Rutgers Addiction Research Center
Brain Health Institute

RARC Fall Symposium Program - September 6, 2024

8:30 AM – 9:00 AM — **Registration and Breakfast**

9:00 AM – 9:15 AM — **Welcome and Introduction**

Danielle Dick, Director, Rutgers Addiction Research Center
Michael E. Zwick, Senior Vice President for Research

9:15 AM – 10:00 AM — **Opening Plenary**

Will Psychedelics Save Us: Thoughts From Two Psychedelic Scholars
Caroline Dorsen, Associate Dean of Clinical Partnerships, Professor, Clinical Educator Track, School of Nursing
Joanna Kempner, Associate Professor, Department of Sociology, Rutgers-New Brunswick School of Arts & Sciences

10:00 AM – 10:30 AM — **Coffee Break**

10:30 AM – 11:15 AM — **Meet the New RARC Associate Directors**

Context Matters: A Better Understanding of Youth Substance Use
Kristina Jackson, Associate Director of Epidemiology, Etiology, & Prevention; Professor, Department of Psychiatry, Robert Wood Johnson Medical School

Building a Clinical Trials Pipeline in Addiction Medicine
Ethan Cowan, Associate Director of Treatment & Recovery; Professor, Department of Emergency Medicine, New Jersey Medical School

11:15 AM – 12:00 PM — **RARC Pilot Awardees**

Developing a Targeted Pharmacotherapy for Pain Without Abuse Liability
Pilot awardees: David Barker; Zhiping Pang
Presenter: **David Barker**, Assistant Professor, Department of Psychology, Rutgers-New Brunswick School of Arts & Sciences

Integration of Genetic, Environmental, and Neural Risk Factors Into Treatment Research
Pilot awardees: Sarah Brislin; David Zald
Presenter: **Sarah Brislin**, Assistant Professor, Department of Psychiatry, Robert Wood Johnson Medical School

Role of Habenula Glucose Inhibitory Neurons in Opioid Use Disorder
Pilot awardees: Jiang Ye; Vanessa Routh
Presenter: **Wanhong Zuo**, Postdoctoral Fellow, Department of Anesthesiology, Physiology and Pharmacology, New Jersey Medical School

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12:00 PM – 1:00 PM — **Lunch - Option to Join Topic Tables (See Page 4)**

1:00 PM – 1:45 PM — **Commercialization of Research**

How Rutgers Tech Transfer Can Support your Commercialization Efforts
Dan Benderly, Associate Director, New Ventures, Rutgers Office for Research

Tales from the Trenches: Addiction Researchers Currently Working to Commercialize Scientific Discoveries
Morgan James, Assistant Professor, Department of Psychiatry, Robert Wood Johnson Medical School
David Barker, Assistant Professor, Department of Psychology, Rutgers-New Brunswick School of Arts & Sciences
Danielle Dick, Director, Rutgers Addiction Research Center

1:45 PM – 2:30 PM — **Advancing Addiction Research & Treatment: New Partnerships with RWJBarnabas Health**

Michael Litterer, Vice President, Institute for Prevention and Recovery
Alexis LaPietra, System Director of Addiction Medicine; Medical Director, Institute for Prevention and Recovery
Elliott Liebling, Director, Institute for Prevention and Recovery
Reyna Maybloom, Senior Manager of Data & Analytics, RWJBarnabas Health
Christine Ramdin, Instructor, Department of Emergency Medicine, New Jersey Medical School
Brittany Simon, Assistant Director of Research, Development, and Project Management, Institute for Prevention and Recovery

2:30 PM – 3:00 PM — **Coffee Break**

3:00 PM – 3:45 PM — **Co-Production and Community-Based Participatory Approaches in Addiction Research**

Alexandria Bauer, Assistant Professor, Department of Applied Psychology, Graduate School of Applied and Professional Psychology
Arielle Estes, Peer Support Specialist III, University Behavioral Health Care
Peggy Swarbrick, Professor, Rutgers Center of Alcohol and Substance Use Studies, GSAPP; Scarlet Well Director, Rutgers New Brunswick

