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Stress and Eating Behaviors

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Abstract

Obesity is a heterogeneous construct that, despite multiple and diverse attempts, has been difficult to treat. One conceptualization gaining media and research attention in recent years is that foods, particularly hyperpalatable (e.g., high-fat, high sugar) ones, may possess addictive qualities. Stress is an important factor in the development of addiction and in addiction relapse, and may contribute to an increased risk for obesity and other metabolic diseases. Uncontrollable stress changes eating patterns and the salience and consumption of hyperpalatable foods; over time, this could lead to changes in allostatic load and trigger neurobiological adaptations that promote increasingly compulsively behavior. This association may be mediated by alterations in the hypothalamic-pituitary-adrenal (HPA) axis, glucose metabolism, insulin sensitivity, and other appetite-related hormones and hypothalamic neuropeptides. At a neurocircuitry level, chronic stress may affect the mesolimbic dopaminergic system and other brain regions involved in stress/motivation circuits. Together, these may synergistically potentiate reward sensitivity, food preference, and the wanting and seeking of hyperpalatable foods, as well as induce metabolic changes that promote weight and body fat mass. Individual differences in susceptibility to obesity and types of stressors may further moderate this process. Understanding the associations and interactions between stress, neurobiological adaptations, and obesity is important in the development of effective prevention and treatment strategies for obesity and related metabolic diseases.

Keywords

Obesity; Food Addiction; Stress; HPA axis; Mesolimbic Dopaminergic System

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CONFLICT OF INTEREST

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Introduction

Defined as “abnormal or excessive fat accumulation that may impair health” [1], obesity is a condition that is increasingly common. In the United States, 35.7% of adults are obese (body mass index [BMI] ≥30 kg/m^2) [2]. Globally, estimates from 2008 suggest that 1.4 billion adults globally were overweight (BMI ≥25 kg/m^2), and that at least 200 million men and 300 million women were obese [1]. Obesity represents an important risk factor for potentially life-threatening health problems including cardiovascular diseases, type II diabetes, osteoarthritis, and certain cancers [3-5].

There have been multiple and diverse attempts to provide mechanisms for individuals to lose weight and maintain a healthy body weight; however, most have failed to sustain lasting effects, with patients often regaining their lost weight within 5 years [6-8]. The difficulty in treating and decreasing the prevalence of obesity may reflect the heterogeneity of obesity as a condition. One conceptualization supported by recent research in the addiction and nutrition fields is that foods, particularly highly palatable and energy-dense ones, may be “addictive” in ways similar to drugs of abuse [9]; these findings have consequently led to the conceptualization of ‘foods as drugs’ [10]. Stress has long been considered a critical risk factor in the development of addictive disorders and relapse to addictive behaviors [11, 12]. However, few studies have reviewed links between stress and food intake, particularly of hyperpalable or “comfort” foods that may be consumed to reduce stress.

Stress and Eating Behavior

The term “stress” refers to processes involving perception, appraisal, and response to noxious events or stimuli [13]. Stress experiences can be emotionally (e.g., interpersonal conflict, loss of loved ones, unemployment) or physiologically (e.g., food deprivation, illness, drug withdrawal states) challenging. In addition, regular and binge use of addictive substances may serve as pharmacological stressors. Acute stress activates adaptive responses, but prolonged stress leads to “wear-and-tear” (allostatic load) of the regulatory systems, resulting in biological alterations that weaken stress-related adaptive processes and increase disease susceptibility [14]. Thus, mildly challenging stimuli limited in duration can be “good stress” or “eustress” and may increase motivation to achieve goal-direct outcomes and homeostasis – this can result in a sense of mastery and accomplishment, and can be perceived as positive and exciting [15]. However, the more prolonged and more intense the stressful situation, the lower the sense of mastery and adaptability and thus the greater the stress response and risk for persistent homeostatic dysregulation [14]. The perception and appraisal of stress relies on specific aspects of the presenting external or internal stimuli and may be moderated or mediated by personality traits, emotional state, and physiological responses that together contribute to the experience of distress.

