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EVALUATING THE MOTOR BEHAVIORAL EFFECTS OF GRADUAL DOPAMINE DEPLETION IN RAT MODELS

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Introduction: Parkinson's disease (PD) is a common neurodegenerative disorder caused by the loss of dopaminergic neurons that project from the substantia nigra pars compacta (SNc) into the striatum; its symptoms include impaired motor functions such as rigidity, tremor, and difficulty with movements and coordination. Most of the current research in Parkinson's disease only examines the symptoms of patients in the late stage of Parkinson's disease. However, parkinsonian symptoms are generally progressive, and the relationship between symptom severity and the degree of dopamine loss is rarely investigated. The goal of our research is to develop a rat model to quantify the relationship between progressive behavioral symptoms and dopaminergic cell degeneration.

Methods: To model different degrees of dopamine loss, the rats are injected with a low-dose of the neurotoxin 6-hydroxydopamine (6-OHDA) every two weeks. After each injection, the motor behaviors of the rats are observed through 3 different tasks: pasta handling, running wheel and a general locomotor task. After collection of behavioral data is finished, rats are sacrificed, and brain samples are analyzed by immunohistochemistry. Microscopic images of the samples are taken, and the percentage of striatal tissue with intact dopamine is quantified and normalized using MATLAB, by comparing the darkly stained area of interest for experimental rats to control rats.

Results: There are 14 rats in total and the brain samples of 8 rats have been analyzed. From the results so far, these samples stained immunohistochemically confirm that the dopaminergic neurons projecting from SNc to striatum degenerate gradually with increasing injections of 6-OHDA. Behavioral data have been collected but have not been fully analyzed yet. However, preliminary results show that the distance travelled for rats in the general locomotor task decreases as the amount of remaining dopamine decreases. We predict that other aspects of motor function, such as balance and coordination, will also deteriorate as the amount of dopamine decreases.

Discussion: Although experimental data have not been fully analyzed, preliminary results confirm that dopamine neurons degenerate gradually with increasing neurotoxin exposure and support the prediction that rat motor deficits will gradually progress as the amount of dopamine in SNc and striatum decreases. One limitation of the study is that analyzing the video data from the behavioral tasks is very time consuming. The next steps of this research will be to develop a computational method that can increase the efficiency of video data quantification, and to finish analyzing the brain samples and behavioral data.