Changes in the neuroendocrine control of energy homeostasis by adiposity signals during aging

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1. Introduction

Neuroendocrine regulation of energy homeostasis involves cross-talk between the periphery and the CNS. Several peptidergic factors, mainly originating in the periphery, interact with specific brain targets such as hypothalamic nuclei or transmit their signal through the vagus nerve and sympathetic fibers, which activate neurons in another brain area, the nucleus of the tractus solitarius (NTS). Thus, hypothalamus and NTS seem to play a key role integrating peripheral signals and generating homeostatic responses, transmitted by the autonomic nervous system which regulate food intake and energy expenditure (Badman and Flier, 2005; Takahasi, 2003).

Peripheral signals regulating energy homeostasis can be classified into one of the three following types: (1) long-term energy balance signals, such as leptin and insulin which act as adiposity signals indicating the amount of fat stored in the organism (Schwartz et al., 2000; Spiegelman and Flier, 2001); (2) hunger and satiety signals, such as ghrelin, glucagon-like peptide 1 (GLP-1) or cholecystokinin (CCK) among others, which regulate the short-term eating behavior (Badman and Flier, 2005; Stanley et al., 2005); and (3) nutrient signals, such as glucose or fatty acids, which reflect the whole-body nutrient status and can modulate appetite, body weight and liver metabolism (Hu et al., 2003; Obici et al., 2003). The first and the last types of signals act mainly through activation of hypothalamic neurons, whereas hunger and satiety signals target additionally to the NTS and other brainstem areas. In addition to these signals, other factors currently under study, such as adiponectin or resistin, seem to have an effect on energy balance acting either centrally on hypothalamus, or peripherally modulating energy metabolism of several tissues. Moreover, it should be pointed out that most of the hormonal factors mentioned above, in addition to their central targets, can modulate peripheral tissues via endocrine and paracrine action.

In this review we examine the role of the long-term modulators of energy balance, leptin and insulin, with special emphasis in the changes that occur during aging in their respective effects on food intake and energy expenditure.

2. Long-term energy balance signals

2.1. Lipostatic theory: leptin and insulin as adiposity signals

The original lipostatic hypothesis of Kennedy aimed to understand how the brain can monitor the status of fat stores in the...