Why do antidepressant drugs fail to work in some people suffering from depression, while for others they quickly bring relief of their symptoms? Are the positive outcomes of antidepressant treatment associated with sensitivity to reward and punishment? And if so, could screening of this sensitivity facilitate finding of the right treatment? Although the relationship between reinforcement sensitivity, affective disorders, and effectivity of pharmacological treatment has been widely postulated and brought together through influential theoretical narratives, until now, there has been no systematic study aimed at investigating these interactions. To address this need, in the present project, we will employ a novel animal model linking various levels of sensitivity to reward and punishment with a putative reactivity to antidepressant treatment. We will also compare the obtained results from animals with the data from humans taking antidepressant medications, using the pioneering online techniques and fully translational behavioural tests. Finally, we will verify, compare, and extend the results from animals and humans using computational modelling of behaviour. Based on the proposed experiments we will be able to conduct complex and multilevel verification of the hypothesis that trait sensitivity to reward and punishment (phenotype of reinforcement sensitivity) can determine the interindividual differences in the effectiveness of antidepressant treatment. Obtained results will be used to understand the phenomena of drug resistance and low effectiveness in antidepressant therapy.