ISSN 2181-

STRESS, APPETITE, AND WEIGHT GAIN: NEUROENDOCRINE MECHANISMS LINKING CORTISOL AND EATING BEHAVIOR.

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Abstract

Chronic psychological stress is a key driver of dysregulated eating behaviors and weight gain. Central to this relationship is cortisol, a glucocorticoid hormone produced by the adrenal cortex in response to activation of the hypothalamic–pituitary–adrenal (HPA) axis. While acute stress tends to suppress appetite, chronic stress leads to sustained cortisol secretion, which alters energy balance, promotes hedonic eating, and increases visceral adiposity. This review explores the neuroendocrine and behavioral mechanisms through which cortisol influences appetite regulation, macronutrient preference, and body fat distribution, emphasizing the interplay between stress physiology, metabolic signaling, and reward pathways in the brain.

Keywords: chronic stress, cortisol, hypothalamic–pituitary–adrenal axis, neuroendocrine regulation, appetite control, emotional eating, hedonic eating, reward pathways

Introduction

Stress is an adaptive physiological response designed to restore homeostasis when an organism faces perceived threats. However, chronic exposure to stressors can lead to maladaptive outcomes, including metabolic disturbances and obesity. Epidemiological data consistently link chronic stress with increased caloric intake, preference for energy-dense foods, and weight gain, particularly in women and individuals with higher cortisol reactivity (Epel et al., 2000). The HPA axis is central to this phenomenon. Through its end-product cortisol, stress exerts widespread effects on metabolism, immune function, and appetite regulation. Understanding the pathways by which cortisol modulates eating behavior is crucial for developing targeted interventions for stress-related obesity.

When a stressor is perceived, the paraventricular nucleus (PVN) of the hypothalamus releases corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP). These hormones stimulate the anterior pituitary to secrete adrenocorticotropic hormone (ACTH), which then prompts the adrenal cortex to release cortisol.

Cortisol exerts negative feedback at the hypothalamic and pituitary levels, maintaining homeostasis. However, chronic stress results in HPA axis hyperactivity, characterized by prolonged cortisol elevation, blunted feedback inhibition, and altered diurnal rhythms (McEwen, 2007).

The hypothalamus integrates metabolic and neuroendocrine cues governing appetite. Under chronic stress, cortisol increases the expression and activity of orexigenic neuropeptides, such as neuropeptide Y (NPY) and agouti-related peptide (AgRP), in the arcuate nucleus (ARC). Concurrently, it inhibits anorexigenic pathways mediated by pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) neurons (Dallman et al., 2003).

This neuropeptidergic modulation shifts the energy balance toward increased food intake and energy storage. Cortisol's metabolic actions further promote appetite and adiposity:

Insulin: Chronic cortisol exposure induces insulin resistance, leading to compensatory hyperinsulinemia, which increases appetite and fat deposition.

Leptin: Elevated cortisol impairs leptin sensitivity, disrupting satiety signaling.

Ghrelin: Stress-induced cortisol release correlates with elevated ghrelin, the "hunger hormone," reinforcing food-seeking behavior (Rouach et al., 2007).

Beyond homeostatic regulation, stress engages dopaminergic reward circuits in the mesolimbic pathway—notably the ventral tegmental area (VTA) and nucleus accumbens (NAc). Cortisol enhances dopamine transmission in these areas, amplifying the rewarding properties of palatable, high-fat, high-sugar foods (Adam & Epel, 2007). This "comfort eating" serves as a coping mechanism, transiently reducing perceived

stress through activation of opioid and dopaminergic systems. Over time, this behavior becomes reinforced, creating a feed-forward loop linking stress, reward-seeking, and metabolic dysfunction.

Chronic elevation of cortisol preferentially promotes visceral fat accumulation, driven by increased activity of 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) in adipose tissue, which locally regenerates active cortisol from cortisone. Visceral adipose tissue, in turn, secretes pro-inflammatory cytokines (IL-6, TNF-α) that exacerbate insulin resistance and HPA axis activation—perpetuating a vicious metabolic cycle (Björntorp, 2001).

Human studies demonstrate that individuals with high cortisol reactivity to stress consume more calories and prefer energy-dense foods (Epel et al., 2001). Furthermore, nighttime cortisol elevations are associated with emotional eating and binge-eating disorder (BED) symptoms. Pharmacological suppression of cortisol with mifepristone (a glucocorticoid receptor antagonist) or stress-reduction interventions like mindfulness-based stress reduction (MBSR) have been shown to improve eating control and reduce abdominal fat.

Managing stress-induced weight gain requires multimodal strategies targeting both physiological and behavioral pathways:

Psychological: Cognitive-behavioral therapy (CBT), mindfulness, and relaxation training reduce HPA axis activation and emotional eating.

Behavioral: Regular physical activity attenuates cortisol responses and improves insulin sensitivity.

Pharmacological: Research is exploring agents that modulate 11β-HSD1 activity or glucocorticoid receptor sensitivity.

Lifestyle: Sleep optimization and balanced macronutrient intake can help stabilize cortisol rhythms and appetite.

Conclusion

The interplay between stress, cortisol, and eating behavior represents a critical axis in the pathogenesis of obesity. Chronic HPA axis activation alters neuroendocrine, metabolic, and reward processes, leading to sustained hyperphagia and visceral fat accumulation. Future interventions should focus on stress regulation and neuroendocrine balance to prevent and treat stress-related metabolic disorders.

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