Description for the general public

GABAergic transmission is the major form of the inhibitory drive in the adult mammalian brain. γ-amino butyric acid (GABA) plays the role of the neurotransmitter in these synapses, which, after release activates the $GABA_A$ receptors located on the postsynaptic neuron. Generally, synaptic transmission consists of its excitable (neurotransmitter glutamate) and inhibitory, GABAergic forms. When the excitatory drive temporarily prevails over inhibition, neurons generate electrical and electrochemical signals which carry the information to respective parts of the brain or other targets in our organism. Synaptic transmission, as any other mechanism of information transduction between cells, can be modulated in various time scales and often synaptic activity itself is a stimulus to modify the synaptic transmission. The processes of continuous alteration of synapse properties is defined as synaptic plasticity. Most interestingly, synaptic plasticity is generally believed to be a major substrate of cognitive processes in our brains**. It can thus be proposed that at least the earliest stages of memory formation in our brains take place in synapses and therefore, at this phase of learning, synaptic plasticity plays a crucial role**. As a consequence of plasticity mechanisms, synapses change their properties and one of the mechanisms underlying this process is alteration of the number of the postsynaptic receptors as well as modification of their kinetic properties. One of consequences of synaptic plasticity is, for instance, a change in the balance between excitatory and inhibitory transmission leading to alteration in the overall network activity. It is worth emphasizing that **in spite of their lower number (than glutamatergic ones), GABAergic synapses play a crucial role in regulating the neural rhythmic network activity, which can be easily observed by using classical EEG technique**. An important, but still poorly understood, aspect of synaptic plasticity is its regulation by astrocytes (which until recently were commonly assigned a merely supportive role). **Recent studies revealed that astrocytes play a role of active partners for neurons, especially in the context of synaptic transmission. However, our knowledge on the mechanisms of interaction between neurons and astrocytes in the context of synaptic plasticity (especially GABAergic one) remains far from being complete and currently is a major challenge in neurobiological investigations. In keeping with these premises, in the frame of the present project, we would like to verify the hypothesis that astrocytic metabolism is a major regulator of GABAergic synaptic plasticity in the model of cultured neurons.** Realization of this project will be based mainly on the use of **electrophysiological techniques** which enable us to perform real time measurements of electrical signals in living cells (including synaptic currents and potentials). In particular, we will assess the GABAergic synaptic transmission, its plasticity and consider the impact of pharmacological manipulations of astrocytic metabolism. In addition, we will use also **confocal microscopy to consider also plasticity phenomena at the morphological level (e.g. to assess the number and size of synapses)**. To verify whether or not the plasticity phenomena in our model are related to the changes in protein expression, standard molecular biology techniques will be used. In particular, we will assess the expression of gephyrin which is the major scaffold protein at the GABAergic synapse and is known to play a critical role in $GABA_A$ receptor docking in the synapse. Owing to the application of these complementary techniques we expect to make an important step forward in our understanding of mechanisms underlying GABAergic neuroplasticity.