TARGETING BIOBEHAVIORAL MECHANISMS IN OBESITY AMONG CANCER SURVIVORS WITH MINDFULNESS-ORIENTED RECOVERY ENHANCEMENT

by

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ABSTRACT

Over the past 50 years, there has been a gradual upward trend in overweight and obesity prevalence, such that current epidemiological estimates indicate that over one-third of U.S. adults are obese and another third are overweight. Cancer prevalence has risen in tandem with excess adiposity in a dose response relationship that may grow stronger with age, suggesting a number of U.S. adults may be at risk. However, prevailing weight loss interventions aimed at disrupting and reversing this alarming trend are predominantly based on an overly simplistic model of energy balance, and consequently have failed to achieve any meaningful long-term results. This may be due in part to interventive focus on the symptomatic expression of excess weight rather than the underlying mechanisms of obesity onset and maintenance. Conversely, identifying malleable traits that promote healthier body composition profiles, as well as their potential mechanistic and behavioral means of conferring clinical benefits, may facilitate the development of the next generation of targeted psychosocial interventions for obesity. Herein is presented an integrated biopsychosocial framework that elucidates cybernetic feedback circuits between stress, reward, homeostatic mechanisms, and both bottom-up and top-down self-regulatory processes that interact to govern obesogenic behaviors. A portion of this conceptual framework was then tested in a correlational study of a sample of overweight and obese female cancer survivors, which revealed that higher dispositional mindfulness was indirectly associated with reduced adiposity via enhanced

capacity to savor nonfood rewards and improved autonomic regulation during attention to food cues. Finally, findings from an early stage pilot randomized controlled trial (RCT) are presented. This RCT investigated the preliminary feasibility and efficacy of Mindfulness-Oriented Recovery Enhancement (MORE), a multimodal intervention designed to target mechanisms underpinning appetitive dysregulation, as an added component to exercise and nutrition counseling to treat excess adiposity among the same sample. Findings revealed that MORE may be an efficacious means of effectively targeting underlying mechanisms explicated by the proposed conceptual framework, in that MORE was associated with significantly enhanced interoceptive awareness, savoring, and responsiveness to natural rewards, and reduced food attentional biases and maladaptive eating behaviors.

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1. INTRODUCTION: A ROLE FOR SOCIAL WORK

The etiology and epidemiology of obesity is complex and multifactorial in nature, involving interactions between biological, psychological, and sociocultural variables. Obesity may therefore be best conceptualized through the biopsychosocial model, which is a core foundation of social work theory, research, and practice. In contrast to reductionistic biomedical models, the biopsychosocial model is inherently nonreductive, integrative, and holistic in nature. Further, it encourages multidisciplinary and transdiagnostic approaches that examine the underlying mechanisms that contribute to a broad array of psychosocial disorders, and facilitate the development of targeted, actionable, and effective interventions (Garland & Thomas, 2015). Such interventions must similarly be multifaceted, moving beyond overly simplistic and largely ineffectual solutions based on the energy balance model, integrating therapeutic mechanisms from biological (e.g., nutrition and exercise), and psychosocial (e.g. mindfulness-based interventions, cognitive behavior therapy, and positive psychology) treatments. The biopsychosocial model explicitly rejects the artificial dichotomy between mind and body. Obesity cannot therefore be viewed as solely a physical health condition when applying a biopsychosocial lens. It must be viewed as the embodiment of biological, psychological, and sociocultural maladaptations.

Within Western societies obesity is highly stigmatized, largely due to limited understandings of the etiological and epidemiological factors that contribute to obesity

onset and maintenance. Prevailing narratives blame obese individuals for their excess weight and fuel weight-based stereotypes which purport that obese persons are lazy, unmotivated, gluttonous, noncompliant, and lacking in self-discipline and willpower (Puhl & Brownell, 2001). Perceptions that obese persons are physically and sexually unattractive also abound (Puhl & Heuer, 2009). Consequently, both institutional (e.g., workplace, healthcare, and education settings) and interpersonal weight discrimination is common (Spahlholz, Baer, König, Riedel-Heller, & Luck-Sikorski, 2016), matching and in some cases exceeding the prevalence of discrimination based on gender and race (Puhl, Andreyeva, & Brownell, 2008). However, in contrast to other forms of inequality that are frequently highlighted and challenged in the public sphere and prohibited legally, weight stigma remains a socially acceptable and largely legal form of bias, contributing to body dissatisfaction, internalized weight stigma, psychopathologies, and experiences of prejudice and discrimination (Jackson, 2016; Pearl, Puhl, & Dovidio, 2017). Further, while weight bias may occasionally be rationalized as a means of motivating behavioral change, recent longitudinal research instead reveals that weight discrimination promotes weight gain and obesity maintenance, as well as obesity onset among participants overweight at baseline (Sutin & Terracciano, 2013). Further, weight stigma heightens stress and doubles the 10-year risk of high allostatic load, the wear and tear of stress on the body (Tomiyama, 2014; Vadiveloo & Mattei, 2017).

Epidemiological studies reveal a nonrandom distribution of obesity that supports the significant role that stress may play in the development of obesity. Racial and ethnic disparities have repeatedly been exposed that demonstrate that non-Hispanic blacks have the highest age-adjusted rates of obesity (48.1%), followed by Hispanics (42.5%) (Flegal

et al., 2016). While cultural variations in body ideals may contribute to such disparities, global trends demonstrate that they may also be related to societal inequities. Recent findings indicate that countries with more equal distributions in income have better health outcomes on many indices including obesity (Pockett & Beddoe, 2017). Whereas wider inequalities in income, financial security, housing, education, health care, sustainable environments, and social inclusion are associated with poorer health outcomes and increased obesity. A recent meta-analysis of over 125 epidemiological studies demonstrated that food insecurity is also associated with increased risk of obesity, specifically among adult women living in high-income countries, which researchers explain through an insurance hypothesis based on evolutionarily selected metabolic efficiency triggered by experiences of stress (Nettle, Andrews, & Bateson, 2017).

Compensatory homeostatic adaptations can also be induced through restrictive eating patterns. Within a context of obesogenic environments (characterized by a profusion of stimuli that elicit evolutionarily-selected and individually-conditioned automatic impulses to consume highly palatable food; Lake & Townshend, 2006) paired with the preponderance of sociocultural idealizations of thinness, health, and self-control (Veit, 2013), internalized weight-based stigma, strong food judgments and moralizations, or efforts to exercise "willpower" to suppress urges to eat, can perpetuate a cycle of stress and weight gain (Ratcliffe & Ellison, 2015; Tomiyama, 2014). Efforts to refrain from eating (reduce calories or restrict food types), can result in internal discomfort, such as amplified craving, feelings of deprivation, and perseverative thoughts about eating food (Forman et al., 2007; Forman & Butryn, 2015). The degree of aversiveness of such discomfort, as well as the level of tolerance for experiencing it, varies widely among

individuals based in part on divergent cognitive appraisals, regulatory capacities, and resources to manage distress. The degree to which one attends to such experiences, rather than attempt to avoid or suppress them also vary widely. When nonacceptance or intolerance of internal experiences exists, which has been demonstrated in overweight and obese samples (Kozak, Davis, Brown, & Grabowski, 2016), relief from distress can be found in a variety of positive and negative coping behaviors, including the consumption of highly palatable foods, which have potent naturally rewarding properties (Volkow, Wang, Fowler, Tomasi, & Baler, 2011), thereby negatively reinforcing consumptive behaviors. Patterns of distress avoidance, which interestingly increase in the face of weight-based stigmatization (Ashmore, Friedman, Reichmann, & Musante, 2008), can become automatized (Tomiyama, 2014), particularly in the face of chronic stress that erodes distress tolerance and generates a sense of powerlessness over time (Wisman & Capehart, 2010).

Prevailing weight loss interventions aimed at disrupting and reversing this alarming trend are predominantly based on an overly simplistic model of energy balance, and consequently have failed to achieve any meaningful long-term results. This may be due in part to interventive focus on the symptomatic expression of excess weight rather than the underlying mechanisms of obesity onset and maintenance. Conversely, identifying malleable traits that promote healthier body composition profiles, as well as their potential mechanistic and behavioral means of conferring clinical benefits, may facilitate the development of the next generation of targeted psychosocial interventions for obesity. While social workers are already engaged in addressing the wide social, economic, and health inequalities that contribute to racial, ethnic, and sex disparities in

obesity prevalence, social workers can also play a significant role in both the development and implementation of such targeted psychosocial interventions that remediate stress, reward, and homeostatic dysregulation. Such mechanistically-informed social work interventions can complement the efforts of social workers to counter weight-based stigma and discrimination by fostering more nuanced, comprehensive, and compassionate understandings that challenge counterproductive and misleading blame narratives. To that end, the following three chapters are presented.

2. TARGETING BIOBEHAVIORAL MECHANISMS IN OBESITY

2.1 Abstract

This article presents a biopsychosocial conceptual framework that integrates features from key theoretical models of appetitive behavior, self-regulation, and stress that have elsewhere been applied to obesity but have underdeveloped treatment implications. This framework explicates how eating pathology is maintained in part by implicit cognitive processes, distress intolerance, appetitive automaticity, and stress-induced allostatic dysregulation of reward processing, which interact with homeostatic biological adaptations to both promote obesity and actively counter weight loss efforts. This framework is then applied to treatment development process by elucidating promising therapeutic mechanisms to be integrated into the next generation of targeted psychosocial interventions for obesity. An argument is then presented that in conjunction with exercise and nonrestrictive dieting approaches, therapeutic interventions which incorporate mindfulness training, cognitive reappraisal, and savoring skills can be a more effective means of targeting underlying attentional bias, cue reactivity, implicit stress appraisals, and reward processing deficits that contribute to the etiology and maintenance of obesity.

2.2 Introduction

Since the 1960s, there has been a gradual upward trend in overweight and obesity prevalence nationwide (Centers for Disease Control and Prevention (CDC), 2017), which has been the subject of significant alarm, investigation, and controversy. Current epidemiological estimates indicate that over one third of U.S. adults are obese (body mass index (BMI) $\geq$ 30) and another third are overweight (BMI $\geq$ 25; (Flegal et al., 2016). Concomitant direct medical costs have surged to approximately $147 billion annually (Finkelstein, Trogdon, Cohen, & Dietz, 2009) due to the extensive comorbid health risks of obesity across cardiovascular, endocrine, gastrointestinal, respiratory, musculoskeletal, and neurological systems (Imes & Burke, 2014).

Prevailing public health recommendations, prevention programs, and traditional weight loss approaches aimed at disrupting and reversing this alarming trend are predominantly based on an overly simplistic model of energy balance in which energy intake minus energy expenditure equals body weight (Hafekost et al., 2013). While the first law of thermodynamics undoubtedly plays a significant role in determining body weight, the energy balance equation does not factor in the complex and multifactorial variables involved in the etiology of obesity, such as the known influence of compensatory homeostatic adaptations that actively counter attempts to alter energy balance through dieting or exercise (Ochner, Tsai, Kushner, & Wadden, 2015). Consequently, medical advice, public interventions, and individual efforts to reduce obesity based on the energy balance model have largely failed to achieve any meaningful, long-term results (Hafekost et al., 2013). Less than 20% of overweight adults have reported success with long-term weight loss (McGuire, Wing, & Hill, 1999),

demonstrating that even when weight loss is realized, for the majority of participants the probability of maintaining weight loss is low. More recently this was supported by a large scale study (*N*=278,982) which reviewed an anonymized database of longitudinal electronic patient health records in the United Kingdom (Fildes et al., 2015). Researchers reported that for obese patients, the odds of attaining a normal body weight were only 1 in 124 for women and 1 in 210 for men, increasing to 1 in 1290 for men and 1 in 677 for women with morbid obesity during a maximum of 9 years follow-up.

The "calories in, calories out" energy balance model has also fueled weight-based stereotypes that blame obese and overweight persons for their condition due to assumed sedentary lifestyles and lack of self-discipline when faced with highly palatable foods (Hebebrand et al., 2014; Puhl & Brownell, 2001). Such blame narratives have resulted in both institutional and interpersonal weight discrimination that matches and, in some cases, exceeds the prevalence of discrimination based on gender and race (Puhl et al., 2008); promotes weight gain, obesity onset, and obesity maintenance (Sutin & Terracciano, 2013); erodes distress tolerance (Ashmore et al., 2008); and compounds the negative health risks associated with obesity (Rudd Center for Food Policy & Obesity, 2009). Conversely, a more nuanced and comprehensive understanding of obesity, which considers the dynamic interactions between biological, psychological and sociocultural variables, could lead to more targeted, effective, and compassionate interventions.

2.3 Beyond Energy Balance

The etiology and epidemiology of obesity is complex and multifactorial in nature. Strong evidence supports genetic predispositions for obesity (Albuquerque, Stice,

Rodríguez-López, Manco, & Nóbrega, 2015; Choquet & Meyre, 2011; Wardle, Carnell, Haworth, & Plomin, 2008). Genetic risks extend beyond phenotypic propensities based on biological processes; they also contribute to behavior. Animal models have demonstrated that rats living in identical environments that differed in their genetic predispostions for obesity express varying anxiety-like, locomotor, and reward behaviors, which contributed to phenotypic obesity outcomes (Vogel et al., 2017). Similarly, genetic risks among humans can be both amplified by negative health behaviors, such as television watching (Xue, Zhang, Li, Luo, & Cheng, 2017) or consuming sugar-sweetened beverages (Brunkwall et al., 2016; Qi et al., 2012) or fried foods (Qi et al., 2014), or blunted by health promoting behaviors such as exercise (Reddon et al., 2016), adequate sleep (Tremblay & Pérusse, 2017), and healthy eating (Grimm & Steinle, 2011; Jääskeläinen et al., 2013). Genetic factors also interact with environmental factors to contribute to obesity (Silventoinen, Rokholm, Kaprio, & Sørensen, 2009).

The modern environment has been characterized as "obesogenic" based in part on increasingly sedentary lifestyles and the abundant availability and ubiquitous markeing of inexpensive, processed, energy-dense, and highly palatable foods (Hebebrand et al., 2014). Other aspects of modern societies have been implicated in contributing to a rise in pathologies include inequality, widening economic disparities, and social isolation (Hidaka, 2012), which may contribute to racial, ethnic, gender, and socioeconomic disparities in the distribution of obesity (Flegal et al., 2016; Kanter & Caballero, 2012; Mitchell, Catenacci, Wyatt, & Hill, 2011). In the last several years, gut microbiota has increasingly been examined as a factor in obesity, through promoting increased energy extraction or through interacting with the gut-brain axis to influence satiety or energy

output (Baothman, Zamzami, Taher, Abubaker, & Abu-Farha, 2016; Kelly et al., 2015). Preclinical studies have shown that when fecal microbiota is transplanted from obese donors to lean recipients, donor adiposity and metabolic phenotypes are also transmitted (Le Roy et al., 2013; Ridaura et al., 2013). The gut microbiome is sensitive to both genetic and environmental factors (Org et al., 2015), and can be altered negatively through diet (Claus & Swann, 2013; Rodríguez et al., 2015), antibiotic treatment (Cox et al., 2014; Keeney, Yurist-Doutsch, Arrieta, & Finlay, 2014), or exposure to synthetic chemicals (Claus, Guillou, & Ellero-Simatos, 2016).

Endocrine disrupting chemicals (EDCs) also abound within modern environments and may contribute to obesity and adipogenesis, a cell differentiation process wherein preadipocytes become adipocytes (Grün & Blumberg, 2006; Janesick & Blumberg, 2011). Common EDCs (e.g., bisphenol A, tributyltin, and hydrocarbons) may be found, for example, in hydrocarbon emissions, pesticides, packaging products, seafood, and water supply lines (Airaksinen et al., 2010; Chamorro-García et al., 2013; Grün & Blumberg, 2006; National Institute of Environmental Health Sciences, 2016; Tracey, Manikkam, Guerrero-Bosagna, & Skinner, 2013). These pervasive obesogens heighten obesity risk not only for those directly exposed, but also transgenerationally, passing phenotypic alterations to subsequent generations through epigenetic processes, which can activate and compound genetic predispositions for obesity (Chamorro-García et al., 2013; Manikkam, Tracey, Guerrero-Bosagna, & Skinner, 2013; Tracey et al., 2013).

Significant proportions of people within Western environments, however, maintain normal eating patterns and body weights despite shared environmental and genetic factors that are largely outside of individual control (Flegal et al., 2016).

Subgroup exposure rates to sociocultural risk factors also far exceed obesity prevalence, indicating that while environmental and sociocultural factors play a role in obesity, individuals are differentially susceptible. Individual differences in biobehavioral vulnerabilities such as homeostatic regulation, reward processing and stress response, can interact to engender, maintain, and exacerbate obesity, as well as impede weight loss efforts. Mounting evidence indicates that some of these underlying mechanisms of obesity may indeed be tractable to psychosocial interventions. Mechanistically-focused interventions may be a more effective means of improving health among obese individuals than traditional weight loss programs grounded in the energy balance model.

This article presents a novel biopsychosocial conceptual framework that integrates features from key theoretical models of appetitive behavior, self-regulation, and stress. This framework is then applied to the treatment development process by elucidating promising therapeutic mechanisms to be integrated into the next generation of targeted psychosocial interventions for obesity.

1.4 The Conceptual Framework: An Overview

Based on an integration of neurobiological processes related to eating, Lazarus and Folkman's transactional model of stress and coping (1984), Herman and Polivy's restraint theory (1975), Koob's allostatic model of addiction (2008), and Robinson and Berridge's incentive sensitization theory of addiction (1993), we provide a biopsychosocial conceptual framework of stress-precipitated obesity (depicted in Figure 1) to inform targeted psychosocial interventions for obesity. In brief, this framework elucidates key mechanisms in the risk chain leading from negative stress appraisals to

loss of control over eating and obesity. Within the context of obesogenic environments, blame and shame discourses, and epigenetic risks, patterns of distress avoidance that rely on food as a means of distress relief can trigger a self-perpetuating cycle of palliative coping that further erodes distress tolerance and alters reward systems such that rewards become more powerfully craved while reward responsiveness is reduced. Further, efforts to suppress urges to eat can increase stress and trigger compensatory homeostatic adaptations, such as reducing metabolism, increasing hunger, and inducing fatigue, which can both promote obesity and subvert weight loss efforts.

