

Stress and Obesity

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Several types of psychological stress influence eating behavior; however, these associations vary widely across a number of psychological and physiological individual differences. Some individuals tend to eat more when stressed, whereas others tend to eat less. Furthermore, eating can itself influence stress arousal. Eating and the experience of stress are critical survival functions that share neurobiological pathways that are regulated by overlapping neuroendocrine systems. Here we review classic and recent literature on mechanisms linking stress and obesity; the intersection of stress, reward, and eating; laboratory and longitudinal associations among stress, eating, and weight gain; and societal implications of this body of findings.

Mechanisms Linking Stress and Obesity

Acute, isolated stressors, as well as chronic, ongoing stressors, impact eating behavior in both animals and humans. Most animal studies demonstrate that eating decreases under stress, unless highly palatable food is available, in which case selective eating of highly palatable food increases. This aligns with human studies documenting increased eating of widely available, highly palatable, calorie-dense “comfort foods” in response to the experience of stress.

Stress responses involve a neural network that comprises neurons in the hypothalamus, brainstem, and afferent nerves, as well as several areas within the limbic system and frontal cortex. Stress responses operate along two interacting pathways. One pathway is the limbic–hypothalamic–pituitary–adrenocortical (LHPA) axis, which produces a cascade of hormone secretions that represent an endocrinological stress response. These hormones include corticotropin-releasing hormone (CRH), adrenocorticotropic hormone (ACTH), and glucocorticoids (GCs).

A second pathway, the sympathetic–adrenal–medullary (SAM) axis, is a part of the autonomic nervous system (ANS) that involves the catecholamines adrenaline and

noradrenaline. Acute stress-induced catecholamine release leads to increased lipolysis (breaking down of triglycerides in the cell) and weight loss by stimulating beta-adrenergic receptors. Chronic stress, combined with a highly palatable diet, can lead to changes in the SAM and LHPA axes. In the SAM axis, this combination leads to impaired beta-adrenergic activation, release of neuropeptide Y (NPY), and subsequent growth of adipocytes. Chronic arousal of the LHPA axis leads to both larger adipocytes and dysregulated physiological satiety mechanisms. Hence, regulation of LHPA axis activity has a well-known, critical role in the neural regulation of eating and peripheral energy balance. Below, we focus on the intersection of dysregulation of the LHPA axis, stress, and obesity.

The LHPA Axis: An Intersection of Stress, Eating, and Obesity

The adrenal glands release GCs in response to real or perceived stress, and increases in GCs are associated with greater caloric intake, especially from highly palatable foods, in both humans and animals. Accordingly, experimental laboratory studies assessing eating behavior in response to acute stressors, naturalistic case-control studies examining longer-term changes in GCs and weight gain, and medical studies of hypercortisolism (as in Cushing syndrome), provide clear evidence linking chronically elevated GCs to greater adiposity, especially visceral adiposity.

One prominent mechanism by which activation of the LHPA axis alters glucose metabolism and hunger is via action on feedback loops involving appetite-regulating hormones. Specifically, increases in GCs are associated with elevations in insulin and leptin, which, paradoxically, are hormones that signal satiety. GCs can, however, reduce tissue sensitivities to both insulin and leptin. During chronic stress, sustained high levels of GCs can result in hyperinsulinemia, reduced insulin sensitivity, and resultant accumulation of visceral abdominal fat. That is, insulin resistance can blunt signaling in the satiety and reward areas of the brain, leading to reduced control of the physiological hunger system, overeating, and an increased drive to eat. Recent studies have suggested a similar pattern of increased leptin, leptin resistance, and reduced resting energy expenditure.

Chronic stimulation of the LHPA axis also inhibits the reproductive, growth, and thyroid hormonal axes. The effects of LHPA axis activation on these major endocrine axes serve to selectively redirect nutrients and all vital substrates to the brain and stressed areas of the body. Though adaptive in the short-term, prolonged, chronic stress can lead to long-term disruptions in metabolic homeostasis via these axes. These disruptions can contribute to weight gain, insulin resistance, and metabolic syndrome. For example, stress-induced activation of the LHPA axis decreases production of thyroid-stimulating hormone (TSH), which, in turn, can reduce basal metabolic rate and increase energy conservation.

Stress, Eating, and the Reward System

In addition to disruptions in the regulation of energy homeostasis, stress-induced LHPA axis activity can alter the mesolimbic reward area, which is replete with dopaminergic neurons. This can cause highly palatable, calorie-dense foods to be perceived as especially rewarding. Such foods have been termed "comfort foods" to signify their stress-dampening and rewarding properties. In animal models, stress-induced eating dampens the stress response by increasing dopamine secretion in the mesolimbic pathway,

including the ventral tegmental area (VTA) and nucleus accumbens (NAc). LHPA axis activation amplifies this rewarding experience by stimulating the release of endogenous opioids, which increase palatable food intake and additional opioid release. This sustained opioid release decreases LHPA axis activity and attenuates the stress response in a negative feedback fashion.

