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Challenges of Sex Differences Research in Neuroscience: The role of central estradiol in heroin extinction memory retention in male and female rodents[†]

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OBJECTIVES/GOALS: Misprescription of opioids has led to an epidemic of opioid use disorder (OUD). Females, among other differences, have increased susceptibility to the addictive properties of opioids. Yet, the exclusion of female subjects from many foundational studies on reward processing had hindered our ability to fully understand these disparities. **METHODS/STUDY POPULATION:** Estradiol (E2), a neuronal sex steroid, may play a role in sex differences in OUD. In this study, we used fadrozole, an aromatase inhibitor, to characterize the role of centrally produced E2 in heroin cue extinction memory retention (EMR, “remembering to forget”). Male and female rats self-administered heroin in a long-access paradigm (6hr/day) for 8 days, where a light/tone cue was co-presented with each infusion of heroin. This was followed by 1 day of cued extinction (6hr; light/tone but no heroin). Just prior to this session, fadrozole was infused into the basolateral amygdala (BLA) through implanted cannulas. The next day, subjects were given a cued EMR test (1hr; light/tone but no heroin) following another infusion of fadrozole. **RESULTS/ANTICIPATED RESULTS:** Females took more heroin than males (mg/kg) despite having similar active nose poke responding during acquisition. Regardless of aromatase inhibition, females had higher active nose pokes during the first hour of cued extinction relative to males. Both males and females treated with fadrozole in the BLA prior to cued extinction had impaired EMR on test, evidenced by increased active nose pokes and lower extinction indices relative to vehicle controls. Upon examination of the brains, we expect that aromatase inhibition will have impaired neuronal plasticity, as evidenced by decreases in numerous measures of plasticity. Furthermore, we expect to find sex differential expression of estrogen receptor (ER) subtypes throughout the BLA, suggesting a convergent sex effect of E2 on heroin EMR. **DISCUSSION/SIGNIFICANCE:** This study is the first to examine a behavioral role for central E2 in the BLA. Future studies will examine specific roles for ER subtypes on this behavior and synaptic plasticity. A better understanding of sex specific E2 signaling will promote further research on sex differences and allowing us to better address disparities in disorders like OUD.

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The design of a virtual museum to address social disconnection and pain among individuals with chronic pain (IWCP)

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OBJECTIVES/GOALS: Engagement with art may reduce the social disconnection that accompanies chronic pain. Disaggregating specific from non-specific effects of arts-based programs is challenging. This study creates an experimental virtual museum to identify the separate and joint effects of art and social connection. **METHODS/STUDY POPULATION:** Two x two factorial experiment with repeated measures: (1) Artwork present condition is a virtual exhibition featuring

paintings from the Google Arts & Culture collection; (2) Artwork absent condition is the same exhibition space but with the paintings removed; (3) Social connection condition asks participants to write about a situation in which they felt more socially connected to others; (4) Social disconnection conditions asks participants to write about a situation in which they felt more socially disconnected from others. Participants: (1) English language proficiency; (2) ≥18 years; (3) Chronic moderate to severe pain; (4) Lonely; (5) Has electronic device with internet connection. **RESULTS/ANTICIPATED RESULTS:** Participants will be recruited through a 3-month social media campaign conducted by StudyPages, a clinical trial recruitment and management platform. This study will evaluate the effects of virtual art exposure and social connectivity priming on pain and social disconnection reduction among lonely IWCP. Pre-intervention scores for pain intensity, pain unpleasantness, and perceived social disconnection will be compared to post-intervention scores. Secondary outcome measures include (a) Museum visit data (e.g., user movement, click, object interaction, open comments) and (b) perceptions about artwork. **DISCUSSION/SIGNIFICANCE:** Psychosocial support for IWCP may improve pain-related outcomes. This study's data will help to optimize virtual museum interventions and provides the first data we are aware of to evaluate the specific effects of art in virtual museum engagement to reduce pain and social disconnection among IWCP.

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Inpatient Quality Indicators Risk-Adjustment Using Interactions Selected by Machine Learning Methods

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OBJECTIVES/GOALS: Predictive models for health outcomes often have poor calibration potentially due to interactions that are ignored by standard methods. Using AHRQ models for Inpatient Quality Indicator (IQI) 11 Abdominal Aortic Aneurysm Repair and IQI 09 Pancreatic Resection mortality, we hypothesize that identifying interactions may improve model calibration. **METHODS/STUDY POPULATION:** We used adult discharge data from 16 states obtained from AHRQ Healthcare Cost and Utilization Project (State Inpatient Database), California Department of Health Care Access and Information, and New York State Department of Health. We used AHRQ's v2021-1 Clinical Classifications Software Refined (CCSR) with present on admission flags to create features for risk-adjustment. We compared the performance of Least absolute shrinkage and selection operator (LASSO) model and first-order interaction models estimated using Hierarchical Group Lasso Regression (HGLR), after splitting the data into training and test sets. C-statistics, area under the precision-recall curve and Hosmer-Lemeshow calibration plots are reported. Finally, logistic regression models with selected CSSRs were evaluated on the test set. **RESULTS/ANTICIPATED RESULTS:** IQI 11 has four strata: open and endovascular repair of ruptured aneurysms (39% and 21% mortality, respectively); open and endovascular repair of unruptured aneurysms (6% and 0.8% mortality, respectively). IQI 09 has two strata: with and without pancreatic cancer (2% and 2.5% mortality, respectively). Comparing the HGLR model (with interaction effects) with Lasso models (without interactions), we noticed meaningful improvements in discrimination and calibration. However, for IQI 09, the extremely low mortality rate did not result in good HGLR or LASSO models. Interactions involving