**Identification of genetic variants that contribute to compulsive cocaine and oxycodone intake in rats: Preliminary data and establishment of the cocaine/oxycodone biobanks**

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Identification of the mechanisms that underlie compulsive drug use in animal models is a major goal for understanding the genetic risk factors for substance use disorder and facilitating the identification of novel druggable targets. However, genome-wide association studies (GWAS) in humans have only begun to identify specific genes that confer this risk. One major impediment to studies of substance use disorder is the complexity of the phenotype and the lack of control of environmental variables. We have initiated a complementary approach that leverages a multidisciplinary, highly collaborative consortium that combines next-generation sequencing with state-of-the-art behavioral screening in a unique, genetically diverse, nonhuman animal model.

We show that it is possible to perform high-throughput behavioral screening of addictive-like behaviors in N/NIH heterogeneous stock male and female rats to perform GWAS. We developed a highly-standardized protocol allowing us to measure escalation of intravenous cocaine and oxycodone self-administration that include objective measures of compulsive-like responding combined with longitudinal assessment of emotional states and pain threshold as well as responses to FDA-approved drugs for the treatment of opioid use disorder.

We also established two biological repositories containing brains, blood and various organs with a variety of tissue preservation protocols that will facilitate follow up and replicative studies by allowing the generation of induced pluripotent stem cells as well as neuroanatomical, molecular, biochemical, and pharmacological studies on behaviorally and genetically characterized animals.

The results from these studies and the use of the Cocaine/oxycodone Biobank have the potential to identify novel druggable targets, provide a comprehensive analysis of compulsive cocaine/oxycodone use in both males and females, and provide a unique data/tissue repository that will facilitate follow-up and replication studies.