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Not a Dad Joke: Paternal Alcohol Exposure Affects the Offspring

Dr. Therese Kosten received her BA in Psychology from Purchase College in 1978 and her PhD from Yale University in 1986. She began conducting research on addictions in the Psychiatry Department at Yale University Medical School in 1987 where she was on the faculty until 2006. She then became an Associate Professor and later Professor in Psychiatry at Baylor College of Medicine. In 2014, she joined the UH faculty as a Professor of Psychology. Dr. Kosten directs the Gibson Addiction Research Laboratory at UH. This program investigates precipitants and consequences of alcohol and addiction disorders by employing sophisticated behavioral models in rodents with the aim of developing more effective treatment strategies and elucidating underlying mechanisms. She has been a PI or co-I on over 30 federal, foundation, or internal grants over the past 30 years and has over 160 publications. Her work has been cited almost 8,800 times resulting in an h-index of 55 and an i-index of 142. Dr. Kosten is Head of the Developmental, Cognitive, and Behavioral Neuroscience Program, the Scientific Director of the Animal Behavior Core, a member of the advisory board for Texas Institute of Measurement, Evaluation, and Statistics, and a member of the steering committee for the Drug Discovery Institute at UH. She teaches undergraduate and graduate courses and supervised 30 undergraduates and over 10 Master's, Medical, and PhD student theses. She served on numerous NIH and internal grant review committees, many department and college committees, and is active in national and international scientific organizations.

Abstract: Heritability of alcohol use disorders (AUD) is about 50% but less than 1% of familial transmission can be explained by genomic effects. Epigenetic alterations induced by environmental factors likely influence susceptibility to AUD. This includes paternal alcohol exposure that impacts behavior and physiology of the offspring. Previous research finds decreased alcohol consumption and altered *Bdnf* DNA methylation levels in VTA of male but not female offspring of alcohol-exposed male mice. To expand upon this finding of altered consumption, we utilized operant self-administration procedures to test various appetitive behaviors in acquisition, motivation, persistence, and reinstatement of lever pressing for alcohol in offspring of

alcohol-exposed male rats. We first assessed acquisition of operant alcohol self-administration. Next, a progressive ratio schedule was imposed to examine motivation. Then, alcohol was replaced with water to test persistence of responding during extinction. This was followed by tests of cue-induced reinstatement and reinitiation of responding for alcohol. Both male and female offspring of alcohol-exposed sires showed lower levels of responding across all operant procedures. Thus, paternal alcohol exposure prior to conception protects against the appetitive effects of alcohol. Finally, alcohol-exposed sires had lower *Bdnf* DNA methylation levels in NAc and greater levels in mPFC. But while alcohol-sired offspring of both sexes showed aberrant *Bdnf* DNA methylation patterns in NAc compared to control-sired offspring, the pattern of dysregulated *Bdnf* methylation in reward-related circuitry did not mimic changes seen in sires.