Recently, frightening epidemiological data shows that worldwide leading cause of death and disability are cardiovascular diseases. Social and economic consequences force scientist to undertake detailed analysis of the risk factors for those disorders. Despite connection between psyche and development of cardiovascular disease has been noticed for years, involvement of psychosocial factor in its etiology is not fully understood. Clinical and epidemiological data have strongly indicated that early life stress (ELS) may be considered as a silent risk factor for chronic diseases later in life. Most of them can occur later in life, even though they might have developmental origins. These facts relate to various disorders, including cardiovascular disease, diabetes, mental illnesses (depression, bipolar disorder) and neurodegenerative diseases (Alzheimer's and Parkinson's disease). According to a study published by the World Health Organization WHO, ELS leads not only to increased risk of mental illness, but also greatly accelerates its outcome.

The blood–brain barrier (BBB) is a highly selective permeability barrier that separates the neural tissue within the brain from the circulatory system. It protects the central nervous system from the direct impact of the external environment. Disorders that occur due to disruption of BBB continuity have become common medical issue. The brain's blood vessels are linked with endothelial cells that are wedged tightly together. Continuous tight junctions (TJs) are present in-between them and help block harmful substances from entering the brain. Some evidence suggests the weakening of the BBB is linked to activation of immune responses within the brain and on periphery. They refer to any of the body's reaction to foreign substances, such as an antigen, as a result inflammatory molecules are produced. Studies suggest a leaky BBB and concomitant inflammatory processes contribute to mentioned diseases.

For nearly a decade, our team have been applying animal model of ELS. Procedure is based on repeated maternal separations of rat pups for 3 hours each day, during two first weeks of their lives. In rodents, this period is particularly important because some brain regions (e.g., medial prefrontal cortex (mPFC)) are still under development. Thus, they are especially susceptible to environmental factors insults during postnatal stages. Referring to our previous studies based on ELS model, we suggest that early life adversity may result in impaired functioning of the various brain regions. Among them we can distinguish mPFC and other structures especially important for neurodegenerative and mental illnesses, such as substantia nigra, ventral tegmental area and hippocampus.

Summing up above-mentioned facts, we hypothesize that during a critical period for brain development, ELS may affect the development and functioning of BBB together with an activation of inflammatory processes, on the periphery and within brain structures engaged in pathology of neurodegenerative and mental illnesses. We are planning a comprehensive study in all stages of rats' postnatal development: in juvenility - when BBB is still immature, in preadolescent-when BBB becomes tight and in adulthood. Furthermore, we would like to examine whether other environmental factors operating in later life, such as an infection, interfere with ELS. What is more, taking into account sex differences, we would like to study presented consequences of ELS in both males and females. The main goal of this project will be to study the integrity and functioning of BBB in case of ELS. Therefore, we will examine BBB permeability and continuity and distribution of TJ proteins. Marker of BBB endothelium activation and inflammation processes will be investigated on gene and protein level expression within brain. Additionally, we are planning to test blood to asses a level of stress and inflammatory markers (proinflammatory cytokines, C reactive protein (CRP). Furthermore, the project will analyze if ELS may lead to an activation of microglia cells, represents of immune system within brain.

The results will help to understand if ELS may disrupt functioning of BBB and inflammatory processes, thus underlying their contribution to disturbance in structures important for neurodegenerative and mental disorders. Therefore, the project will potentially expand the current knowledge on etiological factors and sex vulnerability in the context of these diseases. Thanks to advances in non-invasive neuroimaging and diagnostic test, it would be possible to identify dysfunctions within selected brain regions, BBB and also inflammation. Finally, given that early-life trauma has the potential to program brain function and behavior throughout individual's life, the project and its results addresses important social and informational issues. Hopefully, this study may help early diagnose and introduction of preventive treatment in children and adolescents with a history of early-adversity, and underlie its importance in public life. Proposed research may also contribute to an increase in social awareness and sensibility to problem of child abuse showing irreversible effects of stress experienced during childhood.