated a trend for a greater SSRTs Post-Stress in the stress condition ($M \pm SEM_{Stress} = 325.050 \pm 17.574$ vs. $M \pm SEM_{No\ Stress} = 279.539 \pm 11.574$) in comparison to the no stress condition ($U = 59.00$, $n_1 = 13$, $n_2 = 16$, $p = 0.05$). See **Figure 4B**.

Figure 4

Acute Stress Impairs Inhibitory Control Performance



Note. Figure 4A. The no stress condition demonstrated decreased SSRTs across blocks.

Figure 4B. The stress condition demonstrated a trend for greater overall SSRTs.

Errors bars are ± SEM. Greater SSRTs are indicative of poorer inhibitory control.

3.5. Correlations

To probe stress links with facets of eating pathology in BED, exploratory Spearman's bivariate correlations between Post-Stress anxiety scores, EDE-Q eating pathology, binge urge scores, negative urgency, and SSRTs were examined. Results revealed that in the stress condition, Post-Stress anxiety related positively with overall eating pathology (EDE-Q total scores; $r_s = .492, p < 0.05$), and with Post-Stress urges to binge ($r_s = .493, p < 0.05$). Other EDE-Q subscales were examined to see which facet of eating pathology was driving this effect, demonstrating it was primarily the restraint subscale ($r_s = .529, p < 0.05$). Additionally, significant correlations emerged between Baseline BUS urges with both Post-Stress ($r_s = .847, p < 0.05$) and Post-Task ($r_s = .822, p < 0.05$) urges to binge, suggesting those with high levels of binge urges at Baseline demonstrate high levels of binge urges throughout the other timepoints. There were no significant relationships that emerged between Post-Stress anxiety and negative urgency scores or SSRT (See **Table 2**).

In the no stress condition, Post No Stress anxiety did not relate to eating pathology, urges to binge, negative urgency, or SSRT values. Unexpectedly, weight concerns in the no stress condition was negatively correlated with SSRT, such that the greater the weight concerns, the shorter SSRT (better inhibitory control) participants demonstrated ($r_s = -.661, p < 0.05$), although, this effect was driven by one participant. Additionally, similar to the stress condition, there was a significant positive correlation between Baseline BUS urges with both Post No Stress ($r_s = .596, p < 0.05$) and Post-Task ($r_s = .729, p < 0.05$) binge urges, indicating a similar pattern of heightened baseline urge scores carrying over across timepoints (See **Table 3**).

Table 2

Correlations Between Stress, Inhibitory Control, Binge Urges, Negative Urgency, and Eating Pathology in the Stress Condition

			Urges			Eating Pathology					
Stress Condition	Post-Stress Anxiety	SSRT	Baseline BUS	Post-Stress BUS	Post-Task BUS	EDE-Q Total	Restraint	Eating Concerns	Shape Concerns	Weight Concerns	Negative Urgency
Post-Stress Anxiety	-	0.181	0.342	**.493***	0.482^{T}	**.492***	**.529***	0.278	0.452^{T}	0.395	-0.024
SSRT		-	0.106	0.04	0.115	-0.299	-0.209	-0.302	-0.264	-0.229	-0.115
Baseline BUS			-	**.847****	**.822****	0.209	-0.079	0.234	0.417	0.222	-0.255
Post-Stress BUS				-	**.888****	0.18	0.077	0.12	0.331^{T}	0.165	-0.12
Post-Task BUS					-	0.15	0.09	0.149	0.336	0.169	-0.051
EDE-Q Total						-	**.716****	**.799****	**.885****	**.936****	-0.167
Restraint							-	0.437^{T}	**.527***	**.532***	-0.114
Eating Concerns								-	**.663****	**.685****	-0.173
Shape Concerns									-	**.893****	-0.149
Weight Concerns										-	-0.059
Negative Urgency											-

Note. Spearman's rho (r_s) bivariate correlations. *$p < 0.05$, **$p < 0.01$, $^{T}p < 0.10$. N = 17; N = 16 for SSRT correlations; EDE-Q = Eating Disorders Examination Questionnaire; SSRT = Stop Signal Reaction Time; BUS = Binge Urge Scale.

Table 3

Correlations Between Stress, Inhibitory Control, Binge Urges, Negative Urgency, and Eating Pathology in the No Stress Condition

			Urges			Eating Pathology					
No Stress Condition	Post No Stress Anxiety	SSRT	Baseline BUS	Post No Stress BUS	Post-Task BUS	EDE-Q Total	Restraint	Eating Concerns	Shape Concerns	Weight Concerns	Negative Urgency
Post No Stress Anxiety	-	0.351	-0.099	0.323	0.33	-0.268	-0.346	-0.151	-0.252	-0.27	0.457[T]
SSRT		-	0.199	0.11	0.13	-0.412	-0.243	-0.201	-0.391	**-.661***	0.249
Baseline BUS			-	**.596***	**.729****	0.33	0.423	0.187	0.437	0.148	0.231
Post-Stress BUS				-	**.856****	0.155	0.248	0.227	0.214	0.003	0.266
Post-Task BUS					-	0.013	0.25	0.102	0.062	-0.114	0.411
EDE-Q Total						-	**.796****	**.732****	**.955****	**.929****	-0.149
Restraint							-	**.670****	**.696****	**.652****	0.02
Eating Concerns								**-**	**.618***	**.585***	-0.102
Shape Concerns									-	**.892****	-0.104
Weight Concerns										-	-0.175
Negative Urgency											-

Note. Spearman's rho (r_s) bivariate correlations. *$p < 0.05$, **$p < 0.01$, [T]$p < 0.10$. N = 16; N = 13 for SSRT correlations; EDE-Q = Eating Disorders Examination Questionnaire; SSRT = Stop Signal Reaction Time; BUS = Binge Urge Scale

3.6. Treatment Outcome

To evaluate whether Post-Stress anxiety and inhibitory control were linked to treatment outcome, exploratory correlations were conducted across conditions. In the stress condition, two significant, negative correlations emerged. Post-Stress anxiety and SSRTs were negatively correlated with binge episodes during the *Nutrition and Self-Monitoring* treatment module (r_s = -.665, $p < 0.05$; r_s = -.624, $p < 0.05$, respectively). There was also a trend for a negative correlation between Post-Stress urges to binge with binge episodes reported during the *Nutrition and Self-Monitoring* module (r_s = -.552, $p = 0.078$).