Habitual behavior can become embedded in the stress–reward pathway. Repeated and strong opioid responses in the reward neural circuitry promote the encoding of habits in the basal ganglia, which regulate habit-based behavior. Memories involving strong emotions, and the solutions that people use to cope effectively with them, are especially likely to be encoded. Hence, stress-induced eating of comfort foods is easily learned, remembered, and repeated. Functional magnetic resonance imaging (fMRI) data indicate that upon viewing images of highly palatable food, individuals endorsing greater chronic stress show exaggerated activity in regions of the brain involving reward, motivation, and habitual decision making, and reduced activity in areas linked to strategic planning and emotional control. It is therefore not surprising that many people increase their eating of highly palatable comfort foods when stressed.

Longitudinal Associations between Stress and Obesity

Large studies have examined cross-sectional and longitudinal associations between weight change and chronic psychological stress, such as that following from work-related issues (e.g., low job control), psychosocial factors (e.g., interpersonal relationships, bullying, social rejection), and cumulative stressful life events (e.g., traumatic early life experiences). Most associations have been weak to moderate, possibly due to the heterogeneity in eating behavior in response to stress. Some individuals tend to eat more, whereas others tend to eat less, and averaging responses obfuscates these individual differences. Thus, this potential bimodal distribution may account for small effects reported in the literature. Furthermore, prospective studies have found that stress-induced weight gain is contingent on baseline weight status and biological sex. For example, the Midlife in the United States (MIDUS) study, which examined 1,354 adults over a 9-year period, found that psychosocial stress was associated with weight gain among those with a higher body mass index (BMI) at baseline. Additionally, the types of stress associated with weight change differed across men (e.g., work-related stress) and women (e.g., family relationship stress). The Whitehall II Study, which investigated 7,965 British civil servants over a 5-year period, found that work-related stress was associated with weight gain for the most obese men. In contrast, work-related stress was associated with weight loss for the leanest men. In summary, obese status is a risk factor for further stress-induced weight gain, and different types of stressors differentially impact men's and women's weight gain over time.

Stress Reactivity, Eating, and Obesity

Laboratory studies have documented associations between stress responses and weight, especially abdominal adiposity. Laboratory paradigms designed to induce acute psychological stress have allowed researchers to investigate associations among acute stress responses and adiposity. A number of findings show associations among these acute stress responses (e.g., GC and autonomic reactivity) and measures of adiposity (e.g.,

abdominal obesity, generalized obesity, elevated BMI). A growing body of evidence suggests that abdominal obesity, relative to general obesity, may be more strongly correlated with LHPA axis dysregulation (both hypo- and hyperreactivity) and slower cardiovascular and endocrine recovery following acute stressors.

Though earlier research documented positive associations between GC reactivity and eating of palatable food in the laboratory, recent studies have demonstrated mixed results that may be due to important individual differences in dietary restraint, disinhibition, food insecurity, adiposity, and chronic stress levels, which we examine next. It remains important for researchers to develop research designs that will maximally clarify the extent to which acute stress reactivity in the laboratory can predict real-world eating of highly palatable food.

The Special Case of Chronic Stress

Recent research suggests that chronic stress is one important determinant of the association between GC reactivity and obesity. While several studies indicate that greater GC reactivity in the laboratory is associated with increased eating of palatable foods and abdominal adiposity, new studies indicate that lower GC reactivity (hyporeactivity) is also a risk factor for stress-induced eating. These discrepant associations may be due to varying levels of chronic stress, as explained by the *chronic stress response network model* (Mary Dallman and colleagues), which posits that chronic stress increases eating of palatable food, which, in turn, increases abdominal fat and inhibits acute stress-induced LHPA axis responses. Thus, chronically stressed individuals who habitually overeat highly palatable food may evidence blunted GC reactivity in response to acute stressors. This model has been demonstrated in animal studies (e.g., rats, rhesus monkeys) and, more recently, has been observed cross-sectionally in humans. The phenotype of blunted GC reactivity is in fact a common profile in stress-related disorders, and it is possible that chronic eating of palatable food may partially underpin this profile. To test this idea, we recently examined the extent to which a high-sugar diet suppressed stress responses. Results showed that 2 weeks of increased sugar consumption dampened GC reactivity to acute stress, thus demonstrating a metabolism-to-brain negative feedback loop. In summary, data from animals, and a small but growing body of data from humans, suggest that chronic stress is associated with greater eating of palatable food, and that stress-induced eating of palatable food alters LHPA axis activity.

Conclusion and Future Directions

The eating of highly palatable, calorie-dense comfort foods to reduce stress can foster problematic weight gain. The neural networks that regulate eating and psychological stress are tightly intertwined. In the past three decades, the modern food environment has swelled with increasing cues and opportunities to eat highly palatable food, and researchers have documented small but significant population-level increases in psychological stress. Mechanistic and longitudinal studies in animals and humans have demonstrated that the experience of stress can promote eating of highly palatable foods which, in turn, can reduce stress responses. Coupled with increased chronic stress, widespread chronic eating of highly palatable foods promotes habitual stress-induced eating as an extremely accessible coping strategy.

