

Gender-related Differences in Food Craving and Obesity

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Food craving is often defined as a strong desire to eat. Much work has shown that it consistently and prospectively predicts eating and weight-related outcomes, contributing to the growing obesity epidemic. Although there are clear gender differences in the prevalence and health consequences of obesity, relatively little recent work has investigated gender differences in craving, or any sex-hormone-based differences as they relate to phases of the menstrual cycle. Here, we propose that gender-related differences in food craving contribute to gender-related differences in obesity. Drawing on findings in the addiction literature, we highlight ways to incorporate gender-based differences in food craving into treatment approaches, potentially improving the efficacy of obesity and weight loss treatment. Overall, this review aims to emphasize the importance of investigating gender differences in food craving, with a view towards informing the development of more effective treatments for obesity and weight loss.

Popular culture often portrays gender differences in food cravings, such as the notion that men crave savory foods (e.g., burgers) whereas women crave sweet foods (e.g., chocolate), especially as they approach menses [1]. While this is not always the case, some research has supported gender differences in not only the type of food craved, but also in clinically-important characteristics of craving such as frequency, severity, and regulation of food craving [2-5]. In the sections below, we will first define craving and discuss how food craving can predict eating and weight gain [6]. We will then argue that due to this predictive relationship, craving is a likely explanatory mechanism for rapidly-increasing rates of obesity, which is the second leading cause of preventable disease and death in the United States [7,8]. Next, we will review key findings on gender differences in food craving, and explain how these differences may underlie gender differences in obesity and obesity-related health consequences. Then, we will discuss evidence that hormonal differences between men and women, and hormonal variations across women's menstrual cycles contribute to such differences. Finally, drawing on findings in the drug addictions literature, we will highlight important impli-

cations of gender differences in food craving for obesity research and treatment.

THE IMPORTANCE OF FOOD CRAVING

Defining and Measuring Food Craving

Food craving can be defined as *a strong desire to eat* [9-11] and is extremely common; it is experienced by more than 90 percent of the population (e.g., [2,12,13]). Several types of food craving are commonly defined and studied (see Figure 1). *Tonic craving* reflects a general feeling that is experienced either over time or in a particular moment, in the absence of environmental stimuli. It is often related to abstinence from a particular food (e.g., consistently craving chocolate when on a diet; [14]), and is typically measured with multi-item self-report scales/questionnaires, including the Food Craving Inventory (e.g., "*I frequently desire fried chicken*" [12]). Such measures of tonic craving are typically higher in restrained eaters and increase after deprivation [15]. Nevertheless, tonic craving is not the same as hunger, and can be experienced in the absence of caloric need [13,16].

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†Abbreviations: VS, ventral striatum; OFC, orbitofrontal cortex, BMI, Body Mass Index; fMRI, functional magnetic resonance imaging; CERP, Cue Exposure and Response Prevention; CBT, Cognitive Behavioral Therapy; MBT, Mindfulness-based Treatments.

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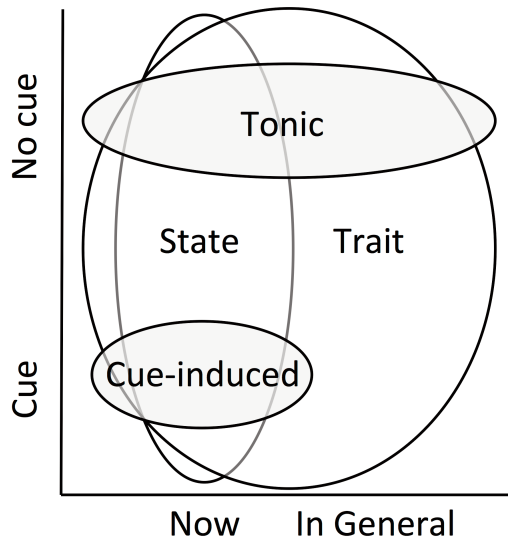


Figure 1. Conceptual overlap of commonly-defined forms of food craving. Schematic and conceptual representation of the overlap in definitions and types of craving. *Tonic craving* refers to a general feeling of craving that is experienced either over time or in a particular moment, in the absence of environmental stimuli. *Cue-induced craving* is an acute period of craving, elicited by environmental/external stimuli. *State craving* is a feeling of craving in a particular moment, regardless of whether a cue is present. *Trait craving* refers to a tendency to feel craving in general; it can refer to craving in general both in the presence of cues and without cues. Sizes of the bubbles reflect definitional overlap across Time and Cue dimensions.

