INTRODUCTION
Stress is increasingly recognized as a factor leading to overeating and obesity. Here we present the evidence that stress-related eating follows well-defined neural pathways that involve control over volitional behavior (prefrontal cortex [PFC]), and subcortical areas controlling stress arousal and energy storage (limbic hypothalamic-pituitary-adrenal [L-HPA] axis) and strong motivational drive and impulsivity (nucleus accumbens [NAcc]). The PFC and limbic system inhibit activity in each other, promoting a balance between slower reflective analytic reasoning, necessary to promote goal-directed behavior, and quick reactive survival instincts. Shifts in activity of this neural network, what we call here the “PFC/limbic balance,” has well-demonstrated effects on cognition and behavior during acute stress. It is now becoming clear that this neural network shapes eating behavior. We propose that a low PFC/limbic balance can lead to energy imbalance and, in particular, abdominal obesity.

We first review neural and hormonal control of eating during basal conditions and then under stressful circumstances, showing that in large part = stress affects activation of reward pathways and impairs attempts to control eating. We conclude with suggestions for treatment of this widespread common behavior.

BASIC MECHANISMS UNDERLYING HOMEOSTATIC EATING AND STRESS-RELATED OVEREATING
We are equipped with highly evolved regulatory systems that monitor the amount of stored energy and are attuned to the need to find and eat more calories. In chordates, this system resides primarily in the brainstem and hypothalamus, and it is sensitive to hormonal and nutrient signals acting directly on receptors decorating the neurons within this network. Regulation of homeostatic eating is covered in detail elsewhere. Left alone, the homeostatic regulation of feeding behaviors is remarkably accurate and over weeks, months, and years the organism neither gains nor loses much weight. Despite the complex coordination between gut, pancreas, vagus, and brain, this regulatory system is easily overridden by our emotions. As more brain was added to mammals, such as limbic and cortical networks, regulation of food intake became far more complicated and far less driven by maintenance of energy stores. Higher brain structures also innervate the brainstem and hypothalamic network and, at each level, can subvert or reinforce their normal operations of maintaining energy homeostasis. In particular, eating for reward, or hedonic eating, contributes to a large proportion of our caloric intake. We posit that stress is a major factor that promotes hedonic eating and strengthens networks toward tonic hedonic overeating. This makes sense in that the stress response is likely a mere subset of the metabolic networks that maintain caloric balance, our primary survival need. The focus of this review is the mechanisms for stress eating and the outcomes of energy balance and fat distribution.

Stress Drives Specific Intake of Comfort Food
Both acute, single stressors and chronic, sustained stressors are likely to change feeding behaviors in people and rats. Roughly 40% of people reduce and 40% increase their total caloric intake during stressors, with only 20% maintaining intake at normal
levels. Rats and mice, given only chow to eat, uniformly decrease food intake during stressors. This is an important observation to note, as historically it was assumed that stress led to weight loss in animals. However, if supplied with highly palatable foods to eat, rats still decrease chow intake but maintain intake of the same or more palatable food, as people do. Whether they decrease or increase caloric intake, people change the type of food ingested, with negative emotion driving a shift away from healthy foods toward highly palatable food—usually sweet, sometimes salty, and high fat, and sometimes moderated by high dietary restraint.

THE STRESS-HEDONIC EATING MODEL

In Figure 40.1, we pose a simplified version of the neural networks regulating stress-induced hedonic eating. There are interactive connections between structures regulating eating—the limbic system, reward system, basal ganglia, and PFC. Differential patterns of activation shape two distinct types of eating behavior—stress-induced hedonic eating (S-EAT) versus homeostatic eating (H-EAT), which is eating solely in response to caloric need.

Limbic Structures, Stress, and Regulation by the Stress Hormone Cortisol

Stressors engage a network of limbic (phylogenetically ancient) structures that reflect interoceptive as well as exteroceptive inputs: the insula, extended amygdala, and anterior cingulate cortex, as well as thalamic, hypothalamic, and lower brainstem sites. This recruitment of the stress network appears to depend on the actions of glucocorticoids secreted from the adrenal cortex in response to stressors, and the network is engaged to a large extent through the positive actions of glucocorticoids on corticotropin releasing factor (CRF) expression in extrahypothalamic neurons. Acute cortisol reactivity appears to acutely promote comfort food intake both in the lab and naturalistically.

