

The nerve cell is the fundamental element of the brain. Neurons which number in the human brain is estimated at 86 billion, are organized in a complex network that enables mutual communication between different regions. One of the most intriguing aspects of neurons and neuronal networks is their ability to reorganize upon diverse factors – including these coming from the external environment. Synapse, a place where neurons communicate, is thought to be one of the main elements of a neuronal network that undergo remodeling. Most synapses are located on small dendritic protrusions called spines. Accordingly, synaptic remodeling can be measured as structural alterations of the individual dendritic spine or/and changes in spine number. Up to now, many normal and abnormal cognitive processes, as well as neuropsychiatric and neurodegenerative disorders, have been shown to correlate with different kinds of spine structures, density, and dynamics. Among factors that significantly influence synapse organization by dendritic spines remodeling is also stress.

Cortical and hippocampal neurons have been shown critically involved in several neuropsychiatric disorders. Their proper functioning is essential for aspects of life crucial for survival, including memory and attention. At the same time, they appear particularly sensitive to chronic stress effects and dendritic spines plasticity. Chronic stress and one of its characteristic features – sustainably elevated corticosterone (CORT) level decrease dendritic spines density in both the cortex and hippocampus. These morphological changes of dendritic spines have functional significance as they correlate with depressive-like behaviors and cognitive impairments. Despite significant advances, little is known about mechanisms involved in CORT/stress-evoked structural and density changes of spines in the cortex and hippocampus.

According to our preliminary data, one of the candidate proteins which disturbed activity may contribute to CORT/stress-associated morphological alterations of the cortical and hippocampal neurons is focal adhesion kinase (FAK). Thus, in the proposed project, we will characterize the role FAK and its associated molecules play in the CORT/stress-mediated structural changes of dendritic spines in cortical and hippocampal neurons.

In experiments, we will use cortical and hippocampal cell cultures and tissues of chronically stressed mice. Further, transfection of plasmid encoding green fluorescent protein gene and confocal microscopy will be adapted to visualize dendritic spines' structure. Viral vector-based techniques will be used to manipulate the expression and activity of FAK and FAK-related proteins. Finally, biochemical methods will be utilized to assess the expression level of synaptic markers and selected proteins (western blot, immunofluorescence).

By utilizing primary cell cultures, and mice stress models, we plan to investigate FAK and its associated mechanisms involvement in CORT/stress-associated neuroplasticity in cortical and hippocampal neurons. Reliably conducted research and detailed analysis will provide insight into the previously unknown molecular underpinnings of CORT/stress-associated morphological alterations. All this, in turn, will expand knowledge with new signaling pathways potentially involved in neuropsychiatric disease, including depressive disorder, which is known to correlate with structural alterations in neuronal morphology.