In humans depression is debilitating psychiatric disorder often associated with prominent cognitive symptoms. Clinical evidence has revealed that patients with depressive disorder frequently ruminate over their perceived failures and criticism and display an altered response to negative performance feedback characterised by increased sensitivity to punishments. Although there is now relatively consistent evidence that altered sensitivity to negative performance feedback co-occurs with depressive episodes, whether this sensitivity could predict the probability of occurrence and/or course of depression is still unclear. This is due to the difficulty in obtaining information regarding the past sensitivity to performance feedback of patients who experience their depressive episode for the first time.

Proposed project has been designed to verify, in an animal model, whether or not the altered sensitivity to negative performance feedback, measured as a stable behavioural trait, could be used to predict individual vulnerability to depression, its course, likelihood of relapse and treatment options.

In order to assess individual sensitivity of animals to negative feedback, the rats will be subjected to a series of probabilistic reversal learning tests. In these tests the animals chose between 2 levers; pressing one of them is associated with a high probability of receiving a reward and a low probability of receiving a punishment while pressing the other, is associated with a high probability of receiving the punishment and only a small chance of receiving the reward. The animals have to adjust their behaviour by responding to the appropriate levers to maximize reward and minimize punishment delivery, ignoring the occasional misleading positive or negative feedback. To assess the sensitivity of the animals to true and misleading positive and negative feedback, we will apply win-stay/lose-shift analysis where animal' behaviour is assessed according to the outcome of each preceding trial. The win-stay ratio, that represents the sensitivity to positive feedback, is the proportion of times the subject decided to press the same lever again after it resulted in a reward in the previous trial. The lose-shift ratio that represents the sensitivity to negative feedback is the probability of switching the lever in response to a punishment in the previous trial.

On basis of the median sensitivity to negative feedback obtained from multiple probabilistic reversal tests, the rats will be divided into subgroups of 'sensitive to negative feedback' and 'insensitive to negative feedback' and subsequently they will be subjected to a battery of behavioural tests aimed at evaluation of motivational, anhedonic (anhedonia – inability to experience pleasure), cognitive, and affective (anxiety) correlates of depression in animals.

Because chronic stress is one of the most prominent factors precipitating depression in humans, we will also investigate, using above mentioned battery of behavioural tests, the differences in reaction to chronic stress, between the 'sensitive to negative feedback' and 'insensitive to negative feedback' animals.

In the last stage of the project we will evaluate potential differences between the animals classified as 'sensitive to negative feedback' and 'insensitive to negative feedback' in their reaction to acute and chronic treatment with antidepressant drugs in an animal model of depression based on chronic stress.

Accomplishment of the aims of proposed project will allow better understanding of cognitive mechanisms implicated in depressive disorder. Proposed experiments will also advance our understanding of how sensitivity to feedback biases cognition towards depression and whether this bias could interact with the effects of antidepressant drugs. A combination of sophisticated behavioural techniques applied in animal models will create a unique opportunity to perform studies that for logistic reasons cannot be performed in humans.