CHAPTER 17

BIOLOGY OF APPETITE, WEIGHT, AND OVEREATING: METABOLIC, PSYCHOLOGICAL, AND BEHAVIORAL INFLUENCES AND CLINICAL DIRECTIONS

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Eating behaviors, appetite, weight regulation, and chronic diseases are multiply determined and highly intertwined (see Figure 17.1). Eating and weight are driven by both physiological processes and psychological processes. Interventions that target weight reduction are largely ineffective in the long term because they fail to target dysregulated eating behavior that may be the underlying source of weight gain. Eating behavior can be classified into one of two primary categories: *homeostatic eating*, defined as what is required to meet basic energy needs for survival and is rooted in evolutionary hormonal-biochemical survival mechanisms (e.g., motivation to eat when energy stores are depleted); or *nonhomeostatic eating*, defined as eating for reasons other than energy needs, including hedonic eating (i.e., for pleasure, sensory perception, or stress reduction), overeating, compulsive overeating (e.g., sense of loss of control while eating), and binge eating.

The first part of this chapter explores traditional homeostatic mechanisms of eating behavior and appetite. Often, in spite of abundant energy stores to ensure survival, nonhomeostatic eating drives override these homeostatic negative feedback mechanisms (Lutter & Nestler, 2009; Rossi & Stuber, 2018). In fact, hedonic eating drive is very common and a primary contributor to excess adiposity and metabolic dysregulation. Thus the second part of this chapter focuses on characteristics of nonhomeostatic eating, in particular hedonic eating, and those found in binge eating disorder, as well as factors that hijack homeostatic eating behavior, including stress (acute and chronic) and emotional regulation, food types (e.g., processed foods), and health behaviors (e.g., sleep and exercise). We emphasize the importance of psychological processes in understanding eating behaviors.

Finally, given that hedonic eating may be a modifiable target that affects weight and metabolic health, we end with a review of established and emerging treatments of excessive hedonic drive. We conclude with a discussion of ways to rewire the hijacked mechanisms of eating, appetite, and weight through behavioral, medical, and pharmaceutical interventions, emphasizing the implications for clinical and health psychologists.

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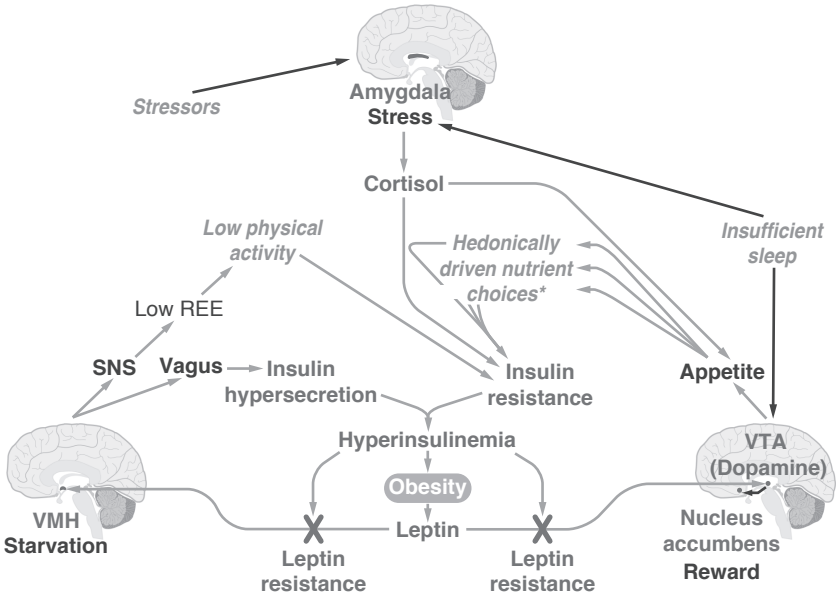

FIGURE 17.1. The Limbic triangle. Adapted, with permission of Annual Reviews, from Mietus-Snyder, M. L. & Lustig, R. H. (2008). Childhood obesity: Adrift in the "limbic triangle." *Annual Review of Medicine*, *59*(1), 147–162; permission conveyed through Copyright Clearance Center, Inc. *Note:* Three areas of the CNS conspire to drive food intake and reduce physical activity, resulting in persistent weight gain. The ventromedial hypothalamus (VMH) transduces the leptin signal from adipocytes to reduce energy intake and increase energy expenditure; however, hyperinsulinemia prevents leptin signaling, promoting the "starvation response." The ventral tegmental area (VTA) transduces the leptin signal to reduce dopamine neurotransmission to the nucleus accumbens (NA), reducing food intake; however, hyperinsulinemia prevents leptin signaling here as well, increasing dopamine and promoting the "reward" of food. The amygdala transduces fear and stress, which results in increased cortisol release from the adrenal cortex. The elevated cortisol also drives energy-rich food intake and promotes insulin resistance, further interfering with leptin signaling at the other two CNS sites. Thus, activation of any aspect of the limbic triangle turns on a positive feedback loop, promoting continued weight gain and obesity. REE, resting energy expenditure; SNS, sympathetic nervous system. Lifestyle choices, or external modifiers of eating, reward, and stress pathways are indicated in orange (sleep, stressors, nutrient choices, and physical activity). *Processed food, including food high in fructose, fat, and carbohydrates.

