The Functional Role of Local Circuit Interneurons in Behavioral Flexibility
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This summer I continued my work in the lab of Dr. Marc Fuccillo in the Department of Neuroscience, whose research focuses extensively on the striatum and its implications in neuropsychiatric disease. The striatum is a subcortical forebrain structure that serves as the primary input of the basal ganglia, which subsequently controls voluntary motor output, routine behaviors, procedural learning, associative plasticity, and goal-directed decision making. Because of the broad functional domains related to or governed by the basal ganglia, it has been thought for some time that the striatum might serve as a possible nexus for the overlapping behavioral phenotypes associated with many neuropsychiatric disorders, particularly autism spectrum disorder (ASD). ASD is typically characterized by deficits in social reward processing. More recently, however, ASD has been associated with deficits in goal-directed decision making and value-based action selection.

With this knowledge, we decided to assess value-based action selection in mouse models of ASD. Past studies have shown that lesions in the orbitofrontal cortex (OFC), which is integral in decision-making, led to deficits in reward processing, specifically deficits in processing the magnitude of a reward. We wanted to recapitulate the lesion studies in a reversible way, so rather than lesioning the OFC we introduced inhibitory receptors called Designer Receptor Exclusively Activated by Designer Drugs (DREADDs) into that specific region. Ten mice were surgerized in this way to introduce the DREADDs such that, when injected by the designer drug clozapine N-oxide (CNO) prior to behavioral testing, neurons in the OFC should be inhibited from firing. At the beginning of each session over the course of two months, each mouse was placed in an operant box meant to reinforce the repetition of a particular behavior, namely seeking out a liquid chocolate reward. Once the mouse got close enough to the empty tray, two hidden levers were released and the mouse had the chance to press either level for an equal magnitude of reward. With the OFC cells inhibited, we could then observe these deficits in reward processing by varying the reward amounts on a day-to-day basis.

The experience afforded by this grant has proven invaluable in my growth as a future scientist. I learned how to carefully read through and dissect journal papers and use that knowledge to plan and execute an experimental design from beginning to end. I gained experience in performing stereotactic surgery on a mouse for viral injection into specific brain regions, coding in Med-PC language for our various behavioral paradigms, scruffing mice for IP injection, and cutting and mounting brain slices for analysis. Most importantly, I learned that scientific research is, at its core, art and so must be continuously refined and perfected to produce results. My research provided foundational data for my planned independent research project in the BBB department under Dr. Fuccillo in the upcoming semester, with the ultimate goal of arriving at a circuit-level understanding of the deficits and abnormalities in the mutant mice that drives phenotypes associated with neuropsychiatric disease.