

Name: Jill Turner

Email: jill.turner@uky.edu

**Phenotyping Individual Differences in Escalation of Fentanyl
Self-Administration in Sprague-Dawley Rats.**

PI Ortinski¹, R Charnigo², M Xia¹, BA Humburg³, ED Denehy³, J Keady⁴, MT Bardo³,
and JR Turner⁴

¹Department of Neuroscience, ²Departments of Biostatistics and Statistics,
³Department of Psychology, ⁴Division of Pharmaceutical Sciences, University of Kentucky,
Lexington KY, 40536 USA.

A hallmark criterion of opioid use disorder (OUD) is taking the drug in larger amounts than intended. Phenotyping the escalation of opioid intake may reveal the underlying genetic markers associated with OUD. Male and female Sprague-Dawley rats (n=58) were trained in a sucrose reinforcement task using a progressive ratio schedule; individual differences in responsivity to sucrose were hypothesized to predict escalation of fentanyl intake. Rats were then trained on an FR1 schedule to self-administer fentanyl (2.5 µg/kg/infusion, i.v.) using a 2-lever procedure with a 20-sec signaled time-out (TO). The first 7 sessions were 1 hr and the next 21 sessions were 6 hr. Using latent growth curve modeling, sucrose breakpoints did not predict fentanyl infusions across 1-hr sessions nor escalation of infusions across 6-hr sessions; however, sucrose breakpoints did predict overall infusions earned during 6-hr sessions (p<0.05). A mixed effect model showed greater fentanyl intake in females than males during 1-hr sessions (p<0.01), but not during 6-hr sessions. Most important, across 6-hr sessions, we used group-based trajectory modeling that probabilistically clustered animals into phenotypes based on the combination of (1) infusions, (2) non-reinforced responses during TO, and (3) inactive lever presses. Four behavioral phenotypes were identified: (1) low escalators (n=17), (2) medium escalators (n=24), (3) high escalators (n=15) and (4) inverted-U escalators (n=2), the latter possibly being aberrations. These results inform ongoing assessment of sequencing-based genomic markers of susceptibility to OUD based on phenotypic expression of escalated opioid intake.