FOUNDATIONS OF THE BIOLOGY OF WEIGHT

Here we review the basic biological mechanisms that help us understand how eating and weight are controlled by complex, interacting processes.

Homeostatic Mechanisms

Appetite and eating behaviors are regulated by the three arms of the energy balance system. The first is the afferent arm, which sends signals of hunger and metabolism from the body, via hormonal and neural inputs, to the hypothalamus, which helps regulate hunger and satiety. Second are the brain systems within the hypothalamus, such as the ventromedial hypothalamus, arcuate nuclei, and other regions that regulate signals for changes in eating and energy expenditure. Third is the network of autonomic effectors that drive appetite and activity (Morton et al., 2006). Disruptions in these overlapping pathways (Figure 17.1) can alter energy intake versus

expenditure and contribute to obesity (Weiss & Lustig, 2014).

The afferent arm regulates hunger and satiety through a few key neural pathways. The vagus nerve is the largest nerve in the body, and the afferent vagus sends energy balance signals related to feelings of fullness that originate from the gut (Hellström et al., 2004). Ghrelin, an amino acid peptide, is released during fasting and decreases on nutrient intake. Ghrelin binds to the growth hormone secretagogue receptor in the arcuate nucleus to increase feelings of hunger and to drive both food intake and fat deposition (Kamegai et al., 2000). It also increases the respiratory quotient to reduce fat oxidation and promote fat deposition. Several peptides are implicated in feelings of satiety. Peptide YY_{3-36} sends hormonal signals that control meal volume and is secreted from exposure to nutrients in the distal ileum. Glucagon-like peptide-1 inhibits gastric emptying, prolongs the time of meal absorption, and has specific hypothalamic effects which reduces appetite. Cholecystokinin is released in response to caloric intake and promotes satiety. Leptin is a peptide hormone that is released from fat cells, reaches the hypothalamus, and signals long-term energy sufficiency, thus reducing appetite and increasing energy utilization. Insulin is a peptide hormone released by pancreatic beta-cells that induces acute feelings of satiety. Neurotransmitters in the brain and gut may play a role in regulating appetite and energy balance. Endocannabinoids within the brain stimulate food intake, whereas signals from the gut such as serotonin travel retrograde via the afferent vagus nerve to promote feelings of satiety.

The sympathetic nervous system (SNS), which is responsible for controlling the body's heart rate and blood pressure, increases energy expenditure by increasing thyroid hormone release, innervating skeletal muscles, and stimulating β_3-adrenergic receptors in adipose tissue to promote lipolysis (the metabolic process of breaking down fats into glycerol and fatty acids). SNS activation promotes fatty acid and glucose oxidation, and increases protein synthesis. By contrast, the efferent vagus promotes energy storage by slowing heart rate and reducing myocardial oxygen consumption, promoting energy substrate absorption, increasing insulin sensitivity to increase energy conversion to adipose tissue, and increasing post-meal insulin secretion which promotes energy deposits to adipose tissue.

Hedonic Mechanisms

Hedonic eating (one important form of non-homeostatic eating) is defined as eating for pleasure or stress, thus distinguished from forms of homeostatic eating (i.e., eating in response to physiological hunger cues). Hedonic eating is common (Hill & Heaton-Brown, 1994) among adults with a higher body mass index (BMI; Delahanty et al., 2002) and among those attempting to lose weight (Massey & Hill, 2012). Virtually everyone at some time participates in eating due to hedonic pleasure or stress, or both. Hedonic eating is characterized by the consumption, and especially overconsumption, of highly palatable and energy-dense foods. Many such foods are engineered by the food industry for their palatability, that is, the "bliss point" (Moss, 2013). Such foods increase the release of the neurotransmitter dopamine (the "feel good" neurotransmitter) in the nucleus accumbens, the region of the basal forebrain implicated in eating, reward, and stress-related behaviors, and frequently referred to as the "pleasure center" of the brain (Baik, 2013). Hedonic eating is believed to be driven by the activation of this pleasure-related, dopamine signaling pathway from the ventral tegmental area (VTA) to the nucleus accumbens, with additional inputs from components of the limbic system (e.g., amygdala, hypothalamus, hippocampus, prefrontal cortex; see Figure 17.1). Eating behavior increases based on palatability, more than energy need (homeostatic drive). This pathway responds similarly to drugs of abuse (e.g., nicotine), promoting greater derived pleasure and reward from substances and motivation for obtaining these substances.

When the nucleus accumbens receives appropriate negative feedback from the prefrontal

cortex, food intake is negatively regulated. Indeed, this pathway mediates feelings of fullness when energy stores are replete. However, in the face of increased stress, which reduces prefrontal cortical inhibition, alterations in this reward pathway within the brain (likely through the increased consumption of highly palatable, ultra-processed foods) may promote excess weight gain and obesity due to a strong activation of hedonic eating behavior. Many are susceptible to hedonic eating behavior through the chronic exposure to highly palatable, ultra-processed foods that are ever present in our modern food environment. Women with (vs. without) obesity have increased activation of several limbic areas when presented with pictures of highly palatable foods (Lutter & Nestler, 2009), suggesting a greater reward value of highly palatable foods among those caught in a cycle of hedonic eating. Furthermore, leptin and insulin play a large role in the activation of these reward pathways, particularly after food deprivation (e.g., rigid diets; Hommel et al., 2006). The VTA has receptors for both insulin and leptin, and both of these hormones normally tamp down the rewarding properties of substances (e.g., processed foods) when the brain is insulin and leptin sensitive (Shalev et al., 2001). However, when insulin and leptin signaling are attenuated (as in both starvation and obesity), hedonic eating is unrestrained. These physiological processes likely explain why restrictive dieting and subsequent weight loss can be followed by rapid weight gain, as food quite literally becomes more rewarding and pleasurable when in a "brain-starved" state.

