

Name: Randy J Nelson

Email: randy.nelson@hsc.wvu.edu

Light at Night Drives Sex-Specific Increases in Fentanyl Reward-Related Behaviors

Randy J Nelson, Darius Becker-Krail, and A. Courtney DeVries*

Departments of Neuroscience and *Medicine, West Virginia University, Morgantown, WV

The US opioid epidemic continues to grow unchecked despite increased opioid addiction awareness and reduced dispensing rates. One new area of investigation examines circadian rhythm disruptions (CRDs) that are associated with increased substance use and aberrant reward regulation. Here, we investigated the role artificial light at night (ALAN)-induced CRD may play in driving opioid reward-related behavior in mice. Male and female mice were first exposed to 4 weeks of either light days and dark nights (LD: 14 h of 150 lux:10 h of 0 lux) or light days and dim ALAN (14 h of 150 lux: 10 h of 5 lux). Mice were then run through a two-bottle choice (2BC) task, wherein they had access to a control quinine solution and a bottle containing fentanyl (4 days: 1 µg/ml, 4 days: 10 µg/ml). Notably, female mice exposed to ALAN (but not males) demonstrated a striking increase in fentanyl consumption across both doses.

Fentanyl consumption also significantly correlated with the degree of CRD for females, but not for males. Preliminary analyses of RNA sequencing of the nucleus accumbens revealed 84 overlapping differentially expressed genes (DEGs) between fentanyl versus water and ALAN versus LD conditions. Metascape analyses determined that immune-related processes were enriched among the overlapping DEGs. These results highlight a mechanism by which light at inappropriate times of day may increase propensity for opioid abuse. Future experiments will assess the effects of ALAN on opioid withdrawal, and we will continue to analyze the RNA-sequencing data to investigate potential molecular mechanisms underlying this differential phenotype and generate molecular hypotheses.