2.5 Neurobiological Processes

2.5.1 Homeostatic Regulation

Despite daily variations in food intake, for the majority of adults body weight remains fairly constant (Sumithran & Proietto, 2013), which is remarkable given that most Americans live in the obesogenic environments previously described. Normal weight maintenance occurs due to a process known as energy homeostasis, which is an active physiological adjustment of both energy intake and expenditure (Gale, Castracane, & Mantzoros, 2004). Departures from balanced set points generate homeostatic tension, which in turn motivates subsequent behavior in order to dissipate this tension. These adjustments are made predominantly by the hypothalamus, which senses blood glucose levels (Chan & Sherwin, 2012) and receives potent peripheral signals, such as leptin, produced in adipose tissue, and ghrelin, produced by the stomach, (as well as other regulatory neuropeptides such as insulin and orexin) in order to regulate appetite, food intake, activity levels, and metabolism and thereby maintain homeostatic equilibrium

(Coll & Yeo, 2013). Leptin levels increase in proportion to fat mass, and function, in part, to suppress food intake and stimulate metabolic processes in order to reduce excess energy stores. Conversely, ghrelin increases in response to a negative energy balance and functions to stimulate both food intake and energy storage. Stress has also been shown to increase ghrelin and reduce leptin levels, which may be an endogenous stress coping mechanism intended to relieve excessive anxiety (Bali & Jaggi, 2016), that correlates with increased food intake generally (Lutter et al., 2008), as well as preferential consumption of high-fat foods (Teegarden & Bale, 2008). Leptin and ghrelin can also influence eating motivation through exerting effects on mesolimbic dopamine signaling (Farooqi et al., 2007; Malik, McGlone, Bedrossian, & Dagher, 2008; Skibicka, Hansson, Egecioglu, & Dickson, 2012) indicating homeostatic interactions with reward systems (Volkow, Wang, & Baler, 2011).

In cases of food insecurity or scarcity induced by dieting, caloric deprivation can also reduce metabolism and increase appetite and consummatory behaviors (Jiménez Jaime et al., 2015; Martin et al., 2007). Such evolutionarily selected metabolic efficiency, while advantageous for promoting energy surplus and survival when food is in fact scarce (Faulconbridge & Hayes, 2011), may play a role in both the overall obesity trend, and in racial and sociodemographic disparities in obesity prevalence in modern obesogenic environments. Research demonstrates that compensatory biological adaptations such as metabolic reductions can remain salient for up to 6 years following weight loss (Rosenbaum, Hirsch, Gallagher, & Leibel, 2008), resulting in an upward trend in BMI over time (Garner & Wooley, 1991; Sarwer & Wadden, 1999).

2.5.2 Neural Circuits

To understand the neurobiological processes that subserve obsesity, dual-process models have been developed based on neuroimaging data which implicate dysfunction in two major neural systems: a "bottom up" limbic system centered on the amygdala which generates impulsive responses to emotionally salient cues (e.g., palatable foods), and a "top-down" prefrontal cortical system that aligns these responses with goal states (e.g., maintaining a healthy body weight) (McClure & Bickel, 2014). Both bottom-up and top-down systems are integrally involved in regulating typical eating behaviors and when disturbed can alter eating patterns in maladaptive ways.

Rather than there being a hunger center within the brain, multiple complex, redundant, and distributed structures within these two major neural systems are involved in regulating eating behavior and energy expenditure through bidirectional processes (Faulconbridge & Hayes, 2011; Lenard & Berthoud, 2008). Top-down mechanisms are initiated at the cerebral cortex level through mental processing that modulate sensory experiences through descending pathways, while bottom-up mechanisms are initiated from the periphery to the cerebral cortex through ascending pathways when various viscero-, somato-, and chemo-sensory receptors are stimulated (Taylor, Goehler, Galper, Innes, & Bourguignon, 2010). Bottom-up processes, which may be initiated by the circulating neuropeptide hormones described earlier that communicate caloric needs and motivate behavior, may be overridden by top-down cognitive processing of sensory and reward information by corticolimbic striatal networks, which can motivate or inhibit eating even regardless of metabolic requirements (Berthoud, 2011). This could be based on conscious execute decision-making that is conducive with goal states (e.g., food eating

contests or politically motivated hunger strikes), or it could be directed by implicit cognitive processes such as perception, learning or memory (Berthoud, 2011).

Top-down and bottom-up modulation of eating behaviors can also occur through input from cortical-amygdala circuits (stress appraisals), or through reward processing systems primed to elicit appetitive consumption (Berthoud, Lenard, & Shin, 2011). The ventral limbic neural circuit is involved in identifying emotionally significant stimuli, including rewards, and generating affective responses to these stimuli, while the dorsal executive function neural circuit modulates selective attention, planning, and effortful regulation of affective states (Kaye et al., 2013; Phillips, Drevets, Rauch, & Lane, 2003). Together these systems assess reward value and affective valence of stimuli, and determine both response selection, inhibition, and execution, whereas dysfunction in these regions is thought to underpin addictive behavior (Feil et al., 2010; Goldstein & Volkow, 2002).

2.5.3 Associative Learning

While internal cues involved in homeostatic regulation play a significant role in food consumption, eating behavior can also be controlled by external factors that prime behavioral responses due to conditioned associative learning processes, termed cue-potentiated feeding (Holland, Hatfield, & Gallagher, 2001; Holland & Petrovich, 2005; Johnson, 2013). This type of feeding need not be inherently tied to food palatability, hence, even bland food when tied to a conditioned stimulus can trigger a conditioned response (Walker, Ibia, & Zigman, 2012). Cue-potentiated feeding is particularly enhanced when food availability has been interrupted previously, causing binge-like

eating behaviors based on nonconscious predictions of future famine and learned incentive motivation (Galarce & Holland, 2009; Holland, 2014), which may in part explain the potential ineffectiveness of restrictive dieting approaches. Associative learning can also be applied to regulating eating behaviors, when caloric consequences of food are experienced. However, reward-based associative learning impairments specific to food have been demonstrated in obese women, which may be attributable to higher cognitive loads due to body dissatisfaction or efforts to suppress appetitive urges that exhaust cognitive capacities (Zhang, Manson, Schiller, & Levy, 2014).

2.5.4 Reward Processing

Cognitive and emotional processing of food-related reward in cortico-limbic-striatal circuits motivates nonhomeostatic consumption of palatable foods to obtain pleasure, termed hedonic eating (Berthoud, 2011). A variety of neurotransmitters, such as dopamine, serotonin, opioids, and cannabinoids, as well as the neuropeptides involved in homeostatic regulation of eating behaviors described previously, contribute to the rewarding effects of food (Atkinson, 2008; Cason et al., 2010; Cota, Tschöp, Horvath, & Levine, 2006; Kenny, 2011; Volkow, Wang, & Baler, 2011). Among these, dopamine has been the most thoroughly investigated, and while dopamine is released in response to novel or unexpected rewards, dopamine responses become habituated and are gradually transferred to stimuli associated with food rewards (e.g., smell of food, food pictures, time, etc.) which then become conditioned cues that induce appetitive responses. Stressors can also become conditioned cues for eating when food is used as a means of distress relief.

Highly palatable foods are potent rewards that can become powerful motivators through associative learning processes. Preclinical studies have demonstrated that palatable foods can be even more powerful rewards than cocaine, even among drug-sensitized and addicted rats (Lenoir, Serre, Cantin, & Ahmed, 2007; Tunstall & Kearns, 2014), potentially due to evolutionarily selected preferences. Both reward and homeostatic systems can become dysregulated in response to chronic exposure to such hyperpalatable foods, which can upset the balanced interaction between regulatory systems through prolonged activation of the limbic system, resulting in cellular and molecular adaptations that serve to maintain homeostasis in dopamine signaling (Nestler, 2005), but can weaken control circuits and reduce sensitivity to natural rewards (Volkow, Wang, & Baler, 2011). Animal models have demonstrated that such reward deficits both antedate the development of obesity and are exacerbated as adiposity increases (Valenza, Steardo, Cottone, & Sabino, 2015).

2.6 Theoretical Models

2.6.1 Transactional Model of Stress and Coping

Nonacceptance or avoidance of distressing internal experiences may explain the short-term utility of compulsive eating behaviors as a means of distress relief (Merwin, Zucker, Lacy, & Elliott, 2010). This has been supported by a recent study which revealed distress tolerance is negatively correlated with BMI and markers of eating pathology (Kozak et al., 2016). Stress is a nonspecific demand for adaptation, but manifestations and responses to stress are highly specific based on one's appraisal and management of the stressor (Selye, 1976). According to Lazarus and Folkman's seminal

transactional model of stress and coping, stress is cognitively mediated, and distress results when a determination is made that the event is both critical to well-being and exceeds one's coping resources (1984). Distress tolerance and resilience are related to positive appraisals of one's capacity and social, economic, or cognitive-emotional resources to effectively manage stress and challenges within one's environment, which can promote a sense of self-efficacy and positive affect. Based in part on associative learning processes, stress appraisals can become automatized and implicit (Ohman, Carlsson, Lundqvist, & Ingvar, 2007), or they can be the product of explicit reasoning and perseverative thinking patterns (Ellsworth & Scherer, 2003). When negative stress appraisals and resultant negative emotions become automatic, they can become deeply rooted and lead to the development of dysphoria and distress avoidance action schemas perpetuated largely by unconscious processes. Maladaptive schemas have been associated with disordered eating (Talbot, Smith, Tomkins, Brockman, & Simpson, 2015), and shown to mediate the relationship between stress and compulsive eating patterns (Moloodi, Dezhkam, Mootabi, & Omidvar, 2010; Zhu et al., 2016). Emotional eating action schema can be based on avoidance of negative affects either through preemptive strategies to avoid stress activation, or through palliative strategies to reduce the experience of negative emotions once activated (Luck, Waller, Meyer, Ussher, & Lacey, 2005).

For example, socioenvironmental stressors such as poverty, discrimination, interpersonal conflict, isolation, or increased workload, may promote the development of distress avoidant emotional eating schema that can trigger food cravings and promote learned appetitive behaviors. While one person may appraise their capacity to be

sufficient to handle this trigger due to their ability to tolerate distress or using positive coping skills in order to reappraise negative thoughts, another person might become overwhelmed by distressing emotions and turn to emotional eating behaviors in order palliatively cope with emotional distress. One key distinction between the two, aside from the difference in the appraisal, is the duration of the activation of neuroendocrine stress response systems including the sympathetic adrenal-medullary (SAM) axis and the hypothalamic-pituitary-adrenal (HPA) axis (Engelmann, Landgraf, & Wotjak, 2004; Herman & Cullinan, 1997). Stress reactions occur in response to aversive encounters that are appraised to have threat or harm value, prompting the adrenal glands to release cortisol, epinephrine, and norepinephrine which cause increases in heart rate and respiration, decreases in digestive activity, gluconeogenesis, and lipolysis, as well as behavioral reactions such as increased arousal and vigilance (Engelmann et al., 2004). The experience of both stress generally and distress specifically is therefore dependent on cognitive appraisals, which then activate and continue to modulate physiological stimulus-response relationships.

Allostasis, or the process by which the body responds to stressors in order to regain stability or homeostasis through physiological or behavioral change (Sterling & Eyer, 1988), can be highly effective in the short-term in response to acute stress situations. However, when prolonged due to chronically stressful environments wherein stressful stimuli persist and individuals lack either the capacity or the resources to manage stressors, activation of the HPA is sustained, leading to an allostatic state wherein allostatic mechanisms perpetuate a positive feedback loop that increasingly sensitizes the amygdala to stressors and heightens the experience of distress over time

(McEwen, 2007). In such cases, stress can have a cumulative effect and create what has been termed an allostatic load, which is the wear and tear on the body and makes one vulnerable to both disease and the development of disorders (McEwen & Wingfield, 2003; Sterling & Eyer, 1988), including obesity, hypertension, cardiovascular disease, and Type II diabetes (McEwen & Seeman, 1999).

As illustrated in our conceptual framework, the path that leads from stress to loss of control over eating and negative health effects has been characterized as a downward spiral involving positive feedback loops that become self-perpetuating systems in which distress tolerance erodes and patterns of avoidance emerge characterized by conditioned appetitive automacity that becomes strengthened over time (Garland, Fredrickson, et al., 2010). Recurrent activation through appetitive behaviors may lead to further sensitivity of the stress response and antireward systems (Koob et al., 2014; Koob & Le Moal, 2008; Moberg, Bradford, Kaye, & Curtin, 2017), contributing to the generation of insensitivity in the dopamine system (Volkow, Wang, Fowler, Tomasi, & Telang, 2011), creating ever more tightly integrated feedback loops that maintain and intensify maladaptive behavior. Individual resilience to comparative stress varies in accordance with executive functioning abilities including impulse control, cognitive flexibility, decision-making, and working memory, all of which have been identified as deficits associated with obesity and compulsive eating behaviors (Alarcón, Ray, & Nagel, 2016; Manasse et al., 2015; Mole et al., 2015; Murphy, Stojek, & MacKillop, 2014; Perpiñá, Segura, & Sánchez-Reales, 2016; Volkow, Wang, Fowler, Tomasi, & Baler, 2011; Weygandt et al., 2013). Where these vulnerabilities exist, even comparatively low-level chronic stress may induce allostatic load.

2.6.2 Restraint Theory

Restraint theory was first described by Herman and Polivy (Herman & Polivy, 1975) as an extension on Nisbett's theory of weight set points that, when suppressed through dieting or restrictive eating patterns, cause overeating behaviors (Nisbett, 1972). Humans are biologically and evolutionarily designed to promote weight gain through homeostatic adjustments following famine as a protective measure and buffer against starvation and variable, stressful environments (Keys, 1950; Ochner, Barrios, Lee, & Pi-Sunyer, 2013; Speakman et al., 2011). Famine-like experiences can be caused by a lack of resources or replicated through self-imposed dieting with similar resultant deleterious physiological, psychological, and behavioral effects that demonstrate a potential link between both eating disorders and obesity (Macpherson-Sánchez, 2015).

The dieting industry emerged in response to the construction of the concept of ideal weights, which was first developed by insurance companies in the 1940s and was one of the bases for variable premiums, making weight loss desirable (Czerniawski, 2007). Weight ideals used today, such as body mass index (BMI), are based on societal norms and perceptions of health and do not allow for individual variance in set points (Crawford & Campbell, 1999; Macpherson-Sánchez, 2015). Rigid weight ideals have also contributed to the growth of weight stigma, which when internalized increase body dissatisfaction and the risk for maladaptive eating behaviors (Macpherson-Sánchez, 2015). Further, it has been repeatedly shown through meta-analytic review and both observational and experimental longitudinal research that while dieting produces short-term weight loss, it leads to long-term weight gain (Field et al., 2003; Mann et al., 2007; Neumark-Sztainer, Wall, Story, & Standish, 2012; Stevens et al., 2012).

Obesity could also arise from aberrant schema related to food, self, and others (Anderson, Rieger, & Caterson, 2006), accompanied by symptomatic behaviors such as restricting (dieting), bingeing, and exercise avoidance, which could also then create abnormal physiological feedback that induces reward dysfunction (Berridge, 2009; O'Hara, Campbell, & Schmidt, 2015). Cognitive models assert that appetitive behavior may become automatized and executed without conscious volition (Tiffany, 1990). Exposure to conditioned appetitive cues is thought to trigger the automatic compulsion to eat, which, when consciously restrained, results in food- and weight-related cognitions and cravings (Wansink, 2006). Wegner's theory of ironic processes of mental control maintains that attempts to control thoughts and counterintentional inner states initiate both intentional operating processes that promote mental control and ironic monitoring processes that assess the need for operating processes and can result in intensification of unwanted inner states (Wegner, 1994). Thus, maladaptive coping with appetitive urges via attempts to suppress thoughts of eating may result in cognitive and behavioral rebound, manifested by intensification of food cravings and increased food consumption (Erskine & Georgiou, 2010). As such, although many compulsive eaters engage in traditional dieting, long-term results are rarely maintained as the individual's craving and maladaptive coping habits remain unaddressed (Kristeller & Wolever, 2011).

The connection between dieting and its effects have been explored and debated extensively since the inception of restraint theory, and the relationship between dietary restriction, obesity, and eating disorders has since become well established through both prospective studies and experimental research (Field et al., 2003; Irving & Neumark-Sztainer, 2002; Neumark-Sztainer et al., 2006, 2012). Research examining the effects of

dieting on food intake is not new, and has demonstrated increased salivation to food stimuli among restrained eaters (e.g., dieters) (Wooley & Wooley, 1973), as well as an increase in hedonic responsiveness to palatable food stimuli, measured through a modified affect misattribution procedure designed to capture immediate versus delayed hedonic responses to tempting-food stimuli (Hofmann et al., 2010). Restrained eaters have been shown to consume more food after exposure to dietary disinhibitors such as high-calorie preloads and fear than without exposure, a phenomenon termed the "counterregulatory eating" effect, whereas unrestrained eaters consumed less food in both conditions (Herman & Mack, 1975). Herman and Polivy downplayed biological set points and instead emphasized counterregulatory cognitive mechanisms that determine hunger and satiety boundaries that may, in fact, be outside of biologically determined limits, which over time habituate restrained eaters to sensations of hunger and oversatiety (Herman & Polivy, 1980). More recently, fasting has been identified as a risk factor for bingeing (Stice, Davis, Miller, & Marti, 2008), and an ecological momentary assessment study provided further support for the association of dietary restriction and bingeing behaviors (Zunker et al., 2011). Thus, traditional models of weight loss may, in fact, contribute to suppression of sensations or urges that promote ironic monitoring processes and consequent intensification of unwanted inner states.