In the no stress condition, Post No Stress anxiety positively correlated with reported binge episodes during the last treatment module, *Fine-Tuning and Emotional Triggers* (r_s = .615, $p < 0.05$). Additionally, there was a trend for binge urges following No Stress and following the SST to positively correlate with binge episodes reported during *Fine-Tuning and Emotional Triggers* (r_s = .541, p = .056; and r_s = .526, $p = 0.065$ respectively). There were no significant relationships between binge episodes reported across treatment modules and SSRT, or negative urgency ($ps > 0.05$).

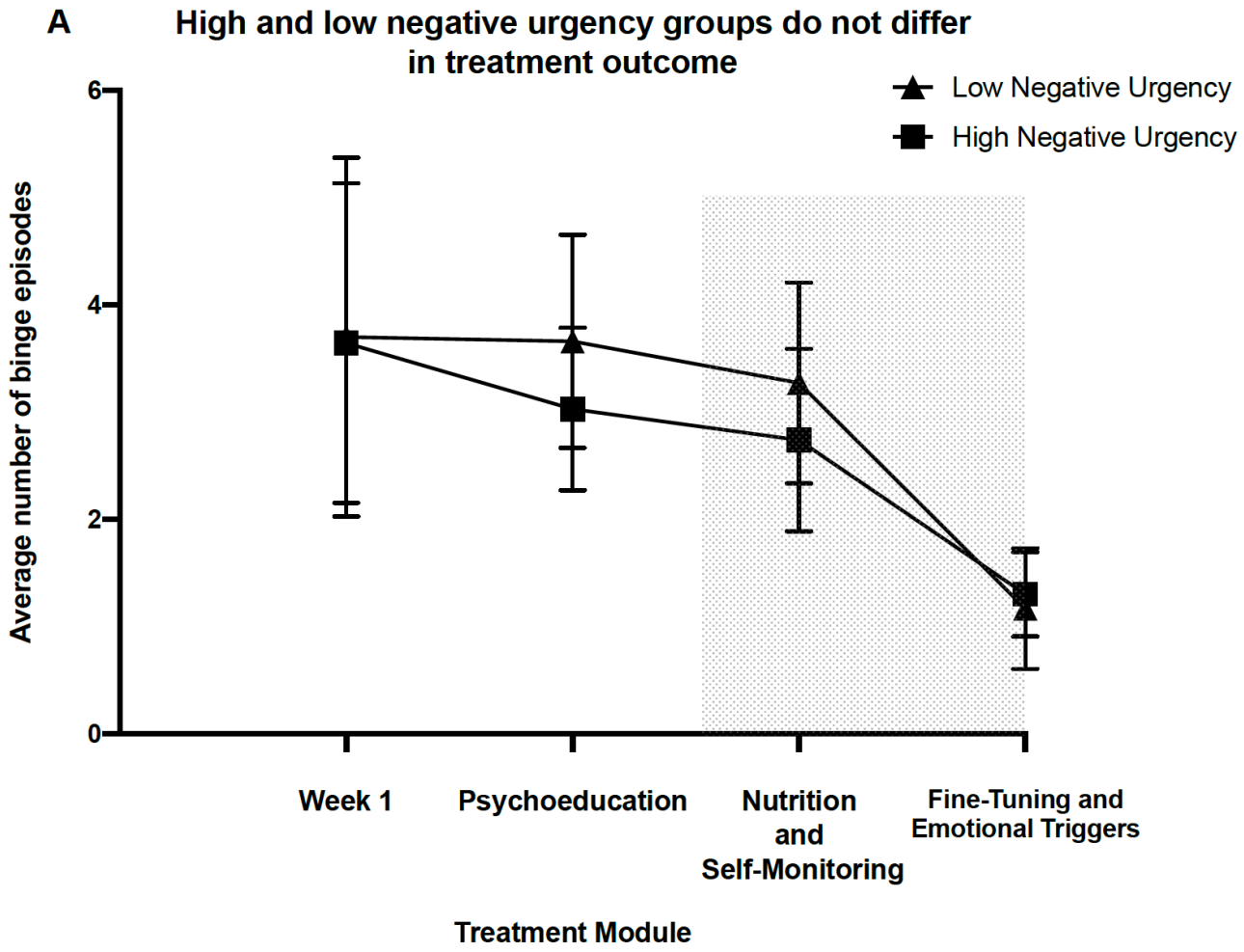
Next, the ED clinic sample (n = 27; 1 missing treatment outcome data) was sub-grouped using the median split technique (median = 2.75) into high (above 2.75) and low (2.75 or below) negative urgency groups, similar to Manasse, Espel, et al. (2016; 28). This was possible, given that conditions had relatively even and normally-distributed negative urgency scores. A 2 Group (high/low negative urgency) by 4 Treatment Module (average number of binge episodes during each module, including Week 1) linear mixed model demonstrated a significant main effect of Treatment Module on the number of binge episodes ($F(3, 67.709) = 7.570$, $p < 0.05$). There was no main effect of Group ($F(1, 25.073) = 0.213$, $p > 0.05$) or Treatment Module by Group

