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Invited review

The link between stress and feeding behaviour

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ABSTRACT

Exposure to stress is inevitable, and it may occur, to varying degrees, at different phases throughout the lifespan. The impact of stress experienced in later life has been well documented as many populations in modern society experience increasing socio-economic demands. The effects of stress early in life are less well known, partly as the impact of an early exposure may be difficult to quantify, however emerging evidence shows it can impact later in life. One of the major impacts of stress besides changes in psychosocial behaviour is altered feeding responses. The system that regulates stress responses, the hypothalamo-pituitary-adrenal axis, also regulates feeding responses because the neural circuits that regulate food intake converge on the paraventricular nucleus, which contains corticotrophin releasing hormone (CRH), and urocortin containing neurons. In other words the systems that control food intake and stress responses share the same anatomy and thus each system can influence each other in eliciting a response. Stress is known to alter feeding responses in a bidirectional pattern, with both increases and decreases in intake observed. Stress-induced bidirectional feeding responses underline the complex mechanisms and multiple contributing factors, including the levels of glucocorticoids (dependent on the severity of a stressor), the interaction between glucocorticoids and feeding related neuropeptides such as neuropeptide Y (NPY), alpha-melanocyte stimulating hormone (α-MSH), agouti-related protein (AgRP), melanocortins and their receptors, CRH, urocortin and peripheral signals (leptin, insulin and ghrelin). This review discusses the neuropeptides that regulate feeding behaviour and how their function can be altered through cross-talk with hormones and neuropeptides that also regulate the hypothalamo-pituitary-adrenal axis. In addition, long-term stress induced alterations in feeding behaviour, and changes in gene expression of neuropeptides regulating stress and food intake through epigenetic modifications will be discussed.

This article is part of a Special Issue entitled 'SI: Central Control of Food Intake'.

1. Introduction

Stress has been shown to affect food intake in a bidirectional manner, inducing either increases or decreases food intake, as is well evidenced in both in human and animal studies (Martí et al., 1994; Harris et al., 1998; McIntosh et al., 1999; Pecoraro et al., 2004; Foster et al., 2006; Ryu et al., 2008; Groesz et al., 2011; Tomiyama et al., 2011; Schulz and Laessle, 2012). In animals, most studies demonstrate that stress reduces food intake, unless access to palatable food is given during the stress period, and this is in line with human studies reporting feeding responses to stressful situations (Pecoraro et al., 2004; Dallman et al., 2006; Adam and Epel, 2007; Tomiyama et al., 2011). Stress-induced eating of palatable food is also known as non-homeostatic eating. This eating behaviour has been hypothesized to activate the brain reward system and decrease activity of the hypothalamo-pituitary-adrenal (HPA) axis, dampening the stress response, as evidenced by lower cortisol (Tomiyama et al., 2011) and corticosterone (Pecoraro et al., 2004) concentrations (Pecoraro et al., 2004; Adam and Epel, 2007; Tomiyama et al., 2011). The phenomenon of stress induced positive energy intake has been associated with increased risk for developing obesity and its associated diseases such as diabetes and cardiovascular disease, which have become a primary public health concern.

Stress is defined as a state in which homeostasis is disrupted or perceived to be threatened (Chrousos, 2009). This infers that insults

Abbreviations: ACTH, adrenocorticotophic hormone; AgRP, agouti-related protein; alphaMSH, alpha-melanocyte stimulating hormone; 5-HT, serotonin; 11 beta HSD, (11 beta hydroxysteroid dehydrogenase); CRH, corticotrophin releasing hormone; GR, glucocorticoid receptor; MC, melanocortin; HFD, high fat diet; HPA, hypothalamic-pituitary-adrenal; ICV, intracerebroventricular; LPS, lipopolysaccharide; npEW, Edinger-Westphal nucleus; NPY, neuropeptide Y; POMC, proopiomelanocortin; VTA, ventral tegmental area.

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in any form, including emotional fluctuations, an adverse physical environment, social disruption (isolation or overcrowding), or a change in diet that interrupts homeostasis can represent a stressor. The system that regulates stress responses, the HPA axis, plays an essential role in feeding responses because the neural circuits that regulate energy intake converge on the paraventricular nucleus, which contains the cell bodies of corticotrophin releasing hormone (CRH) containing neurons. Thus this region regulates HPA axis responsivity and in addition responds to circulating glucocorticoids and insulin (Dallman et al., 1995; Nieuwenhuizen and Rutters, 2008) providing overlap between the stress and feeding systems. Glucocorticoids secreted by the adrenal gland (released in response to stress) and insulin secreted from the pancreas, have opposite effects on feeding responses (Strack et al., 1995). In addition, glucocorticoids stimulate insulin secretion however evidence shows that the action on food intake is partly mediated through the potently orexigenic neuropeptide, hypothalamic neuropeptide Y (NPY) (Hanson and Dallman, 1995; Strack et al., 1995). Glucocorticoids also alter the expression of other feeding neuropeptides; adrenalectomy decreased proopiomelanocortin (POMC) and agouti-related peptide (AgRP) in the hypothalamus while replacement of glucocorticoids reversed these effects in rats (Savontaus et al., 2002). Glucocorticoids also interact with the adipose-derived hormone, leptin and induce changes in feeding responses (Cavagnini et al., 2000); this is extensively discussed in the subsections below.