2.6.3 Addiction Model

Intense and ongoing debate about the validity and utility of applying the addiction model to eating pathology can be found within the academic literature (Avena, Gearhardt, Gold, Wang, & Potenza, 2012; Ziauddeen, Farooqi, & Fletcher, 2012a, 2012b). These

debates seem to center on bingeing behaviors in binge eating disorder (BED) and compulsive eating patterns in obesity, but have included bingeing behaviors in bulimia nervosa (BN) as well (Hadad & Knackstedt, 2014; Meule, von Rezori, & Blechert, 2014). The concept of "food addiction," while not new (Randolph, 1956), has gained increasing support (Brownell & Gold, 2013; Davis & Carter, 2014; Gearhardt, Boswell, & White, 2014; Rosa et al., 2015; Schulte, Avena, & Gearhardt, 2015; Shriner & Gold, 2014; Smith & Robbins, 2013; Volkow, Wang, Tomasi, & Baler, 2013; Wolz et al., 2016) due to worldwide increases in the prevalence of obesity over the past 30 years (Finucane et al., 2011). Critics of the addiction model for eating pathology argue that while some overlap related to craving, loss of control, and coping with stress with food exists between substance abuse and binge eating, key characteristics of addiction or substance use disorders such as tolerance, physical dependence, and withdrawal reactions are absent among disordered eaters (Wilson, 2001). Furthermore, the notion of food addiction is not supported by preferential consumption of any type of macronutrient, but instead control over the amount of food eaten seems to distinguish the appetitive abnormality among both individuals with BN (Walsh, 1993) and BED (Yanovski et al., 1992).

While some components of substance-related disorders, such as physical withdrawal, that are absent in behavioral addictions have come to dominate conceptualizations of addiction, research demonstrates clinical, genetic, neurobiological, and phenomenological similarities between substance use disorders and behavioral addictions (Potenza, 2014). Some of the similarities of note include preoccupation, cravings, compulsive urges to engage in behaviors, continued use despite resultant functional impairments and adverse consequences, loss of control, and tolerance

evidenced through escalations in intensity, duration, or frequency of appetitive behaviors in order to achieve relief from dysphoria (Halmi, 2009). Recurrent activation of reward systems through appetitive behaviors, whether through substance abuse or compulsive eating patterns, establishes the automated appetitive action schemas discussed previously that perpetuate compulsive behaviors in part through biasing attention towards appetitive stimuli (e.g., alcohol, opioids, food) (Pierce & Vanderschuren, 2010; Tiffany, 1990). Attentional bias, which is a phenomenon found in all addictions, can be identified through cognitive tasks such as the dot probe, wherein reaction times to probes replacing images of appetitive cues are shorter comparative to probes replacing neutral images (Field & Cox, 2008). Attentional bias towards unhealthy food has been identified as a driver of maladaptive eating behaviors and obesity (Deluchi, Costa, Friedman, Gonçalves, & Bizarro, 2017; Hendrikse et al., 2015) and is predictive of future weight gain (Yokum, Ng, & Stice, 2011). Impaired impulse control has also been significantly associated with obesity, which mirrors behavioral studies on substance disorders (Weygandt et al., 2013). Further, there is clinical and empirical support for reciprocity between addictions, that is addictions may covary and engaging in one addiction increases the risk for another (Haylett, Stephenson, & Lefever, 2004). Such covarying of addictions indicates that underlying etiological mechanisms may be shared across addictions. For example, women with substance use disorders or eating disorders have been shown to be over four times more likely to develop the other disorder than women in the general population (Gadalla & Piran, 2007).

Due to these similarities, the allostatic model of drug addiction proposed by Koob (2008) may be effectively applied to compulsive eating. Koob conceptualized addiction

as chronically relapsing disorder characterized by patterns of impulsivity (positive reinforcement) that lead to patterns of compulsivity (negative reinforcement) through a cycle that involves three core psychological features of addiction: compulsion to seek the appetitive substance, loss of control in limiting use, and emergence of a negative emotional state following use such as anxiety, dysphoria, or irritability. Koob describes three stages of this cycle, which include binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation (Koob & Le Moal, 1997), and correspond with dysregulation in three functional domains that are reciprocally reinforced by the others (Koob, 2017). Binge/intoxication is mediated by the ventral striatum and extended amygdala reward system, and is associated with dysregulation of conditioned responses and incentive salience; withdrawal/negative affect is mediated by decreases in function of the extended amygdala and brain stress neurocircuitry; and preoccupation/anticipation is mediated by the prefrontal cortex and corresponds with dysregulated executive functions (Koob, 2008, 2017). The allostatic model of addiction asserts that pathological over-stimulation of the reward systems has been shown to eventually cause a down-regulation of incentive systems wherein reward thresholds are increased due to a reduction in the number of dopamine receptors in order to compensate for the over-stimulation (Koob & Le Moal, 2001, 2006). Elevated reward thresholds reflect decreased sensitivity of the brain reward system, resulting in reduced capacity to experience pleasure regardless of reward type. Animal model research has provided empirical support for such allostatic shifts in hedonic set points (Kenny, 2011). Researchers demonstrated that reward thresholds remain stable and unaltered in control rats that have access to standard lab chow and that remain drug naïve. However, thresholds gradually elevate in rats with

extended daily access to an energy-dense palatable diet consisting of tasty food items (e.g., cheesecake, bacon, chocolate, etc.). Similarly, reward thresholds progressively elevated in rats that have extended daily access to intravenous cocaine or heroin infusions. These effects suggest that overconsumption of palatable foods and associated weight gain can induce profound deficits in brain reward similar to those induced by excessive consumption of addictive drugs. Substance use disorders have consequently been referred to as reward deficit disorders (McArthur & Borsini, 2008).

Of particular interest is Koob's reconceptualization of withdrawal as being neither physical nor somatic, but rather a motivational withdrawal syndrome that reflects dysregulation of hedonic homeostatic processes. Solomon's opponent-process theory of motivation posits that once hedonic, affective, or emotional states are initiated, the central nervous systems automatically modulates and reduces the intensity of hedonic feelings through recruitment of stress systems. These opponent processes are integral to normal homeostatic function, but can fail to return to normal homeostatic ranges (Koob & Le Moal, 2008). Koob describes how these processes are mediated by within-system neuroadaptations (at the molecular or cellular level) and between-system adaptations (circuitry changes), wherein overactivation of the reward system also triggers activation of stress systems, resulting in heightened sensitivity to appetitive cues, reduced sensitivity to natural rewards, and to the allostatic state described previously (Koob & Le Moal, 2008).

While the ability of exogenous substances to alter central nervous system signaling and create hedonic dysregulation is well established (Feng et al., 2012; Mechoulam & Parker, 2013), in some circumstances, and among predisposed individuals,

endogenous opioids, released through pleasure-inducing behaviors such as eating or sexual stimulation, can produce similar effects and alterations in complex central regulatory systems, which can result in dysregulation of reward system function coupled with signs of tolerance, dependence and withdrawal (Hebebrand et al., 2014). Hence, behavioral addictions, such as compulsive eating, can similarly be described as reward deficit disorders. Indeed, preclinical experiments have documented that overeating results in reduced dopamine receptor availability, as well as reduced responsivity to both food and drug rewards (Geiger et al., 2009; Johnson & Kenny, 2010). Similarly, reduced reward response to food, as well as a reduced number of dopamine receptors has been found clinical studies of obesity (Stice, Spoor, Bohon, & Small, 2008; Wang et al., 2001). As with substance addictions, individuals with behavioral addictions such as maladaptive eating report compulsive urges to engage in addictive behaviors, discomfort and anxiety when engagement ceases, resultant increases in craving and anxiety (Bradley, 1990), and ultimately loss of volitional control of compulsive eating behaviors (Halmi, 2009). Whether by food or by drug, the complex activation of the reward system, rather than specific means of activation, may therefore be viewed as the initial step in a path that can end in addiction (Hebebrand et al., 2014).

2.6.4 Incentive Sensitization Theory of Addiction

In line with the addiction model, obese persons have also been shown to find food more reinforcing than nonobese individuals (Saelens & Epstein, 1996; Temple, Legierski, Giacomelli, Salvy, & Epstein, 2008). The Incentive Sensitization Theory of Addiction asserts that addiction results from neuroadaptive changes to repeated drug use, which

results in increasing reward salience (wanting), with concomitant increases in craving and appetitive urges (Robinson & Berridge, 1993), which has been supported in applications to other reinforcers including food (Temple & Epstein, 2012).

2.6.4.1 Wanting versus liking

It is critical to note that increases in incentive sensitization or salience result in increases in the wanting of a stimulus, but not the liking of that stimulus (Berridge, 1996). As described previously, pathological overstimulation can in fact shift hedonic set points such that tolerance is developed, causing liking, or pleasure, induced from both the addictive stimulus as well as other natural rewards, to diminish over time. Neurobiological systems drive attention and motivated behavior towards seeking and obtaining an appetitive stimulus (construed as a wanting of the stimulus) as well as govern the sensory pleasure derived from consuming the appetitive stimulus (construed as a liking of that stimulus) (Berridge, 1996). However, from a biological perspective, sensory experiences are not innately pleasant or unpleasant; rather, their hedonic value evolves over time through both heritable epigenetic processes, the state of the organism, and individual conditioning (Berridge & Kringelbach, 2008).

The internal milieu, or state of the organism, also plays a significant role in liking through appetitive signals generated based on the physiological needs of the moment (Cabanac, 1971). Following receipt of these signals a hedonic shift occurs called alliesthesia wherein tastes can then become either more pleasant in response to hunger or less pleasant in response to satiety (Berridge, 2009; Cabanac, 1971). The lateral hypothalamus and ventral pallidum are sensitive to physiological needs and actively

influence appetite, illustrated by the fact that when these systems are severed both food wanting and liking are abolished (Cromwell & Berridge, 1993), but when intact can generate enhancement or aversion to natural rewards (Smith & Berridge, 2005, 2007). The process of alliesthesia can generate both obsessive aversions and desires through individual conditioning that can both co-exist and reinforce each other (Faure, Reynolds, Richard, & Berridge, 2008; Reynolds & Berridge, 2008). For example, food insecurity, restrictive eating patterns, or fasting can create an internal milieu of lack and starvation which increases the hedonic value of food due to alliesthesia, which increases the palatability of food, demonstrating the role alliesthesia plays in subverting the effectiveness of restrictive dieting interventions.

With repeated exposure and resultant experiences of pleasure, primary reinforcers, such as palatable food, or the cues associated with them, such as food advertisements or packaging, can trigger conditioned cue-induced appetitive responses and become increasingly salient, thereby increasing their motivational value and the Pavlovian effect (Pavlov, 1927; Volkow et al., 2013). Conscious, cognitive desire which involves the orbitofrontal cortex, is not necessarily a component of incentive salience, which depends on subcortical mesolimbic dopamine neurotransmission (Berridge, 2001; Dickinson & Balleine, 2010). In fact, excessive incentive salience may cause an individual to powerfully want rewards that are not consciously desired or even liked (Berridge & Aldridge, 2008; Robinson & Berridge, 1993).

The orbitofrontal cortex, anterior cingulate cortex, and insular cortex, however, do play a role in liking, along with mesolimbic and subcortical forebrain limbic structures including the amygdala, nucleus accumbens, and the ventral pallidum (Berns, McClure,

Pagnoni, & Montague, 2001; Cardinal, Parkinson, Hall, & Everitt, 2002; Craig, 2002; Everitt & Robbins, 2005; Kringelbach, 2004; Kringelbach, de Araujo, & Rolls, 2004; Levine, Kotz, & Gosnell, 2003; O'Doherty, Deichmann, Critchley, & Dolan, 2002; Pelchat, Johnson, Chan, Valdez, & Ragland, 2004; Schultz, 2006; Small, Zatorre, Dagher, Evans, & Jones-Gotman, 2001; Volkow et al., 2002; Wang et al., 2004). Of these, the areas that have been singled out as the most significant to hedonic responses are hotspots within the nucleus accumbens, ventral pallidum, the parabrachial nucleus, and possibly the amygdala and orbitofrontal cortex as well, which all work together as an integrated liking system (Berridge, 2009; Berridge & Kringelbach, 2008; Smith, Tindell, Aldridge, & Berridge, 2009). Endogenous opioid or cannabinoid receptor activation has been found to mediate food liking (Barbano & Cador, 2007; Berridge, 2009; Cooper, 2004; Dallman, 2003; Higgs, Williams, & Kirkham, 2003; Jarrett, Limebeer, & Parker, 2005; Kelley et al., 2002; Kirkham, 2005; Kirkham & Williams, 2001; Le Magnen, Marfaing-Jallat, Miceli, & Devos, 1980; Levine & Billington, 2004; Panksepp, 1986; Sharkey & Pittman, 2005). But whereas hedonic liking involves an estimated 10% of the nucleus accumbens, the entire nucleus accumbens and surrounding brain structures, including the amygdala and neostriatum, are stimulated by opioidergic signaling during food wanting (Kelley, 2004; Kelley, Baldo, & Pratt, 2005; Levine & Billington, 2004; Peciña & Berridge, 2005; Yeomans & Gray, 2002). Pleasure centers are, therefore, much smaller than motivational and appetite-increasing centers of the brain, which may indicate a potential neurological basis for overconsumption or bingeing even in the absence of food liking or when counter to individual health goals.

2.7 Targeting Mechanisms with Therapeutic Approaches

Our model identifies key mechanisms involved in the risk chain leading to obesity identified through integration of prominent theoretical models and biobehavioral research findings. These cognitive, affective, and psychophysiological mechanisms of obesity development and maintenance are overlooked or potentially even exacerbated by traditional weight loss approaches, yet remain tractable to psychosocial interventions. Underlying mechanisms to be targeted by intervention include attentional bias, cue reactivity, distress intolerance, appetitive automaticity, and stress-induced allostatic dysregulation of reward processing. Nonetheless, traditional behavioral interventions for obesity have largely focused on an analysis of individual interaction patterns with the surrounding environment through self-monitoring, goal-setting, stimulus control, and problem-solving in order to promote behavioral change (Berkel, Carlos Poston, Reeves, & Foreyt, 2005; Foster, Makris, & Bailer, 2005). Systematic reviews demonstrate that behavioral treatment is more effective than exercise and dieting approaches alone (McTigue et al., 2003; Shaw, O'Rourke, Del Mar, & Kenardy, 2005). However, mindfulness, cognitive reappraisal and savoring skills specifically target underlying mechanisms implicated in the obesity risk chain that are largely unaddressed by extant therapies and may therefore confer additional therapeutic effects beyond those provided by standard treatments. Here, we will detail these three therapeutic mechanisms of action and their applications to the treatment of obesity.

2.7.1 Mindfulness

Mindfulness-based interventions (MBIs), which have been shown in meta-analyses to be effective means of addressing other disorders of appetitive self-regulation, such as substance dependence (Li, Howard, Garland, McGovern, & Lazar, 2017), may target an array of mechanisms underlying maladaptive eating behavior. In the same way that substance dependent individuals feel overwhelming urges to consume drugs or alcohol when triggered by stress or negative affect, in spite of the often severe consequences for doing so, maladaptive eaters may similarly be plagued by thoughts of eating and the drive to self-soothe distress with food, continuing to binge-eat or overeat irrespective of the negative outcomes they may experience. MBIs may target such stress- and cue-induced appetitive processes, disrupting automaticity and ameliorating intrusive thoughts and cravings (Garland, Froeliger, & Howard, 2013), including those related to food (O'Reilly, Cook, Spruijt-Metz, & Black, 2014). MBIs also offer training in practices that evoke a mindful mental state characterized by a nonreactive, nonevaluative monitoring of moment-by-moment cognition, emotion, perception, and sensation without fixation on thoughts of past or future (Garland, 2007). Mindfulness practice involves both focused attention and open monitoring (Lutz, Slagter, Dunne, & Davidson, 2008; Vago & Silbersweig, 2012). Focused attention involves sustained attention on an object, (which could include sensations such as breathing, pain, hunger, or fullness), while gently acknowledging and letting go of distracting thoughts and emotions (Lutz, Dunne, & Davidson, 2007). Open monitoring practices instead cultivate broadened metacognitive awareness, wherein thoughts are not suppressed but are merely observed without judgment (Lutz et al., 2008). Together these practices can exercise and strengthen

cognitive capacities such as attentional vigilance, attentional reorienting, response inhibition, and emotion regulation (Vago & Silbersweig, 2012). Consistent mindfulness practice may induce cognitive plasticity and promote durable changes in dispositional capacities and propensities to be mindful in everyday life (Baer, Smith, Hopkins, Krietemeyer, & Toney, 2006; Garland, Gaylord, Boettiger, & Howard, 2010). Repeated activation of the mindful state may also result in salutary outcomes, such as improved distress tolerance (Luberto et al., 2014; Nila, Holt, Ditzen, & Aguilar-Raab, 2016) and reduced stress reactivity (Smith et al., 2008), as well as lead to the extinction of maladaptive behaviors such as compulsive eating (Katterman, Kleinman, Hood, Nackers, & Corsica, 2014). The self-compassion inherent in practicing acceptance of one's body and food urges may be especially therapeutic for maladaptive eaters, who typically engage in self-denigration and avoidance of intrusive, eating-related thoughts (Kristeller & Wolever, 2011). In fact, in one study when compared to challenging thoughts via CBT, acceptance-based approaches produced greater reduction in cravings and food consumption (Forman, Hoffman, Juarascio, Butryn, & Herbert, 2013).

