The use of different types of club drugs, especially by young people, is a great concern for EU societies. Novel psychoactive substances (NPS) is the common name for various kinds of products containing psychoactive substances. One of these substances is mephedrone. Mephedrone is a derivative of phenylethylamine, the same as methamphetamine and methylenedioxymethamphetamine (MDMA). For a long time mephedrone has been easily accessible for sale both online and in some stores called "smart shops". An increase in the popularity of mephedrone in Europe and in the whole world has resulted in fatal cases among abusing adolescents. In Poland, the production, use and sale of mephedrone was banned on the 25th of August 2010. Unfortunately, this action has only slightly reduced the drug sale, which has moved to the Internet. Thus far, mephedrone use has not been seriously affected by its legal status and it appears to be a common product for designer drug manufacturers, which suggests that long-term mephedrone use is going to continue. Mephedrone is also increasingly used to supplement more established club drugs such as MDMA and cocaine. Mephedrone, like other psychoactive drugs, including MDMA, enhances extracellular dopamine and serotonin in the nucleus accumbens (NAc). Therefore, chronic use of this substance can lead to the development of addiction. The process of addiction is associated with functional disorders of the rewarding system. The system consists of the ventral tegmental area (VTA), giving projections to the NAc (the mesolimbic pathway) and to the prefrontal cortex (PFC) (the mesocortical pathway). VTA stimulation causes an increase of dopamine release at the synapses, connecting VTA neurons with NAc and further with PFC. Furthermore, NAc implements backward inhibition of VTA, thus, preventing from their excessive agitation. The other structures involved in drugs addiction are: the amygdala and hippocampus. Despite dopaminergic neurons building the mesocorticolimbic pathway, other very important components for the development of addiction are neurotransmitters such as glutamate, gamma-aminobutyric (GABA).

However, the neuropharmacological profile of mephedrone remains incomplete, because here is a lack of research concerning the involvement of GABA-ergic and glutamatergic neurotransmission in the rewarding actions of mephedrone.

The research has been planned so as to apply an interdisciplinary approach, including biochemistry, spectroscopy and animal behavior studies to assess the GABA-ergic and glutamatergic mechanisms underlying the rewarding properties of mephedrone. In behavioral studies NMDA receptors antagonist - memantine, as well as $GABA_B$ receptors agonist (baclofen) and $GABA_B$ receptors positive modulator (PAM-GS39783) will be administered to evaluate the mechanism of mephedrone addiction. For behavioral study conditioned place preference (CPP) test and its modifications will be employed. In biochemical studies the concentration of glutamate and GABA will be determined by two independent methods. One of them will be performed *in vivo*, in sedated animals, and it will employ magnetic resonance imaging (MRI). MRI can be a useful method in obtaining information about the biochemical composition at a selected anatomical location. This technique is based on the interpretation of molecular spectra of chemical compounds. At the end of all the experiments the animals will be decapitated and then their brains will be withdrawn, divided into structures (prefrontal cortex, hippocampus) and homogenized. In the homogenates the concentration of glutamate and GABA will be determined by ion-exchange chromatography. Moreover, human and animal studies have identified stress as a critical factor in drug addiction, including acquisition, retention, and relapse towards the drug of abuse. Our previous studies have shown that chronic as well as acute stress can potentiate both behavioral and neuronal effects of nicotine. However, there is a lack of information about the influence of stress on rewarding effects of mephedrone. Furthermore, it was shown that MDMA increases sociability in humans, as well as in male Long–Evans rats. Therefore, taking into consideration close structural and mechanistic convergence between mephedrone and MDMA we would like to evaluate the influence of mephedrone on social behavior. The rewarding effects of mephedrone may be sex-dependent. Therefore, we plan to evaluate these effects in both male and female Wistar rats. Another aim of the project is to establish and validate the suitability of using non-invasive MRI imaging methods in evaluating the changes in metabolite levels in rat brains resulting from the administration of mephedrone. In particular, we are going to implement existing and develop new magnetic resonance spectroscopy (MRS) methods for the quantitative concentration measurement of glutamate and GABA. In these experiments we are going to compare neurotransmitter concentrations measured *in vivo* to results from analytical techniques performed *ex vivo.*