On the other hand, *cue-induced craving* is an acute period of craving, elicited by environmental/external stimuli (e.g., craving chocolate after seeing a Godiva commercial; [14], for review, see [6]). In response to such stimuli, individuals report their current level of craving, either on a multi-item scale (e.g., [17,18]) or a single-item response (e.g., [19,20]). A large body of studies has consistently shown that exposure to visual, olfactory, or taste cues of salient food items results in cue-induced craving, along with increases in peripheral physiological signals such as heart rate, gastric activity, and salivation, known as *cue reactivity* [21-23]. Such cue reactivity also includes a predictable pattern of neural responses in brain systems previously associated with reward, including the ventral striatum (VS \dagger), orbitofrontal cortex (OFC), and insula (for reviews, see [24-26]). For instance, the VS is thought to play a central role in motivation and learning (e.g., [24-26]), the OFC is involved in value computation (e.g., [24-27]), and the insula has been associated with updating value based on interoceptive states (e.g., [24, 28-29]). Although these brain regions have unique and varied functions, together they form part of a circuit that detects and encodes the salience of reward [24-26]. Further, activation of these regions (measured by functional neuroimaging) correlates with self-reported cue-induced craving (e.g., [30-34]; see [24-26] for reviews). As such, cue-in-

duced craving is a conditioned response, wherein food cues present at the time of food consumption became associated with the reward of eating, and over time come to elicit conditioned physiological, neural, and craving responses [14,35].

Additional forms of craving have been discussed in the literature, which partially overlap with tonic and cue-induced craving: namely, *state craving* and *trait craving*. *State craving* is a feeling of craving in a particular moment, regardless of whether a cue is present; thus, it can describe either tonic or cue-induced craving assessed in a present moment. In contrast, like tonic craving, *trait craving* refers to a tendency to feel craving in general; however, it can also refer to craving in the presence of cues in general. For example, the Food Craving Questionnaire-Trait includes questions about the tendency to experience both tonic craving (e.g., “If I am craving something, thoughts of eating it consume me”) and cue-induced craving (e.g., “Whenever I go to a buffet I end up eating more than what I needed”; [36,37]). Conversely, the Food Craving Questionnaire-State includes questions asking about the present moment only, which could include cue-induced or tonic craving (e.g., “I have an urge for a specific food”; [37]).

Importantly, although studies can be designed to focus on a specific form of craving, the subtypes of craving are not always fully dissociable. For example, studies that measure self-reported craving across a day or week may capture some combination of these types of craving across time. For instance, subtle daily stimuli (e.g., time of day, a location associated with eating, the physical sensation of hunger) may induce craving even when individuals are unaware of the cause of the craving. However, the type of craving may be less important than the severity of the craving in contributing to craving-induced eating, and an interaction of tonic, trait, and cue-induced craving may produce the strongest overall craving in any particular moment [38]. Throughout this review, we do our best to differentiate between the types of craving where possible, based on the definitions above (see Figure 1).

Food Craving, Eating, & Weight Gain

Food craving is clinically important because it is prospectively associated with and predicts eating and weight gain [6]. Individuals who report tonic food cravings display higher caloric intake than those who report rarely experiencing food craving [39]. Tonic craving for certain foods or food groups also predicts consumption of these specific foods [40]. Tonic and trait food craving are related to long-term weight outcomes such as greater weight gain over time and lifetime high body mass index (BMI [41-43]). Similarly, food cues and cue-induced food craving are also associated with food consumption. For instance, exposure to food cues elicits a craving response that predicts subsequent eating, such that higher cue-induced craving levels are associated with greater food consumption [44]. Further, cue-induced food craving predicts

overeating in overweight children [45] and adults [46]. In a nonclinical population, one study found that both neural food cue reactivity in the VS and self-reported state craving predicted subsequent eating over a period of one week [47]. We recently summarized the data on both tonic and cue-induced food craving in a quantitative meta-analysis; we found that both were prospectively predictive of eating and long term weight gain across 45 studies, with a medium effect size [6]. Importantly, these craving measures accounted for 11 percent of the variance in eating-related outcomes, which is greater than any other single predictor of eating and weight [6]. Given that food craving is strongly associated with increased food intake and weight gain, its investigation is key to understanding obesity, and may inform prevention and treatment approaches [48].