Stress is a challenge to the natural homeostasis of an organism; in turn, the organism may react to stress by producing a physiological response to regain equilibrium lost by the impact of the stressor. One such homeostasis that is disrupted is that of feeding behavior. Physiological aspects of eating behaviors have been long studied, and information is often derived from animal models fed standard lab chow. However, experimental results have

been inconsistent. Animals fed a single bland food diet have provided evidence both for acute stress-induced hyperphagia and hypophagia [16, 17]. In humans, individual differences in food intake response are similarly noted – roughly 40% increase and 40% decrease their caloric intake when stressed, while approximately 20% of people do not change feeding behaviors during stressful periods [18-20]. These varying results may relate to the specific type of stressor manipulated, duration of stress provocation, and variations in the satiety and hunger levels at the start of the study. For example, mild stressors could induce hyperphagia, while more severe stressor, hypophagia [21]. However, other individual differences warrant consideration.

The rather complex pattern of results may also be conflated by the lack of food choice. Understanding which foods are selected or avoided under stress is a crucial issue both due to the theoretical interpretation of the mechanisms involved and for the prediction of harmful effects of stress on health. In both human and animals, a shift toward choosing more pleasurable and palatable foods is observed irrespective of caloric intake changes associated with stress. The foods eaten during times of stress typically favor those of high fat and/or sugar content. For example, when rats were presented with a choice of highly palatable food such as lard or sugar, stress consistently increased intake of palatable food specifically [22-24]. Humans similarly turn to hyperpalatable comfort foods such as fast food, snacks, and calorie-dense foods [25-27] even in the absence of hunger and lack of homeostatic need for calories [28]; this effect may be exacerbated in overweight or obese individuals as compared to lean individuals [20, 29]. Taken together, these findings suggest that stress may promote irregular eating patterns and strengthen networks towards hedonic overeating; these effects may be exacerbated in overweight and obese individuals. The factors underlying these and other behaviors that may contribute to obesity are slowly becoming understood.

The present article elucidates potential explanations for the stress-eating paradox, i.e. that stress can lead to both hyperphagia and hypophagia. We review overlaps in key elements of hormonal and brain stress neurocircuitry with that of appetite and motivation for food intake.

Acute and Chronic Stress Response: Role of the Hypothalamic-Pituitary-Adrenal Axis

The stress response, which maintains allostasis, is comprised of a cascade of adaptive responses and is manifested through two interacting stress pathways. First is the activation of the sympathetic adrenal medullary system, with release of catecholamines (adrenaline and noradrenaline) that is typical during periods of acute stress [30]. The second key component is the hypothalamic-pituitary-adrenal (HPA) axis. The HPA axis is a neuroendocrine system with inhibitory feedback loops involving hormone secretion from a remote target gland. Stress stimulates the release of corticotropin-releasing factor (CRF) from the paraventricular nucleus (PVN) of the hypothalamus which in turn stimulates the synthesis of adrenocorticotropic hormone (ACTH) from the anterior pituitary. ACTH subsequently triggers the production of glucocorticoids (GCs) such as cortisol or corticosterone in the adrenal cortex. In addition to these mechanisms of HPA axis activation, cytokines produced by immune cells or adipocytes can also stimulate the HPA axis, at the levels of the

hypothalamus, anterior pituitary gland, and the adrenal cortex. The first evidence that cortisol levels may be related to obesity and metabolic disease was derived from clinical observations of Cushing's syndrome; the pathological hypercortisolemia in Cushing's syndrome is associated with upper body obesity, atherosclerosis, glucose intolerance, and hypertension. Conversely, adrenalectomy in Cushing's syndrome patients reversed impaired glucose intolerance and obesity [31].

Acute stress-related sympathetic arousal and GC release supports behavioral, automatic and endocrinological changes which promote energy mobilization including heighted cardiac output, blood pressure, gluconeogenesis, triglyceride levels, and redirection of blood flow to fuel the muscles, heart and the brain [32]. Such responses are evolutionarily adaptive and serve to promote an immediate fight-or-flight reaction; activities requiring energy expenditure that may conflict with this response (e.g., food intake, digestion, and reproduction) are typically inhibited. Thus, part of the stereotypical acute stress response includes suppression of appetite and food intake [18]. GCs terminates the acute effects of stress on CRF and ACTH via negative feedback signals to the hypothalamus [33]; this serves to protect the organism from prolonged, detrimental cortisol exposure. The hypothalamus is also responsive to insulin concentration, which is secreted from the pancreas and is integral to glucose metabolism and glycogenolysis [34], as well as levels of other hormones such as leptin and ghrelin, which are involved with appetite inhibition and promotion respectively. Moreover, GCs alter the expression of a number of hypothalamic neuropeptides, such as CRF, orexigenic neuropeptide Y (NPY), agouti-related peptide, and proopiomelanocortin (POMC), all of which play a role in feeding behaviors [35]. Together, these findings indicate the hypothalamus is a critical region in the stress-response circuit as well as in the regulation of feeding and energy balance.