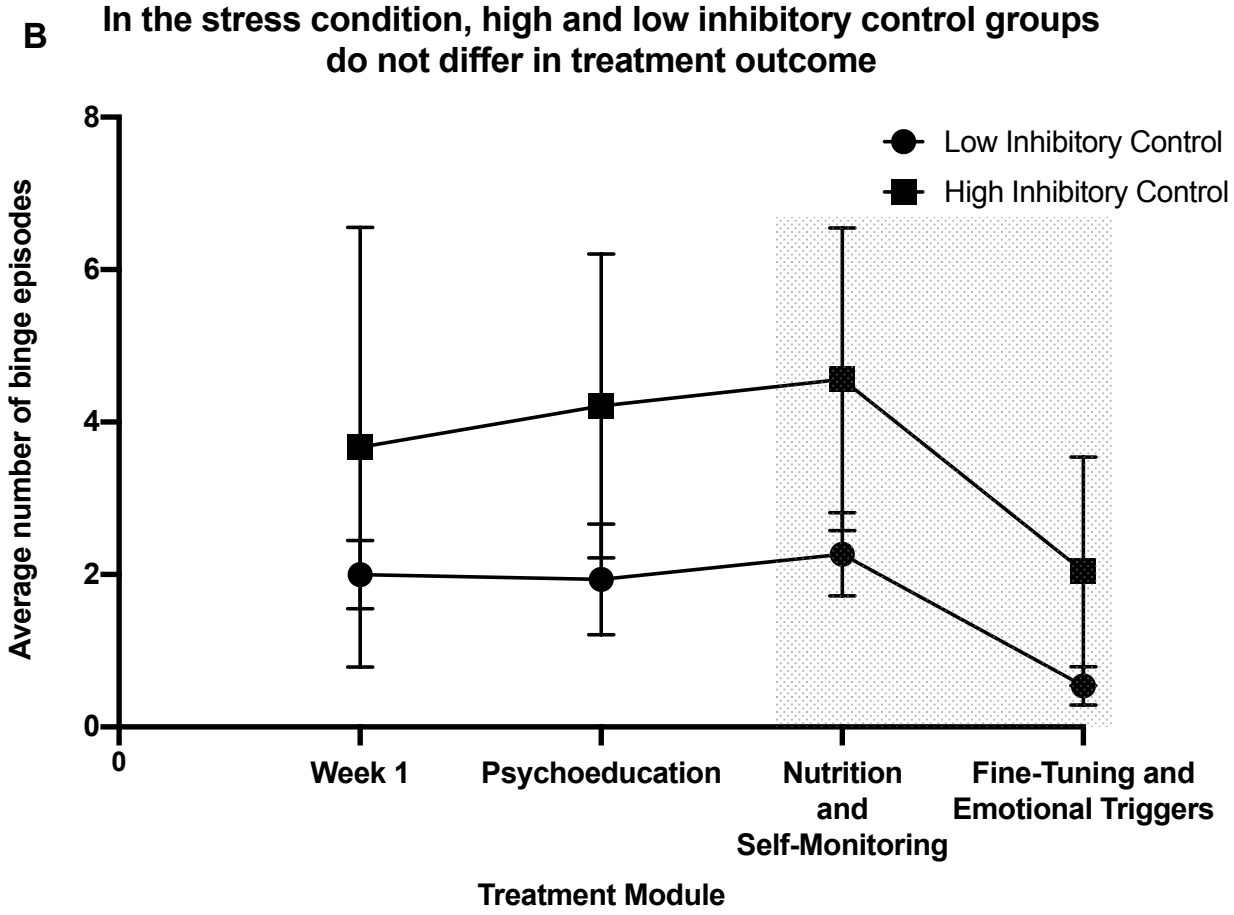
interaction ($F(3, 67.709) = 0.093, p > 0.05$). Post-hoc Bonferroni-corrected pairwise comparisons showed that both groups displayed significant decreases in binge episodes between treatment modules *Psychoeducation* (M ± SEM = 3.309 ± 0.600) and *Fine-Tuning and Emotional Triggers* (M ± SEM = 1.238 ± 0.331) and between *Nutrition and Self-Monitoring* (M ± SEM = 2.984 ± 0.619) and *Fine-Tuning and Emotional Triggers* (*ps* < 0.05), but not between *Psychoeducation* and *Nutrition and Self-Monitoring* ($p > 0.05$). Binge episodes at Week 1 (M ± SEM = 3.667 ± 1.091) only differed from *Fine-Tuning and Emotional Triggers* ($p < 0.05$). These results demonstrate that irrespective of trait levels of negative urgency, individuals are able to achieve a similar treatment outcome (See **Figure 5A**).

To examine stress-induced alterations in inhibitory control relationships with treatment outcome, the stress condition ($n = 12$ for individuals with SSRT and ED clinic data) was sub-grouped using the median split technique (median = 304.45) into high (SSRT above 304.45) and low (SSRT 304.45 or below) inhibitory control groups. A 2 Group (high/low inhibitory control) by 4 Treatment Module linear mixed model demonstrated a main effect of Treatment Module on the number of binge episodes ($F(3, 25.259) = 3.854, p < 0.05$). There was no significant Treatment Module by Group interaction ($F(3, 25.259) = 0.242, p > 0.05$), or main effect of Group ($F(1, 10.058) = 0.748, p > 0.05$). Post-hoc Bonferroni-corrected pairwise comparisons revealed that both groups reported significant decreases in the number of binge episodes between *Psychoeducation* (M ± SEM = 3.075 ± 1.069) and *Fine-Tuning and Emotional Triggers* (M ± SEM = 1.207 ± 0.680), and between *Nutrition and Self-Monitoring* (M ± SEM = 3.309 ± 0.964) and *Fine-Tuning and Emotional Triggers (ps* < 0.05*)*. Week 1 (M ± SEM = 2.909 ± 1.540) did not significantly differ from the treatment modules and there were no significant differences between *Psychoeducation* and *Nutrition and Self-Monitoring* (*ps* > 0.05). See **Figure 5B**.

Figure 5

High/Low Negative Urgency and High/Low Inhibitory Control Groups do not Differ in Treatment Outcome (continued on next page)





Note. Figure 5A. High and low negative urgency groups did not differ in treatment outcome. n = 24, Week 1, n = 27 Psychoeducation, n = 26 Nutrition and Self-Monitoring, n = 23 for Fine-Tuning and Triggers**.**

Figure 5B. High and low inhibitory control groups within the stress condition did not differ in treatment outcome. n = 11 Week 1, n = 12 Psychoeducation, n = 11 Nutrition and Self-Monitoring, n = 9 Fine-Tuning and Emotional Triggers

Only includes ED clinic sample. Error bars are ± SEM.

