

The reproduction, especially in females, is an energy-requiring process, therefore the relation between the functioning of reproductive system and the organism energy status has been intensively studied. Both short and chronic food deficiency results in the inhibition of the gonadotrophic axis activity, which consequently leads to a lower number of offspring or temporary infertility. Activity of the gonadotrophic axis is conditioned by a number of metabolic and nutritional signals, suggesting that common regulatory pathways are involved in the joint control of reproduction and energy balance. New compounds (hormones and neurotransmitters) are still being discovered and further studies confirm their involvement in the regulation of the gonadotrophic axis activity.

In recent years a new family of regulatory peptides, RF-amide peptides, have been described. RF-amide peptides have a characteristic amino acid sequence occurs at the C-end in the protein chain. So far properties of two peptides belonging to this group: kisspeptin and GnIH have been very well documented. They play an important role in the regulation of reproductive axis, mainly by modulating the activity of neurons that express gonadotrophin releasing hormone (GnRH). One of the peptides belonging to this family is 43RF-amide (43RFa) whose expression has been demonstrated in all vertebrate groups. C-terminal sequence of this peptide, which is responsible for its biological activity, remained unchanged in the course of evolution. Such kind of phenomenon is characteristic for the compounds performing the key functions in the organism.

Research planned in the proposed project focuses on the neuromodulatory impact of 43RFa on the gonadotrophic axis secretory activity, which is the most important part of a complex system responsible for the control of the reproductive processes in the organism. Our research hypothesis assumes that 43RFa can modulate activity of GnRH neurons in the hypothalamus, thereby regulating the functioning of the gonadotrophic axis (at the hypothalamic-pituitary level).

In order to verify our research assumptions, we plan administration of 43RFa directly into the third ventricle of sheep brain. During the experiment, blood samples will be collected for determination of changes in the level of LH and FSH by using radioimmunoassay method. The selected structure of the hypothalamus and the pituitary gland will also be collected to determine the changes in chosen gene expression using a Real Time RT qPCR method. Moreover, using the immunohistochemical analysis we will determined the location of interesting us hormones in the structures of the hypothalamus and pituitary gland.

The presented research is part of the current trend of research on the molecular basis explanation for interactions between the appetite control peptides and the reproductive axis activity at the CNS level. The unquestionable, innovative advantage of the designed project is the simultaneous examination of changes occurring in key regulatory systems: the gonadotrophic axis and the GnRH pulse generator system. This experimental system, difficult to perform and requiring a lot of experience, will enable to trace simultaneously the dynamics of changes in gene expression, location and concentration of GnRH, LH and FSH material. Used technique will allow to monitor changes of selected neurons, after the precise 43RFa administration, closely to the hypothalamus structures where the examined neuropeptide is active.

Performed experiments concern the understanding the molecular basis of the neuronal interactions and the plasticity of neuroendocrine networks located in the hypothalamus and allow to proper and easier designee of pre-clinical studies in human medicine. Obtained results provide new unique data on the effects of anorexigenic/orexigenic neuropeptides on the reproduction modulation.