Associations between stress and obesity depend on multiple risk factors and moderators. Chronic stress increases risk for weight gain among individuals who are already overweight or obese; however, there are important differences between men and women in terms of which types of stressors confer this risk. Furthermore, it is important to understand risk factors for stress-induced eating at multiple levels, which include prenatal stress exposure, trauma and poor nutrition in childhood, family and relationship issues, employment and work-related factors, food insecurity and neighborhood food accessibility, and individual differences in the experience of a drive to eat for reward and sensitivity to food cues.

In summary, mechanistic research has shed light on pathways linking stress and weight change in animals and humans, as well as some of the complexities of these associations. Although more basic research, especially with humans, is needed, we should use what we know about associations between chronic stress and eating behavior to inform prevention efforts that target individuals who are at increased risk for weight gain. We believe this will require societal efforts focused on reducing population-wide increases in psychosocial stress, cultivating stress resiliency across the lifespan, and fostering the growth of and access to healthy food environments.

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Suggested Reading

- Adam, T. C., & Epel, E. S. (2007). Stress, eating, and the reward system. *Physiology and Behavior*, 91(4), 449–458.—The authors propose a theoretical model of reward-based stress eating and uses animal and human literatures to explain how different types of psychological stress impact eating.
- Block, J. P., He, Y., Zaslavsky, A. M., Ding, L., & Ayanian, J. Z. (2009). Psychosocial stress and change in weight among US adults. *American Journal of Epidemiology*, 170(2), 181–192.—This article reports on associations between weight gain and several domains of psychological stress among adults enrolled in the MIDUS study.
- Dallman, M. (2010). Stress-induced obesity and the emotional nervous system. *Trends in Endocrinology and Metabolism*, 21(3), 159–165.—This article reviews emotional and regulatory brain networks, and outlines processes by which stress and GC secretion can impact behavior that increases risk for obesity.
- Kyrou, I., Chrousos, G. P., & Tsigos, C. (2006). Stress, visceral obesity, and metabolic complications. *Annals of the New York Academy of Sciences*, 1083(1), 77–110.—The authors discuss stress physiology with an emphasis on metabolism, and highlight data suggesting that multiple neuroendocrine and inflammatory mechanisms impact the paths through which chronic stress can contribute to central obesity and metabolic syndrome.
- Maniam, J., & Morris, M. J. (2012). The link between stress and feeding behaviour. *Neuropharmacology*, 63(1), 97–110.—This article reviews the neuropeptides that regulate eating behavior and how their function can be altered by cross talk with neuropeptides and hormones that also regulate the HPA axis.
- Mietus-Snyder, M. L., & Lustig, R. H. (2008). Childhood obesity: Adrift in the “limbic triangle.” *Annual Review of Medicine*, 59, 147–162.—This article reviewed three interacting

neural systems that regulate eating and food choices—the ventromedial hypothalamus (hunger), the VTA, and the NAc (reward seeking), and the amygdala (emotional responding)—and how factors such as stress and leptin resistance can dysregulate these systems.

- Nyberg, S. T., Heikkilä, K., Fransson, E. I., Alfredsson, L., De Bacquer, D., Bjorner, J. B., et al. (2012). Job strain in relation to body mass index: Pooled analysis of 160,000 adults from 13 cohort studies. *Journal of Internal Medicine*, 272(1), 65–73.—The authors performed a pooled analysis to examine cross-sectional and longitudinal associations between job strain and BMI in adults enrolled in 13 European studies.
- Rosmond, R. (2005). Role of stress in the pathogenesis of the metabolic syndrome. *Psychoneuroendocrinology*, 30(1), 1–10.—This article reviews the pathways by which GC secretion plays a pathogenic role in the development of obesity and is associated with factors comprising metabolic syndrome.
- Sinha, R., & Jastreboff, A. M. (2013). Stress as a common risk factor for obesity and addiction. *Biological Psychiatry*, 73, 827–835.—This article reviews the role of stress as a risk factor for obesity and addiction, and proposes an integrative heuristic model that outlines the hypothesis that chronically high stress levels alter stress biology and both appetitive and energy regulatory systems in ways that promote stress-induced overeating of highly palatable food, thereby increasing risk for weight gain.
- Ulrich-Lai, Y. M., Christiansen, A. M., Ostrander, M. M., Jones, A. A., Jones, K. R., Choi, D. C., et al. (2010). Pleasurable behaviors reduce stress via brain reward pathways. *Proceedings of the National Academy of Sciences USA*, 107(47), 20529–20534.—This article presents experimental data showing that the hedonic properties of highly palatable foods have stress-reducing effects that can therefore increase motivation to eat in times of stress.