IMPACT OF WEIGHT GAIN AND OBESITY

In the United States, more than two-thirds of the population (68.5 percent) is now defined as overweight (BMI > 24.5; [49]). This stands in contrast to U.S. rates of overweight 30 years ago, when only 15 percent of adults were overweight (a 400 percent increase; [49]). This is problematic because obesity has been directly and causally linked to increasing rates of obesity-related disease, including diabetes, cardiovascular disease, and hypertension [50], such that obesity is now the second leading cause of preventable disease and death in the United States [7,8]. These health outcomes illustrate that obesity is a critical clinical and public health issue, necessitating the development of effective interventions. Thus, the sections below will illustrate how understanding gender differences in food craving could lead to improved interventions for obesity.

LINKING CRAVING AND OBESITY

As reviewed above, craving is a strong predictor of eating and weight gain [6]. One society-level mechanism whereby craving influences obesity is through the increase in food cues in the environment which, in turn, increases craving and eating at the population-level. Indeed, the rising rates of overweight and obesity have been associated with increases in the availability and advertisement of unhealthy/calorie-dense foods [51,52]. Accordingly, individuals who live in an environment that includes high caloric foods (e.g., fast food, such as McDonalds) eat those foods more frequently, which results in a higher BMI [53-56]. Moreover, the omnipresence of “junk food” advertisements serves as a salient food cue, leading to even more frequent unhealthy food consumption [57]. Some have termed this an “obesogenic” or “toxic” food environment, wherein ultra-prevalent food and food cues lead to increased craving, food consumption, and weight gain [52,58,59]. While this environment affects everyone to some degree, some individuals may be more sensitive

to food-related cues or experience more craving, such as overweight individuals [60,61].

GENDER DIFFERENCES IN WEIGHT GAIN AND OBESITY

Importantly, there are gender differences in risk for and consequences of obesity. Gender is considered a risk factor for obesity; being female doubles the chance of becoming overweight [62]. Worldwide, women are 3 percent more likely to be overweight or obese than men [63]. Similarly, in the United States, women are 3.3 percent more likely than men to be overweight [64] and are 3 percent more likely to be morbidly obese [49]. Furthermore, some work has shown that women shoulder a greater burden of obesity-related health problems, including diseases such as high blood pressure and heart disease [65,66]. In other words, greater proportions of overweight and obese women suffer from obesity-related diseases [65]. Specifically, the rate of disease is 6.6 times greater in women compared to men [66,67]. One reason for this is that health-related impairments occur at lower BMIs in women than in men [65], and this is evident on both physical [68-72] and psychological health indices [73-76]. Finally, overweight women have twice the risk of mortality compared to overweight men [66], suggesting that they are more likely to die from weight-related disease.

GENDER DIFFERENCES IN FOOD CRAVING

Because women are disproportionately affected by obesity, there may be a gender-related mechanism that explains these differences. Given the role of craving in obesity, one mechanism underlying gender-based health disparities in obesity could be gender differences in craving. Indeed, men and women have different experiences of craving, and different behavioral responses to it. Specifically, as reviewed below, gender differences have been reported in: (1) the kinds of foods craved, (2) the intensity and frequency of craving, and (3) the ability or tendency to regulate craving.

Gender Differences in Kinds of Foods Craved

Men and women tend to crave different kinds of foods. Several studies have shown that men report more craving for savory foods (e.g., meat, fish, eggs), whereas women report more craving for sweet foods (e.g., chocolate, pastries, ice cream; [3,4]). Further, men may crave different types of sweets than women do (e.g., sugar-sweetened beverages, but not chocolate; [3]). Consistently, a few studies have shown that more than 92 percent of those who experience strong cravings for chocolate are female [77,78].

