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Exploring Genetic Influences on Alcohol Use Disorder: A Comprehensive Study of Addiction-like Behaviors in Heterogeneous Stock Rats

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Alcohol use is prevalent among over 175 million Americans each year, with approximately 16% developing Alcohol Use Disorder (AUD). This indicates the presence of significant individual differences in the development of problematic drinking, potentially attributable to genetic variations.

In this extensive study, over 400 male and female HS rats were characterized for addiction-like behaviors. Rats self-administered oral ethanol (10% v/v) on a fixed ratio 1 schedule of reinforcement until a stable baseline of intake was measured. Subsequently, multiple addiction-related behaviors, such as preference for ethanol over water, progressive ratio responding, and level of quinine-adulterated ethanol intake, were assessed. Dependence was induced using chronic intermittent ethanol vapor exposure (14 hours/day x 4 weeks, achieving blood ethanol levels of 150-250 mg%) and behavioral experiments were conducted during acute withdrawal (6-8 hours after vapor) from ethanol. Assessments included escalation of ethanol intake, motivation to obtain ethanol, compulsivity, sensitivity to alcohol, somatic withdrawal signs, and withdrawal-induced hyperalgesia. An Addiction Index was computed from the mean Z scores of the five measurements. The robust individual differences in the Addiction Index suggest that HS rats present diverse AUD-related phenotypes, likely associated with genetic factors influencing AUD development.

These findings, derived from characterizing addiction-like behaviors in over 300 rats, emphasize the importance of pharmacogenetic studies and suggest the potential application of precision medicine in AUD treatment.