

Michael Lattanzi Abstract

Pharmacological Interventions for Repetitive Behaviors

Repetitive behaviors are a common feature of many neurodevelopmental disorders. Despite their clinical importance, there are currently no efficacious medications for the treatment of these behaviors. Previous work in our lab using deer mice (*Peromyscus maniculatus*) as a model of repetitive behavior has implicated reduced activation of the indirect basal ganglia pathway in these behaviors. Use of a novel drug cocktail developed in our lab that targets indirect pathway neurons has been successful in attenuating repetitive behavior in our model, suggesting the possibility of pharmacological modulation of these behaviors. Experiments from several other groups have provided evidence for the GABA_B agonist r-baclofen in reducing repetitive behaviors. The present experiments sought to determine both the behavioral effects of both the novel drug cocktail and r-baclofen as well as drug-induced neuronal activation of the striatum, the major input nucleus of the direct and indirect basal ganglia pathways. We tested the behavioral effects r-baclofen in two different mouse models of repetitive behavior and the novel drug cocktail in deer mice. No significant behavioral effects were found for r-baclofen when delivered in oil, and only a small window of significant effects were found when it was delivered in saline. The novel drug cocktail significantly reduced repetitive behavior in our deer mice. Preliminary immunohistochemical analysis of the striatum of animals treated with this drug cocktail showed increased neuronal activation as indexed by c-Fos expression in the striatum. This increased neuronal activation is likely due to the activation of receptors in the striatum expressed on the indirect pathway basal ganglia neurons.