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Characterization of addiction-like behaviors to alcohol in Heterogenous Stock rats

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Twin and genome-wide association studies have clearly established the heritability of alcohol use disorder and have shown that it has highly a polygenic architecture, meaning that numerous single nucleotide polymorphisms and other polymorphisms with individually small effects confer risk. One major impediment to studies of alcohol 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-administer alcohol in 30 min sessions for 3 weeks and then made dependent through the chronic intermittent ethanol vapor exposure (CIE) model. The rats were then allowed to self-administer alcohol during acute withdrawal (8h after the vapor was turned off) for 5 consecutive weeks. The animals were screened for their addiction-like behaviors using an addiction index that incorporates the key criteria of alcohol-use disorder: escalated intake, compulsive-like responding, motivation for alcohol, somatic withdrawal signs and withdrawal-induced hyperalgesia. The measures were analyzed across sexes and experimental subgroups. The results showed significant interindividual variability and sex differences in all the behavioral measures tested. Future studies, will allow us to identify genetic variants that predict the vulnerability to alcohol use disorder. Such data will have considerable translational value for designing pharmacogenetic studies in humans.