Submitter Name: Eamonn Duffy
Submitter Email: Eamonn.duffy@colorado.edu
PI Name: Marissa Ehringer
PI Email: marissa.Ehringer@colorado.edu
Ryan Bachtell
ryan.Bachtell@colorado.edu

Sex and genetic background influence intravenous oxycodone self-administration in the Hybrid Rat Diversity Panel

Eamonn P. Duffy[1,2], Jack O. Ward[3], Luanne H. Hale[3], Kyle T. Brown[3], Andrew J. Kwilasz[3], Erika A. Mehrhoff[1,2], Laura M. Saba[4], Marissa A. Ehringer[1,2], Ryan K. Bachtell[3]

[1] Department of Integrative Physiology, University of Colorado Boulder, Boulder, CO, USA
[2] Institute for Behavioral Genetics, University of Colorado Boulder, Boulder, CO, USA
[3] Department of Psychology and Neuroscience, University of Colorado Boulder, Boulder, CO, USA
[4] Department of Pharmaceutical Sciences, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

Opioid Use Disorder (OUD) is an ongoing worldwide public health concern and relatively little work has addressed the contributions of genetic background and sex to oxycodone self-administration. Here, we present findings from a behavioral phenotyping protocol using male (n=216) and female (n=208) rats from 15 genetically diverse inbred strains from the Hybrid Rat Diversity Panel (HRDP). We used a self-administration paradigm to measure the acquisition of oxycodone intake during ten 2-hour sessions, escalation of oxycodone use during ten 12-hour sessions, and motivation to obtain oxycodone in progressive ratio tests. During the acquisition and escalation phases of self-administration, we observed an effect of both sex and strain on oxycodone consumption. Measures of oxycodone intake (e.g., median daily intake and total intake) displayed mild to high levels of heritability (h^2=0.24-0.55). The acquisition and escalation of oxycodone intake were evaluated using the median intake during the first and last three days of the 2-hour or 12-hour sessions, respectively. Strain, but not sex, accounted for variation in the acquisition and escalation of oxycodone self-administration, and these phenotypes displayed moderate heritability (h^2=0.28-0.33). Animals underwent a progressive ratio test to examine motivation to obtain oxycodone before and after the escalation phase. We observed strain differences in motivation to obtain oxycodone before escalation, but no differences after escalation. The heritability of pre-escalation progressive ratio performance was quite modest (h^2=0.14). Our results demonstrate that both sex and genetic background drive behavioral differences in oxycodone self-administration.