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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[†]

Jordan S. Carter[1], Dhruvi Patel[1] and Carmela M. Reichel[1]
[1]Medical University of South Carolina

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)

Ian Koebner[1] and Jorge Pena[1]
[1]University of California, Davis

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 studys 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

Monika Ray[1] and Patrick S. Romano[1]
[1]General Internal Medicine, University of California Davis Health and Center for Healthcare Policy and Research

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 CCSRs 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

CCSRs could be identified using the novel HGLR method, which improved model performance given a heterogeneous population in IQI 11 with a mix of high and low event rates, unlike the more homogeneous patient population in IQI 09. DISCUSSION/SIGNIFICANCE: Standard implementations of regression models fail to address critical issues that arise in healthcare data – (a) quadratic explosion of potential interactions that cannot be manually identified, and (b) categorical variables with multiple levels or values (e.g., age categories). We propose innovative use of HGLR to robustly address these issues.

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Neonipple Formation After Implantation Of Acellular Ovine Xenograft

Nicholas Andrew Vernice[1], Sarah Caughey[1], Nabih Berri[1], Xue Dong[1], Jason Harris[1], Ryan J. Bender[1] and Jason A. Spector[1]
[1]Weill Cornell Medicine

OBJECTIVES/GOALS: To determine if decellularized costal cartilage (DCC), which could theoretically be obtained "off the shelf," would provide similar results to autologous cartilage grafts previously studied in this lab, thereby widening the application of our novel nipple engineering approach to all patients undergoing nipple reconstruction. METHODS/ STUDY POPULATION: PLA scaffolds (diameter: 1.0 cm, height: 1.0 cm) were printed using a PRUSA 3D printer and sterilized. Lamb costal cartilage was minced (1 mm3) or zested (<0.2 mm3) and then decellularized. The quality of decellularization was assessed using DNA quantification and histological analysis. DCC was then packed into PLA scaffolds and implanted subcutaneously into immunocompetent Sprague Dawley rats using a CV flap technique. The constructs were explanted and evaluated up to 6 months after implantation. RESULTS/ANTICIPATED RESULTS: All nipple reconstructions showed well-preserved diameter and projection due to persistence of the external scaffolds at 1, 3, and 6 months. Mass and volume of engineered tissue was well-preserved over all timepoints. Compared to implantation values, engineered zested nipples demonstrated a 12% mass increase and a 22% volume increase at 6 months. Minced nipples illustrated a similar mass and volume gain with a 21% increase in mass and a 13% increase in volume at 6 months secondary to infiltration of fibrovascular tissue and growth through scaffold wall pores, respectively. Histologic analysis demonstrated a mild inflammatory infiltrate 1 month after implantation which was replaced by fibrovascular tissue by 3 months that remained stable through 6 months. The processed DCC structure remained unchanged over time. DISCUSSION/ SIGNIFICANCE: Using acellular ovine xenograft within bioabsorbable scaffolds, we have engineered neonipples that maintain their volume for at least 6 months. DCC architecture is well-preserved with minimal evidence of immune-mediated degradation. By using DCC, this novel approach to nipple engineering may be applied to any patient requiring reconstruction.

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Search Solutions: Investigation into CTSA Hubs COVID-19 Vaccine Information

Hasan M. Bashir[1] and Barbara Tafuto[2]
[1]Robert Wood Johnson Medical School, Rutgers University and [2]Rutgers University

OBJECTIVES/GOALS: While CTSA hubs have contributed to the successes in COVID-19 clinical research, understanding the role of the CTSA consortium in translating vaccine efficacy and availability to awareness and implementation. The goal of this study is to quantitatively assess the use of social media in the dissemination of COVID 19 vaccine content across 60+ CTSA Hubs. METHODS/ STUDY POPULATION: Structured search terms in the CTSA Search Solutions database were used to identify CTSA Hub website pages highlighting "COVID-19 Vaccination Information." Each link identified was manually reviewed for vaccination content. The links and content identified by CTSA Search Solutions were then validated by advanced Google search operator "vaccine site" and manual review of CTSA Hub websites. Official CTSA Hub social media platforms were searched for vaccine proliferation content from January 1, 2020 to November 11, 2021. Data points collected included Community Targeted Vaccine Content, Vaccine Awareness, Vaccine Distribution, Vaccine Clinical Trial, Vaccine Related Media, Social Media Presence, and Social Media Vaccine Proliferation. RESULTS/ANTICIPATED RESULTS: In examining content, of the 64 listed CTSA Hubs, 52 of (67.2%) hosted one or more categories of COVID-19 vaccine information, and 16 (25%) hosted three or more categories. The most common category was "Community Targeted Information" with 27 (42.2%) hubs; the least common category was "Vaccine Distribution" with 5 (7.8%) hubs. Examining social media for vaccine proliferation, 41 (64.1%) hubs had connected social media and 23 (35.9%) hubs had vaccine proliferation posts. The most common platform was Twitter with 37 hubs; the least common platform was Instagram with 5 hubs. DISCUSSION/SIGNIFICANCE: Our investigation demonstrated varying Phase 4 translational efforts via social media among the CTSA Hubs for COVID-19 vaccine implementation. These novel findings identify promising opportunities for enhancement while emphasizing proven strategies from CTSA hubs nationwide. Further research will elucidate granular trends among CTSA hubs.

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A Longitudinal, Multi-Method, Pilot Triangulation of Family Intensive Care Unit Syndrome

Grant Pignatiello and Ronald L. Hickman[1], Jr*
[1]Case Western Reserve University

OBJECTIVES/GOALS: The objectives of this study are to: 1) Examine the feasibility of using concurrent multi-methodology to quantify the affective, decisional, physical symptom domains of Family Intensive Care Unit Syndrome. 2) Describe the associations between the Family Intensive Care Unit Syndrome symptom domains (affective, decisional, physical). METHODS/STUDY POPULATION: Using a repeated-measures, correlational design, we recruited surrogate decision makers of incapacitated, mechanically ventilated patients within four adult intensive care units at a tertiary medical center in northeast Ohio. We collected baseline data (T1) after obtaining informed consent and follow-up data three (T2) and seven (T3) days post-baseline. We used self-report instruments, behavioral tasks, and accelerometry to measure affective (anxiety & depression), decisional (working memory ability & decision fatigue), and physical (sleep quality & sleep disturbance), symptom domains. For objective 1, we computed completion percentages of each time-point and overall compliance with wearing the accelerometer device. For objective 2, we inspected Spearman correlations. RESULTS/ANTICIPATED RESULTS: We recruited and collected baseline data (T1) for 33 participants. Nineteen participants completed the T2 interview and twenty participants completed T3. Eight participants wore the accelerometer device for less than 72 hours and 15 wore the accelerometer for the full study period.