Project 1.5 Role of astrocytes in chronic stress resilience

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Background:

Major depressive disorder (MDD) represents a significant public health challenge. Despite the considerable efforts invested in research, effective treatments for MDD remain limited underscoring the need for a deeper understanding of its underlying mechanisms.

Within the realm of MDD, there is a growing recognition of the concepts of resilience and susceptibility to stress. Resilience refers to the ability of individuals to maintain psychological and emotional well-being in the face of adversity, while susceptibility relates to an increased vulnerability to developing depressive symptoms under similar circumstances. Unraveling the factors that contribute to resilience and susceptibility is crucial for identifying potential therapeutic strategies and developing personalized interventions.

While traditional research on MDD has largely focused on neurons and neurotransmitters, emerging evidence points to the involvement of non-neuronal cells, particularly astrocytes, in the pathophysiology of the disorder. Astrocytes which were once regarded as mere “brain glue”, are now recognized as active participants in the brain function, influencing synaptic connectivity, neurotransmitter regulation, neuroinflammatory responses and other. Several studies highlight the involvement of astrocytes rather than neurons in decreasing volume of prefrontal cortex, amygdala, or hippocampus in patients with depression. Rodent studies provide compelling evidence by demonstrating that selective ablation of cortical astrocytes or blocking their function, causes depression-like behavior. Additionally, there is also mounting evidence demonstrating the direct effect of commonly used antidepressant drugs on astrocytes.

A key astrocytic marker implicated in MDD is glial fibrillary acidic protein (GFAP), an intermediate filament protein predominantly expressed in astrocytes. GFAP undergoes upregulation in wide range of brain pathologies like trauma, ischemia or neurodegeneration; however, GFAP expression has been found to be downregulated in MDD. Studies utilizing postmortem brain samples have consistently shown decreased GFAP expression in regions associated with mood regulation, such as the prefrontal cortex and hippocampus. This downregulation of GFAP suggests a potential impairment in astrocyte function and highlights the significance of investigating astrocytic involvement in MDD.

Interested Applicants, please contact:
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Aim:

1) Testing the influence of GFAP on chronic stress resilience in mice and astrocytes function.

For that purpose, we will use GFAP KO mice. In particular we will study astrocyte morphology and coverage of synapses by glutamate transporters, as well as Ca2+ signalling.

Requirements:

- Bachelor in the field of biology, medicine, veterinary, physics, chemistry or equivalent,
- interest in conducting scientific research,
- previous laboratory experience,
- proficiency in English,

NCN OPUS26 grant (Role of astrocytes in chronic stress resilience).