Various types of MBIs have also been applied to eating pathology with promising results. The most recent systematic review and meta-analysis of the effects of mindfulness training on weight loss and health behaviors demonstrated that while, overall, changes in BMI from pre- to postintervention were not significant, longer term measures from baseline indicated increased and continued weight loss over time (Ruffault et al., 2016). This review did demonstrate significant reductions in impulsive (d = -1.15) and binge eating (d = -1.26) that may explain the increased effects in weight loss over time. Another systematic review of MBIs for obesity-related eating behaviors

reported that of the twenty-one studies included in their review, 86% reported positive changes in eating behavior outcomes, which included emotional eating (Cohen's *d* ranged between 0.53 to 0.90) and external eating (*d* = 0.53 to 0.70), as well as only small effects on body weight outcomes (O'Reilly et al., 2014). Both systematic reviews determined that MBIs held promise, but that future studies should use longitudinal designs, active control arms, and examine whether mindfulness is the mechanism for improved eating behavior outcomes or can be attributed to other therapeutic mechanisms unique to various interventions. Each also noted the wide differences between interventions and a need to determine the most efficacious components of those interventions.

While Mindfulness-Based Cognitive Therapy (MBCT: Segal, Williams, & Teasdale, 2002) has been adapted for binge-eating disorder (Baer, Fischer, & Huss, 2005), mindfulness therapies have also been developed that are specifically designed to target eating pathology, such as Mindfulness-Based Eating Awareness Training (MB-EAT: Kristeller & Hallett, 1999). MB-EAT, which was modified from Mindfulness-Based Stress Reduction (MBSR: Kabat-Zinn, 1982) and specifically developed for binge eating disorder, has been shown to significantly reduce binge eating behaviors (such that 95% of those meeting full criteria for binge eating disorder (*N* = 99) no longer met criteria postintervention), promote weight loss comparative to wait list controls, and that the amount of mindfulness practice predicted the amount of weight lost ($r = -0.38$, $p < 0.05$; Kristeller, Wolever, & Sheets, 2014). While these interventions include a number of diverse approaches, principles, and practices, explicit mindful skill development that engenders nonjudgmental present moment awareness of both internal and external stimuli, while encouraging openness, curiosity, and acceptance are key components of

MBIs (Bishop et al., 2004) that have been shown to be particularly effective for conditions characterized by intolerance of negative affect states and subsequent behavioral avoidance (Hofmann et al., 2010). Reduced attentional bias (Garland, Gaylord, et al., 2010) and increased parasympathetic control during attention to emotional information (Garland, Froeliger, & Howard, 2014) are likely key mechanisms of MBIs that produce clinical benefits, such as improved health and stress coping (Grossman, Niemann, Schmidt, & Walach, 2004), indicating the significance of explicit mindful skill development. The most recent systematic reviews of mindfulness training for adults with overweight and obesity reveal that mindfulness training holds significant promise as a means of producing short-term benefits in health-related behaviors and obesity, but further longitudinal research with active control arms is necessary in order to determine the endurance of treatment outcomes and comparative effectiveness (Katterman et al., 2014; Ruffault et al., 2016).

2.7.2 Cognitive Reappraisal

MBIs such as MBSR (Kabat-Zinn, 1982), MB-EAT (Kristeller & Hallett, 1999), and MBCT (Segal, Williams, & Teasdale, 2012) provide formal mindfulness training, but are divergent from cognitive behavioral interventions in that they eschew cognitive reappraisal, a meaning-based adaptive coping strategy through which stressful events are cognitively reconstrued as nonthreatening or beneficial, or wherein appetitive cues are reframed as unhealthy rather than appetizing (Garland, 2016; Kober et al., 2010), in favor of complete nonjudgment, nonstriving and noneffort. Evidence demonstrates, however, that cognitive reappraisal can effectively downregulate craving (Dutra et al., 2008;

Giuliani, Calcott, & Berkman, 2013; Kober et al., 2010), indicating its significance in disrupting implicit cognitive processes and improving self-regulatory skills. Importantly, cognitive reappraisal of food stimuli has also been shown to modulate neural responsivity to palatable food, inhibiting appetitive motivation and reducing intake of unhealthy food (Yokum & Stice, 2013). It is important to note, however, that reappraisal strategies elicit differential neural responses and vary in their effectiveness. Whereas thinking in terms of the long-term costs of eating unhealthy foods has been shown to be effective with lean individuals (Kober et al., 2010; Siep et al., 2012), among obese samples thinking of the benefits of not eating was far more effective (Yokum & Stice, 2013).

However, mindfulness and reappraisal skills need not be exclusive, and incorporating both in therapeutic interventions may in fact reciprocally enhance the efficacy of both skillsets when practiced sequentially. Cognitive theorists assert based on dual-system models that patterns of impulsivity and compulsivity are counteracted by deliberative and goal-directed cognitive and behavioral control (McClure & Bickel, 2014). But cognitive behavioral therapy may depend on individual capacity for attention (McClure & Bickel, 2014), which can be enhanced through mindfulness training (Jha et al., 2015; Semple, 2010). Bi-directional relationships have been theorized wherein attentional broadening developed through mindfulness practice increases capacity for positive emotions, which can facilitate reappraisal (Garland, Farb, Goldin, & Fredrickson, 2015a, 2015b). When maladaptive stress appraisals and subsequent dysphoria arise, mindfulness may disrupt automatic cognitive processes and facilitate a shift into a metacognitive state (Garland, Farb, et al., 2015a; Teasdale, Segal, & Williams, 1995) that reduces cue reactivity (Garland et al., 2014; Keesman, Aarts,

Häfner, & Papies, 2017; Westbrook et al., 2013), broadens attention to include previously unattended to information, and facilitates reappraisal such that maladaptive schema can be restructured (Garland, Farb, et al., 2015b). Mindfulness has also been shown to reduce thought suppression and its deleterious effects in perpetuating unwanted thoughts and increasing associated avoidant behaviors (Bowen, Witkiewitz, Dillworth, & Marlatt, 2007; Garland, Gaylord, et al., 2010; Garland & Roberts-Lewis, 2013; Moss, Erskine, Albery, Allen, & Georgiou, 2015), which may enhance the effectiveness of cognitive reappraisal when these two cognitive strategies are combined.

2.7.3 Savoring

Mindful and intuitive eating approaches encourage food savoring practices as a means of slowing eating, reducing calories consumed, and increasing satiety (Kristeller & Wolever, 2011; Rossy, 2016; Somov, 2012; Tribole & Resch, 1995). However, more broadly, savoring of natural rewards has shown promise as a means of remediating reward processing deficits in addiction, which have been implicated in the mechanistic model of disordered eating (Feil et al., 2010; Goldstein & Volkow, 2002; Kaye et al., 2013). Mindful savoring involves focusing attention on the sensory experiences of natural rewards and the positive emotions induced therein (Garland, Froeliger, & Howard, 2015b), which can both increase exposure to positive emotions and counter emotion dysregulation, thereby supporting lasting affective dispositional changes (Garland et al., 2013). The recently proposed Mindfulness to Meaning Theory (MMT) posits that such dispositional changes transpire through an attentional shift away from maladaptive perseverative cognitive processes, which frees attentional resource to be

reallocated to engagement with healthful or naturally rewarding stimuli (Garland, Farb, et al., 2015a). Enhanced responsivity to natural rewards may in turn decrease appetitive responses towards addictive substances (Garland et al., 2016). Natural rewards include but extend far beyond food experiences. Music, social interaction, physical intimacy, nature, pets, hobbies, and even work are all examples of sources of pleasure that can be savored. In fact, savoring alternative sources of reward outside of those used for palliative coping may be integral to remediating reward processing. Hence, obesity treatments that focus solely on food savoring may be insufficient to countering reward dysregulation.

Because compulsive eating involves dysfunction in both controlled and automatic processes, it may best be targeted by mental training programs that unite complementary aspects of mindfulness training, cognitive behavioral therapy, and positive psychology principles in order to target both top-down and bottom-up mechanisms in the risk chain elucidated by our conceptual framework (Garland, 2016). While the energy balance model is overly simplistic, it remains pertinent. Hence, therapies that combine mindfulness, cognitive reappraisal, and savoring mechanisms with exercise and nutrition counseling informed by principles of mindfulness and the complexities of obesity maintenance may not only produce additive but also multiplicative or synergistic effects. Among the various types of mindfulness-based interventions, Mindfulness-Oriented Recovery Enhancement (MORE) is distinct in that it integrates formal mindfulness training, cognitive reappraisal skills, and specifically targets reward processing deficits through savoring (Garland, 2013). MORE has effectively been applied to appetitive disorders and has recently shown preliminary efficacy as a means of reducing food

attentional bias and increasing responsiveness to natural, nonfood rewards in obesity (Garland, 2016; Thomas, 2017a). Further research is needed to determine the effectiveness of MORE on compulsive eating and the durability of treatment effects.

2.8 Conclusion

Obesity may be viewed as the endpoint of an equifinal process with multiple biobehavioral generators. Our proposed integrated conceptual framework elucidates the risk chain leading from negative stress appraisals to loss of control over eating and obesity. Negative stress appraisals may be based on either actual or perceived capacity and resources to manage stressors, but tendencies to avoid the resultant distress trigger a self-perpetuating cycle of palliative coping. When the consumption of food is used as a means of distress relief, maladaptive emotional eating behaviors become negatively reinforced, creating a positive feedback loop that leads to further stress sensitization, distress intolerance, and compulsive eating behaviors, resulting in loss of control over weight gain. This process is compounded by exposure to obesogenic environments characterized by a profusion of stimuli that elicit evolutionarily-selected and individually-conditioned automatic impulses to consume food. While traditional weight loss programs assume that conscious self-control efforts can regulate eating behavior, these stress-precipitated processes generate unconscious appetitive automaticity and interact dynamically with homeostatic biological adaptations to both promote obesity and subvert weight loss efforts. Further, efforts to suppress these automatic impulses through restraint and dieting can intensify cravings and increase stress appraisals that trigger compensatory homeostatic adaptations, such as reducing metabolism, increasing hunger,

and inducing fatigue. Countering this cycle requires more than treating its symptomatic expression (e.g., weight). It requires multidisciplinary and administrative action to construct health-promoting environments, advocacy efforts that increase awareness of the multifactorial complexity of obesity and challenge weight-based stigma and discrimination, and the development of biopsychosocial interventions designed to target underlying mechanisms of obesity onset and maintenance. Based on an examination of therapeutic approaches that have demonstrated effectiveness in remediating appetitive disorders, we propose that, in conjunction with exercise and nutrition counseling, mindfulness, cognitive reappraisal and savoring training be incorporated in next generation of treatments for obesity.

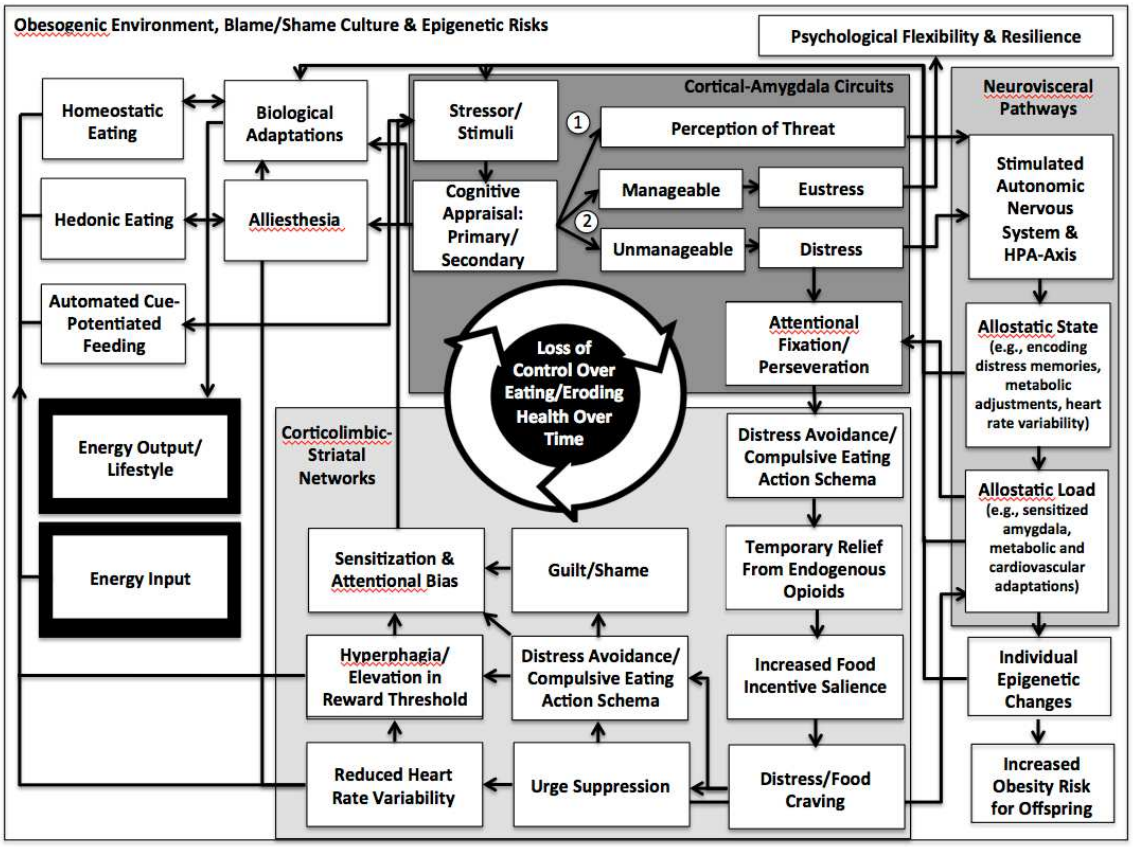

Figure 1. An integrated model highlighting key mechanisms involved in the risk chain of compulsive eating and obesity that are targetable with therapeutic interventions.

3. SAVORING AND CUE-ELICITED HEART RATE VARIABILITY MEDIATE THE RELATIONSHIP BETWEEN DISPOSITIONAL MINDFULNESS AND ADIPOSITY AMONG FEMALE CANCER SURVIVORS

3.1 Abstract

Excess fat is often highlighted as a modifiable risk factor for both cancer prevention and survivorship. However, interventions that aim to reduce adiposity have largely failed to achieve long-term results. Identification of malleable psychological traits that promote healthier body composition profiles, as well as their potential mechanistic and behavioral means of conferring clinical benefits, may facilitate the development of the next generation of targeted psychosocial interventions for obesity. The present study employ data from a sample of 51 female cancer survivors to test a conceptual model in which the association between dispositional mindfulness and reduced adiposity is hypothesized to be mediated by savoring nonfood related natural rewards and autonomic regulation during attention to appetitive information, as indicated by high-frequency heart rate variability (HRV). Multivariate path analyses revealed that the association between dispositional mindfulness and adiposity was mediated by food cue-elicited HRV and savoring, which was consistent with the conceptual model. This study demonstrates that dispositional mindfulness may promote the ability to flexibly regulate attention and emotion, which may promote healthier body compositions.

3.2 Background

Cancer is the second leading cause of death worldwide, with an estimated 14 million new cases and 8.2 million deaths annually (Ferlay et al., 2015). Overweight and obesity are among the most prominent risk factors for the development of several types of cancer, including esophageal, gastric, biliary tract, colorectal, pancreatic, kidney, multiple myeloma, endometrial, ovarian, and breast cancers (Kyrgiou et al., 2017), as well as being risk factors for cancer recurrence and poorer prognosis (Azrad & Demark-Wahnefried, 2014; Chan et al., 2014; Druesne-Pecollo et al., 2012). Among women, endometrial and postmenopausal breast cancers account for nearly two thirds of all cancer cases attributable to excess body weight (Arnold et al., 2015).

Over the past 50 years there has been a gradual upward trend in overweight and obesity prevalence nationwide (Centers for Disease Control and Prevention, 2017). Epidemiological estimates based on the most recent National Health and Nutrition Examination Survey (NHANES), a cross-sectional, nationally representative survey (N=5455), indicate that over 70% of adults age 20 and older within the United States are overweight or obese (National Center for Health Statistics, 2016). Cancer prevalence, along with hypertension, cardiovascular disease, and Type 2 diabetes, has risen in tandem with excess adiposity (Wylie-Rosett & Jhangiani, 2015) in a dose-response relationship (Calle et al., 2003) that may grow stronger with age (Masters et al., 2013), suggesting a significant number of U.S. adults may be at risk.

Body mass index (BMI) is a commonly used scale to assess overweight and obesity, which defines overweight as a BMI of 25 to 29.9kg/m^2, and obesity as a BMI of 30 kg/m^2 or greater (World Health Organization, 2016). While BMI is used as a

surrogate measure of body fat, it does not determine the actual composition of body weight, and it is therefore an imprecise measure of adiposity (Shah & Braverman, 2012); particularly among cancer survivors who may lose skeletal muscle and gain body fat as a side effect of adjuvant chemotherapy (Vance, Mourtzakis, McCargar, & Hanning, 2011). Reliance on BMI rather than directly measuring body fat may be responsible for the oft-cited obesity paradox (Padwal, Majumdar, & Leslie, 2016), as excess body weight indicated by BMI may be due to either muscle hypertrophy or hypertrophy and hyperplasia of adipose tissue (Jo et al., 2009; Schutz, Kyle, & Pichard, 2002). Conversely, low BMIs may indicate low fat mass, or they may represent a higher fat ratio based on deficits in fat-free mass (FFM) due to age-related sarcopenia (Walston, 2012) or cancer cachexia (Fearon et al., 2011), demonstrating the importance of accurately assessing body composition in cancer populations with imaging technologies such as dual X-ray absorptiometry (DXA), computed axial tomography (CAT: Shah & Braverman, 2012), and ultrasound (Wagner, 2013).

