NEUROSCIENCE & PHYSIOLOGY SEMINAR SERIES

MARCH 26TH

12:00PM – 1:30PM | LILY 1117

Conditional restoration of FMRP in PV interneurons partially rescues visual familiarity coding in FX mice

Sanghamitra Nareddula
Dr. Chubykin's Lab

Pizza will be served!

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that widely affects information processing in the brain resulting in deficits in learning and memory. One of the prevalent forms of ASD is Fragile X Syndrome (FXS), which results from a mutation in the FMR1 protein (FMRP). Previous studies have shown alterations in cell morphology, synaptic connections, and neural circuits pertaining to sensory perception in FXS model systems. Consistent with this, our lab has identified significant differences in the visual response of FX mice to a visual perceptual experience paradigm. Visual experience evokes low-frequency (4-8 Hz) theta oscillations in the primary visual cortex of wild-type mice, suggesting these oscillations are a possible mechanism for visual memory encoding. In FX mice, however, these oscillations are attenuated in duration, amplitude, and frequency, potentially leading to the learning disability symptomatic of the disorder. We propose a novel model that predicts the specific interaction between excitatory pyramidal cells and fast spiking inhibitory neurons in V1 which forms the circuitry responsible for the oscillations. Parvalbumin (PV) interneurons are reported to be developmentally impaired in FX mice and have reduced functionality associated with visual perception. To better understand the role of PV interneurons in the observed visual experience evoked oscillations and the subsequent impairments in FX mice, we used a novel Fmr1 conditional restoration mouse strain (Fmr1 cON/PV-Cre) to restore the expression of FMRP specifically and only in PV interneurons. We found that visual experience evoked oscillations in the Fmr1 cON/PV-Cre strain showed improvements from the FX strain. The conditional restoration strain showed a higher number of oscillation cycles, and a shift towards a higher frequency in LFPs. Using an operant conditioning paradigm we evaluated if this network rescue in Fmr1 cON/PV-Cre translates to behavior. We found that the conditional strain perform better than the FX mice, showing significant improvements in the learning deficits. This partial rescue of phenotypes seen in Fmr1 cON/PV-Cre strain emphasizes the importance of the role PV interneurons play in visual memory encoding and could provide a potential therapeutic avenue of treatment for FXS.