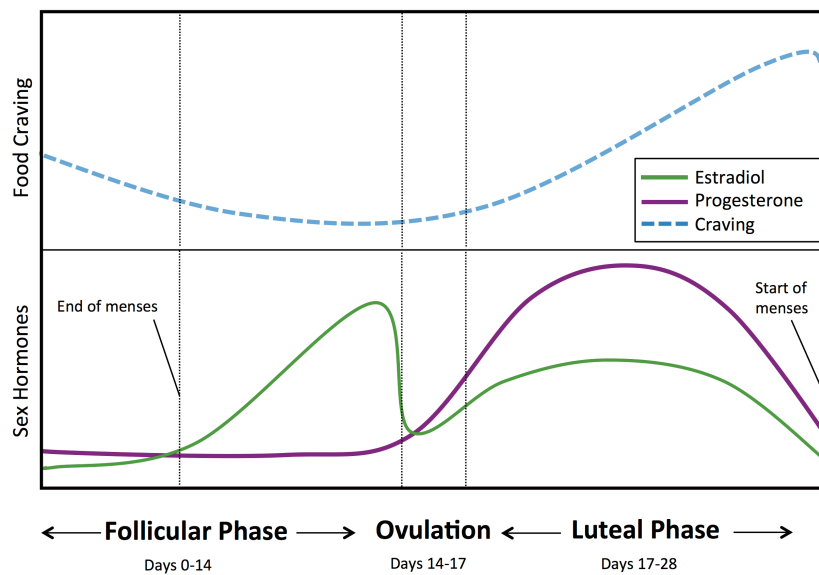


Figure 2. Ovarian hormone levels and proposed variation in food craving for each cycle phase.

Lines represent variation in sex hormones across the menstrual cycle (e.g., Allen et al., 2015; Hirschberg, 2012) and their proposed relationship to craving for food. During the follicular phase (days ~0-14), levels of estradiol increase and craving may decrease. During ovulation (days ~14-17) and the luteal phase (days ~17-28), levels of progesterone increase and then decrease before menses. Such changes may be associated with a rise in craving for food reported during this period (e.g., Hormes & Timko, 2011; Dye & Blundell, 1997; Dye, Warner & Bancroft, 1995).

Gender Differences in Levels or Frequency of Food Craving

Men and women report different intensities and frequencies of tonic and trait food craving, although the literature on cue-induced craving is less clear. Women report experiencing stronger tonic and trait food craving overall [5,36]. For example, one study assessed baseline gender differences in trait food craving in a large sample of college students, and found that women have significantly higher trait craving scores than men, even when controlling for food deprivation and eating disorder symptoms [36]. Overweight and obese women enrolled in a weight loss treatment program also reported higher trait food craving than overweight and obese men, even when controlling for binge eating behaviors and obesity levels [79]. Further, women more frequently report experiencing craving in everyday life [3,5,80]. Indeed, women report more frequent episodes of state craving, as highlighted by a three-day food diary study, in which women reported 15.6 percent more food cravings episodes than men [5]. To our knowledge, no published studies to date specifically tested gender differences in the intensity or frequency of cue-induced food craving. However, some studies have shown gender differences in food cue reactivity, which is related to cue-induced craving. For example, in a functional magnetic resonance imaging (fMRI) study investigating neural reactivity to palatable food images, women showed greater activity in craving and taste-related brain regions such as the anterior insula in response to food cues as compared to men [81]. In another study, women also exhibited greater neural reactivity than men to high-calorie food cues under food deprivation, including in the OFC and insula [82].

Gender Differences in Regulation of Food Craving

Women may find it harder to regulate food craving compared to men. In one study, only 20 percent of women who reported craving indicated that it was “easy” for them to resist cravings, as compared to 50 percent of men; however, men and women ultimately reported equal levels of success in resisting their cravings [5]. Gender differences in the ability to reduce cue-induced craving have also been reported. Wang and colleagues (2009) found that men and women report similar cue-induced craving levels and exhibit similar levels of neural activity in craving-related brain regions after exposure to food cues [83]. However, when participants were asked to reduce craving by distracting themselves or ignoring the food cues, only men showed decreased neural activity in these regions; this is consistent with women being less able to suppress their cue-induced craving for food than men [83]. Importantly, this specific gender difference in regulation of cue-induced craving does not appear to extend more broadly to gender differences in behavioral impulsivity (see [84] for meta-analysis). Taken together, these data suggest that men and women differ in several aspects of craving and in responses to craving.

