

The positive effect of estrogens on the central nervous system (CNS) has been demonstrated in numerous clinical and experimental studies. Among postmenopausal women, who are characterized by a decline in circulating levels of estrogen, there is significantly increased the risk of obesity, osteoporosis, type 2 diabetes, cardiovascular episodes, stroke, cancer and CNS diseases. Moreover, either the epidemiological studies indicate that among women the frequent of neurodegenerative diseases is higher than among man. Furthermore, Alzheimer's disease is twice as often as man. Studies carried out in recent years show that the number of CNS disorders, among others, Alzheimer's, Parkinson's, and depression are propagated by chronic, uncontrolled inflammation within the brain - neuroinflammation. Suppression of neuroinflammation has been suggested as one of the key processes underlying the neuroprotective effect of estrogens. It is well-known that regular physical activity exerts beneficial effects on the functioning of the whole organism and reduces the risk of many chronic diseases. Exposure to regular physical activity in older persons could be hampered by some difficulties related to health or the frequent lack of motivation. A possible strategy to overcome some of these issues could be based on supplementation with exercise mimetics. Exercise mimetics have been shown to partially mimic the signaling events that mediate some of the beneficial effects of physical activity.

In the planned project, we intend to verify the hypothesis that voluntary physical activity or exercise mimetic supplementation can have a positive effect on neuroinflammatory changes associated with a lack of estrogen.

The aim of the planned research is to answer if and how voluntary physical activity and exercise mimetic treatment affects the neuroinflammation in female mice exposed to chronic estrogen deprivation induced by ovariectomy surgery. Mice will be ovariectomized. Simultaneously, on glial cell cultures, there will be performed an assessment of the most potent anti-inflammatory exercise mimetic. The chosen one will be supplemented to animals in further investigation. In order to verify if the voluntary physical activity and exercise mimetic treatment may reduce the adverse effects caused by lack of estrogens, female mice will be allowed to free access to running wheels or subjected with chosen previously exercise mimetic for 6 weeks. Then, molecular examinations will be carried out to assess various neuroinflammatory markers and intracellular inflammation signaling pathways. Measurements will be performed in the frontal cortex - the structure playing an important role in cognitive processes and in the serum.

The research topics of this project fit into the main public health issues of our society. The role of physical activity or exercise mimetics in the modulation of neuroinflammation and therapy of CNS diseases under lack of estrogens is still underestimated either among physicians or society. The study of the effect of physical activity or exercise mimetics on neuroinflammation changes is particularly important because it may contribute to the development of new therapies based on naturally occurring protective mechanisms among postmenopausal women.