Excess fat is often highlighted as a modifiable risk factor for both cancer prevention and survivorship (Whiteman & Wilson, 2016). However, efforts to reduce adiposity based on an overly simplistic "calories in, calories out" energy balance model have largely failed to achieve long-term results (Hafekost et al., 2013). This may be due, in part, to interventive focus on the symptomatic expression of excess weight rather than the underlying mechanisms of overweight and obesity maintenance. Conversely, identifying malleable traits that promote healthier body composition profiles, as well as their potential mechanistic and behavioral means of conferring clinical benefits, may facilitate the development of the next generation of targeted psychosocial interventions

for obesity.

The obesity risk chain involves key cognitive-affective mechanisms that may be explicated by an integrated biopsychosocial framework (see Thomas, 2017b). This framework elucidates cybernetic feedback circuits between stress, implicit cognition, self-regulation attempts, and food consumption driven by homeostatic regulation (based both on actual metabolic requirements and perceived future energy needs determined by experiences of stress or deprivation), associative learning (conditioned responses to appetitive cues that can be strengthened by repeated exposure), and reward processes (hedonic eating based on the experience of pleasure or of distress relief from the consumption of highly palatable foods). Eating behaviors can also be moderated or mediated by dispositional traits (Elfhag & Morey, 2008; Keller & Siegrist, 2015; Murphy et al., 2014; Ouwens, Schiffer, Visser, Raeijmaekers, & Nyklíček, 2015), implicit cognitive and behavioral schemas (Moussally, Billieux, Mobbs, Rothen, & Van der Linden, 2015; Wang et al., 2016), regulatory capacities (Manasse et al., 2015; Mole et al., 2015; Perpiñá et al., 2016; Weygandt et al., 2013), physiological responses to food and stress exposure (Hopkins, Blundell, Halford, King, & Finlayson, 2016), and historical factors (trauma/abuse, major life events, stressful and obesogenic environments) (Laraia, Epel, & Siega-Riz, 2013; Michopoulos et al., 2015; Osei-Assibey et al., 2012). Each of these may represent viable and more effective targets of interventive efforts for adiposity.

Both preclinical and clinical studies have demonstrated reward dysregulation in obesity similar to substance abuse disorders, evidenced by deficits in dopamine signaling that have been linked to both compulsive food intake and decreased metabolic activity (Johnson & Kenny, 2010; Volkow et al., 2008). Decreased dopamine signaling elevates

reward thresholds, thereby reducing sensitivity to food and nonfood related rewards, which may in turn result in heightened reactivity to food cues, cue-elicited food craving, and compensatory compulsive eating (Ferriday & Brunstrom, 2011; Kenny, 2011; Volkow, Wang, & Baler, 2011). Indeed, clinical trials have demonstrated amplified craving (Contreras-Rodríguez, Martín-Pérez, Vilar-López, & Verdejo-Garcia, 2017; Potenza & Grilo, 2014) and increased reactivity to food-cues (Coelho, Jansen, Roefs, & Nederkoorn, 2009; Herman & Polivy, 2008; Jansen et al., 2003) among those who are overweight or obese.

Adaptive cognitive regulation of appetitive reactivity to food cues may be indicated by elevated heart rate variability (HRV), the beat-to-beat modulation of heart rate by parasympathetic activation of the vagus nerve (Berntson et al., 1997; Thayer & Lane, 2000, 2009). Elevated HRV may reflect self-regulation (Segerstrom & Nes, 2007) of attentional and appetitive responses to salient cues (Garland, Franken, & Howard, 2012; Thayer, Yamamoto, & Brosschot, 2010), whereas attenuated HRV may be indicative of impaired abilities to regulate attention, emotion, and appetitive urges (Ingjaldsson, Laberg, & Thayer, 2003; Thayer & Lane, 2009; Garland, Carter et al., 2012). Elevated HRV has also previously been associated with reduced adiposity (Chintala, Krishna, & N, 2015).

While mindfulness practices evoke a state of nonjudgmental metacognitive awareness of internal cognitive, emotional, and sensory experiences in the present moment (Garland, 2007; Garland et al., 2013), dispositional mindfulness refers to the propensity an individual has to be mindful in everyday life (Baer et al., 2006), which varies naturally between persons, but can be increased through mindfulness training

(Carmody & Baer, 2008). Research indicates that dispositional mindfulness is associated with improved biomarkers of physical health, including adiposity (Loucks et al., 2016). Higher levels of dispositional mindfulness have also been associated with better self-reported health, among a sample of women with breast cancer (Tamagawa et al., 2013). Dispositional mindfulness has also been correlated with decreased attentional bias towards appetitive cues, and improved HRV recovery from appetitive cue exposure (Garland, 2011). Therefore, dispositional mindfulness may index ability to regulate attention to appetitive stimuli, as well as cognitive control over appetitive responses, indicated by autonomic recovery from exposure to emotionally salient cues.

According to the Mindfulness-to-Meaning Theory (Garland, Farb, et al., 2015a), mindfulness involves increased awareness and cognitive flexibility that can facilitate the deliberate cultivation of positive experiences through savoring. Savoring, a process of positive emotion regulation, is the ability to intensify and prolong positive feelings by intentionally orienting attention towards the sensory aspects of natural rewards, and increasing appreciation and meaning through metacognitive reflection on those experiences (Bryant, Chadwick, & Kluwe, 2011; Bryant & Veroff, 2007; Garland, 2016; Smith & Bryant, 2016). Importantly, when reward systems have become dysregulated due to repeated exposure to powerful rewards, causing elevations in both reward salience and reward thresholds, savoring may facilitate reward restructuring through reevaluation of the meaning and value of conditioned stimuli, and thereby promote both hedonic regulation and eudaimonic well-being (Garland, 2016). Savoring has previously been shown to engender psychological well-being (Hurley & Kwon, 2012; Quoidbach, Berry, Hansenne, & Mikolajczak, 2010; Smith & Hanni, 2017), which can buffer against or

decelerate age-related declines in physical health (Brummett, Babyak, Grønbæk, & Barefoot, 2011), and lower cortisol and inflammatory markers (Steptoe, Demakakos, de Oliveira, & Wardle, 2012; Steptoe, O'Donnell, Badrick, Kumari, & Marmot, 2008), which have been associated with both obesity and cancer (Deng, Lyon, Bergin, Caligiuri, & Hsueh, 2016; Esser, Legrand-Poels, Piette, Scheen, & Paquot, 2014; Gunter et al., 2015). A cross-sectional test of the Mindfulness-to-Meaning Theory in a sample of cancer survivors found that dispositional mindfulness was significantly associated with savoring, an association that predicted improved cancer-related quality of life (Garland et al., 2017).

The present study tested in a sample of female cancer survivors a conceptual model derived from the aforementioned proposed conceptual framework of the biobehavioral mechanisms implicated in obesity (Thomas, 2017b), in which the association between dispositional mindfulness and reduced adiposity was hypothesized to be mediated by enhanced savoring of nonfood rewards and autonomic regulation during attention to food cues.

3.3 Methods

3.3.1 Sample Characteristics

Potential participants met study inclusion criteria if they were female, 18 and older, English speaking, had a BMI $\geq$ 25, and had a history of a cancer diagnosis (active or in remission). Participants were excluded if they had unstable cardiac disease, substance dependence in the past year, psychotic disorders, and less than 90 days since a surgery procedure. Participants were recruited through direct referrals from oncologists

at the Huntsman Cancer Hospital and through flyers posted in the hospital.

Table 1 represents sample characteristics. Study participants were 51 adult women aged 29-76 (M = 57.92, SD = 10.04) with a mean BMI of 34.69 (SD = 7.39), and a mean fat mass of 113.08lb (SD = 42.33). Most participants were White/Caucasian (96%), with one Black/African-American and one Hispanic/Latino individual in the sample. The majority had a breast cancer diagnosis history (N =45), while six participants had histories of varying types of cancers with associated obesity risks (Azrad & Demark-Wahnefried, 2014; Carlson, Thiel, Yang, & Leslie, 2012; Larsson & Wolk, 2007; Lichtman, 2010; Ma et al., 2013; Onstad, Schmandt, & Lu, 2016), including ovarian (N = 2), endometrial (N = 1), kidney (N = 1), colon (N = 1), and multiple myeloma (N = 1). In the year prior to the study, 14% had a pretax household income of < $25,000, 20% earned $25,000-$49,999, 26% earned $50,000-$74,999, 12% earned $75,000-$99,999, and 28% earned $100,000 or more.

3.3.2 Procedure

Potential participants were preliminarily screened for eligibility over the phone, and then consented and enrolled if they met inclusion criteria following an initial interview at a lab at the University of Utah. Assessments used in the present study included two separate evaluations. The first evaluation included the completion of several standardized psychosocial instruments using REDCap electronic data capture (Harris et al., 2009), as well as a dot probe task during which HRV was recorded in response to food cues. Participants then completed a second evaluation in which a technician who was a registered dietician conducted objective measurement of adiposity.

Participants gave informed consent and received no monetary compensation for their participation in the study. Study procedures met the standards put forth by the Declaration of Helsinki and were approved by the University of Utah IRB.

3.3.3 Measures

3.3.3.1 Dispositional mindfulness

Dispositional mindfulness was assessed with the Five Facet Mindfulness Questionnaire (FFMQ: Baer et al., 2006), a 39-item instrument measured on a 5-point Likert scale (1 = Never or very rarely true, 6 = Very often or always true). This validated scale yields a total dispositional mindfulness score (α = .92 in this sample) that subsumes various facets of dispositional mindfulness including observing and attending to experiences, describing and discriminating emotional experiences, acting with awareness, nonreactivity to inner experiences, and nonjudging of inner experiences.

3.3.3.2 Savoring

Savoring was measured with the "savoring the moment" subscale (α = .79 in this sample) of the Savoring Beliefs Inventory (SBI: Bryant, 2003), a 24-item validated scale that measures an individual's perceptions of their ability to derive pleasure from life experiences.

3.3.3.3 HRV cue-reactivity

HRV responses to food cues were measured during the administration of a dot probe task. Electrocardiogram (ECG) electrodes were attached to participants' right and

left pectoral muscles, and a Biopac MP150 data acquisition system (Biopac Systems, Goleta, CA) acquired raw ECG at a frequency of 1000 Hz, which was recorded continuously throughout the protocol. Prior to the dot probe task a 5-min baseline high-frequency HRV was captured, during which participants were instructed to remain motionless and silent. Automated routines in Acqknowledge 4.1 (BIOPAC, Inc.) were used to detect R-R intervals, and then visually inspected to correct artifacts. During the dot probe task, which was comprised of 64 trials, each trial began with a fixation cross presented for 500 ms. Participants were then presented with both food and neutral pictures selected from the International Affective Picture System (IAPS) based on their valence and arousal ratings. Photos were matched for visual complexity, color, and figure-ground relationships and displayed side by side for either 50 or 2000 ms. Food pictures included 12 photos of highly palatable foods including pizza, hamburgers, french fries, and desserts, while the neutral photos depicted common household items. Following each trial, a target probe replaced one of the photos and was displayed for 100 ms, and participants were instructed to indicate the location of the probe on the screen with a left/right button press. The order and duration of cue presentation, as well as the left or right position of the photos and target probe on the screen, was randomized and counterbalanced.

3.3.3.4 Adiposity

Body composition was measured using BodyMetrix BX-2000 (IntelaMetrix, Inc., Livermore, CA) 2.5 MHz, A-mode ultrasound, and analyzed with Body View Professional software. Recommended 3-point measurement protocol was followed,

which included repeated measurements of the thigh, triceps, and abdomen by an experienced technician (Wagner, 2013). BodyMetrix ultrasound has been shown to be an accurate measure of adiposity comparative to the BodPod (Life Measurement, Inc., Concord, CA; Bielemann et al., 2016) and DXA (Ripka, Ulbricht, Menghin, & Gewehr, 2016).

3.3.4 Statistical Analyses

Previous to hypothesis testing, raw RR intervals were analyzed with Kubios 2.0 (Biosignal Analysis and Medical Imaging Group, University of Finland), and a fast Fourier transform (FFT) was used to extract normalized high-frequency HRV from a de-trended, end-tapered interbeat interval time series. Vagally-mediated HRV was estimated by selecting HRV in the respiratory frequency band (0.15 – 0.40 Hz) and averaged across the 5-min baseline and food cue block presented on in dot-probe task. To assess food cue-elicited HRV, residualized change in HF HRV was computed by covarying HRV levels during the resting baseline from levels during the dot probe task.

Data analyses were performed using SPSS 22.0 (IBM Corp., Armonk, NY). Data were first examined for extreme outliers (z scores ± 2.5 *SD* from the mean) and to ensure they met distributional assumptions for normality. All variables of interest to the present study were approximately normally distributed based on Shapiro-Wilk tests of normality, and no extreme outliers were identified. The conceptual model was tested using a multivariate path analysis conducted in AMOS 22.0 with Full Information Maximum Likelihood (FIML) estimation. Overall model fit was assessed by examining the Comparative Fit Index (CFI; Bentler, 1990), as well as the Root Mean Squared Error of

Approximation (RMSEA) Index (Hu & Bentler, 1998). CFI values approaching 1 indicate better model fit, with .90 being the conventional cut-off for a model with adequate fit. RMSEA scores closer to 0 indicate better model fit, with .05 being a commonly accepted cut-off for a well-fitting model. The Sobel test was first used to calculate the significance of the indirect effect. However, the Sobel test assumes normality of the sampling distribution. As such, multiple mediation analyses were then conducted using the PROCESS macro developed by Hayes (2013), which uses bias-corrected nonparametric bootstrapping techniques with 5,000 bootstrap samples to estimate indirect effects. Normal sampling distribution of the indirect effects is not assumed with bootstrapping mediation tests, making it preferable to other tests of mediation (i.e., Sobel test), and it is also the recommended method for small sample sizes. (Preacher & Hayes, 2008). Point estimates for the bootstrapped indirect effect were considered significant if the 95% confidence interval did not span zero.

3.4 Results

Our hypothesized model (Figure 2) exhibited excellent fit (CFI = 1.00, RMSEA = .00). Results indicated that dispositional mindfulness was negatively associated with adiposity, but not significantly. Dispositional mindfulness was however significantly positively associated with food cue-elicited HRV ($\beta = .29$, $p = .04$) and savoring ($\beta = .51$, $p < .001$). HRV was also significantly negatively associated with adiposity ($\beta = -.38$, $p = .02$), as was savoring ($\beta = -.42$, $p = .02$). Though the direct effect between dispositional mindfulness and adiposity was not significant ($\beta = .11$, $p = .57$), these results suggested a potential inconsistent mediation of the relationship between dispositional mindfulness

and adiposity by food cue-elicited HRV and savoring. While Baron and Kenny's (1986) causal steps approach to mediation, requiring initial significance of the X → Y relationship, are commonly followed and reported, lack of significance of either c path, whether it be the total or direct effect, does not preclude the possibility of observing opposing indirect effects that obscure or suppress the significance of the X → Y relationship (Rucker, Preacher, Tormala, & Petty, 2011). Observed significant indirect effects in the absence of direct or total effects is termed inconsistent mediation, and it can be indicated when the c path of the mediation model is opposite in sign to the ab paths, which can suppress the direct effect due to opposing meditational processes (MacKinnon, Fairchild, & Fritz, 2007). Inconsistent mediation is also indicated when the direct effect is even larger than the total effect (Kenny, 2016), which was demonstrated by subsequent multiple mediation analyses (c' = .11; c = -.21). The Sobel test indicated that the indirect effect of savoring was significant (z = 2.03, SE = .25, p = .04), whereas the indirect effect of food cue-elicited HRV was not (z = 1.51, SE = .17, p = .13). However, in the bootstrapped multiple mediation model, only the bootstrapped indirect of food cue HRV was significant (B = -.34, SE = .25, CI = -1.12, -.01). In the bootstrapped model, model predictors accounted for approximately 31% of the variance in adiposity.

3.5 Discussion

Among this sample of female cancer survivors undergoing a cue-reactivity protocol, higher dispositional mindfulness was indirectly associated with reduced adiposity via enhanced capacity to savor nonfood rewards and improved autonomic regulation during attention to food cues. Participants who exhibited comparatively higher

savoring and higher HRV during exposure to emotionally salient foods may therefore be less vulnerable to increased adiposity. To our knowledge, this is the first study to examine HRV and savoring as mediators of the relationship between dispositional mindfulness and adiposity in a cancer population.

Although the current findings are preliminary in nature, they are congruent with previous research. In a recent prospective birth cohort study, dispositional mindfulness was shown to be associated with reduced adiposity (Loucks et al., 2016). Dispositional mindfulness has also been associated with increased healthy regulatory eating behaviors (Beshara, Hutchinson, & Wilson, 2013; Jordan, Wang, Donatoni, & Meier, 2014; Lattimore, Fisher, & Malinowski, 2011; Ouwens et al., 2015). Findings may be further supported by a recent large-scale cross-sectional study (N = 63,628), which also found a significant negative relationship between dispositional mindfulness and likelihood of overweight and obesity (Camilleri, Méjean, Bellisle, Hercberg, & Péneau, 2015). Further, though the present study examined dispositional mindfulness rather than the effects of a mindfulness-based intervention, mindfulness training has been shown to decrease cue-potentiated and hedonic eating (O'Reilly et al., 2014), reduce craving (Alberts, Thewissen, & Raes, 2012), and help overweight and obese participants maintain (Daubenmier et al., 2011) and reduce weight (Tapper et al., 2009; Timmerman & Brown, 2012), as well as reduce chronic stress (Daubenmier et al., 2011).

