Expression of GALP, alarin and their receptors system in hypothalamo-pituitary-adrenal axis and its role in the regulation of growth, differentiation and function of rat adrenal cortex.

DESCRIPTION FOR THE GENERAL PUBLIC

There are two principal mechanisms of energy homeostasis regulation, central and peripheral with key role of peptides involved in food intake. The first system involves shortly acting mechanism, with principal role of ghrelin, orexins, cholecystokinin, while the second – long acting system is linked to energy storage in the body and the role of leptin and insulin. In the regulatory process of energy homeostasis key role plays hypothalamus. Most of the hunger/satiety signals reach this part of the brain. In response, orexygenic neuropeptides are released, such as neuropeptide Y (NPY), orexins, galanin or agouti related neuropeptide (AGRP) together with decreased secretion of anorexigenic peptides, for example melanocortin (MSH), cocaine- and amphetamine-regulated transcript (CART) or corticotropin releasing hormone (CRH). Some of the neuropeptides regulate food intake by acting through the endocrine system. Key role in this process play adrenocortical hormones (corticosteroids) and the hypothalamo – pituitary - adrenal axis (HPA). As commonly known, corticosteroids stimulate secretion of NPY by hypothalamic neurons, and inhibit CRH and MSH release. Moreover, corticosteroids are known to affect the manner of adipose tissue deposition in the body and thus body weight gain.
Orexigenic and anorexigenic peptides can modify growth, structure and function of adrenal gland. Some of them act at the level of hypothalamus and modify adrenocorticotropic hormone (ACTH) secretion that directly control function of adrenals. They may also act directly on adrenal gland.
Galanin-like peptide (GALP) and alarin belong to a group of newly identified bioactive peptides involved in the regulation of feeding. They are encoded by the same gene. GALP is a 60-aminoacids peptide that expresses in the arcuate nucleus of hypothalamus and in pituitary gland. Alarin arises as a splice variant of GALP mRNA and contains 25 aminoacids. Both peptides share first five aminoacids which are essential for their biological activities. There are evidence that both GALP and alarin are orexigenic and stimulate food intake. Moreover, both alarin and GALP affect hormones release, such as gonadotrophin releasing hormone (GnRH), luteinizing hormone (LH) and ACTH.
Both examined peptides, GALP and alarin, belong to a galanin peptide family. It is commonly known that galanin, the “parental” peptide, plays significant role in the regulation of secretion of adrenocortical hormones. Galanin stimulates corticosterone secretion. However, the question if GALP and alarin also affect function of adrenal gland is still open. Proposed experiments aim to investigate whether both GALP and alarin are involved in the regulation of growth, differentiation and function of the rat adrenal cortex and to explain their mechanism of action on the gland. Experiments will be based on in vitro (freshly isolated adrenocortical cells, adrenal cortex sections, primary cell cultures) and in vivo models (peripheral and central administration of peptides, subcutaneous injections, mini - osmotic pumps). Proposed experimental models allow to determine the expression of GALP and alarin in adrenal gland. They will help to understand whether examined peptides may exert their effects on adrenal gland in paracrine/autocrine manner and if adrenal cortex is involved in the regulation of energy homeostasis by both peptides.