Summary

Maintaining a state of relative internal equilibrium (body temperature constant, electrolyte balance, amount of energy resources) is necessary for the proper functioning of every living organism, regardless of the large number of stimuli generated by changing environmental conditions. The integration and processing of stimuli coming from both the external environment and from inside of the body take place in the central nervous system (CNS), from where information is transmitted to other organs and systems. The most important structure of the brain, controlling the proper course of physiological processes at various levels of the organism’s organization, is the hypothalamus. Hypothalamus is an area of synthesis of many neuropeptides and hormones responsible for the regulation of the body's energy homeostasis. Many of these neuropeptides are simultaneously involved in the regulation of reproductive and growth processes.

One important group of neuropeptides are neurotrophins, which are protein growth factors synthesized by nerve cells. The first studies showed that they play a role in stimulation the differentiation and survival of neurons. Moreover, they participate in processes related to the neuroplasticity of neurons (stimulation of neuronal growth and forming of the synaptic connections) and in neuroprotective processes. There are indications that one of the neurotrophins − brain-derived neurotrophic factor (BDNF) may participate in the modulation of the activity of the hypothalamic neurohormonal network, regulating the energy status of the organism, and thus affecting the activity of the gonadotrophic and somatotrophic axes. However, the available literature lacks information on the interaction between BDNF and key hormones involved in the regulation of appetite or the modulation of reproductive and growth processes, especially at the CNS level.

The research hypothesis assumes that:

1. BDNF is involved in the modulation of the neurohormonal appetite regulating network activity at the hypothalamus level;
2. BDNF is involved in the regulation of the gonadotrophic axis hormones secretion at the hypothalamic-pituitary level;
3. BDNF modulates the somatotrophic axis hormones secretion at the hypothalamic-pituitary level.

The experiment has been performed on Polish Merino sheep (n = 24). Prior to the commencement of the experiment, all animals were implanted with stainless steel guide cannulae leading directly to the third ventricle of the brain (IIIv). Oestrus synchronization has been performed in all experimental animals, and after a period of seven days from the onset of ovulation, a series of four infusions were made into the IIIv on three consecutive days. Sheep from the control group (n = 8) received Ringer-Locke solution (480 μl/day), animals from the BDNF 10 group (n = 8) received Ringer-Locke solution with BDNF at a dose of 10 μg/480 μl/day, while sheep from the BDNF 60 group (n = 8), BDNF at a dose of 60 μg/480 μl/day. During the experiment, blood was taken to determine the concentration of luteinizing hormone (LH), follicle stimulating hormone (FSH) and growth hormone (GH) by radioimmunoassay. Moreover, the concentration of selected hormones (LH, FSH and GH) in the pituitary was determined. Immediately after the end of the experiment, certain structures of the hypothalamus and pituitary were obtained from sheep in order to determine mRNA expression using the Real-Time RT qPCR method.

For the first time in an *in vivo* study, the effect of BDNF in ruminants on the activity of neurons that co-creating the hypothalamic appetite-regulating network was observed: neuropeptide Y, Agouti protein (NPY / AgRP neurons), cocaine and amphetamine regulated transcript, and alpha-melanocortin (CART / α-MSH). At the same time, it has been shown that BDNF modulates the expression of selected microRNAs that may participate in the post-transcriptional regulation of NPY, CART, and proopiomelanocortin mRNA expression. BDNF has also been shown to affect the activity of kisspeptin, neurokinin B, and dynorphin neurons (KNDy neurons) in the mediobasal hypothalamus (MBH) and alters gonadoliberin mRNA expression in the preoptic area. Moreover, exogenous BDNF alters the expression of growth hormone releasing hormone (GHRH) mRNA in MBH, and the expression of GH mRNA, GHRH receptor, and somatostatin type 5 receptor at the pituitary. It has also been shown that BDNF has different effects on the concentration of LH, FSH, and GH, in both pituitary and peripheral blood.

Based on the obtained results, it can be concluded that BDNF is involved in the modulation of the activity of the hypothalamic appetite-regulating network, and in the modulation of the activity of the gonadotrophic and somatotrophic axes in sheep.