Project summary

Neurodevelopmental disorders are increasingly perceived as the consequence of altered developmental trajectories rather than isolated regional dysfunctions. Among the brain regions implicated in these conditions, the cerebellum occupies a unique position due to its early postnatal maturation and its extensive connectivity with associative cortical areas such as the prefrontal cortex and hippocampus. Early disruptions of cerebellar activity have been proposed to influence the maturation of distributed brain networks through mechanisms of developmental diaschisis. However, whether early targeted manipulation of cerebellar activity can reorient altered developmental trajectories remains largely unexplored. **This PhD project aims to determine whether early-life cerebellar low-intensity repetitive transcranial magnetic stimulation (LI-rTMS) can modulate brain network maturation and behavioral outcomes in a genetic mouse model of autism (Shank3$^{\Delta 4\text{-}22}$)**. The project integrates controlled physical manipulation, multiscale functional imaging, cellular analyses, and longitudinal behavioral assessment. **First,** we will use functional ultrasound imaging (fUSi) and ultra-high-field fMRI to assess how early cerebellar stimulation influences large-scale brain networks. fUSi will characterize acute, region-specific hemodynamic responses during stimulation and evaluate its effect on connected regions across development. fMRI will determine whether these early network signatures are associated with persistent reorganization of whole-brain functional connectivity. **Second**, we will examine how early cerebellar modulation affects prefrontal cortical maturation, focusing on synaptic organization and excitation/inhibition balance through structural and molecular analyses. **Finally**, we will evaluate whether early cerebellar intervention produces short- and long-term changes in domains relevant to autism spectrum disorder using automated and longitudinal behavioral assessments. Together, this project will **establish a causal and multiscale framework linking early cerebellar physical manipulation to brain network maturation, cellular plasticity, and behavioral developmental trajectories**, providing new insights into mechanisms of developmental reprogramming in neurodevelopmental disorders.