Hedonic drive leads to overeating of highly palatable foods and ultimately weight gain and obesity for many adults (Rossi & Stuber, 2018). Obesity (defined by a BMI ≥ 30 kg/m^2) remains a public health crisis, with rates steadily rising (Flegal et al., 1998; Kuczmarski et al., 1994). In 2017, 42.4% of U.S. adults were obese (CDC, 2021). This rate is alarming, given the well-established increased risk for heart disease, respiratory problems, hormonal dysfunction, and osteoarthritis (Bray, 2003). Obesity is associated with the metabolic syndrome, which increases risk for heart disease, Type 2 diabetes, certain cancers, liver disease, and dementia (Zimmet et al., 2007).

FACTORS THAT OVERRIDE HOMEOSTATIC MECHANISMS

Understanding the basic biology of eating behavior, appetite, and weight regulation is important for understanding how these systems are overridden (or "hijacked") in the modern, obesogenic environment. In this section, we review the primary factors implicated in distorting these homeostatic systems, namely, stress (acute and chronic), negative affect, exposure to highly and ultra-processed foods, and disruptions in circadian rhythms, such as with sleep. We highlight disordered eating patterns, particularly binge eating, that result from overriding homeostatic mechanisms of appetite and weight regulation.

Although genetics play a strong role in the biology of appetite and weight, genetics within our society have not changed in the last fifty years. However, our environment has shifted dramatically over this time. Genome wide association studies argue that only 15% of the variance in metabolic syndrome is explainable by genetics, the rest likely by changes in the environment (Lusis et al., 2008). These changes include but are not limited to increases in perceptions of stress, higher rates of exposure to chronic stressors, alterations in the food supply, food composition, and food availability (Figure 17.1). We review each of these in the following section.

How Stress and Emotional States Alter Appetite and Weight

Population-based data shows that chronic work stress can lead to weight loss or weight gain, weight gain being more common (Nyberg et al., 2012). The neuroendocrine bases to these changes in adiposity are now well understood. During chronic, long-lasting stress, cortisol can increase appetite by mobilizing glucose, and contributing to increased food intake. Exogenous cortisol administration increases appetite, as seen in

Cushing's disease (Starkman, 2013). Some forms of chronic stress, such as states of severe depression, can decrease appetite, as part of the anhedonia classic symptoms, and contribute to weight loss (Simmons et al., 2020).

Stress-related imbalances in hormones can lead to abdominal fat and metabolic dysregulation. Substantial evidence from clinical studies demonstrates that elevated cortisol, combined with secondary inhibition of sex steroids and growth hormone, results in the accumulation of fat in visceral adipose tissues as well as metabolic abnormalities, as seen in the metabolic syndrome (Adam & Epel, 2007; Björntorp, 2001). Furthermore, chronic stress can lead to insulin resistance, by activating the hypothalamic-pituitary-adrenal (HPA) axis, and producing higher than normal levels of cortisol, which can interfere with insulin's ability to turn glucose into usable energy for the body (Björntorp, 2001). Cortisol also acts to reduce both prefrontal cortical inhibition of the amygdala and the nucleus accumbens and to increase hedonic eating (Mietus-Snyder & Lustig, 2008). The effects of chronic stress and excess cortisol production on appetite and weight are indeed so strong that the typical pathways through the ventral tegmental area (VTA) and nucleus accumbens that mediate satiety are easily overridden. Furthermore, substantial evidence from animal and human research implicates the essential role of cortisol in the full expression of obesity, explaining why many struggle to maintain their weight when facing chronic stressors (Dallman et al., 2005).

Following acute stressors, adults tend to exhibit increases in caloric intake of comfort foods (Adam & Epel, 2007), and this stress response contributes to leptin resistance (Tomiyama et al., 2011). Chronic stress (e.g., related to caregiving) is linked to dysregulation of the HPA axis (hypoarousal), greater reward-driven eating (one form of hedonic eating), and increased waist circumference over time (Radin et al., 2019). Additionally, in humans, cortisol administration increases food intake, and in rats, corticosterone stimulates eating, particularly of high-fat food (Tataranni et al., 1996). One extreme case of this form of homeostatic dysregulation of appetite is binge-eating disorder (BED).

A Well-Studied Prototype of Hedonic Eating

Binge-eating disorder is considered a prototype of dysregulated eating and overactive hedonic drive. It is characterized by eating rapidly until feeling uncomfortably full and by marked feelings of guilt or depression with oneself (American Psychiatric Association, 2013).

Biological mechanisms and correlates. It has been proposed that binge eating represents an interplay between the dopaminergic reward centers (striatum, amygdala, VTA) and the prefrontal impulsivity-control networks (prefrontal cortex, the anterior cingulate cortex, and the insular cortex; Weiss & Lustig, 2014). BED may be the result of a transition from a reward- or goal-directed drive to consume food to an impulsive drive to consume food that involves changes in how the ventral and dorsal striatum communicate. This change may be due to the expression of two receptors for the neurotransmitter dopamine in the striatum. Eventually, this change decreases reward sensitivity (less dopamine release) and is associated with decreased inhibition of reward from the prefrontal cortex (Kessler et al., 2016).

