

Major depressive disorder (MDD) is a serious problem of modern medicine. Despite the fact that many antidepressant drugs are widely used in MDD treatment, new pharmacological solutions are still very desirable. Currently prescribed antidepressant drugs have delayed onset of action and limited clinical efficacy. Therefore, fast onset of action and long-lasting activity observed after a single dose are desired features for novel antidepressants. In recent years, ketamine has shown very interesting profile of antidepressant activity both in clinical and preclinical conditions. Ketamine reversed depression symptoms after administration of a single dose and its effects lasted even two weeks. Unfortunately, its use on a large scale is controversial. Ketamine evokes a few serious side effects that radically limit its application in the MDD patients. In particular, ketamine as few other NMDA receptor antagonists can induce psychomimetic symptoms and cognitive disturbances. Additionally, some researchers postulate that ketamine should be considered as an addictive drug.

In my recent studies, I have shown that co-administration of single doses of hyperforin and an NMDAR antagonist can be an alternative to pharmacological strategy based on ketamine alone. In the present project, I would like to examine antidepressant-like activity of combined administration of single doses of hyperforin and ketamine in mice. Hyperforin is an active compound extracted from *Hypericum perforatum*. Antidepressant properties of hyperforin have been described both in clinical and preclinical studies. Since ketamine is a racemic mixture of two molecules: R and S-ketamine, both racemic mixture and particular enantiomers will be administered with hyperforin. Antidepressant-like activity of the combination of hyperforin and ketamine will be evaluated in numerous behavioral tests. Moreover, I would like to assess potential antidepressant mechanisms of action of the combination of hyperforin and ketamine or its enantiomers. The set of biochemical methods will be applied to this task. The implementation of the present project is a chance for finding a new pharmacological strategy in the treatment of MDD. Moreover, a better understanding of biological mechanism of action of the combination of hyperforin and ketamine can give a new insight into the molecular basis of the MDD treatment.