Behavioral and molecular consequences of a ‘double-hit’ challenge on the pathogenesis of mouse models of depression and amyotrophic lateral sclerosis (ALS)

Valorization

Relevance for society

Major depressive disorder (MDD) remains to be one of the most common neuropsychiatric disorders recognized among the top causes of health loss worldwide. The etiology of MDD is multifactorial and comprises both hereditary and environmental factors, including stressful and pro-inflammatory triggers. A combination of disease-driven 'sterile' inflammation due to emotional stress or genetically-determined neurodegeneration and pathogen-induced inflammation is a common clinical situation. An interaction of various factors when combined may lead to an altered progression of pathological processes in the CNS, including possible exacerbation of neuropsychiatric outcomes. Investigation of molecular mechanisms of such interactions is necessary for better understanding of the factors influencing the onset and progression of MDD, which will be used for the development of therapeutic approaches. Additionally, the FUS[1-359]-tg mouse line used in this study can serve as a useful model to further explore the role of microglia and inflammation in the mechanisms of ALS/FTLD syndrome.

Target groups

Patients with specific etiological factors of neuropsychiatric disorders, such as abnormal HPA activity due to chronic stress or neurodegenerative processes, and systemic inflammation. The combination of both factors may exacerbate neuropsychiatric symptoms.

Activity / Products

My work has demonstrated that the use of anti-inflammatory treatments can be beneficial in the management of neuropsychiatric and neurodegenerative disorders. The exploitation of coxibs in the management of depressive-like syndrome can be such example, suggesting that this therapeutic approach needs further investigation and development.

Innovation

My work is innovative in terms of exploitation of animal models that mimic an interplay between etiological factors of neuropsychiatric disorders rather than use a single challenge. This approach is likely to result in more valid translational research, as a combination of various etiological factors for neuropsychiatric disorders with a systemic inflammation represent a common clinical situation, and an interaction between systemic inflammation and specific etiological factors of neuropsychiatric disorders can exacerbate their symptoms.

Implementation

The results of my research have been published in peer-reviewed international journals, presented at international conferences, and contributed to our understanding of the overlapping molecular mechanisms underlying depressive syndrome induced by emotional stress, neurodegeneration, and systemic inflammation.