Increased savoring, as measured by the SBI, may indicate increased ability to upregulate natural reward responses to intentionally induce positive affect states. According to a restructuring reward hypothesis, mindfulness can enhance cognitive resources that enable the restructuring of reward-learning through promoting attentional

flexibility, enabling disengagement from emotional processing and automatic appetitive schemas, and facilitating reevaluation of behaviors and their conduciveness to goal states (Garland, 2016). Attentional flexibility engendered through mindfulness can also broaden attention such that novel targets for savoring can be drawn from previously unattended information, facilitating the cultivation and regulation of positive emotions (Garland, 2016). Elevated cue-elicited HRV may indicate increased parasympathetic response to emotionally salient food cues due to enhanced regulatory capacities that promote autonomic recovery from cue-exposure, which may correlate with reduced craving. Both increased HRV and savoring may therefore be accounted for by the enhanced attentional flexibility occasioned by dispositional mindfulness, which may facilitate contextually-appropriate disengagement of neurocognitive resources from automatic schemas and emotionally processing in order to free resources to instead restructure rewards and behaviors in line with goal states, thereby cultivating positive affect and meaning (Garland, 2016; Garland, Farb, et al., 2015b; Thayer, Hansen, Saus-Rose, & Johnson, 2009; Thayer & Lane, 2000, 2009), which promote healthier body composition profiles. This may be particularly important for a cancer population who endure significant distress related to unknown outcomes and may greatly benefit from both the capacity to counterbalance emotional experiences and to engage in meaning making. Further, findings indicate that dispositional mindfulness may either buffer against or promote recovery from skeletal muscle losses and increased adiposity caused by adjuvant chemotherapy (Vance et al., 2011). Current study findings are consistent with the aforementioned conceptual framework of the obesity risk chain (Thomas, 2017b), which posits that broadened metacognitive awareness and vigilant attention to

emotionally-salient cues and internal experiences, evoked by mindfulness, may enhance regulatory abilities that inhibit automatic eating habits and thereby promote healthier body compositions. Determining such malleable protective traits is crucial to the development of more effective obesity interventions.

The greatest limitation of this study is that it was cross-sectional in nature, and therefore causality cannot be determined. These findings also cannot be generalized beyond a cancer population. The number of study participants was relatively small, limiting statistical power. Further, the conceptual framework that contributed to the hypothetical basis of the tested model is based on stress-precipitated appetitive urges. While food cues can elicit appetitive urges on their own based on salience generated through conditioning and reward processes, urges can become heightened when primed by stress, but the protocol for the present study did not incorporate stress primes. Subsequent experimental research should replicate these findings in a larger sample employing longitudinal designs, and incorporate stress-primed stimulus presentation into study protocols.

Insofar as dispositional mindfulness is associated with savoring nonfood rewards and autonomic regulation during attention to food cues, participation in mindfulness-based interventions should alter these mechanistic targets. If so, HRV and savoring may prove to be key indicators of ability to self-regulate appetitive responses and maintain healthy body composition.

Table 1

Sample Characteristics

Variables	Total number	Percentage	*M* (*SD*)
Age (range = 29 – 76)	50	98	57.92 (10.04)
29 – 50	13	25	45.08 (6.20)
51 – 60	18	35	56.94 (3.19)
61 – 76	19	37	67.63 (4.43)
Overweight (BMI 25 – 29)	7	14	27.51 (1.57)
Obese (BMI ≥ 30)	26	51	36.19 (7.12)
Fat mass	29	57	113.08 (42.33)
White/Caucasian	48	96	
Black/African American	1	2	
Hispanic/Latino	1	1	
Breast Cancer	45	88	
Ovarian Cancer	2	4	
Endometrial Cancer	1	2	
Kidney Cancer	1	2	
Colon Cancer	1	2	
Multiple Myeloma	1	2	

Notes. *N* sums within variables range due to missing data.

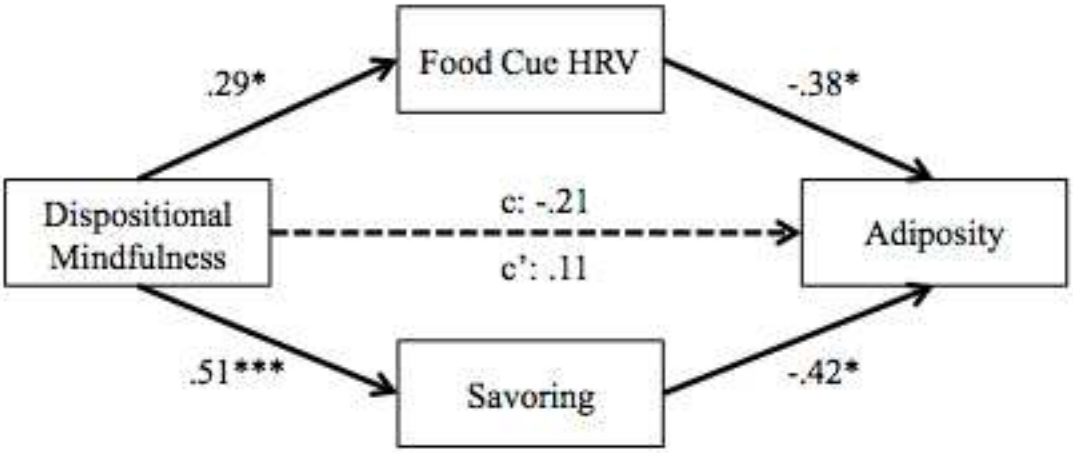

Figure 2. Results for the multiple mediation model, * $p < 0.05$, *** $p < 0.001$. For each of the mediators, the standardized path coefficients are indicated. The dotted line represents the nonsignificant direct and total effects, indicating inconsistent mediation.

4. MINDFULNESS-ORIENTED RECOVERY ENHANCEMENT RESTRUCTURES REWARD PROCESSES AND PROMOTES INTEROCEPTIVE AWARENESS IN OVERWEIGHT CANCER SURVIVORS: RESULTS FROM A STAGE 1 RCT

4.1 Abstract

In order to address the risks associated with obesity for cancer survivors, Huntsman Cancer Hospital developed a weight loss program that includes dietary counseling and exercise prescription. Similar programs have achieved modest short-term weight loss, but do not target the underlying causes of obesity, limiting the duration of treatment effects. The primary aim of this study was to assess the preliminary efficacy of Mindfulness-Oriented Recovery Enhancement (MORE), a multimodal intervention designed to target mechanisms underpinning appetitive dysregulation, as an added component to exercise and nutrition counseling. Female overweight and obese cancer survivors ($N = 51$; mean age = 57.92 ± 10.04; 88% breast cancer history; 96% white) were randomized to one of two 10-week study treatment conditions: a) exercise and nutrition counseling; or b) exercise and nutrition counseling plus the MORE intervention. Measures were administered at pre- and postintervention, as well as at 3-month follow-up. Primary outcome examined was BMI; secondary outcomes included interoceptive awareness, maladaptive eating styles, mindfulness, and savoring. Natural reward

responsiveness and food attentional bias were also evaluated. Primary analyses showed no significant differences between groups on any physical health markers, however, statistically significant changes did occur in waist circumference across the entire sample. Mixed effects linear models revealed significant time x treatment interactions on interoceptive awareness, savoring, and food attentional bias. Subsequent path analyses demonstrated that the effect of MORE on reducing food attentional bias was mediated by increased smiling during attention to natural rewards. Findings indicate that MORE may be an efficacious means of effectively enhancing responsiveness to natural rewards and reducing food attentional biases.

4.2 Objective

Obesity within the United States remains at an all-time high, and continues to increase rapidly across the world (Imes & Burke, 2014). Current population-based estimates indicate that over two-thirds of U.S. adults are overweight (Body Mass Index (BMI) $\geq 25 kg/m^2$), and that of those, 37.7% are obese (BMI $\geq 30 kg/m^2$) (Flegal et al., 2016). Excess adiposity has been identified as the greatest cause of preventable morbidity and mortality (Sniehotta, Simpson, & Greaves, 2014) due to extensive co-morbid health risks that include Type 2 diabetes, hypertension, cardiovascular disease, respiratory problems, sleep apnea, stroke, and osteoarthritis (Jensen et al., 2014; Seidell & Halberstadt, 2015). Cost of illness studies estimate that obesity incurs an estimated $147-210 billion per year in concomitant direct medical costs, representing over 20% of U.S. health care expenditures (Cawley & Meyerhoefer, 2012). Overweight and obesity are also highly associated with increased risk for the development and recurrence of some

of the most common types of cancer (including esophageal, gastric, biliary tract, colorectal, pancreatic, kidney, multiple myeloma, endometrial, ovarian and breast cancers; Jackson, Heinrich, Beeken, & Wardle, 2017; Kyrgiou et al., 2017), and have been identified as the leading cause of cancer death (Torre et al., 2015).

Among the myriad of identified risks associated with cancer development and poorer prognosis, behavioral risk factors, which include poor diet, physical inactivity, and overweight/obesity, are frequently highlighted as some of the most modifiable, and hence, often become the focus of both preventive and interventive efforts. One such weight loss program, Personal Optimism With Exercise Recovery (POWER), was developed by the Wellness Survivorship Center at the Huntsman Cancer Hospital in order to address the increased risks associated with overweight and obesity for cancer survivors. POWER incorporates dietary counseling, individualized exercise prescription, and self-monitoring. Similar programs have achieved modest short-term weight loss, but do not target the underlying mechanisms of obesity onset and maintenance, resulting in over 85% of individuals regaining weight lost or even exceeding pretreatment weight within 3 – 5 years (Kraschnewski et al., 2010; Wadden & Osei, 2004). Systematic reviews indicate that while behavioral interventions focused on physical activity and dieting components have effected statistically significant differences in weight loss compared to controls, studies averaged only -1.36 kg (3 lb) to -1.56 kg (3.44 lb) more weight loss at 12 months, which is unlikely to be clinically relevant (Booth, Prevost, Wright, & Gulliford, 2014; Dombrowski, Knittle, Avenell, Araújo-Soares, & Sniehotta, 2014). These reviews also determined that heterogeneity of studies was high, and data were insufficient to examine duration of effects beyond 24 months. Effective long-term

behavioral treatments for obesity therefore remain elusive.

Given the lack of effective noninvasive treatment alternatives, bariatric surgery has emerged as the most effective excess adiposity treatment option, although accompanying risks and lack of follow-up data beyond 5 years preclude valid inferences related to long-term outcomes (Arterburn & Fisher, 2014; Courcoulas et al., 2014). Findings from a systematic review of health-related quality of life following bariatric surgery also demonstrated that preoperative risk factors associated with excess adiposity, such as psychological factors (e.g., anxiety), personality traits (e.g., neuroticism), negative body image, and both emotional and compulsive eating behaviors, persist following surgery (Wimmelmann, Dela, & Mortensen, 2014). There is therefore a pressing need for therapeutic interventions that target the underlying maladaptive dispositional traits, and cognitive and affective mechanisms of obesity development and maintenance, rather focus primarily on symptomatic phenotypes such as weight.

Targetable mechanisms have been identified by an integrated biopsychosocial framework that proposes that the risk chain leading from stress to loss of control over eating involves cybernetic feedback circuits between stress, reward, and both bottom-up and top-down regulatory processes that interact to reinforce automatic appetitive action schema that, when suppressed, promote perseverative thinking patterns and avoidance of unwanted internal experiences (Thomas, 2017b). Highly palatable food is a potent reward that, when used as a means of avoidance of thoughts, emotions, or sensory experiences, can be become increasingly salient and overconsumed in patterns that mirror other disorders of appetitive regulation such as substance abuse (Hebebrand et al., 2014). Common mechanisms underlying the maintenance of maladaptive coping behaviors

include sensitization and attentional bias towards appetitive cues (Deluchi et al., 2017; Garland, Franken, et al., 2012; Garland & Howard, 2013; Hendrikse et al., 2015), urge suppression that may interfere with adaptive autonomic regulation of stress (Erskine & Georgiou, 2010; Garland, Carter, Ropes, & Howard, 2012), implicit cognitive schema and behavioral automaticity (Garland, Boettiger, & Howard, 2011; Moussally et al., 2015; Stice, Lawrence, Kemps, & Veling, 2016), and decreased sensitivity to natural rewards (Garland, Froeliger, & Howard, 2015a; Volkow, Wang, & Baler, 2011). To target these mechanisms, a therapeutic integration of mindfulness, reappraisal, and savoring techniques has been proposed (Garland, 2016). Specifically, mindfulness may be used to enhance attentional flexibility, interoceptive awareness, and autonomic regulation of cue-reactivity, whereas reappraisal can facilitate contextually-appropriate inhibitory control over appetitive urges. Based on the restructuring reward hypothesis (Garland, 2016), mindfulness, reappraisal, and savoring synergistically interact to disrupt the cycle of craving, distress, and automatic appetitive action schema by decreasing the valuation of appetitive stimuli, craving, and related attentional bias, as well as by amplifying natural reward processing. While previous studies have separately examined the clinical efficacy of mindfulness, cognitive reappraisal, and savoring food rewards in treating excess adiposity, to date, no previous studies have combined these three therapeutic mechanisms, including savoring of nonfood rewards, shown to be effective in the treatment of other disorders characterized by appetitive hedonic dysregulation. Dual-process models assert that such appetitive dysregulation results from both allostatic shifts in the bottom-up neural circuitry related to the salience of natural rewards, as well as impaired top-down cognitive-control processes, including the regulation of attention and

emotion (Garland, 2016). When extant interventions for excess adiposity do move beyond symptomatic expressions (excess adiposity) to target the underlying mechanisms related to homeostatic dysregulation of weight, they fail to target both top-down and bottom-up mechanisms.

The primary aim of this study was to assess the preliminary efficacy of Mindfulness-Oriented Recovery Enhancement (MORE), a multimodal intervention designed to target both top-down and bottom-up mechanisms underpinning appetitive dysregulation, as an added component to exercise and nutrition counseling. MORE is unique among extant therapies in that it unites traditional mindfulness training with cognitive reappraisal and savoring strategies designed to reverse the allostatic shift in reward salience, which may exert salutary effects on addictive behaviors and the neurobiological processes that drive them (Garland, 2016). MORE has demonstrated efficacy in disorders of appetitive dysregulation such as alcohol dependence (Garland, Gaylord, et al., 2010), opioid misuse (Garland, Froeliger, et al., 2015b), nicotine addiction (Froeliger et al., 2017), and gaming addiction (Li, Garland, et al., 2017), but has previously not been examined in obese or disordered eating samples. The primary outcome of the present study was BMI and excess adiposity. Secondary outcomes included interoceptive awareness, maladaptive eating styles, and savoring. We also examined natural reward responsiveness and food attentional bias as therapeutic mechanisms of the intervention. Specifically, based on previous studies which have shown that MORE increases autonomic and electrophysiological indices of reward responsivity among chronic pain patients misusing prescription opioids (Garland et al., 2014; Garland, Froeliger, et al., 2015b) and nicotine-dependent smokers (Froeliger et al.,

2017), we hypothesized that increases in natural reward responsiveness would mediate the effect of MORE POWER on food attentional bias.

4.3 Methods

4.3.1 Participants

Participants met study inclusion criteria if they were female, 18 and older, English speaking, had a BMI ≥ 25, and had a history of a cancer diagnosis (active or in remission). Participants were excluded if they had prior experience with mindfulness training, current participation in a regular exercise program, unstable cardiac disease, presence of a clinically unstable systemic illness judged to interfere with treatment (determined by physician evaluation), substance dependence in the past year, psychotic disorders, and less than 90 days since a surgery procedure. Participants were recruited between 2014-2015 through direct referrals from oncologists at the Huntsman Cancer Hospital and through flyers posted in the hospital. Over the course of 1.5 years, 3 iterations of intervention delivery were conducted, resulting in cohort sizes of no more than 10 participants per condition. In total, 110 participants were screened, 51 of whom met study criteria and were randomly assigned to treatment. From this pool, 38 participants began treatment, 34 completed treatment, and 30 completed postassessment measures. See Figure 3 for the CONSORT study flow diagram. Approval was obtained from the University of Utah Institutional Review Board prior to contacting potential participants and the collection of data.

4.3.2 Procedures

Following a preliminary phone screening for eligibility, potential participants were further screened in a face-to-face interview. Individuals who met eligibility criteria and agreed to participate in the study completed two separate evaluations. In the first, participants reported demographic information and completed several standardized psychosocial instruments using REDCap electronic data capture (Harris et al., 2009), as well as a dot probe task, during which psychophysiological data were collected by graduate students with a Biopac MP150 data acquisition system (Biopac Systems, Goleta, CA). Following this assessment, participants were randomly allocated to either MORE POWER or POWER alone. Random assignments were computer-generated, and the allocation list was stored in a protected file inaccessible to assessment personnel in order to ensure staff were blind to each participant's group assignment.

Participants then completed a second evaluation at the hospital, where a physician, dietician, and exercise specialist evaluated various markers of physical health. After participants completed the 10-week MORE or MORE POWER intervention, they returned to the lab to complete postintervention assessments, which included the same questionnaires, psychophysiological evaluations, and physical health evaluations administered at pretreatment. Informed consent and study procedures were conducted in compliance with the University of Utah IRB and standards set forth by the Declaration of Helsinki. Participants received no monetary compensation for their participation in the study.

4.3.2.1 MORE intervention

MORE unites complementary aspects of mindfulness training, third-wave cognitive-behavioral therapy (CBT), and principles from positive psychology into an integrative intervention strategy (Garland, 2013). MORE was originally developed to address substance abuse, but given similarities between conditions characterized by appetitive dysregulation, the MORE manual was modified for treating maladaptive eating behaviors, exercise avoidance, and excess adiposity. MORE sessions involved mindfulness training to broaden awareness, promote interoceptive awareness, target appetitive automaticity and foster nonreactivity; cognitive reappraisal training to promote affective and autonomic regulation, and engender a sense of meaning; and positive affect regulation training, which teaches savoring as a means of cultivating positive affect and ameliorating reward processing deficits. MORE is typically conducted in weekly 2 hr sessions over a period of 10 weeks, but in order to match MORE to the established POWER program, MORE was modified into 1.5 hr weekly sessions. MORE sessions were administered by Masters-level licensed clinical social workers, including the first author, who received intervention training and supervision directly from the second author, Dr. Garland, the developer of MORE. The same therapists administered MORE for all three cohorts in order to control for therapist effects. Each session was audio-recorded and reviewed by Dr. Garland to monitor therapist adherence to the modified treatment manual via a fidelity checklist that specified both prescriptive and proscriptive therapist behaviors. Deviations from manualized treatment protocol were reviewed during weekly clinical supervision meetings and corrected by the therapist in subsequent sessions. No major deviations were noted and minor deviations were observed

infrequently, particularly as adherence improved over time.