In order to explore if stress-induced alterations in anxiety related to treatment outcome, an additional linear mixed model was conducted examining stress reactivity (calculated by subtracting *Tension-Anxiety* subscale scores at Post-Stress from Baseline) in the stress condition

only. Results demonstrated that there was a main effect of Treatment Module ($F(2, 16.486) = 5.108$ $p < 0.05$), but no main effect of Group (high/low anxiety reactivity; $F(1, 10.267) = 1.61$, $p > 0.05$) or Treatment Module by Group interaction ($F(2, 16.361) = 0.583$ $p > 0.05$). These results demonstrate that stress reactivity, or stress-induced alterations in anxiety do not relate to treatment outcome.

4. Discussion

The purpose of this study was to examine the effects of acute psychosocial stress on inhibitory control and to evaluate stress effects on binge urges. The study also explored whether there were links between subjective anxiety with inhibitory control, eating pathology, and trait negative urgency. Additionally, it explored whether these measures predicted treatment outcome in BED. There were 4 significant major findings of this study: 1) acute stress impaired inhibitory control as evidenced by the absence of improvement in performance across blocks in the stress condition, 2) across conditions, urges to binge eat increased over time, 3) there was a positive correlation between Post-Stress anxiety and Post-Stress binge urges and Post-Stress Anxiety and restraint eating pathology in the stress condition, and 4) high/low negative urgency and inhibitory control groups did not differ in their treatment response. Finally, it is also worth noting that the stress condition reported an increase in state anxiety following stress, but also reported a significant reduction in anxiety by the end of the SST.

4.1. Stress Effects on Inhibitory Control

Consistent with our hypothesis, the current study found that individuals in the stress condition showed a trend for higher SSRTs relative to the no stress condition on the SST. The mean SSRT in the no stress condition (M = 279.538) is consistent with previous inhibitory

control studies in BED examining SSRT performance without stress effects (23, 24, 58), and those reported in other eating disorders (59). Notably, the SSRT observed in the current study was higher than that reported in healthy controls (59), which is consistent with other SST findings in BED.

In the current study, SST findings were further examined over trial blocks, which showed that the no stress condition exhibited a significant decrease in SSRTs across time, while the stress condition remained elevated across the entire session. Specifically, conditions significantly differed at block three, such that the stress condition has significantly greater SSRTs than the no stress condition. This suggests that although the no stress condition showed a practice effect by improving their inhibitory control performance across blocks, this ability was impaired by acute psychosocial stress in the stress condition. This finding is novel to the literature and provides clinical implications around stress-induced binge episodes. Specifically, binge episodes initiated by acute stress may be more difficult to control or stop than ones not triggered by stress. Additionally, this finding is similar to a previous study examining acute stress effects on general inhibitory control in healthy control participants that showed those who underwent the TSST had poorer inhibitory control performance following stress and did not experience the same practice effects as the no stress condition (22). Here, this effect is replicated in a BED sample, and poses implications for deficits in general impairments in inhibitory control in BED, as these results demonstrate that an acute stressor can significantly impair inhibitory control. Further extending this finding, this poses implications for investigation of chronic stress effects on individuals' inhibitory control mechanism. Previous research has demonstrated individuals with BED display no significant change in cortisol levels or even blunted cortisol activity in comparison to BMI-matched control participants following psychosocial stress (15, 16), which may be indicative of

chronic activation of their stress response. Additionally, individuals with BED show decreased recruitment of brain areas (e.g., the inferior frontal gyrus) involved in response inhibition (60). Therefore, the finding that even acute stress can impair inhibitory control in BED warrants further investigation on stress effects on inhibitory control, particularly following repeated or chronic stress.

4.2. Stress Effects on Anxiety

The current finding of acute stress increasing self-reported anxiety is consistent with a previous study showing an increase in negative affect in BED following stress (17). However, it is in contrast to previous studies showing higher overall negative affect in BED in comparison to control participants (3, 18). Specifically, these previous findings demonstrate that in comparison to BMI-matched and healthy control participants, individuals with BED report significantly greater negative affect before and after stress. Importantly, however, the current study showed that following acute stress, individuals with BED reported a significant increase in subjective anxiety but were able to rapidly return back to their baseline anxiety levels, such that self-report scores did not differ from Baseline at the Post-Task timepoint (~20 minutes post-stressor). This finding provides clinicians and patients undergoing BED treatment with the reassurance that although stress may acutely increase state anxiety, individuals show that they are able to recover relatively quickly.

It is noteworthy that in the no stress condition, anxiety scores remained relatively stable and even slightly increased over the Baseline, Post-Stress, and Post-Task timepoints. In healthy control men and women, one study shows no increases in negative mood and anxiety in the no stress condition, with participants actually reporting a decrease over the experimental session (38). The steady or slightly rising anxiety levels in the no stress condition could relate to these

individuals maintaining a state of vigilance, or the experience of an anticipatory anxiety response, which could be due to greater anxiety scores on the BAI and the high level of anxiety disorders present in the group. To our knowledge, this is the first study in BED comparing stress response from the TSST to a no stress BED condition, and this subtle increase in anxiety is a novel finding. In contrast, individuals in the stress condition were able to experience a stressor and adapt.

4.3. Stress Effects on Urges

Additionally, Post-Stress anxiety was significantly and positively related to Post-Stress urges to binge in the stress condition only. This is consistent and a replication of findings from Rosenberg, Bloch, et al. (2013; 16) who found greater desires to binge eat following stress were significantly related to anxiety levels following stress. This finding is also different from individuals with anorexia nervosa, who show a decreased desire for food, and individuals with bulimia nervosa who show no significant change in desire for food following the TSST (61). Instead, these binge urge findings are similar to elevated craving in substance users following acute psychosocial stress (e.g., 62, 63).

