Depression is a serious mental disorder, which unfortunately is becoming more and more prevalent in the general population. It is often characterized by long-term lowered mood levels, the lack of sensitivity to pleasure (anhedonia), as well as high levels of anxiety. The question is, why has there been a dramatic increase of psychiatric disorders such as depression and anxiety? The World Health Organization (WHO) prognosis indicates that, within the next 10 years, depression will become the main cause of illness-related leave from work and that the combined costs of therapy and absence from work due to depression will outweigh the summary cost of the treatment of other illnesses. The main blame for this situation is put on stress. And it is true that the world surrounding us is bombarding us with different kinds of stressful stimuli. The levels of chronic stress that we are currently experiencing are unprecedented in our history. In prehistoric times, mankind had to deal with immediate, life-threatening dangers, resulting in a dramatic fight-or-flight response – a fast, intensive set of behaviors focused on surviving the threat. Fortunately, today that is often not the case. However, life today is a constant barrage of demands and high intensity information, which, while not posing an immediate threat to our lives, results in chronic levels of stress. This is very harmful in the long run, as chronic stress is the leading cause of affective disorders worldwide.

During the development of depression, stress related stimuli deeply affect the structure and function of many brain areas associated with the so-called limbic circuit, where emotional processing takes place. In particular, these changes affect the amygdala, an almond-shaped collection of brain nuclei participating in various aspects of memory and emotional processing. Patients with diagnosed depression have decreased amygdala volume and disrupted connections of this structure with other brain areas. In terms of therapeutic potential, it is very important to learn more about that role of serotonin – a neurotransmitter classically targeted for depression therapy – in regulating amygdala activity. Serotonin acts through a myriad of receptors, however recent studies have shown a very large density of the serotonin 5-HT_7 receptor subtype in the amygdala. What is surprising is the extremely small number of scientific publications regarding the role of 5-HT_7 receptors in the amygdala, which seems to be a major oversight due to its reported effects in other brain areas associated with the pathophysiology of depression and the known antidepressant effects of blocking 5-HT_7 receptor activity in animal models of depression.

This project aims, as a world-first, to fully and exhaustively characterize the anatomy and physiology of 5-HT_7 receptor signaling in the main amygdala nuclei. Taking into account the current problems with existing medications for depression (several weeks of delay before therapeutic effects, side effects etc.), the planned experiments will greatly contribute to the theoretical basis underlying future attempt to create better therapeutic solutions to various affective disorders.