Each MORE session included formal mindfulness meditation and experiential exercises, debriefing of those exercises, homework review (mindfulness, reappraisal and savoring practice over the previous week), and weekly didactic material covering the following topics: gaining awareness of automatic habits and coping behaviors; disrupting automaticity through mindful reappraisal; refocusing attention from stressors and food cues to savor pleasant experiences derived from nonfood rewards; regulating craving through mindful attention and awareness; overcoming craving by coping with stress; promoting acceptance instead of suppression of experience in order to challenge both attachment and aversion; impermanence of the body; defusing relationship triggers; cultivating interdependence and meaning; and developing a mindful recovery plan.

4.3.2.2 POWER intervention

Both experimental and control groups received 2 exercise sessions a week directed by a physical trainer over the 10-week period, as well as 4 sessions of nutrition counseling from a certified dietician dispersed over the course of the 10 weeks. Exercise sessions were an hour long and were conducted in a group format in order to replicate social support. Based on their initial physical health assessment, exercises programs were individualized in order to accommodate various physical capacities and conducted in circuit training format. Participants were monitored throughout each session in order to ensure both safe and optimal exercise techniques. All participants also maintained daily journals recording their eating and exercise activities.

4.3.3 Measures

4.3.3.1 Body composition

Certified dieticians assessed Body Mass Index (BMI) and waist circumference. Adiposity was measured by experienced technicians using BodyMetrix BX-2000 (IntelaMetrix, Inc., Livermore, CA) 2.5 MHz, A-mode and analyzed with Body View Professional software. Recommended 3-point measurement protocol was followed, which included repeated measurements of the thigh, triceps, and abdomen by experienced technicians (Wagner, 2013). BodyMetrix ultrasound has been shown to be accurate measure of adiposity comparative to the BodPod (Life Measurement, Inc., Concord, CA: Bielemann et al., 2016) and DXA (Ripka et al., 2016).

4.3.3.2 Eating behaviors

The Dutch Eating Behavior Questionnaire (DEBQ: van Strien, Frijters, Bergers, & Defares, 1986), a 33-item instrument, was developed to measure eating styles that may contribute to excess adiposity. All items are answered on a 5-point Likert scale (1 = Never, 5 = Very often). The DEBQ includes three subscales that were used to assess restrained (α = .89 in this sample), emotional (α = .96 in this sample), and external (α = .93 in this sample) eating behavior.

4.3.3.3 Interoceptive awareness

The Multidimensional Assessment of Interoceptive Awareness (MAIA: Mehling et al., 2012) was used to measure interoceptive awareness, which relates to the conscious perception of one's internal state. The MAIA is a 32-item multidimensional instrument

that utilizes a 6-point Likert scale (0 = Never, 5 = Always) in order to assess eight constructs including noticing (α = .76 in this sample), not distracting (α = .88 in this sample) not worrying (α = .49 in this sample), attention regulation (α = .82 in this sample), emotional awareness (α = .91 in this sample), self-regulation (α = .67 in this sample), body listening (α = .90 in this sample), and trusting (α = .72 in this sample). Not worrying and self-regulation subscales demonstrated poor internal consistency in this sample.

4.3.3.4 Mindfulness

Mindfulness was assessed with the Five Facet Mindfulness Questionnaire (FFMQ: Baer et al., 2006), a 39-item instrument measured on a 5-point Likert scale (1 = Never or very rarely true, 6 = Very often or always true). This validated scale yields both a composite score (α = .92 in this sample) and five subscales that distinguish between distinct and internally consistent facets of mindfulness: observing and attending to experiences (α = .70 in this sample), describing and discriminating emotional experiences (α = .85 in this sample), acting with awareness (α = .80 in this sample), nonreactivity to inner experiences (α = .85 in this sample), and nonjudging of inner experiences (α = .89 in this sample).

4.3.3.5 Savoring

Savoring was measured with the Savoring Beliefs Inventory (SBI: Bryant, 2003), a 24-item validated scale that measures an individual's perceptions of their ability to derive pleasure from life experiences. The SBI yields both a positive scale and a negative

scale, which can be used to create a composite score (α = .93 in this sample), as well as three subscales relating to anticipating (α = .93 in this sample), savoring the present moment (α = .86 in this sample), and reminiscing (α = .92 in this sample). SBI scores are positively correlated with affect intensity, optimism, life satisfaction, and frequency of experienced happiness, and negatively correlated with hopelessness and depression.

4.3.3.6 Food attentional bias

Attentional bias towards food cues was measured through the administration of a dot probe task. This task was generated in E-Prime 2.0 (PST Inc., Pittsburgh, PA) and presented on a lab computer. During the task, which was comprised of a block of 64 trials, each trial began with a fixation cross presented for 500 ms. Participants were then presented with both food and neutral pictures selected from the International Affective Picture System (IAPS: Lang, Bradley, & Cuthbert, 2008) based on their valence and arousal ratings. Photos were matched for visual complexity, color, and figure-ground relationships and displayed side by side for either 50 or 2000 ms. Food pictures included 12 photos of highly palatable foods including pizza, hamburgers, french fries, and desserts, while the neutral photos depicted common household items. Following each trial, a target probe replaced one of the photos and was displayed for 100 ms, and participants were instructed to indicate the location of the probe on the screen with a left/right button press. The order and duration of cue presentation, as well as the left or right position of the photos and target probe on the screen, was randomized and counterbalanced within and between each participant assessment.

4.3.3.7 Reward responsiveness

Responsiveness to reward was measured with facial electromyography (EMG), using two surface 4mm Ag/AgCI shielded electrodes with signal-conductive gel that were attached to the participant's left cheek in order to detect activity in the zygomatic major muscle regions (which produce smiling expressions) using the placement recommended by Fridlund and Cacioppo (1986). Raw EMG signals were recorded continuously at a sampling rate of 1000 Hz through an EMG100C electromyogram amplifier, which interfaced with the Biopac MP150 (Biopac Systems, Goleta, CA) and Acqknowledge software to provide a detailed frequency analysis. Zygomatic activity during attention to rewards was monitored during the administration of a dot-probe task, also generated in E-Prime and structured identically to the food cue task, but using pictures of nonfood natural rewards paired with neutral pictures all selected from IAPS. Reward pictures included smiling people, babies, puppies, and beautiful scenery. Neutral pictures were also matched for visual complexity, color, content (e.g., people if reward picture contained people) and figure-ground relationships. Picture sets were displayed side by side for either 50 or 2000 ms.

4.3.4 Statistical Analyses

For food attentional bias data, trials with extreme response times (more than 3 *SD* above the individual mean) were discarded as outliers (Garland & Howard, 2014; Kemps, Tiggemann, & Hollitt, 2014; Ratcliff, 1993). Error trials were also discarded (Garland & Howard, 2014; Kemps et al., 2014; Townshend & Duka, 2007). Food attentional bias scores were calculated by subtracting their mean response time to probes replacing

palatable food images from their mean response time to probes replacing neutral images. Positive bias scores indicated an attentional bias towards visual palatable food cues. Raw EMG signals were bandpass filtered at 10-500 Hz (Tassinary, Cacioppo, & Vanman, 2007) to remove signal noise not owing to muscle activity, and analyzed using an automated routine in Acqknowledge software to derive average rectified EMG values.

Intention-to-treat (ITT) analyses were conducted on the entire randomized sample ($N = 51$). Of the 51 participants who were assessed and randomized to intervention conditions, 38 (75%) attended one or more sessions, and 34 (67% of the randomly allocated sample, 89% of those who attended one or more sessions) completed the treatments. Four participants were lost to posttreatment assessment. The majority (77%) of non-starters cited inability to meet the time commitment required by study involvement as a reason for their withdrawal from the study prior to the beginning of treatment. The remainder of the nonstarters withdrew due to unrelated medial issues that precluded their continued participation in the study. In order to assess any significant differences between participants who dropped out and those who completed the study, independent t-tests and chi-square test for independence were conducted, which revealed that there were no significant differences between completers and noncompleters across demographic and physical health variables, including age, income, education, BMI, and fat mass. Similarly, there were no significant differences in a number of clinical variables including eating behaviors, cue-reactivity, savoring, and interoceptive awareness as measured by the MAIA.

Little's MCAR test (Little, 1988) was used to analyze patterns of missing data, which demonstrated that patterns were completely random, therefore enabling maximum

likelihood estimation to be employed to handle missing data. Maximum likelihood estimation procedures include data from all cases, included those measured at only one time point (e.g., treatment noncompleters or nonstarters), reducing potential bias resulting from listwise deletion or last-observation carried forward techniques. Primary and secondary outcomes were analyzed using mixed effects linear models, treating study condition and time (baseline vs. postintervention) as fixed effects. Primary analyses modeled time as a repeated measure, subject condition, and a time x treatment interaction term.

4.4 Results

4.4.1 Participant Characteristics

Study participants were 51 adult women aged 29-76 (M = 57.92, SD = 10.04) with a mean BMI of 34.69 (SD = 7.39), and a mean fat mass of 113.08lb (SD = 42.33). Most participants were White/Caucasian (96%), with one Black/African-American and one Hispanic/Latino individual in the sample. The majority had a breast cancer diagnosis history (N =45), while six participants had histories of varying types of cancers with associated obesity risks (Azrad & Demark-Wahnefried, 2014; Carlson et al., 2012; Larsson & Wolk, 2007; Lichtman, 2010; Ma et al., 2013; Onstad et al., 2016), including ovarian (N = 2), endometrial (N = 1), kidney (N = 1), colon (N = 1), and multiple myeloma (N = 1). In the year prior to the study, 14% had a pretax household income of < $25,000, 20% earned $25,000-$49,999, 26% earned $50,000-$74,999, 12% earned $75,000-$99,999, and 28% earned $100,000 or more.

Participants in the MORE POWER condition indicated a significantly higher

comparative food attentional bias $t(46) = -2.16$, $p = .04$, and significantly lower levels of noticing (MAIA subscale; $t(46) = 2.30$, $p = .03$), as shown in Table 2. The two treatment groups did not differ on any other measured characteristics at baseline.

4.4.2 Treatment Effects

To determine the effects of the MORE POWER and control programs, mixed effects linear models analyzed primary outcomes (BMI, fat mass, WHR) on the ITT treatment sample, which indicated no time x treatment interactions on any physical health outcomes (Table 3). However, both MORE POWER and POWER conditions showed significant weight loss at 3 months follow-up (M weight loss = 9.85; $F(1,21.20) = 9.14$, $p = .006$). MORE POWER ($M_{diff} = -4.66$, $SD_{diff} = 1.18$, $d = .002$) and POWER ($M_{diff} = -4.74$ cm, $SD_{diff} = .93$, $d < .001$) condition groups also showed statistically significant decreases in waist circumference from pre- to postassessment, though the clinical significance of such change may be modest. Hazard ratios have recently been estimated to be 1.09 per 5cm increment of waist circumference (95% CI, 1.08-1.09; (Cerhan et al., 2014), which may indicate change approaching clinical significance.

Subsequent mixed effects linear models analyzed secondary outcomes on the ITT sample (Table 4) that revealed significant time x treatment interaction on MAIA subscales related to noticing ($F(1,32.82) = 7.41$, $p = .01$), attention regulation ($F(1,26.12) = 6.66$, $p = .02$), self-regulation ($F(1,8.45) = 8.15$, $p = .006$), and body listening ($F(1,31.49) = 14.78$, $p = .001$), indicating that MORE significantly increased several constructs related to interoceptive awareness to a greater extent than the control condition. There were also significant time x treatment interactions on external eating

($F(1,38.93) = 6.80$, $p = .01$) and savoring ($F(1,20.62) = 5.58$, $p = .03$), indicating that MORE resulted in larger increases in these variables over time. No other significant differences on self-report variables were noted.

With regard to effects on psychophysiological mediators, a significant time X treatment interaction was observed for smiling during attention to natural rewards, measured through zygomatic EMG ($F(1,29.56) = 5.56$, $p = .03$), indicating that MORE led to significantly greater increases in smiling to natural reward cues than the control condition. Moreover, a significant time x treatment interaction was found on food attentional bias ($F(1,28.09) = 12.21$, $p = .002$), which indicated that MORE significantly decreased attentional bias to food cues relative to the control condition.

Subsequent path analyses (Figure 4) conducted in AMOS 22.0 with Full Information Maximum Likelihood (FIML) estimation demonstrated that the effect of MORE on reducing food attentional bias (c: $\beta = -.51$, $p = .006$) was mediated by increased smiling during attention to natural rewards (zygomatic EMG; $\beta = .55$, $p = .004$), and that smiling was significantly associated with decreased food attentional bias ($\beta = -.55$, $p = .006$). After controlling for responsiveness to natural rewards, treatment was no longer a significant predictor of food attentional bias (c': $\beta = -.19$, $p = .32$). Overall model fit was excellent (CFI = 1.00), and the Sobel test indicated that the indirect effect of change in zygomatic EMG was significant ($z = -1.96$, $SE = 13.19$, $p = .04$). The PROCESS macro was then used to test the bootstrapped indirect effect without the distributional assumptions required for the Sobel test, which was significant ($B = -29.94$, $SE = 16.11$, $CI = -66.53, -5.37$). Findings are consistent with the reward-restructuring hypothesis, which proposes that increases in natural reward responsiveness would

mediate the effect of MORE POWER on food attentional bias.

4.5 Conclusion

This study examined the preliminary efficacy and feasibility of integrating a mindfulness-based intervention, MORE, into an exercise and nutrition program for overweight and obese cancer survivors. While there were no significant differences between study intervention groups related to measures of adiposity, a significant trend of reduced adiposity at 3 months follow-up and reduced waist circumference was identified across the sample, highlighting the utility and short-term effectiveness of exercise and nutrition counseling and self-monitoring skills. While BMI reflects a composite of both lean mass and adipose tissue, waist circumference reflects levels of visceral fat that can release inflammatory markers, insulin-like growth factors (IGF), and adipokines (Phillips & Prins, 2008), which may promote cancer development (Chen et al., 2016; Key, Appleby, Reeves, & Roddam, 2010; Khan, Shukla, Sinha, & Meeran, 2013; Rose, Gracheck, & Vona-Davis, 2015). Recent findings from a meta-analysis of prospective studies examined dose-response relationships between adiposity markers and cancer risk indicate that, independent of general obesity, waist circumference is associated with both pre- and postmenopausal cancer, while waist-to-hip ratio is not (Chen et al., 2016).

Though participation in both study interventions was associated with potential clinical benefits, study results indicate that MORE significantly improved markers related to underlying mechanisms that have previously been associated with appetitive dysregulation and obesity maintentenance, such as attentional bias towards food cues (Deluchi et al., 2017; Hendrikse et al., 2015) and related external eating behaviors

(Elfhag & Morey, 2008). While previous studies of MORE have demonstrated reductions in attentional biases, the present study provides preliminary evidence that MORE may indeed modify associative learning mechanisms through strengthening cognitive-control functions and promoting revaluation of rewards in line with goal states. Changes in attentional bias were mediated by responsiveness to visual images of natural rewards, meaning that those who smiled more also experienced greater reductions in food attentional bias. It should be noted that smiling responses were measured at 50 ms, which is generally considered to be preconscious, indicating that MORE participants responsiveness was likely due to structural changes in reward processing systems. MORE also induced improvements in interoceptive awareness, which may promote resilience to overeating in the face of ubiquitous encounters with appetitive cues in the obesogenic socioenvironment (Ferriday & Brunstrom, 2011; Herbert & Pollatos, 2014). As participants in the MORE condition also reported fewer external eating behaviors, study findings further support the restructuring reward hypothesis in that automatic appetitive action schema may have been disrupted through decreasing the valuation of appetitive stimuli, craving, and related attentional bias, as well as by amplifying natural reward processing.

Study results are also congruent with the Mindfulness-to-Meaning Theory. Zygomatic EMG and attentional bias findings from this sample indicated that MORE may promote regulatory abilities to cultivate positive affect by disengaging attention from appetitive cues and thereby freeing cognitive resources to attend to novel targets from which to draw meaning and pleasure (Garland, Farb, et al., 2015b). While the Mindfulness-to-Meaning theory supports the therapeutic approach of MORE, no previous

studies have demonstrated that MORE can enhance reward responsiveness as indicated by facial EMG. The present study findings are significant given the ongoing struggle within the field of contemplative science to reconcile the concept of value tied to Western notions of hedonic and eudaimonic well-being with traditional interpretations of complete acceptance within Buddhist teachings that proscribe both attachment and aversion. Study findings support the Mindfulness-to-Meaning Theory by demonstrating that mindfulness and valuation are not necessarily opposing cognitive processes, but that mindfulness may facilitate more adaptive valuation processes through freeing cognitive resources to proactively regulate attention and emotion. Together, mindfulness and cognitive reappraisal skills may disrupt automatized behavioral repertoires by increasing interoceptive awareness and reducing reactivity to appetitive cues. Further, savoring strategies taught in MORE may enhance responsiveness to natural rewards, thereby reversing the downward shift in natural reward salience characteristic of disorders of appetitive dysregulation (Garland, 2016; Garland, Farb, et al., 2015b).

The primary limitation of the present study was the lack of follow-up data across all variables, which precludes an understanding of the duration of treatment effects. Study findings also cannot be generalized beyond a female cancer population. Measuring adiposity in cancer survivors is also challenging due to the potential detrimental effects that adjuvant therapies including surgery, radiation, chemotherapy, and hormone modulation have on fatigue, reduced mobility, loss of lean muscle mass, increased adiposity (Mullin, Cheskin, & Matarese, 2014). Treatment history was not recording in this study. Future studies should control for individual differences in cancer and cancer treatment due to their potential to confound accurate measures of adiposity.