HORMONAL MECHANISMS UNDERLYING GENDER DIFFERENCES IN FOOD CRAVING AND EATING

A complex interplay of biological, sociological, and environmental factors likely account for gender differences in craving and obesity. Nevertheless, sex hormones such as testosterone, progesterone, and estrogens modulate food consumption and are widely understood to be important factors driving such gender differences. First, men and women differ in their average levels of these sex hormones. Second, women experience monthly hormonal

variation across the menstrual cycle while men do not, and this may contribute importantly to gender differences in food craving and consumption, as will be detailed below (see Figure 2).

Sex hormones are important modulators of food consumption, and interact with neurotransmitters and gastrointestinal systems to change energy intake and expenditure (for review, see [85-87]). Men and women are known to have different absolute levels and ratios of sex hormones, which influence eating and weight. For instance, levels of androgens (e.g., testosterone) are typically higher in men, whereas levels of estrogens (e.g. estradiol, estrone) are typically higher in women. However, there is much variability within and across sex and age, including increases in both hormones in men and women during adolescence and reductions in androgens in men and estrogens in women at older ages [88-90]. Importantly, androgens are associated with reduced risk of obesity and diabetes in men, but increased risk of obesity and diabetes in women [85,91,92]. In contrast, estrogens attenuate appetite and eating in men and women [93,94], such that reductions in estrogen increase food consumption (but c.f., tonically higher estrogen levels correlate with increased body weight and amount of body fat in women; [95,96]).

Women experience monthly variations in sex hormone levels across the menstrual cycle (for review, see [86,87]), whereas men do not have such cycles. The menstrual cycle is often described as having two primary stages based on ovarian changes: the *follicular phase*, when estrogen is more prominent, and the *luteal phase*, when progesterone is more prominent¹ [97]. The *follicular phase* is frequently defined as starting on the first day of menses. During menses, both estrogen and progesterone levels are relatively low. After menses, estrogen levels gradually increase to prepare for ovulation. Approximately mid-cycle (~days 14-17), follicular stimulating hormone (FSH) and luteinizing hormone (LH) peak and *ovulation* occurs. After ovulation, the *luteal phase* begins, and estrogen levels decrease as progesterone levels (an estrogen antagonist) increase. At the end of the luteal phase, estrogen and progesterone levels again drop, initiating menses.

It has long been known that in females, food consumption fluctuates across the menstrual cycle due to these fluctuations of sex hormones, as observed in both animal and human studies [86,87,94,98-101]. Specifically, the reduction in estrogen and increased antagonism of estrogen by progesterone after ovulation increase eating in the luteal phase [86,87]. These effects were first causally demonstrated in animal models. For example, in rats, food consumption and weight gain increase following ovariectomy, which eliminates estrogen. These effects can be reversed by estrogen replacement, and co-administration of

progesterone blocks the effects of estrogen [86,87,102-104]. These effects have also been shown in women, such that those in the luteal phase consume significantly more food and prefer sweeter foods compared to women in the follicular phase [86,87,105]. A meta-analysis across studies in women suggests that the difference in food consumption amounts to ~238 additional calories per day during the luteal phase compared to the follicular phase (and may be as high as 597 additional calories per day; [105]). Such increased caloric intake could result in a yearly weight gain of 10 to 20 pounds.

Importantly, one underlying mechanism of these cyclic variations in eating may be menstrual-phase differences in food craving. Indeed, women's menstrual cycle variations have been shown to influence craving and food cue reactivity [106,107]. Women report increased food craving in the luteal phase, with the strongest craving occurring directly before menses and potentially continuing into menstruation [10,108-113]. In fact, it has been reported that women experience as much as 57 percent more craving in the luteal phase than in the early follicular phase [108]. In one interesting study, 28.9 percent of college age women reported chocolate cravings associated with their menstrual cycle, most frequently occurring 4 days prior to menses and continuing into menses [106]. In another study, 74.3 percent of women reported food cravings in the 7 days prior to menses, as compared to 26.9 percent reporting food cravings after menses [10].

