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COMPARISON OF CORTICOSTRIATAL PROJECTIONS RELATED TO NEGLECT USING DOUBLE RETROGRADE TRACERS

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The connections between the dorsocentral striatum (DCS) and the medial agranular cortex (AGm) are crucial elements of the circuitry of hemispatial neglect in a rodent model. The aims of this study are to use double retrograde tracers to examine the proportions of three types of corticostriatal projections from layer Va of AGm to DCS: ipsilateral, contralateral, and bilateral.

Hemispatial neglect is a severely debilitating condition that occurs after approximately 40% of all cases of brain damage due to stroke. Neglect is characterized by the failure of a patient to recognize any type of visual, auditory, or somatosensory stimuli on their contralesional side. Previous studies using a rodent model have implicated cortical areas AGm, PPC, and CG1 as areas involved in neglect. These areas have connections with DCS and thalamic nuclei LP. Additionally, LP has its own set of connections to DCS and is thought to be a central structure in the neuroanatomy of neglect. Lesions in DCS cause neglect without any potential of recovery, but recovery is possible after lesions in AGm and PPC.

My previous work in Dr. Reep's lab has produced substantial results that will allow us to pursue this new study. Over the past year, I have been working to optimize the tracer efficacy of dextran amines (DA), but have found that a different tracer, cholera toxin subunit b (CTB), would suit our purposes better. CTB is a neuroanatomical tracer that transports in a retrograde direction, from the terminal to the soma. Labeled cells show what area projects to the injection site. CTB is available in several colored fluorescent conjugates, which allows multiple injections in a single animal to be compared.

In order to determine the proportions of cortocostriatal projections, hooded rats will be injected in DCS with AF 488 (green) and AF 594 (red) conjugates of CTB. On one side of the brain in DCS, a small injection of AF 594 CTB will be made while a large injection of AF 488 CTB will be made in DCS on the other side of the brain. Thus, the large injection will overlap the extent of the smaller injection, but be on the other side of DCS. Seven days postsurgery, the brains will be removed, sectioned, and examined under a fluorescent microscope. Since double injections were used, double-labeled cells will appear yellow in AGm, and will represent bilaterally projecting neurons. Similarly, red-only labeled cells in AGm on the same side as the red injection will represent ipsilateral projecting neurons, whereas those in the contralateral AGm will represent contralateral projecting neurons. Thus, the green injection is used simply to ensure that we obtain complete labeling of all the bilaterally projecting neurons. Unbiased sampling procedures will be used to count these three populations of layer Va neurons in AGm.

The results of this study will give us quantitative information that can be used to model in greater detail the circuitry related to neglect. Each of these three neuron populations is known to have cortical as well as corticostriatal projections, so the findings of this study would have implications beyond the specific pathways being evaluated.