Repeated and uncontrollable stress can over time dysregulate the HPA axis, which consequently affects energy homeostasis and eating behavior. Chronic activation of the HPA axis can alter glucose metabolism, promote insulin resistance and influence multiple appetite-related hormones and hypothalamic neuropeptides [36]. Noradrenaline and CRF may suppress appetite during stress, whereas cortisol may stimulate appetite during recovery from stress [37]. Prolonged stress-induced GC secretion can promote abdominal fat deposition; synergistically with insulin, this can decrease HPA axis activity [38]. Moreover, those under chronic stress tend to eat more under acute stress conditions [39] and show heighted preference for and consumption of hyperpalatable, energy-dense foods high in sugar and fat [18, 40].

Potential Role of Insulin

Animal models have demonstrated that GCs act directly in a feed-forward manner that promotes food-associated drives and CRF and ACTH secretion. For example, adrenalectomized rats demonstrate reduced food intake, while GC administration increases food intake by stimulating the release of NPY and inhibiting CRF release [41, 42]. However, these effects do not appear to increase feeding-motivated behaviors under all conditions. Adrenalectomy reduces chow intake, while subsequent corticosterone replacement normalizes it; however, high corticosterone levels neither stimulate nor reduce chow

intake [43]. When rats were made diabetic using streptozotocin (which kills pancreatic B-cells, and therefore reduces/eliminates insulin secretion), a marked, dose-dependent effect of corticosterone on intake of rat chow was noted [44]. Together, these findings suggest that insulin secretion, also stimulated dose-dependently by GCs, partially blocks chow intake stimulated by corticosteroids.

Insulin is secreted in proportion to adiposity; it crosses the blood-brain barrier and serves to reduce food intake and body weight dose-dependently by acting on specific receptors in the hypothalamus. Insulin and corticosterone serve opposing roles in energy balance and storage; GCs inhibit energy storage while insulin promotes adiposity [44]. For example, streptozotocin-diabetic rats displayed depletion of fat reserves, and this effect was prevented when given exogenous insulin treatment [45]. Under conditions where there is a choice diet (chow and lard), corticosterone dose-dependently increases total calorie intake, whereas the proportion of calories derived from a certain food source is influenced by the prevailing insulin levels [44]. In the presence of insulin, passive treatment of rats with high GCs reduces chow intake, body weight, and sympathetic activity but increases fat stores [38]; under chronic stress, a relative increase in abdominal fat is also observed [46]. Insulin contributes importantly to dampening ACTH and GC responses to stress; evidence that indicate plasma insulin levels are negatively correlated with PVN CRF mRNA expression support this notion [40]. As such, the presence of insulin is important to consider when examining the relationship between stress, eating patterns, and energy storage.

Stress, Eating and the Reward System

Activation of the HPA is linked to activation of the mesolimbic dopaminergic system, a network strongly related to reward. Anatomically, stressors can stimulate increased CRF secretion which can in turn impinge on dopamine neurons in the ventral tagmental area (VTA) [47,48], which project not only to the nucleus accumbens (NAcc) but also to prefrontal and limbic regions – all of which are part of the brain reward system commonly implicated in substance abuse [9, 49]. Both food and drugs of abuse may exploit similar pathways in the brain including the dopaminergic and opioidergic systems [9, 50]. Increased drug taking and high-fat diets alter CRF, GC, and noradrenergic activity to increase sensitization of reward pathways (including within the VTA, NAcc, dorsal striatum, and the medial prefrontal cortex regions), which in turn influences preference for addictive substance and hyperpalatable foods and increases craving and intake [48]. Adrenalectomy decreases dopamine release specifically in the shell of the NAcc in response to both drug injection and hypothalamic self-stimulation, and treatment with corticosterone restores both to normal [51]. Moreover, dopamine transporters in the shell of the NAcc that are reduced by adrenalectomy are restored in a dose-dependent manner by corticosterone treatment [52]. Although dopamine release is not equivalent to addictive properties, dopamine has been associated with reward sensitivity, conditioning and control with respect to both food and drugs of abuse. Increased dopamine release has been reported in response to food and food cues [53] - both of which are crucial aspects of food intake [54]. Repeated stimulation of the dopaminergic reward pathways may trigger neurobiological adaptions that may promote progressively compulsive behavior [55]. Further, administration of dopamine antagonists or lesions of the dopaminergic