Analyses demonstrated that, irrespective of condition, binge urge levels significantly increased from the Baseline to Post-Task timepoints. This was inconsistent with the hypothesis that increases in urges to binge eat would occur between Baseline and Post-Stress in the stress condition only. This was also inconsistent with the decrease in subjective anxiety Post-Task, as urges to binge continued increasing, mostly driven by the no stress condition. Two other studies also report higher binge urges in BED in comparison to BMI-matched control participants both preceding and following stress (15, 16). Altogether these findings suggest that binge urges are not directly linked to acute stress in BED, and instead may indicate trait levels of urges. Binge

urge increases in the no stress condition may relate to these individuals experiencing a state of heightened vigilance or anticipatory stress. The anticipation of an acute stressor in BED can increase distress (17), therefore, given the nature of the protocol, and that participants were aware that it was a stress study, this could have increased binge urges in the no stress condition. This phenomenon is similar to elevated binge urges in individuals with bulimia nervosa on days they experience a binge episode in comparison to non-binge days (64). This suggests that these trait levels of binge urges are an important therapeutic and relapse prevention target, since they tend to increase even in the absence of an acute stressor.

Exploratory correlations between stress-induced anxiety, binge urges, negative urgency, inhibitory control, and eating pathology measures demonstrated two noteworthy relationships. First, there was a significant positive correlation between Post-Stress anxiety and the restraint eating subscale from the EDE-Q, suggesting a link between acute anxiety in BED with this specific facet of eating pathology. Restraint is associated with strict dietary rules, including avoidance of food, and desire for an empty stomach; this facet of eating pathology has previously been linked to inhibitory control in BED (58, 60). For example, a previous BED study found reduced activity in the inferior frontal gyrus during a cognitive control task (Stroop Task) was negatively correlated with restraint eating pathology (60). Greater SSRTs are also negatively correlated with restraint scores in BED (58), although the current study did not show relationships between restraint and behavioural inhibitory control on the SST. Instead, there was a significant positive correlation between dietary restraint and anxiety following stress, suggesting that stress-induced anxiety increases also relate to intentions to restrict food.

4.4 Relationships With Treatment Outcome

In the current study, high and low negative urgency groups did not differ in self-reported binge episodes across treatment modules. This is in contrast with findings from Manasse, Espel, et al. (2016; 28) who found that those with higher negative urgency exhibited less reductions in binge eating throughout treatment than those with lower levels of negative urgency. Study differences could be attributed to the study sample characteristics (i.e., mostly treatment-seeking vs. community) of individuals with BED. The current study also included participants undergoing a well-established CBT treatment for BED, in comparison to a novel, pilot treatment. As such, there is potential for differential therapeutic effects of managing stress and inhibitory control between samples. Additionally, the finding that stress-induced alterations in general inhibitory control did not relate to treatment outcome are somewhat similar with a previous finding demonstrating that food-specific, but not general inhibitory control is related to treatment outcome (28), despite previously established general impairments in inhibitory control in BED (24).

4.5. Strengths, Limitations, and Future Directions

A strength of the current study is that the sample includes clinician-diagnosed treatment-seeking individuals with BED, allowing clinical utility of the study findings. The finding that subjective anxiety rapidly decreases following an acute stressor offers clinical significance for developing coping and cognitive restructuring strategies around the effects of acute stress. Additionally, while the inclusion of a baseline Stop-Signal Task may have provided a more potent within-subjects design, the significant practice effects on the SST demonstrated in the current study suggests that a cross-sectional design with a within-task (i.e., block) analysis was a better fit. The current study included mostly individuals who were seeking treatment for BED,

therefore the generalizability to other BED subgroups is unclear, given that some individuals in the community with BED may experience less severe symptoms and not seek treatment (65). Future studies will also benefit from the inclusion of other eating pathology-related measures to examine stress effects in BED considering previous research demonstrates that negative urgency does not correlate with episodes of binge eating, but it does with other measures of eating pathology on the EDE-Q (66). An additional noteworthy limitation is the absence of information about daily and chronic stressors participants face in their lives which may have interacted with the findings.

Although this study did not demonstrate links with treatment outcome, it opens the gateway for future studies to examine the loss of control feature of BED as it relates to stress and treatment outcome. This is because it provides more insight into the fact that other forms of inhibitory control or chronic stress may relate. A future direction includes information about daily and chronic stress as they relate to the stress response and subsequent treatment outcome. Another important next step includes distinguishing between subjective and objective binge episodes across treatment modules. This is because subjective binge episodes, although lacking in the caloric content of objective binge episodes, represent subjective loss of control (67). Future studies could incorporate additional questionnaires following stress, regarding shape/weight concerns, restraint, and body dissatisfaction to examine acute effects on these facets of eating pathology, and their links with treatment outcome. Additional future directions include using different response inhibition tasks, with more affect-related response inhibition, as binge episodes are associated with salient shifts in negative affect, which may show stronger links with stress.

4.6. Conclusion

The current BED study showed that acute stress impairs inhibitory control, which has clinical implications for understanding how a binge episode triggered by stress may be more difficult to control or stop than one not triggered by stress. Additionally, the finding that acute stress significantly increases subjective anxiety, but also that this anxiety rapidly decreases once the stressor is removed is reassuring for patients that they will be able to cope with acute stressors. The role of restraint eating pathology may moderate stress relationships with inhibitory control and warrants further investigation. Finally, findings in the no stress condition highlighted that binge urges are not directly linked to acute stress in BED, and may increase in ambiguous situations.

5. Supplementary Material

5.1. Stop-Signal Task Measures

Supplementary Table 1

Stop-Signal Task Indices Across Stress and No Stress Conditions

Stop-Signal Task Measure M ± SD	**Stress Condition** (*n* = 16)	**No Stress Condition** (*n* = 13)	*t* or U	*p*
Probability of responding on a stop trial (%)	51.82 ± 13.67	47.86 ± 13.32	.784	> 0.05
Average stop signal delay (ms)	289.18 ± 151.49	362.97 ± 171.12	-1.23	> 0.05
Overall stop signal reaction time (ms)	325.07 ± 70.27	279.54 ± 41.73	59.000	0.05^{T}
RT of go responses on unsuccessful stop trials (ms)	543.78 ± 110.60	570.39 ± 113.43	-.637	> 0.05
RT on go trials (ms)	614.91 ± 125.29	642.48 ± 147.46	-.545	> 0.05
Probability of correct choices on no go trials/Probability of choice errors on no go trials (%)	97.63 ± 2.13/ 2.38	96.15 ± 5.33/ 3.85	100.500	> 0.05
Probability of go omissions (no response %)	1.41 ± 1.46	3.05 ± 5.05	103.500	> 0.05

Note. M = mean, SD = standard deviation, ms = milliseconds, RT = reaction time, $^{T}p = 0.05$.

