Description for general public

Due to the scale of the phenomenon, both Alzheimer's disease (AD) and obesity, causing systemic inflammation, constitute a serious modern medical and social problem. The similarity of factors responsible for development of both diseases, their pathophysiology, biochemistry and many pathways of transmitting cellular information, as well as the synergy of signaling pathways at the molecular level, confirm this relationship. The implementation of the project will allow us to deepen our knowledge on the coexistence of both these disorders and examine the impact of the popularly consumed, unhealthy Western diet, leading to obesity and metabolic syndrome developing, on the development of neurodegenerative disease. The results obtained in the project will allow to assess whether the type of diet mentioned above can be classified as a risk factor for the development of AD or may accelerate or intensify the occurrence of characteristic neuropathological changes in the AD brain. In addition, this project will identify the neuropathological molecular mechanisms occurring in the early, pre-symptomatic stages of AD occurring under the influence of peripheral factors, i.e. an unhealthy diet and resulting systemic inflammation, and thus confirm the systemic character of the disease, which until recently was considered as a local brain pathology. Moreover, the results obtained from the project in the future may enable the establishment of new methods of counteracting the progression of the disease through the use of a properly balanced diet.

The aim of this project is to verify a novel, never before tested hypothesis, whether long-term consumption of Western diet (WD), characterized by the intake of highly processed products with an unbalanced composition, including increased saturated fatty acids and cholesterol content, and characterized by an abnormal proportion of simple to complex carbohydrates, may be considered as a risk factor for the occurrence or intensification of AD.

In order to answer the research question, in this pioneering project we will investigate the influence of the described Western dietary pattern and of diet-induced systemic inflammation on inducing brain inflammation and the course of molecular changes reflecting the pathogenesis of the early stages of AD. To this purpose, we will examine whether WD affects brain resident microglia and macrophages infiltrating into the brain from the periphery. We plan to distinguish these two main populations of immune cells found in the brain, what will provide unique and novel data describing the impact of WD on the activation state of these cells, signaling between them and neurons at the early stages of AD. The analysis will be performed in brain tissue derived from transgenic mice carrying the human mutant gene for the amyloid precursor protein (APPswe), fed long-term with food mimicking a Western-type diet. The described animal model is a model of the familiar form of AD in which the detailed pathogenesis is associated with the occurrence of a mutation in the gene encoding the APP protein. In order to determine the sequence of events and the impact of the factors used on the eventual changes in the time points of the appearance of neuropathological changes in the brain, the tests will be carried out in three age groups of APPswe mice: 4-, 8- and 12-month-old. 4- and 8-month-old groups reflect the early stages of the development of the disease, before the appearance of characteristic neuropathological changes in the form of amyloid plaques and cognitive symptoms. The group of 12-month-old APPswe mice constitutes a group in which the characteristic pathology of AD is already fully developed. The obtained results will provide fresh knowledge determining whether the Western type diet should be considered a crucial risk factor contributing to the development of neurodegenerative diseases, and will allow to assess how it affects the processes associated with the developing pathology of the central nervous system in the course of Alzheimer's disease.