A Model of Gradual Dopamine Depletion in the Rat

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Introduction: Parkinson's disease (PD) is a debilitating motor disorder that is characterized by the progressive loss of dopaminergic neurons that innervate the striatum. With the progression of disease pathology, patients experience increasing severity of motor and psychiatric deficits that encompass changes in speech, muscle rigidity, bradykinesia, tremor, and impulsive behavior. Current animal studies induce PD-like symptoms with a large volume injection of 6-hydroxydopamine (6-OHDA) that completely depletes dopamine expression within a short period of time. Though these studies provide significant insight on the pathological effects of complete dopamine loss, this methodology is limited in studying the prodromal stages of PD. Current studies have demonstrated that repeated low-dose injections of 6-OHDA linearly correlates with gradual dopamine depletion. This innovative experimental approach provides an alternative model for studying the early stages of Parkinsonian-like diseases, but the behavioral deficits associated with the linear decline in dopamine levels has not been well characterized in the rat.

Materials and Methods: We gradually depleted dopamine expression by bilaterally administering low-dose intracranial injections of 6-OHDA to the medial forebrain bundle in the rat. One week following each injection, rats underwent a general locomotor task using custom tracking software developed by our lab. Fine motor behavior was also assessed with a pasta handling test.

Results and Discussion: Results from the pasta handling task suggest that small dose 6-OHDA injections can correlate with distinctive deficits in fine motor behavior. However, there were no distinctive changes in general locomotor behavior. Studies have suggested that changes in overall locomotion do not manifest until DA is completely depleted. Therefore, we will increase the number of low dose injections rats receive in future studies.

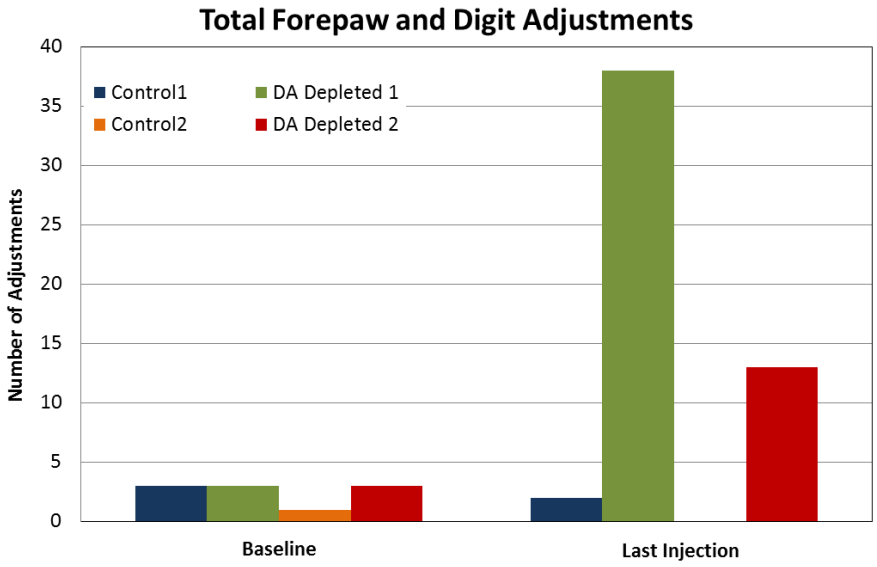

Figure 1: The pasta handling task revealed deficits in fine motor behavior as indicated by an overall increase in forepaw and digit adjustments while eating a 7cm piece of pasta.

Conclusions: This study suggests that deficits in motor behavior with progressive DA depletion may manifest first in fine motor coordination. Studies have suggested that changes in overall locomotion do not manifest until DA is completely depleted. Therefore, future studies would benefit from a larger cohort of animals and behavior tests that analyze gait and step parameters.