Project Title

Aberrant neuroimmune interactions during development contribute to oxytocin system hypofunction in mice lacking an autism-risk gene

Investigators

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Statement of Purpose

The project will study how disruption of an autism spectrum disorders (ASD)-risk gene, Cntnap2, causes developmental disruptions in neuroimmune interactions in the central oxytocin system, contributing to ASD pathophysiology.

Project Summary

Interactions between the immune and central nervous system are critical for proper brain development. Alterations in this process can lead to cellular, circuit, and behavioural abnormalities that persist into adulthood, and are suspected to play a role in neurodevelopmental disorders, such as autism spectrum disorders (ASD).

The *Cntnap2* knockout (KO) mouse is a well-established *in vivo* model of ASD exhibiting core ASD-like behaviours. The lower sociability phenotype of *Cntnap2* KO mice is associated with alterations in the central oxytocin system and decreased synaptic connectivity. Interestingly, maternal immune activation has been linked to ASD, highlighting the importance of neuroimmune interactions during early brain development.

Using *Cntnap2* KO mice, we will study if immune factors contribute to abnormal development of the central oxytocin system, causing behavioral deficits in these mice. To investigate this, we will use super-resolution in situ imaging, *in vitro* electrophysiology, *in vivo* fiber photometry, and behavioural tests. Discovering a potential role of neuroimmune interactions in abnormal neurodevelopment and ASD behavioural phenotypes will advance our understanding of molecular mechanisms of ASD and the role of neuroimmune interactions in these processes.