In recent decades, societies around the world have been struggling with increasing health problems resulting from the negative impact of a polluted environment caused by intensive economic development. An example is the global increase in the production and use of plastics, which leads to the generation of a huge amount of plastic waste, destroying ecosystems and becoming a serious environmental problem. Many recent studies highlight the global impact of plastic pollution on the economy, the environment and, in particular, human health. Currently, plastic waste is responsible for massive contamination of waters, where under the influence of biological, physical, and chemical processes, it disintegrates into micro- and nano-plastic particles (MPs/NPs), which then accumulate in organisms via the food chain. Furthermore, plastic food and water containers also release MPs/NPs, becoming significant source of exposure. The increasing risk of direct or indirect exposure of large populations to ubiquitous MPs/NPs, which is of great concern due to potential health risks, is currently the subject of numerous discussions by regulatory authorities. Growing evidence indicates the toxicity of MPs/NPs, including the induction of oxidative stress, endoplasmic reticulum stress, inflammation, and cell death. Recent studies also suggest their potential neurotoxic effects, as they are able to freely cross the blood-brain barrier and enter the brain. A large accumulation of MPs/NPs was found in the brains of deceased patients with a documented diagnosis of dementia, which draws attention to the possible association of MPs/NPs with brain disorders, especially neurodegenerative diseases (NDs), the incidence of which has significantly increased in recent years. The pathogenesis of many of these diseases remains unknown, however it has been suggested that some unidentified environmental factors with neurotoxic effects may induce or accelerate the development of NDs. Therefore, it is reasonable to search for a relationship between exposure to MPs/NPs and the development of neurodegeneration, especially since some pathological molecular and biochemical mechanisms are common in both cases. In this project, we assume that polystyrene nanoparticles (PS-NPs) penetrate the brain of exposed rat, accumulate there and exhibit neurotoxic effects, inducing biochemical and molecular changes that reproduce some of the pathological features of neurodegeneration. As a biochemical mechanism contributing to neurodegenerative-like changes, we propose PS-NP-induced alterations in mitochondria-associated membranes (MAMs) connecting the endoplasmic reticulum (ER) and mitochondria (Mito). These cellular structures have recently been shown to play a significant role in initiating the molecular processes underlying NDs. Animals will be exposed to an environmentally relevant dose of PS-NPs via the oral route, which is the most likely route of exposure via food and drink containers or contaminated water. In an in vivo model of exposure, we will assess the occurrence of potential behavioral changes indicative of cognitive dysfunctions, investigate the formation and accumulation of pathological proteins characteristic of NDs in the rat brain, as well as biochemical and molecular processes occurring in MAMs. In addition, in vitro studies will be conducted using primary cell cultures to assess possible mitochondrial dysfunction, manifested by calcium ion dyshomeostasis. The second objective of the project is to investigate the fate of PS-NPs in the body and their possible transfer via extracellular vesicles (EVs). We will check whether PS-NPs present in the body affect the protein profile of EVs towards the appearance of neurodegeneration markers. In our opinion, the scientific problem of this project is closely related to the latest trends in global research, which concern both the determination of health risks resulting from environmental exposure to MPs/NPs and the search for possible environmental causative factors of neurodegenerative diseases. As related to public health, the proposed research is also valuable from societal point of view.