

Group Name: Traslational Neuropsychopharmacology

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Title of the MRP:

Sex-specific pharmacological modulation of PTSD-like alterations in a mouse model

Summary of the MRP:

Post-traumatic stress disorder (PTSD) is a debilitating psychiatric condition characterized by persistent alterations in emotional and cognitive processes. Importantly, significant sex differences have been described in PTSD prevalence, symptomatology, and treatment response, highlighting the need for sex-specific therapeutic approaches.

This Master's thesis will focus on the evaluation of pharmacological strategies aimed at modulating PTSD-like behavioral and molecular alterations in a validated mouse model. Male and female C57BL/6J mice will be exposed to a stress paradigm that induces PTSD-like phenotypes. Following model induction, animals will be treated with candidate compounds with potential therapeutic effects, including cannabidiol (CBD) and a PPAR β/δ receptor agonist.

Behavioral assessment will be performed to evaluate anxiety-like, depressive-like, cognitive, and fear-related responses, using tests such as fear conditioning, novel object recognition, light-dark box, and novelty-suppressed feeding. The effects of pharmacological treatments will be assessed in a sex-dependent manner.

In addition, molecular analyses will be conducted in key brain regions involved in stress regulation, particularly the medial prefrontal cortex and the hippocampus. Tissue samples will be obtained using micropunch techniques to ensure regional specificity. Gene expression changes associated with treatment response will be analyzed using transcriptomic approaches, complemented by targeted validation techniques where appropriate.

This project aims to identify sex-specific responses to pharmacological interventions and to elucidate the molecular mechanisms underlying treatment effects in PTSD. The results may contribute to the development of more effective and personalized therapeutic strategies for stress-related disorders.

Methods and technology involved in the MRP:

To address the proposed aims, the student will employ a combination of state-of-the-art approaches, including:

- Behavioral assays in a validated mouse model of PTSD
- Pharmacological interventions targeting stress-related pathways (e.g., cannabidiol (CBD) and PPAR β/δ receptor agonists)
- Region-specific brain dissection using micropunch techniques (medial prefrontal cortex and hippocampus, dentate gyrus)
- RNA extraction and quality assessment from brain tissue samples
- Transcriptomic profiling (RNA-seq), depending on project feasibility

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