It is well established that BED is associated with obesity and affects up to 30% of those who seek weight-loss treatment (de França et al., 2014; Ivezaj et al., 2016). Adults with (vs. without) binge eating are more likely to experience several characteristics of metabolic dysfunction (e.g., hypertension, insulin resistance, and full metabolic syndrome), which may be driven in part by their greater obesity (Abraham et al., 2014). However, even after accounting for obesity status, BED uniquely predicts the development of cardiovascular and endocrine disorders, including heart disease and Type 2 diabetes (Hudson et al., 2010). There may be independent and intersecting pathways through which compulsive overeating can promote metabolic disease, including the well-established impacts of obesity and the

less-studied effects of hedonic eating and its physiological consequences, such as episodic insulin spikes, altered circadian rhythms, and stress, with adrenergic and cortisol dysregulation, as described in the next section.

Physiological stress reactivity. Adults who report BED may differ in both endocrine and autonomic functioning from those who do not report it (Lo Sauro et al., 2008), but data have not consistently supported these associations. Abnormalities of the HPA axis among those with BED are likely due primarily to excess weight, although research has not systematically controlled for weight and fat mass. In fact, a significant limitation of much of the research in this field is a failure to examine the contributions of fat mass to cortisol reactivity, and to rely instead primarily on measures of overall BMI. Visceral fat, rather than subcutaneous fat, is strongly linked to cortisol production, above and beyond weight status. Further, hyperresponsiveness of the HPA axis, including increased cortisol response to stressors, has been observed among individuals with central obesity (Incollingo Rodriguez et al., 2015).

Behavioral and emotional correlates. Although BED is biologically driven, it is also psychologically driven. Here we discuss existing models to understand the triggers and maintenance of this extreme form of hedonic eating. Some theoretical models suggest that binge eating is a way of coping in the face of acute or chronic stress. Adam and Epel (2007) propose that prolonged psychological stress can result in chronic overactivation of the HPA axis, producing excess cortisol, which in turn contributes to visceral adiposity. Psychological stress can trigger increases in appetite, energy intake, and the occurrence of stress-induced food intake that is reflected during binge episodes. We posit that binge behaviors are maintained and reinforced by stimulating the release of opioids, which have analgesic effects. Opioids can counter the body's response to chronic stress, at least temporarily increasing the reward value of food, particularly sweets. Thus a feedback loop of stress cortisol, overeating, and pleasure is possible. Conversely, stress may have an anorectic effect for some, and this phenomenon is sometimes referred to as the stress-eating paradox. Depending on the nature and intensity of a stressor, undereating and poor appetite may ensue (Stone & Brownell, 1994).

Negative affect models of BED. Numerous affect regulation models of binge eating have been proposed and studied. It is commonly believed that binge eating is a way of coping with negative emotion. The affect regulation model of binge eating describes the importance of negative emotional experiences in triggering binge eating episodes (Heatherton & Baumeister, 1991; Telch & Agras, 1996). This model proposes that binge eating occurs during times of distress, when individuals lack the skills to adaptively cope with negative affective states. Binge eating thus becomes the primary way of coping to relieve or escape emotional pain. Binge-eating episodes induce a cognitive narrowing such that adverse emotional states and their associated attributions are minimized. As a result, binge eating functions as a temporary coping mechanism to escape emotional distress. Ecological momentary assessment research largely supports this model (Haedt-Matt & Keel, 2011; Smith et al., 2021).

In sum, BED is a well-studied prototype of excessive hedonic eating with links to acute and chronic stress, altered physiological stress response, negative affect, obesity, and dysregulated metabolic function. Understanding pathways that contribute to and maintain BED is clinically useful for establishing effective treatments to reduce hedonic eating drive and promote improved metabolic function.

How Does Nutrient Type Alter Appetite and Weight?

Apart from the effects of stress, negative affect, and binge eating (as discussed), food composition plays a vital role in appetite regulation and hedonic eating. Foods high in fat are energy dense, highly palatable, and essential for good health. However,

trans fat consumption (e.g., fried foods, commercial baked goods, and margarine) is harmful to the body and is associated with cardiovascular disease (Islam et al., 2019). Foods with a high glycemic index (e.g., bread, rice, pasta, and potatoes) increase insulin response and can lead to energy being shunted to adipose tissue. Conversely, a balanced diet high in fiber-rich foods (e.g., beans and lentils) can slow the rate of glucose absorption, which contributes to lower surges in insulin and decreased adipogenesis.

Given the strong overlap within the reward neural circuitry in the brain for both food and substances of abuse, a popular question has been whether particular foods or specific macronutrients are addictive. Processed foods (defined as foods with added fat, refined carbohydrates, or salt) have been investigated most frequently (Schulte et al., 2015). The question of whether food addiction exists and whether it can contribute to excess weight gain has been controversial, especially for those associated with the food industry (Ziauddeen et al., 2012). Animal studies suggest that high levels of sugar induce addictive-like behaviors such as bingeing, withdrawal, and cravings (Avena et al., 2008). Among humans, fast food, sugar, and caffeine are substances that satisfy the DSM-5 criteria for dependence (Garber & Lustig, 2011).

