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Comfort food is comforting to those most stressed: Evidence of the chronic stress response network in high stress women

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Summary Chronically stressed rodents who are allowed to eat calorie-dense "comfort" food develop greater mesenteric fat, which in turn dampens hypothalamic—pituitary—adrenocortical (HPA) axis activity. We tested whether similar relations exist in humans, at least cross-sectionally. Fifty-nine healthy premenopausal women were exposed to a standard laboratory stressor to examine HPA response to acute stress and underwent diurnal saliva sampling for basal cortisol and response to dexamethasone administration. Based on perceived stress scores, women were divided into extreme quartiles of low versus high stress categories. We found as hypothesized that the high stress group had significantly greater BMI and sagittal diameter, and reported greater emotional eating. In response to acute lab stressor, the high stress group showed a blunted cortisol response, lower diurnal cortisol levels, and greater suppression in response to dexamethasone. These cross-sectional findings support the animal model, which suggests that long-term adaptation to chronic stress in the face of dense calories result in greater visceral fat accumulation (via ingestion of calorie-dense food), which in turn modulates HPA axis response, resulting in lower cortisol levels.

1. Introduction

Obesity and obesity-related disease states such as metabolic syndrome are highly prevalent (Crawford et al., 2010). Concurrently, the United States is faced with historically high levels of psychological stress (American Psychological Association, 2009). Both of these trends are taking place within a "toxic" food environment that promotes overeating—particularly overeating of calorie-dense, nutrient-poor foods (Wadden et al., 2002). There are robust and complex connections between obesity, psychological stress, and eating behavior (Adam and Epel, 2007; Dallman, 2010; Warne, 2009). The role of stress in promoting eating and obesity has been relatively well characterized. For exam-

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ple, stress has been shown to promote both obesity (Dallman, 2010; McEwen, 2008; Wardle et al., 2010) and food intake (Born et al., 2010; Epel et al., 2001; Pecoraro et al., 2004; Rutters et al., 2009). In the former, *abdominal* obesity is most affected by stress due to the role of prolonged stress-induced glucocorticoid secretion in promoting abdominal fat deposition (Bjorntorp and Rosmond, 2000; Dallman et al., 2005). In the latter, also primarily driven by glucocorticoids, stress promotes consumption of highly palatable, nutrient-dense foods high in sugar and fat (Adam and Epel, 2007; Torres and Nowson, 2007; Warne, 2009). Further, acute and chronic stress can interact to exacerbate stress eating. For example, those who are under chronic stress tend to eat more under acute stress conditions (Gibson, 2006).

In the current study, we focus on the converse—eating and obesity affecting stress responses. Although this converse relationship is undoubtedly equally important, it has to date only been directly studied in non-human animal models (Dallman, 2010; Pecoraro et al., 2004). In this model, termed the *chronic stress response network* model, rats exposed to repeated chronic restraint stress that are then given lard or sucrose demonstrate *attenuated* stress responses compared to those given chow. Specifically, the otherwise expected CRF expression and ACTH secretion in response to stress is reduced (Foster et al., 2009; la Fleur et al., 2005; Pecoraro et al., 2004). Similarly, rats given sucrose show attenuation of stress-induced activation of the lateral septum (Martin and Timofeeva, 2010). Early life stressors such as maternal separation in rats also appear to activate the chronic stress response network. A palatable cafeteria high-fat diet normalized the effects of prolonged maternal separation in rats, reversing increases in anxiety and depressive behaviors, increased cortisosterone, increased hypothalamic CRH, and increased hippocampal glucocorticoid receptor expression (Maniam and Morris, 2010). In other words, it appears that rats are ''self-medicating'' through the use of food to regulate their stress responses—specifically their hypothalamic–pituitary–adrenocortical (HPA) axis responses.

These rats, over time, develop greater mesenteric fat, and this mesenteric fat has been found over multiple studies to be negatively correlated with CRF mRNA expression in the paraventricular nucleus (Dallman et al., 2003a,b; Laugero et al., 2001). This process is one purported mechanism explaining how, over time, chronically stressed humans appear to have hypocortisolism (Fries et al., 2005), but this has not yet been directly tested in humans. One study (Arce et al., 2009) found evidence of the chronic stress response network in rhesus monkeys: subordinate females consumed more calories, gained more weight, and subsequently showed lower diurnal cortisol responses and dampened cortisol responses to an acute social separation stressor.

In sum, greater mesenteric fat, likely developed through repeated consumption of palatable foods, appears to dampen the activity of the HPA axis in chronically stressed rodents and appears to be conserved across species to monkeys. The chronic stress response network has to date only been tested in non-human animal species, and thus we test the potential relevance of this model to humans in the current study. Prior studies of eating, obesity, and stress responses have not directly tested for evidence of the chronic stress response network, and instead have focused on a main effects model whereby greater stress and cortisol is associated with greater obesity. Indeed, in community samples, there may be and have been documented (Epel et al., 2004; Newman et al., 2006) positive associations between abdominal fat and cortisol output in response to acute stress. There is reason to believe, however, that in *highly* stressed humans we might find the opposite relationship due to the chronic stress response network. These individuals likely have coped with high levels of stress by engaging in stress-eating, thereby developing blunted HPA axis responses like the rats given the opportunity to consume comfort food. Here, we isolate a very high stress group and test for evidence supporting the chronic stress response network.

Given that the prior studies show greater intake of comfort food during stress and recovery from stress, greater mesenteric fat pads, and the amount of the pad is directly related to lowered CRF in the brain and lowered HPA axis response to acute stress, we can make several hypotheses about what to expect in humans under stress who have recruited the chronic stress response network. Specifically, if the chronic stress response network is activated in humans, we would expect the following observations, cross-sectionally:

1. Those with high stress will have greater self-medication with palatable food, and thus will thus report higher scores on self-reported emotional eating.
2. Those with high stress should have greater abdominal fat distribution, as measured by sagittal diameter and overall adiposity as measured by BMI.
3. If those with high stress do tend to have greater abdominal fat distribution, they should also show dampened HPA axis activity in response to acute stress, and diurnally and greater sensitivity to dexamethasone.

2. Methods

2.1. Sample

Fifty-nine healthy premenopausal women aged 20–50 participated in this study. To capture a wide range of chronic psychological stress, this sample contained caregivers of chronically ill children ($n = 40$) and caregivers of healthy children ($n = 19$). Exclusion criteria included post-menopausal status, heavy drinking (7+ drinks per week), major depression, and chronic health conditions except controlled hypertension with beta blockers or ACE inhibitors ($n = 2$) and controlled hypothyroidism with Synthroid supplementation ($n = 1$). Smokers were included but were asked to refrain from smoking on the day of the lab session.

2.2. Procedures

All procedures were fully approved by the University of California, San Francisco Committee on Human Subjects Research. To control for menstrual cycle-related effects on cortisol reactivity, all women were tested within the first seven days of their follicular cycle. To control for diurnal