Sickness is a normal response to infection, just as fear is normal in the face of a predator. It is triggered by soluble mediators that are produced at the site of infection by activated accessory immune cells: proinflammatory cytokines. One particular group of these mediators are known as chemokines (chemotactic cytokines). They coordinate the local and systemic inflammatory response to microbial pathogens. For a long time, the brain was considered as an immune privileged tissue, due to the tight blood brain barrier which prevented the spread of inflammation. However, later it was discovered that brain cells express receptors for immune molecules and that these molecules can act on our brain, influencing our mood and behaviour. Many symptoms that we experience when we are sick are similar to symptoms of depression (e.g. depressed mood, fatigue, anorexia, disturbed sleep). Of particular interest is the idea that the action of cytokines and stress overlap to some extent, because both factors induce aforementioned behavioral changes as well as endocrine changes (e.g. dysfunction of hypothalamic-pituitary-adrenal [HPA] axis, described below). Each year there is more and more behavioral and biochemical data on this subject, however we still lack the functional evidence on the role of chemokines in the brain.

The impact of stress on brain function is increasingly recognized. Various substances are released in response to stress to deal with a stressful situation and ensure the proper functioning of the body. Two main stress responses can be distinguished. The first, fast stress response is connected with activation of the sympathetic nervous system, which triggers the fight-or-flight response. The second, slower phase of a reaction is related to the activation of the HPA axis. This response is characterized by release of corticotropin-releasing hormone (CRH) from neurons of the paraventricular nucleus of hypothalamus (PVN). When CRH binds to its receptors in the anterior pituitary gland, adrenocorticotropic hormone (ACTH) is released to blood system. ACTH binds to receptors in the adrenal cortex and stimulates adrenal release of glucocorticoids, called stress hormones. In humans it is mainly cortisol, whereas in rodents the main hormone is corticosterone. The HPA axis is tightly regulated by a negative-feedback loop, and its proper functioning plays a crucial role in limiting the stress response. The increase in the concentration of glucocorticoids leads to the inhibition of the hypothalamus and pituitary, stopping further release of glucocorticoids from the adrenal glands. However, when the exposure to a stressor is prolonged or too strong, it causes an increase in the level of stress hormones and interferes with the normal regulation of the HPA axis, which can lead to the development of different kinds of psychiatric disorders. Strong or prolonged stress is considered a risk factor in the development of affective disorders including depression or schizophrenia.

Exogenous corticosterone administration used in this research project is one of the better characterized animal models of depression and it enable to investigate acute as well as chronic changes with no risk of animals adaptating to the procedure. Stress causes changes in a wide range of brain structures, including the frontal and prefrontal cortex, hippocampus and, last but not least, the amygdala. This region is a crucial component of the brain network that forms the neural response to systemic immune activation as well as participates in mood regulation and the central and peripheral stress response. The proposed project aims to determine how chemokines interact with the stress hormone corticosterone, and how they affect the proper functioning of amygdala neurons and their synaptic activity using electrophysiological recording techniques. The description of these changes will contribute to the better understanding of mechanisms that underlie chemokine involvement in the stress response and their impact on the development of mood disorders.