Very little work has investigated menstrual cycle variations specifically in cue-induced food craving and associated cue reactivity, a component of cue-induced food craving. A recent study in animals found that renewal of cue-induced food consumption decreases with estradiol levels [114]. In women, neural reactivity to food cues across the menstrual cycle varies in brain regions typically associated with craving and reward (like the OFC and VS; [107]). Specifically, women showed greater neural reactivity when viewing pictures of high calorie foods during the luteal phase as compared to the follicular phase [107]. However, one behavioral study reported no significant influence of menstrual phase on cue-induced food craving [109]. In sum, both animal and human work demonstrate that food craving fluctuates along the menstrual cycle, and could explain variations in food consumption. However, there is a clear need for additional studies in this area to establish the effects of menstrual cycle variations on cue-induced food craving specifically.

LESSONS FROM CRAVING IN DRUG USE AND ADDICTION

Over several decades of research on addictions, it has been firmly established that craving contributes substantially to drug use (e.g., [115-118]) and relapse (e.g., [119-

¹Although researchers have used a variety of definitions for phases, and mechanisms for determining phase status, efforts to systematize this are under way (Allen et al, 2015).

133]). More recently, researchers have pointed to similarities between food and drug craving. For example, the subjective experience of drug craving is thought to resemble the experience of food craving [134]. The two are also similar in their predictive utility and in their underlying mechanisms. For instance, as with drug craving, there is emerging evidence that food craving contributes substantially to and predicts eating and weight outcomes [6,48]. Mechanistically, meta-analyses have shown that cue-induced drug craving is consistently associated with neural activity in a network of regions including the VS, the OFC, and the insula [135,136], which are also consistently associated with neural activity in response to cue-induced food craving [34]. Further, it has been proposed that drugs “hijack” a hedonic reward system, which is thought to have originally evolved for food and other natural rewards (e.g., [137-147]), and that this system is responsible for craving for food and for drugs, including in addictions, obesity, and eating disorders (e.g., [141,148,149]). This suggests that parallel mechanisms contribute to drug- and food-related problems. Therefore, because of this shared circuitry, there may be (1) gender differences and (2) treatment approaches that are effective across disorders. As such, a review of gender differences in drug craving may provide useful insights into food craving and related problems.

Gender differences have been frequently reported in multiple antecedents, clinical course, subjective effects, underlying mechanisms, consequences, and outcomes of drug use and addiction (for reviews, see [150-155]). For instance, gender differences have been reported in drug craving, including cue-induced drug craving, drug cue reactivity, and drug-cue-induced neural activity in craving-related brain regions, such as the VS, OFC, and insula [156-160]. However, the precise nature of these differences remains elusive; for example, in some studies, women report more cue-induced craving, but others find no differences (for review, see [160]). Such inconsistencies may reflect variations in menstrual phase; indeed, menstrual-phase-based variations in drug craving have been reported in female drug users. For example, non-abstinent women smokers report significantly more tonic [161-164] and cue-induced craving [165] in the luteal phase than in the follicular phase of the menstrual cycle (see [166] for review). In contrast, nicotine-abstinent women have been shown to report greater state craving in the follicular phase [162,167]. Inconsistencies in findings may be due to methodological differences between studies, including in abstinence itself [97,168]. Abstinence is important especially when considering the parallel to food, as craving for food is never measured in a fully-abstinent state.

Importantly, in the addiction field, findings on menstrual-phase-based variations in craving have been applied to the realm of treatment. Specifically, several studies have shown that menstrual cycle phase at the date of smoking

cessation predicts smoking status during and after treatment [166,169], such that smoking cessation quit attempts initiated during the luteal phase (when progesterone levels are dominant) are associated with better treatment outcomes than in the follicular phase (e.g., [162]; but c.f. [170,171] with nicotine replacement). These treatment effects may be due to fluctuation/reduction of perceived withdrawal symptoms, including craving [166,172] across the menstrual cycle. Ultimately, these findings suggest that *treatment outcomes may be improved by considering the influence of menstrual cycle phase on cravings* when beginning a substance use intervention. Although drug treatment is not a perfect model for weight control or obesity treatments (where the goal can never be complete abstinence, as it is with drugs), these findings may have applications to obesity treatments, especially because of the importance of craving for both conditions.