3:45 PM – 4:15 PM — **Trainee Research Lightning Presentations**

Dorsal Striatum Astrocytes Modulate Alcohol-Related Behaviors
Cherish Ardinger, Postdoctoral Fellow, Department of Cell Biology & Neuroscience, Rutgers-New Brunswick School of Arts & Sciences (PI: R. Huda)

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3:45 PM – 4:15 PM

Trainee Research Lightning Presentations - Continued

The Effects of High-Fat Diet on Emotion-Like Behaviors and Dopamine Receptors in the Amygdala
Brigitte Gonzalez Almo, Postdoctoral Fellow, Department of Pharmacology, Physiology & Neuroscience, New Jersey Medical School (PI: M. Bocarsly)

Drug and Food Craving in Daily Life
Sergej Grunevski, Ph.D. Candidate, Department of Psychology, Rutgers-New Brunswick School of Arts & Sciences (PI: A. Konova)

Timing Matters: The Effect of Suvorexant on Cocaine Behaviors in the Active vs. Inactive Periods
Shayna O'Connor, Ph.D. Candidate, Department of Psychology, Rutgers-New Brunswick School of Arts & Sciences (PIs: D. Barker; M. James)

4:15 PM – 4:45 PM

Late Breaking News: Research Presentations

Normalizing the Mesocorticolimbic Reward Circuity in Opioid Users Using Transcranial Magnetic Stimulation
Travis Baker, Associate Professor, Center for Molecular and Behavioral Neuroscience, Rutgers-Newark School of Arts & Sciences

Targeting Exon 7-associated 7TM C-Terminal Variants of the Mu Opioid Receptor Gene, Oprm1, via Antibody and Antisense Oligonucleotide for Diminishing Adverse Effects of Clinically Used Mu Opioids Without Altering their Analgesia in Pain Management
Ying-Xian Pan, Professor, Department of Anesthesiology, New Jersey Medical School

Insights From a 40-Year National Prospective Study of Over 10,000 Persons With Opioid Use Disorder
Stanley Weiss, Professor, Department of Medicine, New Jersey Medical School

4:45 PM – 5:00 PM

Concluding Remarks

Danielle Dick, Director, Rutgers Addiction Research Center

5:00 PM – 6:00 PM

Poster Session and Reception

RARC Topic Tables

During lunch, we invite you to join a topic table (optional) to connect with colleagues who share your interests and enjoy lunch over an informal conversation.

Table 1 - Behavioral Addictions

Lia Nower, Associate Dean for Research & Distinguished Professor, School of Social Work; Director, Center for Gambling Studies; Co-Director, Addiction Counselor Training (ACT) Certificate Program

Table 2 - Addiction Treatment Research at Rutgers

Ethan Cowan, Associate Director of Treatment & Recovery; Professor, Department of Emergency Medicine, New Jersey Medical School
Nina Cooperman, Associate Professor, Department of Psychiatry, Robert Wood Johnson Medical School

Table 3 - Community Engaged Research

Peggy Swarbrick, Professor, Rutgers Center of Alcohol and Substance Use Studies, GSAPP; Scarlet Well Director, Rutgers New Brunswick
Arielle Estes, Peer Support Specialist III, University Behavioral Health Care

Table 4 - Addictions in Underserved Populations

Alexandria Bauer, Assistant Professor, Department of Applied Psychology, Graduate School of Applied and Professional Psychology
Carolyn Sartor, Associate Professor, Department of Psychiatry, Robert Wood Johnson Medical School

Table 5 - Addiction Training

Chris Pierce, Professor, Department of Psychiatry, Robert Wood Johnson Medical School
Kristina Jackson, Associate Director of Epidemiology, Etiology, and Prevention; Professor, Department of Psychiatry, Robert Wood Johnson Medical School

Table 6 - Eating Disorders

Morgan James, Assistant Professor, Department of Psychiatry, Robert Wood Johnson Medical School
Miriam Bocarsly, Assistant Professor, Department of Pharmacology, Physiology and Neuroscience, New Jersey Medical School