Sample size was also relatively small, limiting statistical power. There were a significant number of attriters and nonstarters in the study, which may be due in part to the unstable health of recent cancer survivors. Further, the conceptual framework that contributed to the hypothetical basis of this study is based on stress-precipitated appetitive urges, which was not incorporated into the present study. In an effort to limit the length of assessment protocols to make recruitment less difficult, certain measures and cognitive task blocks such as stress primes were not included. Subsequent experimental research should replicate these findings in a larger sample employing longitudinal designs, and incorporate stress-primed stimulus presentation into study protocols.

In conclusion, study results indicate that MORE may be an efficacious means of effectively enhancing interoceptive awareness, savoring, and responsiveness to natural rewards, as well as a means of reducing food attentional biases and maladaptive eating behaviors. Whether changes in these mechanisms are necessary or sufficient for clinically-significant weight loss in this population is as yet unknown. Study outcomes appear tied to key therapeutic mechanisms of MORE, including broadened awareness and disengagement from automatic schemas, and reorienting attention towards interoceptive data and natural reward targets. Findings from this early stage pilot RCT demonstrate preliminary feasibility of integrating MORE into an exercise and nutrition program for overweight and obese cancer survivors, and suggest that the intervention may target appetitive dysregulatory mechanisms integral to loss of control over eating and related excess adiposity, which may thereby reduce cancer morbidity and mortality.

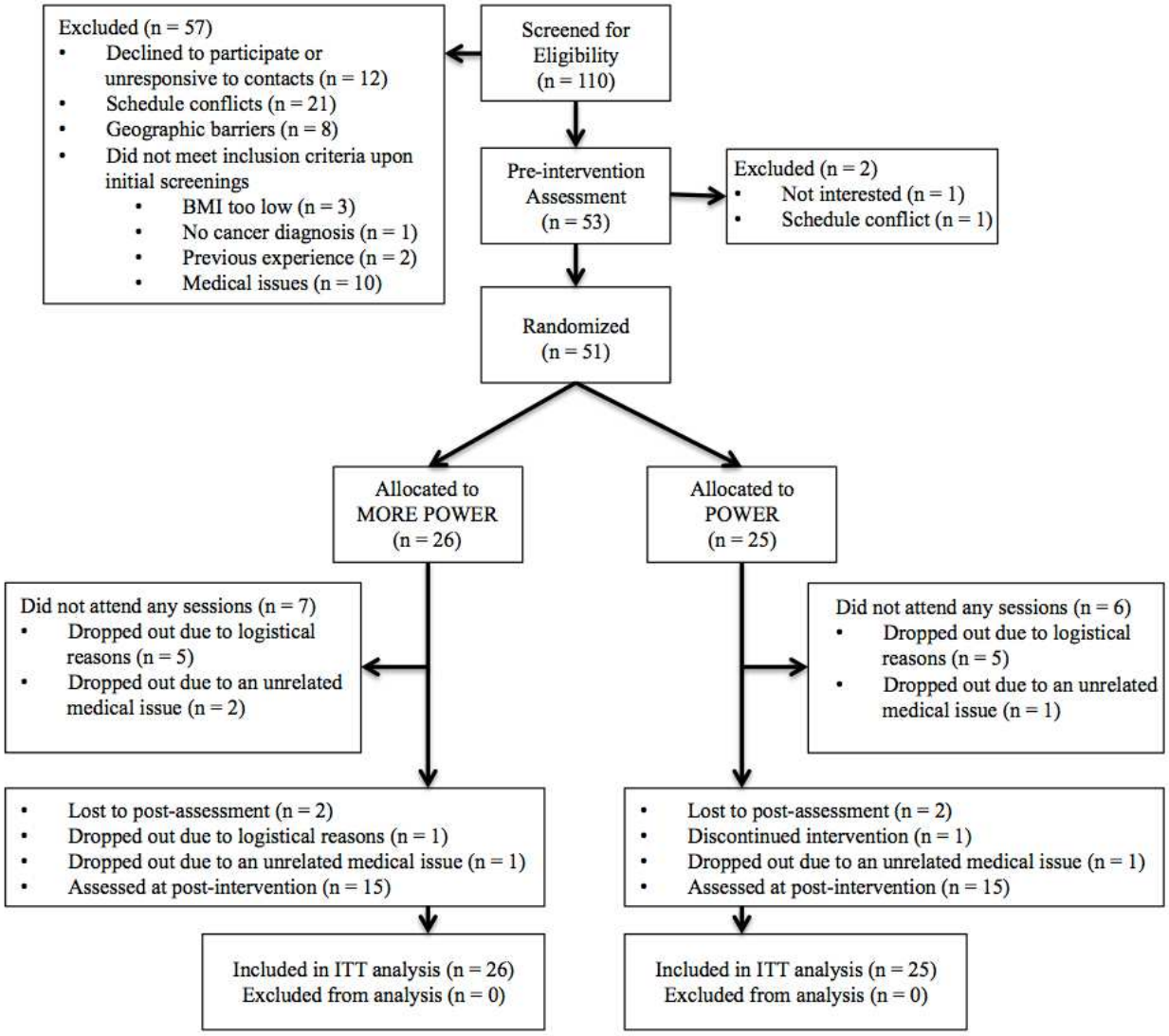

Figure 3. Flow diagram of the progress through the study.

Table 2

Baseline Characteristics of Participants

Characteristic	MORE POWER	POWER	Difference Statistic
Age [*M*(*SD*)]	59.83(9.65)	56.04(9.65)	$t(46) = -1.36$, $p = .18$
Education			$\chi^2(8) = 6.64$, $p = .58$
Income			$\chi^2(7) = 1.74$, $p = .97$
BMI	35.29(9.10)	34.25(6.12)	$t(35) = -.38$, $p = .71$
Waist Circumference	104.27(16.54)	107.42(13.68)	$t(32) = .61$, $p = .55$
Food AB	13.11(33.76)	-6.48(29.18)	$t(46) = -2.16$, $p = .04$
Savoring	129.91(22.19)	130.56(11.82)	$t(46) = .12$, $p = .91$
Mindfulness	123.30(16.00)	122.24(18.44)	$t(46) = -.21$, $p = .83$
Noticing	2.53(1.02)	3.14(.80)	$t(46) = 2.30$, $p = .03$
Not Distracting	2.25(1.29)	2.32(1.03)	$t(46) = .22$, $p = .83$
Not Worrying	2.83(.95)	2.75(.90)	$t(46) = -.30$, $p = .77$
Attention Regulation	2.22(.82)	2.37(1.14)	$t(46) = .51$, $p = .61$
Emotion Awareness	3.20(1.09)	3.07(1.03)	$t(46) = -.19$, $p = .68$
Self Regulation	2.20(.77)	2.49(1.07)	$t(46) = 1.09$, $p = .28$
Body Listening	1.58(1.14)	1.75(1.06)	$t(46) = .53$, $p = .60$
Trust	2,16(.94)	2.23(.83)	$t(46) = .26$, $p = .79$
Restrained Eating	30.00(6.77)	30.40(4.81)	$t(46) = .24$, $p = .81$
Emotional Eating	41.83(12.86)	41.44(11.31)	$t(46) = -.11$, $p = .91$
External Eating	32.52(8.31)	31.92(6.20)	$t(46) = -.29$, $p = .78$

Notes. Condition columns indicate *M*(*SD*).

Table 3

Time and Time x Treatment Interactions

Variable	Time	Time x Treatment Interaction
Weight (3 Month Follow-Up)	$F(1,21.20) = 9.14$, $p = .006$	$F(1,21.20) = .317$, $p = .579$
Waist Circumference	$F(1,24.45) = 29.61$, $p < .001$	$F(1,24.45) = .002$, $p = .97$
Savoring	$F(1,20.62) = 3.20$, $p = .09$	$F(1,20.62) = 5.58$, $p = .03$
Noticing	$F(1,32.82) = 1.00$, $p = .32$	$F(1,32.82) = 7.41$, $p = .01$
Not Distracting	$F(1,23.49) = .24$, $p = .63$	$F(1,23.49) = .73$, $p = .40$
Not Worrying	$F(1,22.84) = 2.71$, $p = .11$	$F(1,22.84) = 1.39$, $p = .25$
Attention Regulation	$F(1,26.12) = 11.45$, $p = .01$	$F(1,26.12) = 6.66$, $p = .02$
Emotional Awareness	$F(1,37) = 3.84$, $p = .06$	$F(1,37) = 3.08$, $p = .09$
Self-Regulation	$F(1,35.02) = 21.40$, $p < .001$	$F(1,8.45) = 8.15$, $p = .006$
Body Listening	$F(1,31.49) = 17.81$, $p < .001$	$F(1,31.49) = 14.78$, $p = .001$
Trust	$F(1,26.87) = 26.56$, $p < .001$	$F(1,26.87) = 2.06$, $p = .16$
Restrained Eating	$F(1,27.04) = 7.61$, $p = .003$	$F(1,27.04) = .09$, $p = .76$
Emotional Eating	$F(1,22.79) = 3.89$, $p = .06$	$F(1,22.79) = 3.10$, $p = .09$
External Eating	$F(1,38.93) = 11.82$, $p = .001$	$F(1,38.93) = 6.80$, $p = .01$

Notes. All variables were measured at postintervention unless otherwise noted.

Table 4

Primary and Secondary Outcomes as a Function of Treatment and Time of Measurement: Intention-to-Treat Analysis (N = 51)

	MORE POWER			POWER		
Outcome	Pre	Post	*ES*	Pre	Post	*ES*
Weight (3 Mo)***	205.13(34.80)	189.50(28.63)	0.5	212.35(37.97)	202.60(41.28)	0.2
Waist***	102.32(12.87)	100.75(15.78)	0.1	107.42(13.68)	104.27(16.54)	0.2
Savoring*	19.64(2.80)	21.40(2.46)	0.7*	19.08(3.75)	18.39(5.19)	-0.2
Mindfulness***	128.93(16.00)	137.20(11.57)	0.6	122.24(18.44)	123.30(16.00)	0.1
Noticing	2.75(0.92)	3.35(1.40)	0.5*	3.14(0.80)	2.53(1.02)	0.7
Not Distracting	2.24(0.79)	2.37(0.97)	0.2	2.32(1.03)	2.25(1.29)	-0.1
Not Worrying	3.31(0.97)	2.93(0.68)	0.5	2.75(0.90)	2.83(0.95)	0.1
Attention Reg*	2.50(1.05)	3.31(0.75)	0.9*	2.37(1.14)	2.22(0.82)	-0.2
Emotional Aware	3.14(0.95)	3.90(0.57)	1.0	3.13(1.08)	3.26(1.14)	0.2
Self-Regulation***	2.86(1.16)	3.95(0.79)	1.2**	2.49(1.07)	2.20(0.77)	-0.3
Body Listening***	1.88(1.42)	3.53(0.72)	1.5***	1.75(1.06)	1.58(1.14)	-0.2
Trust***	2.74(1.12)	3.50(0.86)	0.8	2.23(0.83)	2.16(0.94)	-0.1
Restrained	34.93(5.46	34.50(5.84)	-0.1	30.40(4.81)	30.00(6.77)	0.1
Emotional	41.21(12.48	34.60(5.66)	0.7	41.44(11.31)	41.83(12.86)	0.0
External**	32.07(4.67)	26.50(4.09)	1.3*	31.92(6.20)	32.52(8.31)	0.1

Notes. All variables were measured at postintervention unless otherwise noted. Data are given as mean (*SD*). *ES* = within-group effect size (Cohen's D). Significance next to outcome variables indicates significant interactions. *$p < .05$, **$p < .01$, ***$p < .001$.

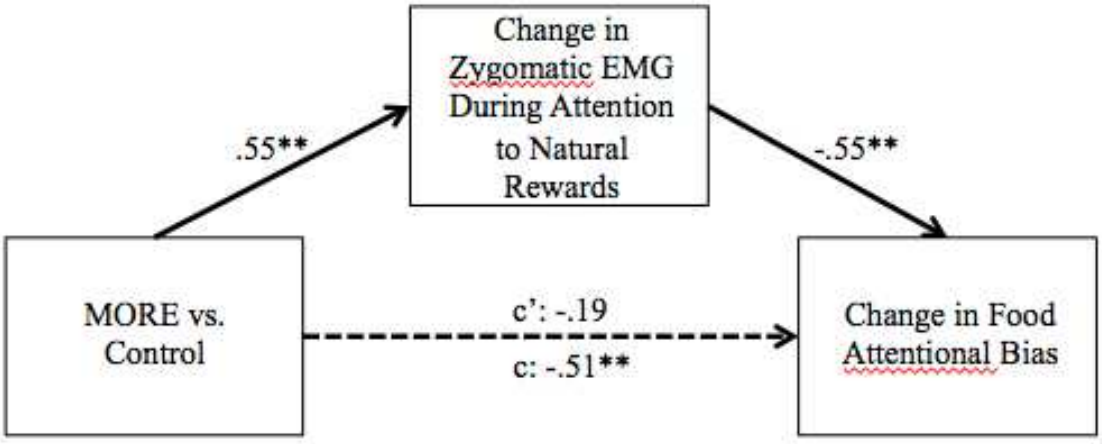

Figure 4. Path analysis results showing that change in zygomatic EMG mediates the time x treatment interaction on food attentional bias. Numbers represent standardized beta coefficients. ** $p < .01$.

5. CONCLUSION

The biopsychosocial conceptual framework that was elucidated within the first paper integrates features from a number of prominent theoretical models of appetitive behavior, self-regulation, and stress that have elsewhere been applied to obesity but have underdeveloped treatment implications. It identifies key biobehavioral mechanisms underlying obesity onset and maintenance that may be overlooked or potentially even exacerbated by traditional weight loss approaches, yet remain tractable to psychosocial interventions. These malleable mechanisms include implicit cognitive schemas, attentional bias, cue reactivity, distress intolerance, appetitive automaticity, and heightened food reward salience paired with unresponsivity to natural rewards. Within a context of obesogenic environments, individuals with low dispositional mindfulness may seek out powerful food rewards impulsively and automatically, and when eating is used as a means of distress relief (even if the stressor is the absence of conditioned food rewards), stressful environments can drive compulsive eating behaviors that can become addictive in nature, particularly when tolerance for distress is low. Compulsive eating patterns lead to an overactivation of reward systems, wherein desires for food rewards are heightened and pleasure experienced from obtaining those and other natural rewards is reduced. Such reward dysregulation is driven by a self-perpetuating cycle of palliative coping that simultaneously increases sensitivity to stress. Countering this cycle requires more that treating its effects (i.e., weight), it requires skills that may be built through

therapeutic mechanisms such as mindfulness, reappraisal, and savoring.

In order to examine the role of these mechanisms in contributing to excess adiposity, a study was conducted utilizing a cue-reactivity protocol. This study tested one hypothetical pathway from the biopsychosocial framework described above; namely, the hypothesis that savoring of nonfood rewards and autonomic regulation during attention to food cues would mediate the relationship between dispositional mindfulness and adiposity. Findings from this study supported the hypothesized model. This study demonstrated that dispostional mindfulness, a malleable trait, may promote the ability to flexibility regulate attention and emotion by enhancing broadened awareness, the capacity to decenter from internal experiences, and thereby strengthening the ability to disengage from automatic appetitive action schema. Once cognitive resources are freed, attention can be shifted towards reappraising the value of food rewards, as well as the comparative value and meaning of nonfood rewards, which can further regulate appetitive reactivity to food cues. Such mindful steps back from experiences therefore provide space to facilitate intentional steps forward in line with goal states, which may in turn promote healthier body compositions.

Therapeutic mechanisms proposed in the biopsychosocial conceptual framework to target the key mechanisms implicated in appetitive dysregulation and excess adiposity, including mindfulness training, cognitive reappraisal, and savoring skills, have been previously shown to be an effective means of targeting underlying attentional bias, cue reactivity, implicit stress appraisals, and reward processing deficits associated with other appetitive disorders. Hence, MORE, a mindfulness-based intervention that incorporates mindfulness training, cognitive reappraisal, and positive affect regulation through

savoring, was tested in a pilot RCT among a sample of overweight and obese female cancer survivors. Findings from this study revealed that MORE may be an efficacious means of effectively enhancing interoceptive awareness, savoring, and responsiveness to natural rewards, as well as a means of reducing food attentional biases and maladaptive eating behaviors. Study outcomes appeared tied to the key therapeutic mechanisms of MORE, including broadened awareness and disengagement from automatic schemas, and reorienting attention towards interoceptive data and natural reward targets. While MORE did not improve weight loss comparative to exercise and nutrition counseling alone, findings indicate that there may be unique and added value in targeting underlying mechanisms that may counter the cycle of obesity onset and maintenance. This study provides preliminary support for the restructuring reward hypothesis and indicates that MORE may indeed induce structural modifications of reward processing systems such that food rewards become less salient, thereby reducing attentional biases, while nonfood rewards become more salient through revaluation processes and the generation of positive emotions through savoring. Participants in the MORE condition also reported fewer external eating behaviors, demonstrating that enhancements in reward responsiveness and cognitive control may also disrupt automatic appetitive action schema, thereby enabling actions in line with goal states. Although findings from this study are preliminary and limited to female cancer survivor populations, they warrant further investigation in larger and more varied samples, as well as in studies that employ longitudinal designs in order to examine the duration of treatment effects.

Social workers, ingrained in the biopsychosocial model, are aptly emplaced to intervene among groups disproportionately affected by obesity. They are also uniquely

equipped with a strengths-based perspective conducive to the application of positive psychology principles. Hence, social workers are well-suited to lead the turn away from prevailing energy balanced based treatments for obesity towards the next generation of more nonreductive, holistic, and mechanistically driven interventions for obesity.

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