system may attenuate the responding for food and reduce the reward value of both high-sugar foods and drugs of abuse in rats [56-58].

Exposure to acute stress during a positron emission tomography (PET) scan revealed that both stress and cortisol release enhanced dopamine release from the NAcc [59]. Another study similarly found that individuals with greater cortisol reactivity released more dopamine in the ventral striatum, suggesting a strong interconnectictivity between the two [60]. In parallel, peripheral homeostatic regulators of energy balance, such as leptin, ghrelin, insulin, and orexin (all of which are associated with the HPA axis), can also regulate behaviors that are non-homeostatic and modulate the rewarding properties of food [54, 61]. These neuropeptides may be involved with food intake regulation by interacting with the dopaminergic system through cognate receptors on VTA dopamine neurons.

Importantly, this motivational circuit overlaps with limbic regions (e.g., the amygdala, anterior cingulate cortex, hippocampus, and insula) that underlie emotions, stress reactivity and learning and memory processes contributing to cognitive and behavioral responses critical to homeostasis [48]. For example, limbic regions have been implicated in the coding of rewards, memories for highly emotional events, and reward-cue-based learning and feeding [62]. In contrast, the prefrontal cortex (PFC) is involved in higher cognitive and executive control functions and the regulation of emotions, impulses, desires, and cravings [62]. While during normal conditions cognition is dominated by reflective cognition, during stress PFC activity is dampened and limbic circuitry hyperactivated, thus promoting “automatic” behaviors that bias survival including being vigilant for food cues. Both acute and chronic stressors increase synaptic branching in the amygdala and anterior cingulate cortex while simultaneously reducing synaptic contacts with the hippocampus and prefrontal regions [63]; this process further sculpts the chronic stress network towards limbic-biased stress responses. The stressed brain expresses both a strong drive to eat and an impaired capacity to inhibit eating – together creating a potent formula for obesity. These findings are consistent with behavioral and clinical research indicating that stress or negative affect decreases emotional and behavioral control and increases impulsivity, which may synergistically contribute to greater engagement in alcohol and substance abuse and eating [48].

Given that food and drugs of abuse appear to share similar mechanisms of action, engaging in one could potentially “cross-prime” for the other. Consistent with this notion, rats administered intra-accumbens opioid injections (versus saline) responded by overeating [64]. Conversely, patients who underwent bariatric surgery and lost a significant amount of weight rapidly increased their alcohol use [65]. Administration of naltrexone, an opioid antagonist, to rats following 17 weeks of hyperpalatable diet exposure did not modify the energy intake but suppressed hyperphagia of hyperpalatable food [66]. As food is an inexpensive resource for providing reward with hyperpalatable foods offering short term pleasure and relief from discomfort, negative reinforcement and distress may motivate stress-related eating as a way to regulate stress responses.

Addictive Properties of Hyperpalatable Food

Food-intake research indicates there is significant overlap with substance addictions, with much to be learned from this relatively well-established field [67], including with regards to the role of stress and hyperpalatable food. Stress, particularly uncontrollable stress, is a potent negative reinforcer that promotes the acquisition of drugs of abuse [48]. Pretreatment with corticosterone, thought to mimic the condition of chronic stress, exaggerates this effect [68]. Conversely, adrenalectomy abolishes the effect of stress on drug acquisition [69].

