

Submitter Name: Dar'ya Pozhidayeva
Submitted email: dyp@pdx.edu
PI Name: Angela Ozburn
PI email: ozburn@ohsu.edu

Effects of Chronic Stimulation of Nucleus Accumbens on Binge Drinking and Transcriptome

Dar'ya Pozhidayeva^{1,2,3}, Sean P. Farris⁴, Kayla G. Townsley^{1,2}, Ovidiu D. Iancu^{1,2} and Angela R. Ozburn^{1,2}

¹Department of Behavioral Neuroscience, Oregon Health & Science University; ²Research and Development, Portland Veterans Affairs Medical Center; ³Chemistry Department, Portland State University; ⁴College of Natural Sciences, Waggoner Center for Alcohol and Addiction Research, University of Texas at Austin

Our recent work revealed that increasing activity in the nucleus accumbens can reduce binge-like drinking in mice. Here, we tested whether chronic administration of CNO given to mice expressing the excitatory DREADD, hM3Dq, in the NAc could produce lasting reductions in binge drinking. We hypothesized that chronic stimulation of hM3Dq could induce behavioral plasticity via transcriptional mechanisms. Mice received AAV-Cre and AAV2-DIO-hM3Dq into the NAc and we measured ethanol intake for 6 weeks using the Drinking in the Dark paradigm. We employed 2 experimental conditions [drinking fluid (ethanol or water) and treatment (1mg/kg CNO or vehicle; administered IP)] with 11-12 mice/condition. Vehicle groups were injected with 1% DMSO in saline daily for 6 weeks 30 minutes prior to DID. Mice in the CNO groups were treated with vehicle during week 1 (baseline) and 6 (washout) and CNO during weeks 2-5. At the end of the study we performed RNA Seq. To determine genes altered chronic binge-like drinking but ameliorated with chronic CNO treatment, we performed Differential Expression analysis (DE), Gene Ontology, and Weighted Gene Network Covariance analysis. Comparison of significantly DE genes in each treatment group revealed 688 unique genes altered with binge drinking, 1431 in binge drinking mice that were treated with CNO, and 612 in water drinking mice treated with CNO. Furthermore, chronic stimulation ameliorated many alcohol-induced changes in gene expression. Since these changes persisted for at least 7d post-treatment, our results suggest that chronically increasing NAc activity (via CNO/DREADDs) induces molecular and behavioral plasticity.