Both acute and chronic stressors increase synapses and dendritic bushing in the amygdala and anterior cingulate cortex, and they reduce synaptic contacts with dendritic atrophy in the hippocampus and PFC, further sculpting the chronic stress network toward limbic-biased stress responses. Chronic stress effects on the brain may alter eating tonically toward greater comfort food. Women reporting greater chronic stress report greater hunger drive and greater high-fat intake.

Stress Stimulates the Reward System

Exposure to psychological stressors can induce a hefty immediate stress response. Stress activates limbic CRF, in particular from the amygdala and hypothalamus, and consequently the L-HPA axis. Activation of the L-HPA is linked to activation of the mesolimbic reward area activity. There are several examples of the tight interconnection between stress and reward areas. Anatomically, increased CRF secretion resulting from activation of this central stress response network impinges on dopamine neurons in the ventral tegmental area and increases dopamine secretion over the NAcc that is stimulated by drugs, and possibly stressors. Stress is linked to craving and drug addiction in people (see Chapter 9). In humans exposed to a lab stressor during a positron emission tomography study, stress

![Figure 40.1. Stress-induced hedonic eating. PFC, prefrontal cortex.](image-url)
exposure, as well as cortisol release, both enhanced dopamine release from the NAcc. In another study on acute stress, those who responded with greater cortisol reactivity released more dopamine in the ventral striatum, showing a very strong coupling of the two.

In turn, the experience of dopamine stimulation is one of craving or drive for pleasure, and food is the most available and inexpensive drug around—a "natural" reward. For example, rats that had opioids injected into their reward area respond by overeating.

Stress Subjugates the Prefrontal Cortex: Impaired Prefrontal Cortex/Limbic Balance
The PFC is a key player in stress neural networks. During normal conditions, the PFC reigns, and cognition is dominated by reflective cognition. During stress, however, the thoughtful PFC activity is dampened and the amygdala and limbic circuitry dominate, promoting automatic behavior geared toward survival, including being vigilant for food cues. In rats, PFC neurons inhibit both dopamine from the NAcc and the L-HPA axis cortisol response.

Conversely, stressors lead both to reduction of PFC function and increased habit expression, thus reinforcing the likelihood of seeking and eating sweet foods after a stressor regardless of whether the stressed individual ranks highly on dietary restraint. The stressed brain expresses both strong drive to eat and impaired capacity to inhibit eating—a potent formula for obesity.

Dietary Restraint: Adaptive Regulator or Additional Stressor?
The construct of dietary restraint is an important individual difference that moderates many of the relationships in Figure 40.1. Dietary restraint is defined as voluntary cognitive control over one’s eating to restrict food intake to control body weight. Some restraint is necessary to have in our abundantly palatable food environment, but high levels are linked to overeating in states of stress.

A critical distinction is the difference between flexible versus rigid restraint. We propose that high PFC/limbic balance is related to high levels of “adaptive restraint,” or the type of flexible dietary restraint behaviors that promote appropriate control over eating. This high balance allows the volitional flexible control needed to self-monitor and adjust to changes in one’s food environment and behavior, such as awareness of how much one has eaten and then adjusting accordingly. Flexible restraint is associated with less disinhibited eating, less frequent/severe binge eating, lower weight, and lower energy intake. In contrast, maladaptive or "rigid restraint" reflects severe behaviors to control eating, based on...
inflexible cognitive rules such as having forbidden foods, and skipping meals. Rigid restraint is associated with disinhibited eating, higher body mass index, greater binge eating, and greater chronic stress. Those high in rigid restraint, therefore, may reflect low PFC/limbic balance and be particularly vulnerable to S-EAT processes. Rigid restraint may itself serve as a stressor, since rigid restraint represents frequent cognitive load or demands on attention and working memory, and violations of one’s desires to eat less. General measures of restraint have been associated with perceived stress as well as increased cortisol. Furthermore, subjective and objective indices of chronic stress are associated with greater rigid and lower flexible restraint. While high stress may promote more rigid restraint, it is also likely that high levels of rigid restraint chronically activate the L-HPA pathways, leading to physiological stress and strengthening the low PFC/high limbic imbalance, promoting a vicious cycle of overcontrol and loss of control.

PUTTING IT ALL TOGETHER: CONTRASTING STRESS EATING VERSUS HOMEOSTATIC EATING

Ingestive behavior can involve many processes, from hunger and satiety detection, to food choice, to cessation of eating. Given that eating is largely a habitual behavior, often done unintentionally with little awareness, it is regulated in part by the PFC/limbic balance, and thus it is affected by states of stress. Table 40.1 summarizes how eating processes are regulated differently under stress versus nondemanding conditions.