Fructose has engendered the most concern, and the most data, supporting a role of food in addiction (Lustig, 2020). Fructose fosters overconsumption, independent of energy need (Lindqvist et al., 2008) and inhibits mitochondrial β-oxidation to reduce peripheral energy expenditure (Softic et al., 2019), thus promoting weight gain. Fructose promotes hedonic eating through both direct and indirect actions on the nucleus accumbens (Banks et al., 2004; Jastreboff et al., 2013; Teff et al., 2009). A comparison of fructose and glucose demonstrates increased risk for bingeing with fructose (Rorabaugh et al., 2015) and human fMRI studies show that acute glucose and fructose administration exert effects on different sites in the brain; glucose increases activity in cortical areas, whereas fructose suppresses the signal coming from those same areas (Purnell et al., 2011). Furthermore, glucose increases blood flow within executive function regions, whereas fructose reduces blood flow within limbic system regions (Page et al., 2013). The effects of fat and sugar both separately and together (adjusting for calories) on fMRI signaling have also been assessed (Stice et al., 2013). High-fat milkshakes increase brain activity in somatosensory areas (i.e., mouthfeel), whereas sugar increases activity in gustatory regions (i.e., reward).

Regardless of their addictive properties, greater consumption of ultra-processed foods is associated with obesity status, worse cardiometabolic outcomes, such as metabolic syndrome (Poti et al., 2017) as well as prospective increases in BMI (Beslay et al., 2020).

Health Behaviors

Life behaviors such as sleep and exercise play a significant role in appetite and body weight, as described here.

Sleep and circadian rhythms. Sleep disturbance (e.g., difficulties falling asleep and/or staying asleep) has clear links to obesity, with those reporting reduced sleep duration being at higher risk for overweight and obesity (Magee & Hale, 2012). Poor sleep quality has also been consistently linked to chronic stress and greater perceptions of stress (Åkerstedt, 2006; Morin et al., 2003) as well as dysregulation of the HPA axis (Meerlo et al., 2008) including exaggerated cortisol reactivity to stressors (Balbo et al., 2010; Goodin et al., 2012). Poor sleep duration is also linked to poor metabolic health, including insulin resistance, even after controlling for BMI (Cappuccio et al., 2008); these links may potentially be explained by changes in energy consumption. Adults who experience restrictions in total sleep duration tend to consume more energy and a greater percentage of calories from energy-dense, high carbohydrate foods, even after adjusting for BMI (Markwald et al., 2013; St-Onge et al., 2011). Changes in appetite hormones may explain the association between

poor sleep and increased hedonic eating behavior, particularly decreases in leptin and increases in ghrelin (Spiegel, Leproult, et al., 2004; Spiegel, Tasali, et al., 2004). Furthermore, preliminary evidence suggests that accelerated cellular aging, as measured by telomere attrition in immune cells, may be a mediator of the sleep–disease relationship (Prather et al., 2015).

Exercise. Aerobic exercise facilitates weight control, partially through appetite regulation. However, mediators of appetite response to exercise are not fully understood (Dorling et al., 2018). Physical activity may modulate appetite control by improving the sensitivity of the satiety signaling system, by adjusting macronutrient preferences or food choices and by altering the hedonic response to food. However, individual responses to appetite following exercise are highly variable and difficult to predict (Blundell et al., 2015). Acute exercise transiently suppresses appetite and increases peptide YY_{3-36} and glucagon-like peptide-1 without stimulating compensatory behaviors in appetite in lean or overweight to obese individuals (Douglas et al., 2017). Conversely, physical inactivity is strongly linked to obesity, waist circumference, and visceral fat mass (Myers et al., 2017; Rottensteiner et al., 2016), and may be linked to altered appetite regulation, including increased hedonic drive (Beaulieu et al., 2018). Physical inactivity may amplify hedonic states and overeating indirectly through increased body fat stores. However, potential moderators of appetite control along the spectrum of physical activity remain to be fully understood.

Our review of the most well-studied hijackers of appetite regulation that promote hedonic eating (e.g., chronic stress response, binge or reward-driven eating, food types that are processed or ultra-processed, sleep disturbance, and physical inactivity) points to adaptive habitual behaviors and clinical pathways that could promote greater appetite regulation and decrease hedonic eating, potentially warding off downstream metabolic health risks such as obesity, heart disease, and Type 2 diabetes.

EXISTING TREATMENTS THAT TARGET APPETITE

Here we review existing and newly developed treatments that may have beneficial or promising impacts on appetite, eating, and metabolic outcomes.

Weight-Loss Interventions

The prevailing standard of care for problems related to weight and overeating are herein referred to collectively as behavioral weight-loss interventions. These interventions, though varied in their approach, generally incorporate diet (i.e., decreasing number of calories ingested) and exercise (i.e., increasing total number of calories expended) components, with the goal of weight loss. Weight loss can result in significant metabolic benefits, including decreased risk for heart disease and Type 2 diabetes (Curry et al., 2018). However, most adults with obesity who lose weight in a behavioral weight-loss intervention will regain lost weight within three to five years (Perri, 1998). Thus current behavioral weight-loss options for obesity fail to produce long-term, sustainable weight loss for many, if not most, adults (Dombrowski et al., 2014; Douketis et al., 2005; Norris et al., 2016).

