How do we know where we are? How can we find the way from one place to another? Finally, how do we store such information that we can immediately find the way, and next time choosing the same way? Our everyday life, like the life of other animals, except for the automatic performance of various activities, requires conscious action. We know that in the hippocampus there are *place cells* that are triggered when we are in the final destination, but also they inform us that we are in a place both related to the appetitive stimulus (e.g. good patisserie we were before) as well as the aversive one (do not come here - because "you felt here electric shock in the past"). At the same time, we know that there are widespread individual differences in motivation, processing of information about pleasure or in anticipation of rewards (differences in the degree of excitation of the reward system). This reaction lies behind the motivation and exploration of space in order to obtain new stimuli that can bring us a subjective feeling of pleasure. The reward system, which is our ally, can lead to a complete destruction of the body in pathological states related to addiction. When a patient tries a drug (a psychostimulant substance) or another strong appetitive stimulus for the first time it releases dopamine in a mesolimbic dopaminergic system - he feels pleasure. As a result of this action, the amygdala "learns" that it was a pleasant experience. The amygdala not only "learns" that the stimulus is rewarding, but also is able to associate the spatial context, and thus can participate in the process of combining the experience of pleasure with a whole range of spatial cues. In this process there are involved among others the hippocampus and cortical structures, ie. prefrontal cortex, entorhinal cortex or retrosplenial cortex. The studies proposed in this project are aimed at transferring labile theoretical considerations about the mechanism of space association with emotion to the level of experimental biology. In the previous studies, the excitation of the reward system by a well-known and appetitatively associated context was examined by the emission level of ultrasonic vocalization in "50-kHz" band. It turned out that contextual response was not uniform in the whole population and such differentiation helped us to conduct correlational studies while creating a mathematical model. We proved that ultrasound vocalization (being a marker of appetitive affective state), induced by 50-kHz context (administration of substance) in context-induced response positively correlates with the concentration of serotonin in the hippocampus, amygdala and prefrontal cortex as well as with the glutamate/glutamine ratio in the nucleus accumbens. We also proved the existence of serotoninergic-glutamatergic co-transmission in the context induced 50-kHz USVs response, and we demonstrated a number of other neurochemical correlations. Using among others methods of machine learning, we created a mathematical model of the relation of many neurotransmitters and their metabolites - a model of activation of the reward system in the processing of information about the space, associated with the administration of substance. We observed this co-transmission among others in the nuclei of amygdala (a structure involved in the processing of information about the reward).

The aim of this project is to study a selective desynchronization of the occurring serotonergic-glutamatergic co-transmission. How do we want to make this? We will use a so-called chemogenetic method (DREADD), where we will introduce designed receptors of **hM3Dq** - activating and **hM4Di** - inhibitory to the amygdala. These receptors (peptide gens) will be transported to amygdala thanks to a creation of viral constructs that will direct them to a designated target (using specific promoters). This target will be serotoninergic or glutamatergic neurons or both. Thanks to this, using CNO (a substance that only matches these receptors) we will be able among others to inhibit serotoninergic activity, without affecting glutamatergic or vice versa. We will also be able to activate one neurotransmission path, while inhibiting another. These studies will be carried out in a specially created space - enabling the study of the navigational capability as well as the place preference (4 corners). While animal will be searching for a preferred place, we will measure the emotional state of the animal and the motivation by recording the ultrasound vocalization - inaudible to humans. Additionally, we will measure the activity of place cells - "produced" during a training-association of the specific corner with the pharmacological reward. Based on our own results and literature data, we expect that the proposed modifications of co-transmission will lead to the lability of place cells, changing at the same time the emotional coloring of the preferred place, and thus the decomposition of emotional states and spatial memory. We also expect that the proposed modifications will switch extreme emotional states from the appetitive state to the aversive one and vice versa, which we will be able to record in the inaudible band for humans (ultrasonic vocalization). What is more, we plan to use the catFISH method that defines which neurons from the neuron population have been active and ready for changes (plasticity) before and after chemogenetic modifications. We believe that in the future these studies may contribute to the creation of innovative addiction therapy.