Cognitive disorders are a group of disorders related to learning and memory. The concept of "cognitive functions" includes processes such as attention, memory and perception. Memory disorders are undoubtedly one of the most disabling and disturbing disorders in everyday life, and as the disease progresses they lead to the exclusion of a patient from normal functioning in society. There are many forms of memory, generally divided into two groups: declarative memory and undeclared memory (latent).

Declarative memory includes sensory memory, short-term memory, long-term memory, episodic memory and semantic memory, while procedural memory, preceded, conditioned and based on non-learning learning, is included in non-declarative memory. Memory disorders accompany many diseases of the brain, both mental and neurodegenerative diseases. Psychiatric disorders with cognitive dysfunctions include schizophrenia, autism or depression. On the other hand the best-known neurodegenerative disease in which progressive cognitive decline (and finally the patient’s death) is Alzheimer's disease. Alzheimer's disease is a complicated process in which variety of pathological processes lead to massive loss of neurons. One of the risk factors that strongly contribute to progression of the disease is dysfunction of the blood-brain barrier system.

So far, there are no satisfying and safe drugs effective in the treatment of cognitive disorders. Therefore a wide research on the field of neuroscience drug discovery has been developed since dozen of recent years. Animal studies indicate that compounds modulating the glutamatergic system in the cortex, by activating glutamate receptors or muscarinic receptors for acetylcholine, can be effective in patients with cognitive impairment, both in mental and neurodegenerative disorders. However, little is known about the mechanisms of action of these compounds, especially about their effects on cellular mechanisms. One of the more interesting aspects of the mechanisms of action of pro-cognitive compounds would be their effect on nitric oxide. Nitric oxide is a gas neurotransmitter involved in a wide range of biological processes. In the central nervous system (CNS), three isoforms of nitric oxide synthase are responsible for its synthesis: endothelial (eNOS), neuronal (nNOS) and produced by immune cells (iNOS). The role of nitric oxide in the CNS is to regulate the cerebral circulation and the proper functioning of the blood-brain barrier, which in turn ensures proper functioning of nerve cells. Nitric oxide is also responsible for the regulation of the NMDA receptor-mediated processes, which is a key receptor, involved in learning and memory processes. In addition, its function is to regulate the post-transcriptional modulation of proteins important in pathological processes.

In our project, we plan to establish the effect of metabotropic receptors for glutamate, or muscarinic receptors for acetylcholine, on the activity of nitric oxide pathways in the context of cognitive disorders. Our main goal will be to establish in behavioral tests, in animal models of both schizophrenia and Alzheimer's disease, whether the effects of mGlu or mAch ligands depend on the level of nitric oxide (the level of nitric oxide will be modulated by giving short- and long-term NO donors or inhibitors of neuronal synthase). In the next stage of biochemical research we will check how particular ligands affect the level of nitric oxide and individual synthases in selected brain structures. As it is assumed that the decreased eNOS isoform level contributes to vascular disorders and dementias, while changes in the nNOS level contribute to cognitive impairment in schizophrenia, these studies will determine which disorders individual ligands may be dedicated to. In addition, we plan to conduct studies to determine the changes in NMDA-dependent NMDA receptor regulation mechanisms and s-nitrosylation processes. The s-nitrosylation processes are particularly important in the pathogenesis of Alzheimer's disease, as they are responsible for the proper assembly of protein chains that lead to the formation of amyloid beta or tau proteins.