IMPLICATIONS FOR GENDER DIFFERENCES IN OBESITY AND ITS TREATMENT

Food Craving and Treatment for Obesity

As reviewed above, food craving is related to eating and weight, and importantly, it directly interferes with weight loss treatments and dieting. One study found that trait food craving is associated with self-reported past dieting failures, such that individuals with higher trait craving report less ability to watch their weight, lose excess weight, and stay in shape [173]. Further, weight cycling in women who diet is associated with increased frequency and intensity of craving and with binge eating behavior [174,175]. In contrast, successful dieters have lower reactivity to food cues, such that exposure to food stimuli elicits lower physiological reactivity (e.g., salivation) and lower neural response in the VS as compared to unsuccessful dieters [176,177]. These findings suggest that individuals with lower levels of craving may be more likely to succeed on diets and in weight loss treatments. Indeed, longitudinal studies have observed that trait craving and cue reactivity can predict weight loss treatment outcomes. For example, Batra and colleagues (2013) found that reductions in trait craving during a weight loss intervention were associated with greater reductions in body weight [178]. Similarly, lower neural reactivity in the VS and insula to images of high-calorie foods was predictive of better short-term and long-term outcomes in weight loss treatment [179]. Thus, it may be more difficult for those with strong food cravings to successfully diet or lose weight. This may be especially relevant to women, particularly during menstrual phases when they may be more sensitive to craving and food cues.

Several treatments that directly target craving and exposure to food cues have been shown to reduce eating and improve outcomes in overweight populations. For example, pharmacotherapies such as bupropion and naltrexone

that reduce craving for drugs of abuse (e.g., opiates and alcohol) are also associated with reduced self-reported craving for food and reduced BMI in weight loss trials [180-184]. Further, psychological treatments have been applied to target the associations between cue exposure, craving, and food consumption, including cue exposure and response prevention treatments (CERP), cognitive behavioral therapy (CBT), and mindfulness-based therapies (MBTs). CERP attempts to extinguish associations between a cue, conditioned responses, and a behavior by preventing the behavior from occurring. In CERP, prolonged exposure to food cues in the absence of food intake reduces self-reported state food craving [185], physiological reactivity in response to cues [186], and binge eating [185,187-189], though results are mixed [190].

In comparison, CBT aims to reduce the influence of food cues and craving on eating behavior and weight, through the use of cognitive and behavioral strategies. Cognitive strategies include the regulation of craving through cognitive reappraisal, which involves reframing a stimulus or situation with the goal of modulating its affective impact (e.g., a delicious slice of pizza might lead to long-term health consequences, including obesity; [191]). Cognitive reappraisal reduces neural reactivity in the VS and self-reported cue-induced craving for high calorie foods [19,32,192,193]. Behavioral strategies include determining the antecedents of eating behavior (e.g., food cues, craving), intervening to prevent consequences (i.e., food consumption), stimulus control (e.g., reduction of food cues in the personal environment), regular meal planning (to reduce vulnerability to food cues and craving), and exposure-based exercises (to reduce the salience of “trigger” foods and contexts; [194]). CBT is effective in the treatment of a range of food- and food craving-related conditions, including eating disorders [195,196] and obesity [197,198]. Finally, MBTs that teach individuals to notice and accept the experience of craving have demonstrated effectiveness at reducing food craving and weight in both lean and obese adults [199-202] as well as reducing episodes of binge eating in individuals with binge eating disorder [203] and bulimia nervosa [204,205], or following bariatric surgery [206]. Thus, further development of these treatment approaches, and others that target craving and/or cue exposure, may improve the effectiveness of treatments for obesity.

