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**Characterization of addiction-like behaviors to cocaine in Heterogenous Stock rats:
Identification of two populations of resistant and vulnerable rats.**

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Twin studies suggest that approximately 50% of the vulnerability to cocaine use disorder is determined by genetic factors, but genome-wide association studies (GWAS) in humans have only begun to identify specific genes that confer this risk. One major impediment to studies of cocaine use disorder is the complexity of the phenotype and the lack of control of environmental variables. To address this issue, we used a unique outbred strain of rats (Heterogeneous Stock) that mimics the behavioral and genetic diversity found in humans and characterized by individual differences in addiction-like behaviors. HS rats were allowed to self-administered cocaine 6h/daily for 14 days. The animals were screened for their addiction-like behaviors using an addiction index that incorporates the key criteria of cocaine-use disorder: escalated intake, compulsive-like responding, motivation for cocaine, and irritability-like behavior. The measures were analyzed across sexes and experimental subgroups. The results showed significant interindividual variability of cocaine intake, compulsivity, and motivation. We found significant sex differences in all measures of cocaine-use disorder. Future studies, will allow to identify genetic variants that predict the characteristics of cocaine use disorder, including 1) escalation of intake, 2) compulsive-like intake, and 3) motivation for cocaine. Such data will have considerable translational value for designing pharmacogenetic studies in humans.