Morphological, functional and behavioral effects of early life immune system activation.

The developing brain is sensitive to a variety of insults. Epidemiology studies indicate that early life immune system activation with bacterial or viral infections plays an essential etiological role in psychiatric and neurological disorders with neurodevelopmental features including autism, schizophrenia, bipolar disorder, cerebral palsy, and mental retardation. A growing body of evidence from postmortem studies of human brains shows malfunctioning of the main inhibitory (GABAergic) system in the brain of patients suffering from psychiatric disorders. Also, models of prenatal inflammation using maternal immune activation or early life immune activation in rodents have been shown to induce changes in GABAergic system in adult. Inhibitory interneurons are very diverse based on differences in morphology, electrophysiological membrane properties, connectivity, features of their synaptic inputs and output as well as the expression of specific molecular markers. Therefore, determining the specific changes of different subtypes of inhibitory interneurons is fundamental to understand brain dysfunctions observed in psychiatric and neurological disorders. Here, the project aims in studying functional changes in 3 main subtypes of inhibitory interneurons in the medial prefrontal cortex of mice subjected to early life immune activation. Using the combination of whole-brain imaging, electrophysiological recordings and behavioral tests, proposed project will answer the following questions how early life immune system activation affects the number of inhibitory interneurons and their electrophysiological properties. Finally, the project will correlate morphological and functional changes after early life immune system activation with the susceptibility to depression and posttraumatic disorder in animals. Thus, results of the project will give essential knowledge required for understanding pathophysiological processes underling psychiatric disorders and potential risks associated with viral or bacterial infections.