Gender Differences in Food Craving and Treatment for Obesity

The data summarized above links craving to eating, weight gain, and obesity, making it an important target for obesity treatment. Given gender differences reported in craving and obesity, considering gender- and sex hormone-based variations in craving and eating may further improve the efficacy of obesity treatments. However, there is a dearth of experimental and clinical work directly comparing treatment outcomes in men and women, and ac-

counting for variation in sex hormones (e.g. across menstrual cycle, pregnancy, and age). In fact, to our knowledge, there are no gender-specific or sex hormone-sensitive interventions for obesity. Furthermore, most clinical trials for obesity do not test for (or report) gender differences in response to treatment, including in reductions in food cravings, eating, or weight-related outcomes. Importantly, recent meta-analyses of the few trials that do report gender differences found that women are less likely to complete treatment [207] and that women lose less weight than men [208], despite comprising more than 50 percent of weight loss trial participants [207]. There may also be gender differences in response to pharmacotherapy treatments; in one study, methylphenidate led to decreases in state food craving, and food consumption, in obese women, but not men [209].

As observed in the addiction literature and described above, targeting and testing treatment based on gender and sex hormone status for women is likely to improve intervention efficacy for eating-related disorders. In smoking cessation trials, it has been shown that women who quit during the follicular phase are less successful, as they are more susceptible to relapse [169]. It may be beneficial to similarly time-lock weight loss treatment so that it begins during the luteal phase of the menstrual cycle to minimize lapses. Alternatively, it may be useful to gradually introduce small dietary changes during this time window across several months; for example, by establishing “quit dates” for particular foods in the luteal phase across the course of a several months, instead of introducing several changes at once. Furthermore, given gender-based differences in food craving, it may be useful to modify the nutritional composition of foods included in weight loss plans between genders and across the menstrual cycle (for women) to adjust for variation in specific food cravings and energy needs. Indeed, as with other biological metrics such as gut microbiota, it may be possible to individualize diet plans based on hormonal profiles and other physiological variations [210]. Additionally, targeting hormonal imbalances or reducing variation across the cycle through pharmacological treatment (e.g., oral contraceptives) may change the intensity of cravings and food consumption across the cycle, influencing treatment outcomes. However, there are currently contradictory findings on this topic, with some studies suggesting that oral contraceptives decrease food craving [211,212], whereas others report no change in food craving [213,214] or eating [215,216]. Finally, providing women with psychoeducation about hormonal influences on craving and food intake may improve self-efficacy and use of coping skills, such as cognitive reappraisal or mindfulness skills, during specific times of heightened craving. Ultimately, what is needed is additional research in this area to uncover the exact effect of sex-based hormones on craving, eating, and the success of diet and obesity treatments.

CONCLUSION

Obesity has become an epidemic, associated with great costs to society including widespread disability, disease, and death. There are gender differences in tonic craving and cue-induced craving, which may underlie documented gender differences in obesity and obesity-related health outcomes. Furthermore, for women, there are sex hormone-related variations in craving and food cue reactivity that may hinder dieting and weight loss attempts. In the field of drug addiction, gender-informed treatments that are time-locked to menstrual phase have shown greater efficacy. We propose that there is much room for further work investigating these issues as they relate to weight loss and obesity. First, further investigation into changes in craving across the menstrual cycle is necessary to fully elucidate its timing and effects on eating. Second, current weight loss studies rarely measure craving or menstrual phase, or test for gender differences in outcomes. Reporting such information in the context of existing interventions would greatly inform our understanding of the mechanisms involved in successful treatment, and allow for the development of more targeted approaches. Third, building on treatments for addiction, studies investigating menstrual-cycle-based timing of weight loss interventions could increase our understanding of how hormonal changes can influence treatment efficacy and weight. Indeed, including assessments of hormone levels as well as craving in such investigations can increase our understanding of the role of these mechanisms in obesity and obesity treatment. Finally, testing targeted interventions to reduce hormonal variability (e.g., oral contraceptives) or to improve coping with cravings (e.g., regulation of craving, mindfulness) may bolster existing treatment approaches. Investigating these issues may improve interventions, so that gender differences in food craving and cue-reactivity are less likely to derail weight loss attempts and contribute to gender-related health disparities in obesity.

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