The bidirectional stress induced changes in food intake are multifactorial and influenced by the type of stressor; effects on food intake are also closely related to the severity of the stress being applied to an organism (see Table 1, and following subsection). We are exposed to stress throughout our life, either before birth, during early development or during adulthood. Both human and animal studies reveal that stress exposure, especially in early life, either during the prenatal or early postnatal period induces changes in brain development, and behavioural outcomes (Heim and Nemeroff, 1999; Heim and Binder, 2012) with both of these possibly affecting eating patterns. This is related to the fact that both the stress and feeding systems, as mentioned earlier, share the same neuroanatomy. Disrupted eating patterns, either hypophagia or hyperphagia were observed following prenatal and postnatal stress in several animal models (Akers et al., 2006; Kaufman et al., 2007; Kumar et al., 2007; Noll et al., 2007; Ryu et al., 2008; Slotten et al., 2006; Weinstock et al., 1992; Zuena et al., 2008).

Amongst the stress exposures during foetal development or the postnatal period that have been shown to alter feeding responses are changes in diet or an adverse environment. In terms of diet, changes in overall food availability (malnutrition or overnutrition), or limitations in selected nutrients (macronutrient and mineral deficiency) during foetal or early postnatal development alters cell structure and metabolism which reprograms stress responsivity. This can lead to altered glucocorticoid secretion in response to stress later in life, and changes in the expression of feeding neuropeptides in the hypothalamus that regulate energy intake including CRH, NPY, POMC, AgRP (Barker, 1998; Chisari et al., 2001; Hirsch and Zukowska, 2012; Nunez et al., 2008; Poore et al., 2010; Schmidt et al., 2008; Venu et al., 2008; Zhang et al., 2011).

In terms of environmental insults, early disruption of the mother–child relationship, or adverse experiences such as child abuse, war, or child-neglect have been shown to modify the neurobiology of stress (neuroanatomy, neurochemical, physiology and response to stress) and feeding behaviour during adulthood (Cohen et al., 2006; Heim and Nemeroff, 1999). Animal models have been extensively used to study the effects of various stressors induced either during the pre-, or postnatal period, or in adulthood. They have been especially useful for examining the mechanism(s) underlying the stress induced changes in feeding behaviour, in addition to other stress responses (Dallman, 2010; Foster et al., 2006; Kaufman et al., 2007; McIntosh et al., 1999).

The following sections will describe how stress of various intensities, and stress at different phases of life can influence food intake and body weight. In addition, this review will attempt to unravel the mechanisms underlying the altered feeding responses induced by stress with a focus on neuropeptide circuits that regulate feeding, the brain regions that are being activated during stress, and potential epigenetic modifications underlying the above changes.

2. Impact of stress intensity and type of stress on food intake

Stress intensity can gauged by the level of activation of the HPA axis, measured by glucocorticoid levels in response to a particular stressor, as well as the post-stress recovery period, the time taken

Table 1
Stress and food intake – rodent studies examining the impact of stress on food intake.

Author & Species	Type of stress	Stressor	Food intake
Rybkin et al., 1997 (Sprague-Dawley rat)	Acute (psychological)	3 h restraint stress morning or evening	Stress in morning resulted in 2 sessions of reduced food intake relative to stress in the evening
Calvez et al., 2011 (Wistar rat)	Acute mild stress	Restraint stress, forced swim test	Reduced food intake 24 h after restraint stress Reduced food intake first hour after forced swim test
Solomon et al., 2007 (Syrian hamster)	Acute stress	Social defeat, footshock	Social defeat had higher reduction of food intake relative to foot shock stress
Dal-Zotto et al., 2004 (Sprague-Dawley rat)	Repeated acute (psychological)	1 min immobilisation stress, followed by 20 min 1 week later	First exposure to stress resulted in higher reduction of food intake compared to second exposure to stress
Vallès et al., 2000 (Sprague-Dawley rat)	Acute single exposure (psychological and immunological)	1 h or 2 h immobilisation, Lipopolysaccharide injection	Immobilisation caused sustained reduced food intake relative to lipopolysaccharide injection
Martí et al., 1994 (Sprague-Dawley rat)	Chronic intermittent stress (psychological)	Immobilisation, handling, restraint	Immobilisation had higher reduction in food intake relative to restraint stress followed by handling
Foster et al., 2006 (Sprague-Dawley rat)	Chronic stress (psychological)	Social defeat	Four and more consecutive social defeats increased food intake relative to non-defeated controls
Harris et al., 1998 (Sprague-Dawley rat)	Chronic (psychological)	Repeated 3 h restraint stress for 3 versus 4 days	3 days restraint stress reduced food intake relative to 4 days restraint stress