

The overall aim of the research proposal is to determine the function of HCN channels in the modulation of neuronal excitability, EEG synchronization recorded in *in vivo* and *in vitro* conditions, and mechanisms underlying spatial memory formation in physiological conditions, as well as in the development of dementia in a rat model of Alzheimer's disease (AD). Firstly, we would like to investigate the role of *I_h* current mediated by HCN channels as a potential pacemaker of membrane potential oscillations and EEG synchronization in the hippocampal theta band *in vivo* and *in vitro*. Secondly we would like to answer the question whether and to what extent hippocampal and cortical EEG oscillations are affected in brains of AD model rats in consecutive stages of the disease. An finally, we would like to establish the modulatory effects of *I_h* current agonist and antagonist long-term treatment on memory functions, neuronal excitability, hippocampal EEG synchronization in theta band and cortical oscillations, as well as neurochemical changes and inflammatory processes in the course of a rat AD model. The designed work plan and the catalogue of experimental techniques will allow us to determine whether and how the pharmacological modulation of *I_h* activity alters all range of electrophysiological, biochemical and genetic aspects in physiological conditions vs. AD rat model.

AD as a serious neurodegenerative disorder characterized by progressive cognitive impairment has become a major healthcare concern. It is expected that the number of patients suffering from AD in the United States and European Union will double by 2040 and yet there is no cure for this disease. According to the amyloid cascade hypothesis, the aggregated form of the amyloid-beta ($A\beta$) initiate pathological processes in neurons of the hippocampus, cortex, and several other structures of the brain. Unfortunately, the full picture of the mechanisms underlying dysfunctions in neuronal networks oscillations and degeneration during AD does not emerge so far. This indicates that further progress and new approaches in the study of excitatory-inhibitory interrelations and, thus, HCN channels and EEG oscillations are necessary in AD developing brain. HCN channels, are often proposed to play an important role in the molecular linkage between epileptic seizures and $A\beta$ generation, and in the aggravation of sporadic AD. However a question remains to be answered whether *I_h* current mediated by HCN channels is rather elevated or lowered in the course of AD in animal models. Moreover, there are very few electrophysiological studies that have attempted to characterize oscillatory activity in animal models of AD. To date, the influence of $A\beta$ central administration on EEG oscillations and synchronization in theta band, as well as spatial synchronization between different areas of the brain has not been well studied. Also, studies planned within the frame of the present research proposal would bring for the first time convergent and comprehensive data concerning the involvement of HCN channels in the mechanisms of synchronization in the theta band production *in vivo* and *in vitro*. This will be possible only through the application of electrophysiological approaches, which may finally bring us closer to understanding the pivotal mechanism of rhythmic activity of neuronal networks in specific brain structures.