Bariatric surgery is perhaps the most effective existing treatment for long-term reductions in weight among individuals with obesity as well as for managing obesity-related medical comorbidities such as hypertension and high cholesterol, relative to standard medical therapy (Cosentino et al., 2021). The effect of surgery on BED and appetite regulation (Zakeri & Batterham, 2018) is less studied. Although the existence of BED before surgery is not considered a contraindication for bariatric surgery and has little influence on weight loss outcomes (Kops et al., 2021), recent data indicate that the development of problems with binge eating before surgery is associated with less weight loss or more weight regain after surgery (Meany et al., 2014).

The tendency toward weight regain following nearly all weight-loss interventions highlights the inadequacy of such programs in targeting

underlying eating patterns to which many individuals return after such interventions, including nonhomeostatic or hedonic eating. Additionally, behavioral weight-loss programs may not be compatible for many people, particularly those who have failed at dieting attempts many times and those who have a tendency toward hedonic eating. Those who endorse binge eating are more likely to drop out of weight-loss programs and tend to regain weight faster following them (Yanovski et al., 1994).

Given prospective links between hedonic eating (e.g., binge eating and grazing patterns of overeating) and worsening metabolic health (Hudson et al., 2010) it would be logical to infer that decreases in nonhomeostatic eating behavior could contribute to metabolic improvements. Preliminary evidence provides some support. For instance, among adults with obesity, rapid reductions in binge eating predict greater weight loss regardless of intervention assignment (Grilo & Masheb, 2007). These preliminary findings raise the question of how interventions might be optimally tailored to target reductions in hedonic drive to promote metabolic health.

Behavioral Interventions

Behavioral interventions fall into one of two categories, psychological or mindfulness-based, which we discuss here.

Psychological interventions. Several existing psychological programs for treating binge eating disorder show established efficacy in reducing binge frequency and severity relative to control conditions. Cognitive behavior therapy (CBT) is considered a gold standard, first line of psychological treatment for BED (Yager et al., 2014) as well as for other hedonically driven eating behaviors. CBT for BED, specifically, targets relationships among thoughts, feelings, and behaviors that are associated with dysregulated eating. One behavioral therapeutic focus is to emphasize moderation in food intake (rather than the binge-restrict cycle typical of BED). Negative cognitions and self-talk about body shape and weight, low self-esteem, and negative affect are also targeted in CBT to reduce dysfunctional thought patterns that perpetuate the binge cycle. CBT may be delivered in various forms (e.g., therapist-led, and self-help). A recent meta-analysis found therapist-led CBT (but not any other type of psychological intervention) to be superior to behavioral weight-loss treatment with regard to reductions in binge eating frequency and abstinence from binge eating (Peat et al., 2017). However, behavioral weight loss such as combination diet and exercise programs may be superior to CBT with regard to reduction in weight. Dialectical behavioral therapy for BED focuses on developing skills to improve emotion regulation, distress tolerance, and interpersonal relationships; its longer-term goal is to help individuals respond more effectively and mindfully to stress and negative affect. Interpersonal psychotherapy for BED focuses on identifying and modifying the role of interpersonal functioning in maintaining hedonically driven eating. The American Psychological Association (APA) recommends a team approach with CBT as the primary form of treatment and medication as an adjunctive treatment. Although most studied psychological interventions targeting BED reduce binge frequency, they have not been found to improve metabolic function or promote weight-loss maintenance. Further, they are not particularly effective for all adults with binge eating (Brownley et al., 2016).

Mindfulness-based interventions. Mindfulness-based therapeutic approaches aim to cultivate a nonjudging awareness of experiences in the present moment and to promote adaptive self-regulation. Mindfulness-based interventions may be a promising treatment modality for hedonic eating because they can reduce perceptions of stress, lower cortisol, and improve physiological stress reactivity (Carlson et al., 2007). Further, general mindfulness interventions may contribute to reductions in the frequency and the severity of binge-eating episodes (Kristeller & Hallett, 1999). However, rigorous, randomized-controlled trials that follow individuals over the long term show only a limited effect on weight and eating (Goyal et al., 2014).

Mindfulness-based approaches that incorporate mindful eating may be a promising avenue for further targeting reductions in hedonic drive. Mindful eating aims to cultivate awareness of internal body states related to eating, such as hunger and fullness, attending to these interoceptive body cues (vs. nonhomeostatic cues to eat, such as feelings of anxiety), in an effort to make more deliberate food choices (Kristeller & Wolever, 2010). Mindful eating programs can lead to reductions in both frequency and severity of binge eating episodes among those with BED (Kristeller et al., 2014) as well as reductions in reward-based eating (Mason, Epel, Aschbacher, et al., 2016) and compulsive eating, as defined by binge-eating behavior (Radin et al., 2020). A particular advantage of mindful eating approaches is that they are not diet based, thus appealing to those who have had many unsuccessful dieting attempts. Preliminary data suggests that even though mindful eating programs may not significantly reduce weight (vs. standard behavioral weight loss), they may contribute to greater improvements in fasting blood glucose and triglyceride/HDL levels at one year (Daubenmier et al., 2016). The mechanisms underlying how and why mindful eating programs can reduce nonhomeostatic eating have not been well studied, although some data points to increases in mindful eating contributing to reductions specifically in sweet food intake (Mason, Epel, Kristeller, et al., 2016). These gaps highlight the need to explore specific mechanisms of change that could produce reductions in hedonic drive.