Several studies have examined the consumption of high-fat, high-sugar diets and activity of the HPA axis. In animal models, palatable non-nutritious food dampens HPA axis activity. For example, rats stressed for 5 consecutive days following a 5-day diet with *ad libitum* access to chow, lard and sucrose (versus chow only) displayed attenuated ACTH responses. In the same study, stress also increased the consumption of hyperpalatable foods above and beyond that consumed by the unstressed group [22]. Similarly, short-term exposure to a high-fat diet reduced anxiety on an elevated-plus maze [70]. Early life stressors such as maternal separation in rats also appear to activate chronic stress responses. A palatable high-fat diet normalized the effects of prolonged maternal separation in rats, reversing increases in anxiety and depressive behaviors, increased corticosterone, increased hypothalamic CRF, and increased hippocampal GC receptor expression [71]. Over time, rats fed a hyperpalatable diet developed greater mesenteric fat, which has been negatively correlated with CRF mRNA expression in the PVN [23]. Taken together, these findings suggest that stress-related eating of hyperpalatable foods serves to provide a short-term gain but may be detrimental in the long-term, contributing to abdominal fat deposition and related metabolic derangements.

Chronic stressors alter brain function and may leave traces after their relief. After the actual stress event, ACTH and GCs activity in the HPA axis may be subnormal, resembling those observed in patients with post-traumatic stress disorder [72] and rats during opioid withdrawal [46]. Hyperpalatable foods given to chronically stressed rats may negate chronic stress-induced inhibition of dopamine release that occurs in the shell of the NAcc. Although acute stress stimulates dopamine secretion in the NAcc, chronic stress inhibits dopamine secretion at this site and in others (such as the PFC) associated with reward pathways [73]. Regular consumption of energy-dense food may be accompanied by concomitant changes in neuronal networks, carbohydrate and fat metabolism, insulin sensitivity, and appetite hormones that modify energy homeostasis closely interact to dynamically affect altering salience, food choice and selection, craving, and motivation for food intake [74, 75]. Based on a diet-induced model of obesity, rats fed a high-sugar diet compared to those on an unrestricted diet showed decreased dopamine release in the NAcc following 26 hours of food deprivation [76]. Furthermore, rats fed on hyperpalatable [77], high-sugar [58], and high-fat [78] diets increased daily food intake over time, developed patterns of copious consumption, and displayed withdrawal symptoms when placed back on a normal chow diet. Such work has been expanded to human samples. For example, healthy adults placed under a nutritionally adequate but monotonous diet, compared to those on an unrestricted diet, showed greater activation of the hippocampus, insula, and caudate in response to cues of foods they favored [79]. Repeated stimulation of the reward pathways through hyperpalatable food may lead to neurobiological adaptations that eventually increase the compulsive nature

of overeating characterized by the frequent drive to initiate eating. Dampening of the HPA axis to stressors in rats eating hyperpalatable foods may account for the interplay between the negative effects of chronic stressors and the positive effects of hyperpalatable foods on inputs to brain regions associated with the reward system.

Factors Moderating the Relationship between Stress and Eating Behavior

Experiencing drive to eat, in the absence of true caloric need, is common but is subject to large individual differences. Discussed below are several common factors and types of stressor that may moderate the risk for stress-induced hyperphagia.

WEIGHT AND DIET-RELATED METABOLISM

Weight-related metabolic changes may alter allostatic load. Animal models have provided evidence that obesity is often characterized by a decreased amount of adipose signal or resistance at the receptor level [80]. In a state of insufficient adipose signaling, which typically serves as a negative feedback by decreasing the hedonic value of food, food intake may be prolonged and termination of eating impaired. In addition to decreased sensitivity to negative feedback, peripheral tissue sensitivity of fat and skeletal muscle tissue may also have altered sensitivity to GCs [81]. Increased weight, insulin resistance and high fat diets are associated with blunted GC responses to stress challenges and altered autonomic and peripheral catecholamine responses [82]. This impaired “brake” system may in part explain the epidemic of non-homeostatic eating [83].

