Mood disorders and depressive behaviours are among the most common mental disorders identified in significant fraction of population. Despite many conducted researches aimed to discover etiology of this disease, the molecular background leading to depressive disorders is still poorly understood. Part of behaviours displayed by depressive patients is connected to impaired action of reward system (loss of energy and interest, anhedonia, lack of motivation to obtain reward). Although role of dopamine in development of depression-like symptoms is usually considered secondary, data from both animal and clinical studies suggest that its involvement in etiology of this disease is underappreciated. Another group of disorders connected with abnormal function of dopaminergic transmission is drug-abuse problem. Even single exposition for cocaine is able to induce persistent changes in number and sensitivity of dopamine receptors, which leads to drug-relapse.

Both depressive disorders and abuses have common feature – abnormalities in functioning of reward system. Since amount of released dopamine in target structures is tightly connected to pattern of displayed activity in dopaminergic neurons, full understanding of neuronal mechanism necessary for developing bursting activity will contribute to description of etiology of disorders listed above.

Dopamine synthesizing neurons are localized within *ventral tegmental nucleus* (VTA) and *substantia nigra pars compacta* (SNc) of the mammalian brain. The key functions of these cells are strongly correlated with firing pattern observed both in primates and in rodents. Tonic release of dopamine, synthesized in VTA and SNc, into these structures supports animals' basal motivation and motor functions, respectively. Phasic increase in amount of released dopamine activates reward and synaptic plasticity. Different modes of dopamine release, tonic and phasic, arise from distinct patterns of electrical activity of dopaminergic neurons. Tonic or irregular (non-bursting) pattern of generation of action potentials maintains basic levels of DA in target structures, whereas bursting pattern of firing leads to phasic increase in amount of synaptically released dopamine. Investigation of mechanisms responsible for developing of bursting activity has well established that presence of fully functional NMDA receptors is crucial to evoke bursting mode of activity.

Results of preliminary data on model of selective, inducible knock-out of NR1 subunit of NMDA receptor spatially restricted to midbrain dopaminergic neurons allowed to connect electrophysiological phenotype of recorded cells with behavioural effects of NMDA receptor disruption. Moreover obtained experiments suggest that despite lack of response to NMDA receptor agonist, cells in mutant animals are able to develop bursting activity mode in presence of cholinergic agonist. Thus our hypothesis is that mechanism involved in this phenomena is NMDA independent.

Obtained results prompt us to propose a project in which we plan to investigate mechanisms of induction of bursting activity in dopaminergic neurons under the influence of cholinergic agonists. The main objective of proposed project is to describe and pharmacologically characterise development of bursting activity in rodent's midbrain dopaminergic neurons, evoked by cholinergic receptors stimulation. Moreover projection targets of dopaminergic neurons displaying robust, prolonged bursting activity during cholinergic agonists application will be described. Proposed project is aimed to verify stated hypothesis in course of electrophysiological and anatomical studies, conducted on urethane anaesthetised laboratory animals (male C57BL/6N mice). Electrophysiological experiments will embrace acute recordings combined with iontophoretic administration of selective nicotinic and muscarinic receptor agonists. Experiments aimed to determine projection targets of recorded cells with advantage of antidromic stimulation, will allow to create spatial map of dopaminergic cells displaying strong response to cholinergic agonists.

Implementation of the planned experiments will allow to precisely determine and describe subtypes of cholinergic receptors engaged in developing bursting activity in animals with non-functional NMDA receptors. Exact description of burst's parameters together with pharmacological characteristic will broaden our knowledge about mechanism controlling activity of reward system. Moreover it will also bring us closer to understand mechanisms responsible for phasic dopamine release in target structures. Since disruption in dopamine release is proposed as one of mechanisms involved in depressive-like behaviours in animal models, better understanding of modulatory and gaiting mechanisms in rodent's midbrain dopaminergic neurons is especially important. It will give the basis for further, important for society, studies on diseases connected with reward and motivation system, including depressive-like behaviours.