Pharmacological Interventions

The causes of obesity are heterogeneous, so the paucity of consistent and effective drug treatment should not be surprising: one therapy does not fit all. In addition, the roles of stress and reward in driving weight gain often complicate the physiological picture and are not particularly amenable to pharmacotherapeutic intervention.

One treatment that has found favor is metformin, which acts to increase AMP (adenosine monophosphate-activated protein) kinase and inhibits target of rapamycin complex-1 to improve hepatic insulin sensitivity (Howell et al., 2017), reducing hyperinsulinemia and attenuating peripheral energy deposition (Seifarth et al., 2013). Other medications that reduce hyperinsulinemia, such as semaglutide, may be beneficial in suppressing appetite and inducing weight loss (O'Neil et al., 2018). Attempts to inhibit cortisol or the stress response have not been successful in promoting weight loss, or have induced significant side effects. Antidepressants have a checkered track record at reducing weight; in fact, the majority have been shown to increase weight (Serretti & Mandelli, 2010). One promising avenue was dashed with the endocannabinoid antagonist rimonabant, which resulted in significant weight loss but accompanying severe depression, and in some cases suicide (Curioni & André, 2006).

Binge eating presents its own challenges. The central nervous system stimulant lisdexamphetamine became the first and only drug approved by the FDA for the treatment of BED in 2015. Drugs of this class (CNS stimulants) are generally used to enhance mental and physical processes (e.g., as in the treatment of attention deficit–hyperactivity disorder) and are widely effective for reducing symptoms of impulsivity, inattention, and hyperactivity. In a recent meta-analysis, lisdexamphetamine was better at increasing abstinence from binge eating than second-generation antidepressants such as fluoxetine and escitalopram (Peat et al., 2017). Lisdexamphetamine, alone or in combination with behavioral interventions such as CBT, promotes clinically meaningful reductions in binge eating frequency in the short term as well as reductions in compulsive and obsessive behaviors related to BED (Brownley et al., 2016; McElroy et al., 2015). It may also be effective in reducing weight among adults with BED, whereas antidepressants used to treat BED fail to have substantial weight-loss effects (McElroy et al., 2012). The mechanism by which lisdexamphetamine works to reduce both binge eating and weight remains unclear, but preliminary data suggests that it may be through reduction in overall food intake and combination actions on appetite

and satiety, reward, and attentional processes (Schneider et al., 2021).

EMERGING METHODS THAT SHOW PROMISE IN TARGETING HEDONIC EATING

Many innovative treatments on the horizon directly target aspects of hedonic eating. We highlight some promising strategies that involve cognitive and physiological strategies, such as modulating attention to palatable foods, inducing a future time perspective, becoming aware of glucose excursions using continuous glucose monitoring, and direct biological manipulation of metabolic balance (time-restricted eating).

Attentional Bias Modification Training

Attentional bias is defined by differential allocation of one's attention to particular stimuli. Those with binge eating tendencies show an attentional bias toward food-specific as well as threat-related cues (Boutelle et al., 2020; Stojek et al., 2018). Across a variety of cognitive tasks, food and threat-related cues tend to capture attention of those with (vs. without) binge eating faster, and those with binge eating spend more time attending to palatable foods, suggesting difficulties with attentional disengagement. Such a tendency may reflect the powerful reward responses and decreased inhibitory control when processing food cues, among those with a tendency to hedonic eating. It is also plausible that those with binge eating will experience decreased inhibitory control and increased impulsivity, making it difficult to disengage from processing of food-related cues. Attention bias modification programs (ABM-food) show initial promise in training attention away from food among adults with binge-eating behaviors (Boutelle et al., 2016; Schmitz & Svaldi, 2017). In particular, ABM may decrease hedonic eating as well as weight, although RCTs comparing ABM with an adequate control group are needed.

Episodic Future Thinking for Modulating Impulsivity

Impairments in the ability to delay immediate gratification and a tendency to devalue larger future consequences in favor of smaller immediate rewards (referred to as delay discounting) are linked to hedonic eating, including consumption of high energy-dense food, as well as impaired glucose control and risk for Type 2 diabetes (Epstein et al., 2014, 2021). Interventions that directly target delay discounting aim to reduce bias for immediate gratification. These interventions are designed to prompt episodic future thinking (EFT) by engaging episodic memory in prospectively experiencing future events, such imagining the long-term rewards of abstaining from a binge episode. EFT may mediate reductions in hedonic eating by activating regions of the brain involved in prospective thinking and planning (Benoit et al., 2011). Preliminary data suggest that EFT reduces delay discounting and energy intake among adults with overweight and obesity when tempted with unhealthy foods (Daniel et al., 2013). In particular, food-related EFT leads to more restricted caloric consumption (Dassen et al., 2016). However, it may not be as effective in reducing demand for fast food, at least under simulations of economic scarcity, which may include abrupt transitions of poverty, which in turn may reduce the salience of EFT in favor of more immediate survival needs (Stein et al., 2021). Although interventions have targeted adults with overweight and obesity, future trials should examine the utility of EFT programs among those with hedonic eating.

