DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)

Living in the modern, rapidly changing world is a task challenging our ability to adapt and manage our lives flexibly. Several decades ago neuropsychologists discovered a set of psychological mechanisms called the executive functions, which are responsible for achieving our goals by selecting and maintaining appropriate behaviors. People with damaged frontal lobes are heavily handicapped in this regard, even though their intelligence remains intact. It is now known, that executive functions are also compromised in people suffering from psychiatric disorders.

One of the most basic of the executive functions is cognitive flexibility, which helps us change habits. When disrupted, it manifests itself as maladaptive rigidity, which causes severe difficulties in everyday life, since there is only one way of doing things for a person with deficits in cognitive flexibility. Another facet of cognitive flexibility is the ability to ignore infrequent failures in order to achieve our goals. This relies on our sensitivity to negative feedback, which is different for every individual. When elevated, negative feedback sensitivity can cause lack of consistence and catastrophic reactions, as seen in patients with depression. Although, as of now, there is no cure for these dysfunctions, a very promising perspective of pharmacological aid in therapeutic interventions is at hands.

Recently a test of cognitive flexibility, commonly used in the clinic, has been developed for testing rodents. In the test, the rat has to chose between two options (levers), one of which delivers a reward with a probability of 80% of choices. The other option is rewarded only in 20% of its choices. After the animal learns which lever is more favorable, the probabilities are reversed.

This test is an exact copy of the human test, and this opens an avenue to conduct studies necessary to elucidate the role of specific receptors in the nerve cells located in brain regions responsible for cognitive flexibility. Much research has been focused on this subject, and we now know that receptors for serotonin in the frontal part of the brain take part in flexible behaviour. A role for dopamine receptors has also been proposed, but the necessary research to confirm it is under way. As both serotonin and dopamine receptors are a target for many of the available drugs, knowledge of the neurobiology underlying cognitive flexibility will be crucial for controlling potential side-effects of future drugs being developed for other dysfunctions.

This research project is aimed at an in depth analysis of two types of receptors for dopamine in the rat brain, to clarify their role in cognitive flexibility and sensitivity to feedback. This will be achieved by administering compounds, that precisely bind to dopamine receptors called D1 and D2 type receptors, directly into the frontal brain areas responsible for flexible behavior in face of uncertainty. Following these injections the animals are going to be tested in automated boxes interfaced with computer software, which records several parameters of rat's behavior. By analyzing these parameters we can assess changes in the animal's cognitive flexibility and feedback sensitivity caused by the tested compounds.

Apart from extending our knowledge of this fascinating function of the mammalian nervous system, we hope that this research will help develop precise drugs, that will not disturb cognitive flexibility, as well as ones, that will help to restore it.