5.2. Stop-Signal Task Instructions

“ WELCOME TO THIS STOP SIGNAL EXPERIMENT
On every trial, you will see a circle or a square and your task is to respond as fast and accurate as possible to these go stimuli:
press the left key with the left index finger when you see a square
and press the right key with the right index finger when you see a circle

Occasionally, the stimulus is presented by a sound, indicating
that you have to stop your response on that trial.
On approximately half of the trials, the sound will be presented
soon after the presentation of the go stimulus
and you will notice that it is easy to stop your response.
On the other half of the trials, the sound will be presented rather late and
it will become very difficult or even impossible to stop your response.

Nevertheless, it is important that YOU DO NOT WAIT
for a stop signal to occur, because if you start waiting,
then the computer will wait with presenting the stop signals

Press one of the response keys to continue”

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Chapter 3: General Discussion

Summary

This study aimed to investigate the effects of acute psychosocial stress on inhibitory control in individuals with BED. Additionally, the study examined whether negative urgency or stress-induced alterations in inhibitory control predicted treatment success. Several major findings emerged, including that acute stress results in general impairments in inhibitory control. Subjectively, following an increase in anxiety from stress, anxiety levels quickly returned back to baseline levels. Acute stress did not affect binge urges, rather, binge urges increased across both conditions throughout the duration of the study. Two noteworthy correlations emerged in the stress condition; subjective anxiety related to binge urges Post-Stress, and Post-Stress anxiety was linked with restraint eating pathology. Additionally, the study did not replicate previous research demonstrating relationships between negative urgency and treatment outcome. Furthermore, inhibitory control performance did not relate to treatment outcome. The implications of these findings are discussed in detail below.

Stress Effects on Tension-Anxiety

Following an acute psychosocial stressor, individuals demonstrated a significant increase, followed by a significant subsequent decrease in subjective anxiety. This finding provides a proof of concept of the stress manipulation – participants reported experiencing increased anxiety from baseline to the timepoint following the stressor. This finding is in contrast with findings from Klatzkin et al. (2015) in which individuals with BED showed significantly greater negative affect and state anxiety at all time points (including before and after stress) in comparison to BMI-matched control participants. Our findings may have differed with previous studies with the inclusion of a BED group acting as the control (i.e., no stress) group; this high

resolution approach allowed us to investigate the effect of stress in BED more closely, and relative to other BED participants. Importantly, however, the stress condition anxiety levels did not differ from baseline to after the SST, therefore demonstrating that participants were able to recover fairly rapidly from this acute anxiety increase. This has clinical implications for clinicians being able to assist with coping and cognitive restructuring strategies around acute stressors that patients may be anticipating. Particularly, offering reassurance that although acute psychosocial stress increases anxiety, that these effects are not long term and that the patient will be able to recuperate.

In the no stress condition, *Tension-Anxiety* subscale scores did not differ at Baseline, however, remained relatively stable and even slightly increased over the course of the experimental timepoints. This may relate to individuals maintaining a state of vigilance or experiencing an anticipatory response, whereas individuals who experienced an acute stressor had a significant relief in anxiety by the Post-Task timepoint. Previous research has shown that the anticipation of an acute stressor like the TSST significantly increases distress in BED, an effect that is not present in BMI-matched control participants (Naumann et al., 2018). This suggests a role for anticipatory anxiety as observed in the no stress condition.

The lack of a main effect of condition could be attributed to high levels of chronic stress, and potentially high levels of anxiety disorders in the sample, or the experience of childhood trauma across conditions, as is common in eating disorders (e.g., Kong & Bernstein, 2009; Rojo, Conesa, Bermudez, & Livianos, 2006; Swinbourne et al., 2012). Rosenberg et al. (2013) found that higher desires to binge following stress was related to subjective stress and anxiety; our findings also demonstrate a significant correlation between Post-Stress anxiety and Post-Stress binge urges in the stress condition only. This finding is similar to studies in addiction

demonstrating that individuals report increased cravings for substances following a stress induction procedure (e.g., Clay et al., 2018; Moran-Santa Maria et al., 2010).

Another novel relationship was reported between restraint eating pathology and Post-Stress anxiety. A previous neuroimaging BED study applying the Stroop Task, found reduced recruitment of the IFG during cognitive control, which negatively correlated with dietary restraint (Balodis et al., 2013). Therefore, future investigations should include restraint eating pathology as it may moderate stress effects on inhibitory control.

Stress Effects on Binge Urges

A significant main effect of time on the Binge Urge Scale showed that collapsed across conditions, binge urges significantly increased from the Baseline to Post-Task timepoints (Chapter 2; See **Figure 3**). This finding was unexpected, because it was hypothesized that the induction of stress would result in greater binge urges in the stress condition only. Although not statistically significant, binge urges marginally increased, and slightly decreased following stress, in the stress condition, whereas in the no stress condition, binge urges continued to increase over time. A post-hoc test on this repeated measures ANOVA revealed that the main effect of increasing binge urges over time was indeed driven by the no stress condition. This suggests that although binge urges in the no stress condition did not relate to the experience of acute stress, they may represent trait characteristics of chronic stress or anxiety. This finding is consistent with other studies reporting consistently higher binge urges in BED both before and after stress (Rosenberg et al., 2013; Rouach et al., 2007). The unexpected increase in binge urges in the no stress condition may indicate more of a trait, rather than state-like construct.

Previous research in BED has shown that the anticipation of an acute stressor can increase distress (Naumann et al., 2018), therefore, given the nature of the no stress protocol

(crossword puzzles instead of undergoing psychosocial stress) participants may be unsure of upcoming events, whereas individuals in the stress condition experienced relief from their anxiety following the TSST. This finding is clinically significant, because it highlights that while individuals with BED experience anxiety following stress, they are able to quickly regain control over their anxiety and there are no longer term effects of acute stress. Conversely, this provides information about states of ambiguity (without the actual presence of acute stress) and how this may relate to gradual increases in anxiety and urges to binge. Accordingly, these heightened trait levels of urges to binge reinforce that this may be an important therapeutic target.