Time-Restricted Eating and Fasting-Mimicking Diets

Time-restricted eating programs (a specific type of intermittent fasting protocol) have received attention in recent years as a potentially effective and simple weight-loss method. Such programs aim to create eating windows separated by defined periods of fasting (e.g., only eating from 12 p.m. until 8 p.m., followed by no more eating until 12 p.m. the next day). Some of these programs do not require particular attention to macronutrients or total caloric intake, thus increasing their appeal to many adults. Meal-timing interventions facilitate weight loss primarily by decreasing appetite,

rather than by increasing energy expenditure. They may also increase fat loss by increasing fat oxidation (Ravussin et al., 2019), particularly in the liver (de Cabo & Mattson, 2019). When compared with continuous energy restriction programs (i.e., typical restrictive diets), intermittent energy restriction paradigms produce equivalent weight loss and body fat loss (Rynders et al., 2019). Recently, however, time-restricted eating, in the absence of other interventions, was not found to be more effective for weight loss than eating three structured meals throughout the day (Lowe et al., 2020); nor was it found to be more effective in improving other indicators of metabolic health, such as fasting glucose or blood lipids. Thus, although time-restricted eating has been the subject of popular media attention and has become a fad, its efficacy may be limited, and trials examining its effects on hedonic eating are lacking.

Fasting-mimicking diets have also received attention for their potential to trick the body into thinking it is in a fasting state while still allowing the consumption of certain foods over the course of five days. Unlike time-restricted eating programs, fasting-mimicking diets are essentially a reduced-calorie diet with specific rules about macronutrient and calorie consumption. Although they are more labor intensive, fasting-mimicking diets, particularly those that incorporate three five-day cycles per month, have been found to have beneficial impacts on BMI as well as a number of metabolic markers of health, such as waist circumference, blood pressure, fasting glucose, IGF-1, triglycerides, total and LDL cholesterol, and CRP (Wei et al., 2017). Despite their promise for targeting eating and weight, fasting-mimicking diets have low adherence, partially due to a high level of commitment needed to follow the program. It is unknown how and whether fasting-mimicking diets affect hedonic drive or whether those with binge eating would potentially have difficulty complying. However, it is possible that they may contribute to physiologic reductions in hedonically driven appetite and reward. Fasting-mimicking diets have the advantage of needing short-term adherence, and deserve further study in terms of effects on cravings and hedonic overeating during the recovery period after people resume normal eating.

Continuous Glucose Monitoring Biofeedback

Continuous glucose monitoring (CGM) is a useful tool in health research and can provide biofeedback and monitor dietary adherence, particularly for those with Type 1 diabetes (Hegedus et al., 2021). Receiving immediate feedback on glucose trends can help individuals understand, on a real-time basis, how specific foods, eating behaviors, and other behaviors (e.g., exercise) affect health trends. More recently, the impact of CGM on glucose regulation among adults with non-insulin dependent Type 2 diabetes has been explored (Dehghani Zahedani et al., 2021). The use of ten-day CGM as a part of multimodal data collection, with feedback to participants via a mobile health app, showed a significant reduction in hyperglycemia, including for those with early stages of glucose dysregulation. This is a promising early finding. The efficacy of CGM could possibly be extended to other populations at risk for Type 2 diabetes, including those with hedonic eating. Given the heterogeneous nature of glucose regulation via CGM, even among those considered normoglycemic, it is plausible that such feedback can provide individuals with important data to change dysregulated eating behaviors that have immediate physiologic effects.

CONCLUSIONS

This chapter reviews the well-established biological mechanisms that control hunger under functional conditions (homeostatic drive), as well as under conditions that contribute to overeating (hedonic drive), with subsequent weight gain and metabolic dysregulation. Hedonic eating, and binge eating in particular, are commonly seen in individuals with obesity. As discussed, dysregulation of nonhomeostatic eating, due to addiction or stress or both, is a major contributor to weight

gain and obesity, especially abdominal adiposity. Hedonic drive likely accounts for the failure of most behavioral weight-loss programs to produce long-term sustainable reductions in weight.

Our review of the most well-studied hijackers of appetite regulation points to clinical pathways that could promote decreases in hedonic eating, and potentially warding off downstream metabolic health risks such as obesity, heart disease, and Type 2 diabetes. These pathways likely involve modulating one or more modifiable factors, including stress management and emotion regulation, dietary changes (e.g., reduction in high glycemic index, high sugar, and processed foods), increased aerobic exercise, improved sleep quality (and quantity), and potentially pharmaceutical treatment.

Existing treatments that seek to return adults to a state of homeostatic (vs. hedonic) eating are broad ranging, from well-established behavioral weight-loss programs and cognitive behavioral therapy and mindfulness-based interventions, to innovative new programs (e.g., attentional bias modification, episodic future thinking, fasting-mimicking diets, and biofeedback interventions).

Yet because obesity is still increasing, this field is rapidly growing as well, and comprehensive, whole person treatment is needed that targets not only hedonic eating drive, but also metabolic regulation and nutrition-specific solutions. Most programs have limited success in reducing both hedonic drive and weight-metabolic dysfunction. In treating clients who present with problems with appetite regulation, clinicians should take a holistic, mind-body view and consider the many domains that can promote both psychological and physiological health. For instance, educating and advising families, families eat together, may be more effective than treating individuals (in certain cases). Further, the prevention of obesity and hedonic overeating should focus on social changes in food sourcing and procurement, in early childhood education programs, schools, and neighborhoods, and in addressing social disparities in health.

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