ABSTRACT

The thesis was focused on characterization of biological activities of two recently discovered anorexigenic neuropeptides: CART (cocaine- and amphetamine-regulated transcript) peptide and prolactin-releasing peptide (PrRP).

In order to find a pharmacophore of CART peptide, shorter fragments of CART(61-102) peptide were tested for binding to PC12 cells and nhibition of food intake in fasted mice. The results showed that a compact structure of CART peptide containing three disulphide bridges is necessary for preservation of its full biological activity.

In the second part of the thesis, synergistic and long-lasting effect of centrally administered peptide CART and peripherally administered cholecystokinin (CCK) is described. In fasted C57BL/6 mice, the anorexigenic effect of CART was enhanced by a subthreshold dose of CCK, while CCK_1 receptor antagonist devazepide blocked the effect of CART peptide on food intake.

In the third part of the thesis, food intake in fed lean and MSG (monosodium-glutamate treated) obese male mice with lesions in nucleus arcuatus (ARC) showed that anorexigenic action of CART peptide was preserved but satiety effect of CCK was completely lost and therefore, effective leptin signaling in ARC is necessary for satiety effect of CCK.

Finally, the PrRP receptor was detected in three rodent tumor pituitary cell lines: rat GH3, mouse AtT20, and rat RC-4B/C cells both with specific antibody and saturation binding of radioiodinated PrRP31 to intact cells. Biological effects of PrRP31 and its shorter analogs were demonstrated in RC-4B/C cells.