

One of the most important issues in modern neuroscience is understanding of the molecular and cellular mechanisms underlying learning. The encoding of memory traces in neural networks largely relies on plastic changes within the synapses, which lead to an increase or decrease in their strength. With regard to excitatory (glutamatergic) synapses, this plasticity most often takes form of long-term synaptic potentiation (LTP) or depression (LTD), the mechanisms of which are relatively well understood. However, in addition to excitatory synapses, almost every region of the brain also contains inhibitory synapses that release the GABA neurotransmitter and play a key role, *inter alia*, in the genesis of cerebral rhythms and are an important pharmacological targets (benzodiazepines, anesthetics and neurosteroids). Until recently, inhibitory synapses were thought to control the stability of neural networks without being affected by plastic mechanisms. This picture has changed in recent years with the discovery of numerous forms of long-term plasticity of inhibitory synapses.

We currently know several types of GABAergic synaptic plasticity, but their induction and expression mechanisms remain virtually unexplored, thus our understanding of the role of more than 20% of brain synapses in learning is limited. Therefore, the aim of this project is to investigate the molecular mechanisms of plasticity of inhibitory synapses in the hippocampus. Only in the CA1 region of the hippocampus we can distinguish more than 20 types of different inhibitory interneurons, thus in this project we have selected a few of them using the criterion of functional diversity. As part of the proposed project, we intend to investigate the molecular mechanisms determining different forms of plasticity in inhibitory synapses formed by various interneurons: cholecystokinin-expressing, neurogliaform, bistratified and OLM on pyramidal cells of the hippocampus. Additionally, we plan to take a closer look at the mechanisms of GABAergic plasticity that underlies the phenomenon of disinhibition, by analyzing the plasticity of interneuron-interneuron inhibitory synapses. Finally, the aim of this project is also to investigate the consolidation phase of GABAergic plasticity and its dependence on local protein translation in the dendrite and nuclear transcription.

We believe that the results of proposed research project will shed new light on the role of inhibitory synapses in memory and cognitive processes. The detailed research objectives of the this project concern the key problems of neuroplasticity: the function of inhibitory synapses, molecular mechanisms of plastic changes in synapses, the role of homo- and hetero-synaptic plasticity and the consolidation process in encoding memory traces. The proposed research project will significantly broaden the understanding of the role of inhibitory synapses in the hippocampus, and in the long run will contribute to a more complete understanding of the mechanisms by which these synapses change their strength and contribute to learning. It is worth emphasizing that inhibitory synapses, in addition to their network function, also play a key role in various neuropathologies. Loss of balance between excitatory and inhibitory transmission underlies numerous pathomechanisms e.g. of epilepsy, schizophrenia and autism spectrum disorders. Therefore, deep knowledge of forms and mechanisms of as yet undiscovered forms of inhibitory synaptic plasticity will open up promising avenues for new pharmacological therapies.