POPULAR SCIENCE SUMMARY

The intensive animal production and a small living space of livestock are a source of both physical and psychological stressors. Working during pregnancy, women are also often exposed to psychological stress. Information on the stressors are integrated at the level of the central nervous system (CNS), modulating secretory activity of the hypothalamic-pituitary-adrenal (HPA) axis. Consequence of HPA axis activation is an increase in cortisol concentration in blood, which can be harmful to the fetus. In lactating and pregnant females evolved adaptive mechanisms, which inhibit activation of the HPA axis by stress. Research carried out in recent years on pregnant mice and rats indicate that a compound inhibiting HPA axis activity during pregnancy can be **allopregnanolone**, a neurosteroid which is synthesized in the CNS from progesterone released from the corpora lutea of pregnancy. Research on the role of neurosteroids in shaping the secretory activity of the HPA axis and its sensitivity to stressors have not been performed on adult livestock animals. In turn, our own research on sheep showed that in the next period of lactation such an action is exerted by other compound, which is synthesized by the dopaminergic system – **salsolinol**. Adaptive changes within the CNS during pregnancy and lactation are related to neuronal plasticity and neurogenesis. One of the compounds playing a significant role in these processes is **brain-derived neurotrophic factor – BDNF.** Linking all these compounds, as a part of the protective mechanism in the CNS in a pregnant female sheep is under investigation in the submitted project. **The main aim of this project is to know the role and mode of action of neurosteroid allopregnanolone, as well as the potential mediators of its activities (salsolinol and BDNF), in the shaping of secretory activity and sensitivity to stressors (stress reaction) of the HPA axis in pregnant sheep.**

Experiments on animals with collection of CSF and blood samples will be performed to answer the research questions raised in the project. In some sheep will be performed a push-pull perfusion of the hypothalamus, while in others selected parts of the brain and the anterior pituitary will be dissected in order to measure the expression of some genes. The experiments will enable monitoring the changes of secretory activity of the HPA axis, noradrenergic and dopaminergic systems and allopregnanolone concentration during treatment of animals by the following factors: isolation stress from the flock and partial restriction of movement, intracerebroventricular infusions of allopregnanolone, and neurosteroids synthesis inhibitor. Analysis of the expression of genes encoding hormones of the HPA axis, BDNF, and CRH, BDNF, and GABAA receptors in some hypothalamic area, the hippocampus and the anterior pituitary will allow to determine changes in some brain structures responsible for pregnant female adaptation to stress condition.

The proposed research will provide answers to following questions: 1) When during pregnancy allopregnanolone, salsolinol and BDNF is present in the CNS? How large is the synthesis of these compounds? Is these compounds remains in the CNS to the early lactation? 2) What is the secretory activity of the HPA axis during pregnancy? What is the allopregnanolone, salsolinol and BDNF impact on HPA axis activity in pregnant sheep? 3) What is the response of the HPA axis, dopamine and noradrenaline to stress after administration of allopregnanolone to the CNS?, and 4) Does allopregnanolone stimulates the synthesis of salsolinol and BDNF? Do these compounds mediate the hypothetical inhibitory activity of allopregnanolone on the HPA axis activity?

All animal procedures will be conducted in accordance with the Polish Guide for the Care and Use of Animals in Science and Education (2015). The project includes procedures minimizing animal suffering. After experiments pregnant sheep will give birth and nurse the offspring in comfortable conditions. Using sheep model will expand our knowledge on the neural adaptive mechanism in pregnant female in ruminants. The obtained results may be the basis for future research in the field of neuroendocrinology of pregnancy and lactation, both in veterinary and medicine sciences, aimed at protecting the mother and the developing fetus from the effects of stressors.