

Since the 1960s, there has been an increase in the abuse of psychoactive substances, which are taken to produce specific psychological effects similar to those seen in psychotic episodes. One group of substances commonly used for this purpose is the group of dissociative drugs that block the NMDA receptor in the brain.

It has been known since 2006 that blockade of the NMDA receptor increases the power of high frequency oscillations (HFO 130-180Hz) in the rodent brain. In 2018, we have shown that the olfactory bulb is the major generator of HFO and they can spread to other parts of the brain, e.g. to cortical or limbic areas. We believe that these oscillations may be related to the abnormal brain functioning that occurs in psychotic episodes.

NMDAR blockade disrupts glutamatergic transmission in the brain and leads to disturbances in the dopamine level. The olfactory bulb is the main source of dopamine neurons in the forebrain of rodents and contains dopamine receptors. In this research proposal, we will check whether dopamine plays a significant role in the generation of HFO. For this purpose, we will use local olfactory bulb infusions of substances that stimulate or block dopamine receptors.

The olfactory bulb receives projections from different parts of the brain, including other olfactory-related structures. The olfactory tubercle projects dopaminergic neurons to the olfactory bulb and may affect its oscillatory activity *via* these projections. In this project we will examine whether stimulation or blockade of the dopamine receptors in the olfactory tubercle may affect HFO recorded in the olfactory bulb.

In the previous research, we have shown that D2 receptor-antagonist based antipsychotics reduced HFO in reward-related brain areas. Here, we would like to check the effect of the same antipsychotics in the olfactory bulb. We will also examine the effect of partial D2 receptor-agonist based antipsychotics, as they have the opposite mechanism of action towards the D2 receptor.

The planned project is therefore of a basic nature, broadening knowledge in the areas of neurophysiology and psychopharmacology. At the same time it may have potentially important implications for preclinical research in the context of antipsychotics tests. All experiments will be performed on rats.