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All of us for rats: multiomic studies of addiction-related traits in outbred rats

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The purpose of the Center for genetic studies of drug abuse in outbred rats is to study the genetic basis of a host of psychologically complex traits that are relevant to drug abuse. We have selected the N/NIH heterogeneous stock (**HS**) rats, which were created in 1984 by intercrossing eight inbred rat strains, and have thereafter been maintained as an outbred population. Because of the numerous accumulated recombinations, HS rats provide the best available mapping resolution. In the initial funding period, we examined Pavlovian Conditioned Approach, Nicotine Self-Administration and Behavioral Regulation (delay discounting, sustained attention, and several other traits). Our center has produced 6,590 HS rats and performed RNASeq on 440 samples from 5 brain regions. During the renewal period, we will continue to increase the sample size of several of the traits from the prior funding period. We have added intermittent access to iv cocaine as a new phenotype. Finally, our center has spawned numerous collaborating grants, including several U01s focused on cocaine, oxycodone and heroin iv self-administration, which will collectively add more than 5,000 additional HS rats to this project. This represents by far the largest rat genetic study ever undertaken, with a final projected sample size of approximately 15,000 rats. All data are stored in a centralized database that will facilitate sharing these date with other groups. We have used these data to perform estimate heritability, to perform GWAS, TWAS and PheWAS, to examine genetic correlations and to map expression QTLs.