Individuals with high BMIs show a stronger association between chronic stress and weight gain than those with low BMIs who experience similar degrees of stress [20]. Consistent with this notion, stress-related eating is significantly associated with obesity in women [84]. Moreover, overweight and obese individuals appear sensitized to food cues, particularly after exposure to stress. A recent study found that among healthy lean participants, mean food craving and energy intake decreased in the absence of hunger in response to both rest and stress conditions [85]. On the other hand, visceral overweight participants showed higher mean food craving and energy intake of hyperpalatable foods (e.g., desserts, snacks) in the absence of hunger when under stress versus rest, potentially as a mechanism to regulate and suppress stress [85]. Obese (versus lean) individuals demonstrated significantly increased activation in brain reward regions including the striatum, insula, and thalamus during exposure to favorite food cue and stress [29]. Moreover, the magnitude of insulin resistance positively correlated with the activation of the striatum and insula in response to both favorite food cue and stress conditions in obese but not lean individuals [29]. Mild hypoglycemia, induced by a hyperinsulinemic clamp, potentiated activation of brain reward and limbic regions preferentially to hyperpalatable food cues, an effect that correlated with increased cortisol levels, while decreasing medial prefrontal activation, an effect that correlated with lowering glucose levels; these effects were moderated by BMI and were more pronounced among obese individuals [86]. Chronic high levels of peripheral insulin and insulin resistance, as observed in many overweight and obese individuals [36], may impair insulin's ability to suppress motivation pathways, resulting in heightened stress- and food-cue-related responses.

EMOTIONAL EATING

Chronic stress is often accompanied by anxiety, depression, anger, apathy, and alienation [87]. Threatening and cognitively meaningful stimuli activate the emotional nervous system which, in part, determines behavioral output (e.g., fight-or-flight). Stress-induced elevations of GC secretion can intensify emotions and motivation [88]. Given the rewarding properties of food, it is hypothesized that hyperpalatable foods may serve as "comfort food" that acts as a form of self-medication to dispel unwanted distress. Individuals in negative affective states have been shown to favor the consumption of hedonically rewarding foods high in sugar and/or fat, whereas intake during happy states favor less palatable dried fruits [89]. Following laboratory exposure to ego threats, people exhibiting high negative affect or greater cortisol reactivity ate more food of high-sugar and high-fat content [28]. Similarly, in naturalistic settings, people with high cortisol reactivity report greater snacking in response to daily stressors [90].

RESTRAINED EATING

Restrained eating refers to the voluntary cognitive control effort to restrict food intake typically for the purpose of weight loss or maintenance. Cognitive restraint has been related to food intake under stress, with highly restrained eaters increasing and unrestrained eaters decreasing their food intake during stressful conditions [91]. This response differs from that of emotional eating – while restraint is associated with greater food intake after stressors, emotional eating is linked to increased intake after an ego-threat stressor [92]. Restraint eating may exacerbate eating in response to food cues, stress and other stimuli, whereas emotional eating may serve to ameliorate negative self-focused emotions. People endorsing higher levels of dietary restraint often show little overall difference in calorie intake compared to people with low restraint, or in food intake when unobtrusively observed in laboratory [93] and naturalistic settings [94]. Restraint may represent unsuccessful attempts at food restriction – eating less than one would during normal (low-stress) conditions, while tending to overeat during stress.

Several studies have found that high cognitive restraint is associated with increased cortisol concentrations [95, 96]. Increased restraint may play an important role in promoting obesity and serve as a vulnerability marker for a reward system sensitized to palatable food. For example, rats exposed to either repeated stress or food restriction alone did not differ from controls in their total food intake, when ignoring food type. With restriction alone, rats increased their chow intake in response to negative energy balance. However, when restricted eating was combined with stress, rats displayed a greater cookie intake over chow, suggesting hedonic feeding and stress arousal reduction rather than feeding for metabolic need alone [97]. In humans, a recent large-scale study reported that stress was related to various indices of increased drive to eat, including disinhibited eating, binge eating, and more frequent intake of hyperpalatable food (e.g., chips, hamburgers, and soda); additionally, greater stress exposure accounted for significantly higher rigid restraint [47]. While flexible restraint may be effective in weight management and prevention of excessive consumption of palatable non-nutritious food, rigid restraint may lead to sensitization of such foods. People who maintain rigid rules around their food appear less attentive to the

physiological cues of hunger and satiety, leading to overeating after a preload [98]. It is hypothesized that people actively trying to restrain food intake may deplete the cognitive resources necessary to deal with stressors, thereby impairing their inhibitory control which in turn increases the likelihood of overeating. Lack of control over life events may lead to desperate and ineffective attempts to control eating such as by deprivation from a particular food followed by later binging. Moreover, chronic food restriction may augment the rewarding (i.e. threshold-lowering) effects of drugs of abuse [99].

