

DESCRIPTION FOR THE GENERAL PUBLIC

The animal models are essential to study the etiology and therapies of central nervous system (CNS) disorders, including disorders associated with anxiety, depression and the stress response (e.g. posttraumatic stress disorder, PTSD). These disorders are an important social and economic problem due to insufficient knowledge about the mechanisms leading to their emergence and development and the lack of effective treatment. The amygdala (Amg), especially its central nucleus (CeA) is one of the key structures regulating reactions associated with fear, anxiety and stress. The rat model of electrical stimulation (ES) of this brain region is most closely related to pathological conditions occurring in patients with psychiatric disorders associated with amygdala hyperactivity. In our preliminary pilot study we showed that the long-term ES of the CeA significantly increased anxiety and behavioural activity (escape behaviour). Moreover, chronic hyperactivity of the CeA influenced the neuroendocrine stress response and immune system, which was reflected in the significant increase in plasma corticosterone concentration and leukopenia in stimulated rats. We found that GOS supplementation alleviated all of these changes, however, additional studies (e.g. neurochemistry analyses) are needed to confirm the efficacy of GOS.

Over recent years, the relationships between the intestinal microflora (microbiome) and CNS functions have become a major research area in neuroscience. Microbiome is involved in the activation of neuronal pathways and thereby contributes to the normal development of the brain, regulates the reactivity of the hypothalamic-pituitary-adrenal stress axis and affects higher cognitive functions. On the other hand, abnormalities in the composition of the bacterial flora can contribute to the development of many diseases from inflammation and obesity to previously mentioned mental disorders by affecting physiological functions.

Galacto-oligosaccharides (GOS) are prebiotics, which are defined as non-digestible polysaccharides that increase the growth and activity of health-promoting microorganisms. GOS probiotic properties have been confirmed in many studies and an anxiolytic and antidepressant-like potential of GOS has been shown recently. Only few studies have examined therapeutical properties of prebiotics in animal models of neuropsychiatric disorders. Furthermore, most of these studies used stress model in which non-specific activity modulation of many brain regions occurs, whereas this project assumes the induction of Amg hyperactivity by electrical stimulation (ES). The influence of GOS on behavioural, neuronal, endocrine and immune effects associated with hyperactivity of the Amg in rat model has not been investigated yet, therefore **the overriding aim of this project is to investigate the potential use of GOS in the treatment of mental disorders associated with stress and anxiety.** Our research hypothesis assumes that ES of the CeA induces abnormalities which are similar to those occurring in patients with PTSD, depression or anxiety disorders. The planned research aims to verify the hypothesis that GOS supplementation alleviates changes induced by ES of the CeA.

This project will apply behavioural tests which allow the assessment of anxiety, social behaviour and locomotor activity. The endocrine and immunological changes will be assessed by blood morphology, plasma corticosterone, norepinephrine, epinephrine and cytokines concentrations. The impact of both GOS and ES of the CeA on CNS processes will be assessed by the biochemical and immunofluorescent analyses of brain tissue taken from animals previously subjected to behavioural procedures.

Demonstration of the efficacy of GOS in this project will initiate further research on models of CNS disorders in animals, allowing the use of these prebiotics as supporting therapy supplementation for patients with anxiety and stress-related disfunctions. Obtained results may also contribute to the widespread use of diet enriched with these prebiotics, which in turn would be a preventive procedure and could minimize the risk of some neuropsychiatric disorders. In addition the use of GOS as a preventive or therapeutic agent would also lead to some measurable economic benefits (e.g. reduction of health care costs, patients returning to professional activity).