Chronic stress is widely acknowledged as a predisposing factor in chronic disease development. This issue is increasingly studied in terms of systemic inflammation or neuroinflammation. As a communication system between the brain and the gut (the gut-brain axis), it was determined to be significant in a systemic stress response, especially including the immune pathway. It is suggested that disrupted signaling throughout the gut-brain axis might contribute to stress susceptibility and enhance the likelihood of developing mood disorders. Individual differences in stress vulnerability have been suggested as an important risk factor for the sex-related prevalence rates of mental disorders. Notably, females were determined to be more vulnerable to unpredictable and social stressors and to develop anxiety- and depressive-like behaviors in shorter time periods than males. Since the effectiveness of commonly prescribed antidepressant treatments was estimated to be approximately 50%. Due to the low effectiveness of pharmacological therapy, additional forms of therapy, such as physical activity, are currently being sought. Regular physical activity was beneficial to CNS functions, improving mood and cognitive abilities (including memory and learning). Multiple studies conducted on rodents confirmed the beneficial effect of physical activity on depressive- and anxiety-like behavior development.

In this grant proposal, we intend to verify the hypothesis that physical activity promotes developing resilience to stress by restoring homeostasis in the gut-to-brain and brain-to-gut communication. In order to verify that, the mice of both sexes will be exposed to a chronic stress procedure that lasts for 21 days. Throughout the experiment, mice will either be housed in their home cages, home cages with a blocked running wheel, or home cages with a free running wheel to enable voluntary physical activity. Blood samples obtained from the animals during stress will be examined for inflammatory factor concentrations, to observe whether their system adapts to stressful stimuli in an enriched environment. The behavioral tests will be conducted after the stress procedure to examine depressive- and anxiety-like behaviors. It is suggested that stress causes disruption of the blood-brain barrier and intestinal barrier, being the cause of widespread neuroinflammation or peripheral inflammation. Therefore, we aim to evaluate the expression of genes and proteins associated with inflammatory processes in the prefrontal cortex engaged in cognition, hippocampus engaged in learning and memory, and colon tissue homogenates, but also confirm the observations made by culturing endothelial and epithelial cells, which are main elements of the blood-brain barrier and intestinal barrier structure, respectively. Moreover, disrupted barriers demonstrate downregulated expression of junctional proteins whose main role is to maintain barriers' integrity and required permeability. Hence, the tissue and cell lysates will be examined for these proteins expression as well. The microbiota composition changes in stress conditions will also be checked for a tendency to adapt via physical activity intervention.

The issue of coping with and developing stress resilience should be publicized, especially nowadays. Measures to improve the treatment of its consequences deserve special attention particularly in such a form as physical activity, which the majority of society can introduce into their daily lives immediately. Research on the impact of physical activity on the acquisition of resistance to stress in the aspect of the gut-brain axis and inflammatory changes will contribute to a better understanding of molecular processes involved in this phenomenon and will also outline the relationship between the above and susceptibility to mood disorders.