Stress Effects on Inhibitory Control

Following an acute stressor, individuals in the stress condition demonstrated greater SSRTs, indicative of poorer inhibitory control. Additionally, results indicated that SST performance gradually improved across blocks, whereas SSRTs in the stress condition remained relatively higher than in the no stress condition. By the end of the third block of the SST, conditions significantly differed with respect to their performance. These findings suggest that acute stress impairs general inhibitory control in BED, while in the absence of stress, individuals are able to improve inhibitory control performance over time. These results are similar to those from Roos et al. (2017) who demonstrated the same effect in healthy control participants. In the current study, however, SSRTs across both conditions were higher than those reported by Roos et al. (2017), consistent with the idea of heightened overall impulsivity/generally worse inhibitory control in BED. The average SSRT values found in the current study collapsed across both conditions are slightly higher than those reported in other BED studies (Svaldi et al., 2014; Wu et al., 2013), which may reflect the clinical study sample, who may experience greater inhibitory control impairments.

Negative Urgency and Inhibitory Control Relationships With Treatment Outcome

High and low negative urgency groups did not show any significant differences in the number of binge episodes reported throughout treatment modules. Additionally, general levels of inhibitory control (i.e., SST performance) and anxiety reactivity did not predict treatment success in BED. Previous studies demonstrate that food-specific, but not generalized, inhibitory control impairments predict treatment outcome, as measured by greater eating pathology on the EDE-Q across treatment timepoints (Manasse, Espel, et al., 2016). The current study did not replicate this finding and may be due to the current study including a clinical level treatment-seeking BED group completing a validated BED treatment. Future studies should attempt to replicate Mannasse, Espel, et al. (2016) by observing if stress-induced alterations in food-specific (rather than generalized) inhibitory control affects treatment outcome in BED. Future studies could also include pre and post measures such as subscales from the EDE-Q to assess treatment outcome. Although the finding that high/low negative urgency and inhibitory control groups did not differ in treatment response, this has direct future research and clinical implications. Specifically, it informs future research about a change in direction. Future research may examine different forms of inhibitory control (i.e., food-specific) and the effects of chronic stress on treatment outcome. Clinically, this allows for reassurance to patients that if individuals feel greater loss of control or heightened negative urgency from stress during treatment, that this will not significantly interfere with their treatment progress or set them back.

Limitations, Strengths, and Future Directions

One study limitation includes the absence of a baseline measure of inhibitory control which could have allowed for greater information on within-subject variations in stress effects on inhibitory control. Nevertheless, the within-task (i.e., by block) analysis of the SST demonstrates

the potent practice effects on the task, which may have longitudinally wiped out group differences. Future studies could include a different baseline measure of inhibitory control to track within-participant changes in inhibitory control across study sessions. Another limitation includes the potential for a treatment effect. While treatment effects are always an important consideration when examining treatment-seeking populations, the treatment outcome analyses confirm that the majority of treatment effects (in terms of binge episodes) occur from week 7 onwards (the start of *Nutrition and Self-Monitoring* to the end of treatment). Therefore, this poses less cause for concern in the current study.

The present study also included a weekly symptom checklist, which is not yet validated, and is also a self-report tool. Although, previous literature suggests that self-report symptomology is relatively consistent with clinical reports in eating disorder populations, this may not necessarily be the case for self-reports of binge episodes (Fairburn & Beglin, 1994). Binge symptomatology could further be distinguished between subjective and objective binge episodes; subjective binge episodes, although lacking the caloric content of objective binge episodes, are accompanied with a loss of control (Palavras, Morgan, Borges, Claudino, & Hay, 2013). Individuals who exclusively engaged in subjective binge eating have similar symptom profiles (i.e., high binge eating severity, co-morbidities) compared to those with both subjective and objective binge eating (Palavras et al., 2013). This demonstrates a need for capturing subjective binge episodes as they may represent an alternative sense of loss of control that may impact the stress response and inhibitory control. Individuals do not necessarily need to only be engaging in objective binge episodes to feel a loss of control. Another potential limitation includes the generalizability of study results to other BED subgroups, as results may not

generalize to subclinical and community individuals with BED, as a proportion of individuals do not seek treatment (Coffino, Udo, & Grilo, 2019).

This study has several strengths, including high construct validity for the *clinical* significance of results and representation of BED. These results stem from one of the few BED studies examining the stress response with a substantial portion of participants that are clinically diagnosed by a certified psychologist, as opposed to a community sample or sample of convenience. Although multiple co-morbidities in the sample exist (e.g., depression, anxiety, panic disorder), this is consistent with a previous epidemiological review demonstrating high levels of similar co-morbidities within BED, suggesting an ecologically valid clinical profile of the patients in the current study (Kessler et al., 2013).

Regarding the study design, a strength includes a laboratory stress-induction procedure, which over other methods, includes the benefit of a systematic, controlled investigation by simulating the threat of a stressor (Razzoli, Pearson, Crow, & Bartolomucci, 2017). This also allows for the induction of negative affect consistent with the psychological effects of the stress response, and allows for direct links between stress, negative affect, and urges to binge to be investigated (Razzoli et al., 2017). Another strength of this study includes the replication of subjective stress effects, and relationships between Post-Stress anxiety with Post-Stress urges to binge. Additionally, a strength is that this current study extended psychosocial stress effect findings to examine relationships with behavioural inhibitory control in BED. These relationships have previously not been examined in a BED sample, making this study novel for introducing this avenue of research. Finally, the inclusion of a no stress BED control group, allowed for a robust approach to understanding how stress impacts individuals with BED, and demonstrated unique increases in anxiety and binge urges in those not experiencing acute stress.

