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### **Characterization of oxycodone use disorder phenotypes in select rat strains of the Hybrid Rat Diversity Panel**

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The opioid epidemic is an ongoing public health crisis in the United States, and little is currently known about genetic mechanisms that contribute to risk for opioid use disorder (OUD). We are using the Hybrid Rat Diversity Panel (HRDP) of 45 inbred rat strains to examine genetic contributions to OUD-related phenotypes. Previous testing of three HRDP strains demonstrated significant differences in oxycodone-related behavioral phenotypes and gene expression patterns in the amygdala and prefrontal cortex. Here, we present preliminary findings from several additional HRDP strains using a longitudinal behavioral phenotyping protocol. This protocol includes a self-administration paradigm to measure acquisition of oxycodone intake, motivation to obtain oxycodone, and progression to compulsive oxycodone use. Tests for allodynia and opioid analgesia are performed prior to and following the oxycodone self-administration period, allowing the assessment of opioid tolerance and withdrawal. Although preliminary, there appear to be emerging strain differences in the various phenotypes. All strains acquired oxycodone self-administration similarly during the acquisition phase. While most strains appear to escalate oxycodone intake, HXB2 rats appear to escalate most rapidly during long-access sessions. As indicated by the tail immersion test, all strains display initial opioid-induced analgesia. Following oxycodone self-administration, SHR rats appear to show a greater tolerance to the analgesic response. Upon conclusion of behavioral phenotypic characterization, brain tissue is collected from several addiction-related brain regions to assess potential changes in gene expression. RNA expression data will be integrated with existing genotypic data to identify genes and pathways involved with oxycodone-mediated behavioral phenotypes.

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