In recent decades, the production and use of plastics in our daily life has increased significantly. Due to their tremendous utility and low biodegradability, plastic-based products are ubiquitous and have raised environmental pollution concerns all over the world. As biologically and chemically inert materials, plastics have long been considered as safe and non-toxic. However, recent evidence indicates that under different physical and chemical factors, plastic undergoes fragmentation forming micro- and nanoparticles. This observation significantly changes the opinion on the safe use of plastic items, as it is known that nanomaterials can pose a health risk. At a nanoscale, the matter acquires new characteristics one of which is a higher surface to volume ratio. This provides the basis for increased reactivity in biological systems, as well as enhanced toxicity. Apart from being formed due to fragmentation, plastic particles are also intentionally manufactured and used in various commercial applications such as personal care products, biomedical products and labware. Micro- and nanoplastics are currently widespread in the oceans, freshwater bodies and sludge but they can also be spontaneously formed from plastic debris in air and soil, as well as can be released from plastic containers and bottles contaminating food and drink. Although global awareness of the problem of environmental pollution with plastics is growing significantly, the knowledge about the impact of MPs/NPs on living organisms is negligible and concerns mainly water organisms. The potential harmful health effects in mammals and particularly in humans remain unclear due to the lack of a comprehensive risk assessment in standardized study designs. Based on the recent findings indicating the potential toxicity and detrimental effects of micro- and nanoplastics in lower organisms, we suggest that nanoplastic would likely have negative consequences in the mammalian brain and particularly in the developing brain. It is known that immature organisms are generally much more vulnerable to the harmful effects of toxic agents, including nanoparticles, relative to the adults. Therefore, in the present project we propose complex *in vitro* and *in vivo* studies on the cellular fate and mechanisms of neurotoxic effects of polystyrene nanoparticles (PS-NPs). The aim of the proposed study is to examine the neurotoxic mechanisms of small PS-NPs in the primary cultures of neurons and astrocytes, as well as in an animal model of developmental exposure in which immature rats are administered chronically with an environmentally-related dose of PS-NPs that was calculated basing upon the available data predicting daily intake of PS-NPs. Animals will be exposed orally in order to mimic the most likely route of exposure through PS-based food and drink containers or contaminated water. Cell cultures will be subjected to various concentrations of PS-NPs in order to compare the susceptibility of different cell types to nanoplastic. In animals we will verify whether chemically inert PN-NPs have the ability to enter the brain of immature rats and exhibit neurotoxic effects. We hypothesize that oxidative stress (OS) and endoplasmic reticulum stress (ERS) may be the main mechanisms of PS-NPs neurotoxicity. Molecular and biochemical analyses of OS/ERS markers will be carried out followed by the investigation of the role of bioactive sphingolipid S1P in these processes. The presence of PS-NPs in brains and comparatively in the peripheral tissues such as liver and kidney, will be confirmed by the measurement of polistyren (PS) concentration. Additionally, ultrastructural analysis of tissues will be performed using electron microscopy.

Due to the extensive production and use of nanoplastic in a wide variety of industrial sectors, and particularly in many consumer products, the risk of human exposure still increases. Therefore, understanding of potential adverse effects of prolonged exposure to nanoplastic is of importance and should be highlighted. The theme of the proposed research is valuable from both the environmental and societal points of view, since the problem of plastic pollution is nowadays in the center of interest of the government agencies in many countries. The scientific problem of this project is tightly coupled with the most recent trends in global research which is the assessment of potential hazard of plastic particles to human health.