Future Research Avenues

Given the impairments in inhibitory control and the finding that stress impairs general inhibitory control in BED, a future avenue of research includes comparing the stress response across similar disorders characterized by inhibitory control impairments. A growing body of literature demonstrates parallels between BED and addictive disorders due to overlapping symptoms including diminished control despite negative consequences, elevated craving, and negative affect (Davis, 2013; Gearhardt, White, & Potenza, 2011). Additionally, comparisons could be made with a subsample of individuals with a diagnosis of bulimia nervosa, which shares the same diagnostic criteria as BED with the inclusion of compensatory behaviours (e.g., purging, laxative use, excessive exercise) in addition to binge eating (APA, 2013).

Future studies could additionally examine the effect of acute stress on food-specific inhibitory control by incorporating a food stimulus in addition to the neutral stimuli used in the current study, given that general inhibitory control did not relate to treatment outcome. Another future direction regarding inhibitory control includes obtaining a greater understanding of the brain mechanisms underlying response inhibition. For instance, it could be that the SST paradigm represents a more general motor response inhibition ability, whereas although there is a motor component to a binge episode, it may be primarily driven by negative affect, or heightened restraint. A future direction includes using a cognitively-demanding and affect-related response inhibition task for examining stress relationships with inhibitory control in BED. Future studies should also consider the role of chronic stress effects on inhibitory control. While the current study does not show relationships between stress-induced inhibitory control impairments and treatment outcome, it does show relationships between acute stress, binge urges, and specific aspects of eating pathology as a small, but incremental effect. In the future, a research direction

would include capturing cumulative stress effects on urges to binge, by examining longitudinally or with chronic stress measures.

An additional, unexpected, but interesting area of research includes the relatively high proportions of cannabis use, the high number of partial/complete hysterectomies, and a subgroup of individuals who have undergone bariatric surgery in the sample. Given that cannabis use has been associated with increased anxiety and an altered stress response (e.g., Hyman & Sinha, 2009; McRae-Clark et al., 2011), and that menstrual status has an effect on the stress response (Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999), examining how these subgroups in BED respond to stress is another noteworthy future direction. Research also shows that impulsivity (specifically, SST performance) is a predictor of weight loss following bariatric surgery (Kulendran, Borovoi, Purkayastha, Darzi, & Vlaev, 2017). Therefore, individuals who have undergone bariatric surgery and subsequently develop loss of control eating/binge eating disorder represent a unique subgroup.

Conclusion

This study shows that acute stress can impair inhibitory control in BED. In addition, the current findings replicated acute subjective stress effects, and extended acute psychosocial stress effects to examine relationships with inhibitory control and treatment outcome. These findings suggest that although individuals with BED quickly recover from stress-induced anxiety, binge urges remain stable or increase, particularly in the absence of acute stressors. This has clinical implications for targeting trait level heightened binge urges. Future work can integrate participants' physiological measures of the stress response (i.e., cortisol) and relate them to subjective stress responses, binge urges, and inhibitory control in BED. These findings will shed further light on other stress relationships with inhibition and BED symptomology.

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Appendix A: Schematic of the Stop-Signal Task

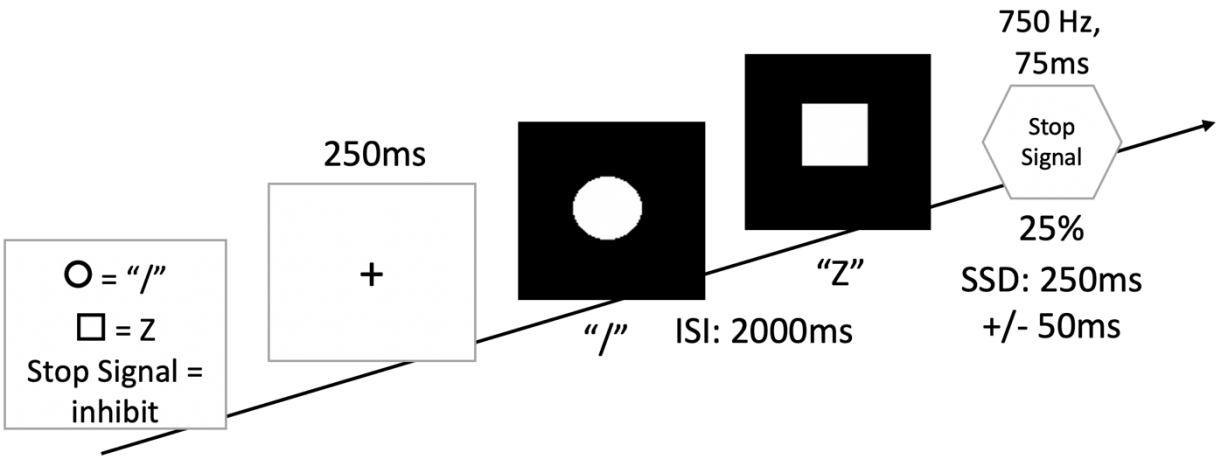

Figure 1. Schematic of the Stop-Signal Task as described by Verbruggen, Logan, and Stevens (2008). Participants are first shown instructions on screen, followed by a fixation cross for 250ms, and either the circle or square stimuli. Participants are to press the "/" when they see a circle and "Z" when they see a square. On 25% of trials, individuals are presented with a tone (i.e., stop signal) indicating to withhold (i.e., inhibit) their response. The interstimulus interval (ISI) is 2000ms. The stop signal is presented with a delay (stop signal delay; SSD) of +/- 50ms depending on the participant's success on the preceding stop trial.

Appendix B: Binge Urge Scale

Binge Urge Scale based on the Gambling Urge Scale (Raylu & Oei, 2004)

Circle the number indicating how much you agree or disagree with each item using a seven point scale:

	Completely Disagree	Disagree	Somewhat Disagree	Neither Agree or Disagree	Somewhat Agree	Agree	Completely Agree
1. All I want to do now is to binge.	1	2	3	4	5	6	7
2. It would be difficult to resist binging this minute.	1	2	3	4	5	6	7
3. Binging now would make me feel so much better.	1	2	3	4	5	6	7
4. I want to binge so bad that I can almost feel it.	1	2	3	4	5	6	7
5. Nothing would be better than binging right now.	1	2	3	4	5	6	7
6. I crave binging right now.	1	2	3	4	5	6	7