SLEEP DEPRIVATION

Sleep deprivation is a common chronic stressor that may contribute to increased risk for obesity and metabolic diseases, including abdominal obesity, insulin resistance, hypertension, atherosclerosis, that may predispose individuals to cardiovascular disease and type II diabetes [100, 101]. It is estimated that roughly 30% of all adults in the United States sleep less than 6h per night [102]. Cross-sectional analyses have found a significant association between short sleep duration and increased prevalence of obesity or higher BMI in both adult and child samples [103]. Two recent meta-analyses have found that short sleep duration (<5h per night for adults, <10h per night for children) significantly predicted obesity. Moreover, BMI was 0.35 kg/m^2 lower for every additional hour of sleep [104, 105].

Sleep deprivation may dysregulate the HPA axis, although data have been inconsistent. In laboratory settings, insulin sensitivity was reduced in sleep-restricted individuals [106]. Studies have demonstrated both increased [107, 108] and decreased [109] night-time and morning plasma cortisol levels. The Wisconsin Sleep Cohort Study reported that following one night of polysomnography in the laboratory, total sleep time from polysomnography was inversely associated with ghrelin levels while average habitual sleep duration was positively associated with leptin levels independent of BMI [110]. In a similar vein, data from the Quebec Family Study of 740 adults sleeping 5-6h per night had leptin levels approximately 15-17% lower than predicted based on body fat alone [111]. However, other studies have reported negative findings. For example, a sample of 173 obese, sedentary post-menopausal women aged 50-74 years found no cross-sectional associations between self-reported sleep duration and total leptin or ghrelin levels [112]. Interestingly, although hunger ratings and average nocturnal sleep were not significantly associated, adolescents who slept 3h or more during the daytime reported greater caloric intake and food cravings, and this association was not confounded by nocturnal sleep duration [113]. More research assessing the relationship between habitual insufficient sleep and food intake is needed.

Conclusion

Feeding is essential for life. The balance between energy storage and expenditure is critical for survival. It is therefore not surprising that neural networks that subserve feeding and stress responses form in early developmental stages [88]. During human evolution, food was scarce and life-threatening stressors frequent; elevated GCs level and depressed insulin levels, except when feeding, therefore served adaptive purposes. However, in our current obesogenic environment where food is plentiful, palatable and easy accessible, the proliferation of stressors may drive non-homeostatic feeding – in other words, eating without metabolic need. Repeated bouts of minor daily stressors that keep the stress system

in a chronically activated state may alter brain reward/motivation pathways involved in wanting and seeking hyperpalatable foods and induce metabolic changes that promote weight and body fat mass. Weight-related adaptions of the metabolic, neuroendocrine, and neuronal pathways can together potentiate food preference, craving and intake under conditions of stress. A sensitized feed-forward process may result in changes that promote elevated desires for and increased consumption of hyperpalatable foods. Individual differences in susceptibility to obesity and types of stress may further moderate this process.

While recent research has elucidated possible pathways for stress-related eating, there is considerable need for trying to better understand and prevent stress-related eating and non-homeostatic eating in general. Despite data suggesting potentially addictive properties of hyperpalatable foods, debate exists regarding the existence of food addiction [114-116]. For this and possibly other reasons, food addiction is generally overlooked in clinical settings. Large-scale prevention and treatment programs for food addiction (like those for substance addiction) are lacking with physicians, nurses, psychologists and other clinicians typically receiving little or no training in food addiction or its management. Identifying specific biomarkers and developing quantifiable measures to assess biobehavioral adaptations associated with stress and food addiction could be beneficial in developing public health intervention. Nonetheless, specific subgroups of individuals appear at elevated risk for food addiction. For example, binge-eating disorder shows a particularly close relationship with elevated odds of about 5 between food addiction and binge-eating disorder [117], and multiple other clinical characteristics (impaired impulse control, altered reward processing) linking binge-eating disorder and food addiction [118, 119]. By integrating information across disciplines in order to promote the development of improved policy, prevention and treatment strategies, significant advances in halting and reversing the current obesity epidemic may be achieved [120].

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