The PFC, particularly the right frontal PFC, plays a crucial role in eating behavior, as demonstrated by certain neurological conditions. Interceptive awareness of hunger and satiety cues uses somatosensory perception, relying on the anterior insula cortex and, for satiety, the orbitofrontal cortex. PFC also promotes inhibition of undesired responses, so it is crucial in controlling overeating. Those with successful weight loss maintenance have higher activity in certain frontal regions and secondary visual cortex in response to food images than those who are obese. The dorsolateral PFC also drives top-down decision making about food choices, enabling one to plan for healthy choices based on goals and nutrition knowledge.

In contrast, stress can disinhibit aspects of PFC circuitry that are so necessary for self-regulation of eating. Emotional states can be misinterpreted as hunger. The limbic brain, amygdala, and hypothalamus drive salience for survival-related cues, making food cues salient and increasing the arousal drive to consume. Stress may thwart careful self-regulation (flexible control) over food portions. Conversely, people with rigid control tend to lose that control under stress, and overeat, at least in laboratory studies. Instead of being a result of thoughtful decisions, S-EATing is driven by ventral tegmental area-driven impulse, and habit circuitry, housed in the basal ganglia. For the stressed brain, food “choices” seem to become predetermined or habitual search for dense calories or highly palatable food, rather than a conscious choice.

**TABLE 40.1. CONTRASTING EATING-RELEVANT BEHAVIOR IN HOMEOSTATIC EATING VERSUS STRESS EATING**

<table>
<thead>
<tr>
<th>Process</th>
<th>Homeostatic Eating (H-EAT) (PFC Driven, Somatosensory Cortex)</th>
<th>Stress Eating (S-EAT) (Amygdala, Limbic, Hypothalamus Driven)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hunger</td>
<td>Awareness of hunger level, sensitivity to somatosensory cues</td>
<td>Confusion of emotions with hunger (arousal drive), blunted awareness of somatosensory cues</td>
</tr>
<tr>
<td>Control over onset and cessation of eating</td>
<td>Flexible restraint</td>
<td>Rigid restraint and loss of control</td>
</tr>
<tr>
<td>Decision making about food choices</td>
<td>Reflective eating enables healthy choices (goal-directed behavior)</td>
<td>Reflexive eating of highly palatable food, pursuit of comfort food (habit-driven behavior)</td>
</tr>
<tr>
<td>Satiety</td>
<td>Awareness of sensations of satiety, physical cues</td>
<td>Blunted sensitivity to satiety and physical cues</td>
</tr>
</tbody>
</table>
CONSEQUENCES OF A CHRONICALLY STRESSED SOCIETY AND INTERVENTIONS FOR STRESS EATING

Living in increasingly stressful times creates a potent formula for low PFC/limbic balance, impaired flexible restraint, and sustained excess energy intake, preferentially stored as “stress fat,” in the visceral area. Although it is hard to determine how pervasive S-EATING versus H-EATING may be, it could account for a large proportion of our societal caloric excess and the obesity epidemic. Given that S-EAT patterns may be maintained by historical stressors, or provoked by the mildest of daily stressors, and masquerade as habit, it is hard to identify the unique contribution of S-EATING to one’s total caloric intake, at least in humans.

Psychoeducational strategies are not enough to counter the strong habitual forces of S-EAT, especially when the food environment is likely the most powerful influence on eating behavior. Exercise improves function of the PFC, but it may not be enough to counter the epidemic. Retraining of the brain to pay effortful attention to eating and to emotions is probably a necessary but not sufficient component in any obesity intervention. Experimental work supports the potential role of techniques that work on reappraisal of emotional stressors, and even simply labeling emotions verbally, in establishing a stronger PFC/limbic balance and control over eating. Mindfulness, or nonjudgmental attention to the present moment, promotes more reflective cognition, awareness of emotions, and separation of emotions from hunger. Mindful eating can reduce binge eating. People high on dispositional mindfulness show stronger PFC/limbic balance (high PFC, low amygdala activity) when simply labeling emotions. Structural data show that meditation is associated with greater volume of right orbital prefrontal cortex, insula, and hippocampus, which are important in self-control. We are currently testing whether mindful eating and mindful stress reduction can reduce S-EAT in obesity. However, given the pervasive exposure of both the toxic food environment and societal-wide chronic stress, it is likely that policies that reduce the toxic food environment and societal stress are both necessary to tide the epidemic.

REFERENCES


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