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TITLE: Alcohol Related Behaviors in Mice Selectively Bred for High and Low Activity

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ABSTRACT:

Open-field activity (OFA) is widely viewed as a proxy for measuring anxiety-like behavior in mice. DeFries et al. (1978) reported a bidirectional selection experiment that resulted in High and Low Activity (low and high anxiety-like behavior, respectively) strains of mice with 7.8-20 fold differences in OFA. These High and Low Activity strains of mice also exhibit correlated differences in other anxiety-related behaviors including light-dark box, elevated plus maze, mirror chamber test, elevated square maze, and novel object exploration (Henderson et al., 2004). Additionally, due to the high correlation of anxiety and alcohol use disorders (AUDs), we have begun to characterize these strains for several alcohol phenotypes. Using a two-bottle choice (2BC) paradigm, it was revealed that male Low mice consume significantly more alcohol than the male High mice. However, female High mice consume significantly more alcohol than the female Low mice, highlighting a sex difference in 2BC behaviors. To evaluate acute sensitivity to alcohol, we tested these strains for the loss of righting reflex. Both male and female High mice regain their righting reflex significantly faster than the male and female Low mice,

respectively. Additionally, we are testing these strains for acute alcohol induced locomotor sensitization and alcohol metabolism. Finally, because the hippocampus may play a role in both anxiety and AUDs, we have collected alcohol naïve brains for hippocampal RNA sequencing, revealing dramatic strain and sex differences in genes associated with mitochondrial function, i.e., up-regulation of several gene ontology terms related to oxidative phosphorylation in female Low mice.

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