Table 7 - Cannabis

Tammy Chung, Director, Rutgers Center for Population Behavioral Health; Professor, Department of Psychiatry, Robert Wood Johnson Medical School

Table 8 - Commercialization of Research

Dan Benderly, Associate Director, New Ventures, Rutgers Office for Research

Poster #1

Elucidating the Role of Dopamine D3Rs in Obesity

Authors: Ali Khawaja, Valentina Vargas, and Miriam Bocarsly

PI Name: Miriam Bocarsly

Obesity is an ever-increasing epidemic within developed nations, with approximately ⅔ of the US adult population being overweight and ⅓ of the US adult population being obese (NIH 2021). Obesity exacerbates the risk for chronic illnesses such as hypertension, hyperlipidemia, type II diabetes mellitus, and other metabolic disease. While this epidemic progressively worsens, obesity remains heavily stigmatized as a behavioral disorder, whilst understanding of the underlying neural mechanisms remains unclear. We propose that obesity is reflective of dysfunction in the neural reward circuitry such that the hedonic value associated with food overrides innate caloric regulation mechanisms. The striatum has long been implicated in driving addiction and overconsumption, specifically through its dopaminergic pathways. While the role of dopamine D1 and D2 receptors (D1R & D2Rs) in these phenotypes are well established, little is known about the role of D3Rs. Through the utilization of novel transgenic D3 floxed mice, we have been able to selectively ablate D3Rs only on D1R-containing neurons within the striatum. Over the course of the study, we have identified a direct relationship between D3R expression and obesity phenotype under standard conditions. Concurrently, preliminary data shows no significant change in locomotor activity across genotypes, thus implicating decreased D3R expression in the overconsumption of standard rodent chow with no other implemented variables. Both populations of mice utilized in this study show significant changes in body weight over the course of the study, with variability in sex differences.

Poster #2

Dorsal striatum astrocytes modulate alcohol-related behaviors

Authors: Cherish Ardinger, Anagha Kalekar, Mariam Mahboob, Wesley Evans, Miriam Bocarsly, and Rafiq Huda

PI Name: Rafiq Huda

Alcohol is a pharmacological agent that targets all brain cells, including non-neuronal glia cells called astrocytes. Astrocytes display robust calcium dynamics reflecting synaptic transmission and neuromodulation. Emerging evidence shows the involvement of astrocytes in multiple behavioral processes important for alcohol misuse. However, we do not understand whether and how astrocytes modulate alcohol-related behaviors. Decades of work in human clinical populations shows that people with a higher stimulant and lower sedative response to alcohol are predisposed for alcohol misuse. Preclinical work in rodent models has further established that the dorsal striatum is a key contributor to the stimulant effects of ethanol. In rodents, stimulant effects of ethanol manifest as an increase in locomotor activity. We tested how astrocyte calcium activity modulates the stimulant properties of ethanol. Male and female mice were stereotaxically injected into the dorsal striatum with viruses expressed under an astrocyte specific promoter. We expressed in mice the mCherry fluorophore

(control) or CalEX, a calcium extruding pump that reduces astrocyte calcium activity. After ~4-weeks of viral expression, mice were given intraperitoneal (IP) injections with a range of ethanol doses (0-2g/kg) and placed in an open field arena for 30 minutes. Perturbing astrocyte calcium activity increased the stimulant effect of ethanol, evidenced as increased locomotion following ethanol injection in CalEX mice as compared to the mCherry expressing mice. We are currently using fiber photometry to determine the effect of ethanol exposure on astrocyte calcium activity. Together, our findings suggest that astrocytes may play a protective role against behavioral stimulation to ethanol.

Poster #3

Binge sucrose and saccharin-induced neuroadaptations: A focus on the orexin/hypocretin system

Authors: David De Sa Nogueira, Sarah Delcourte, Rachel Kim, Samad Arastu, Elise Grelet, and Gary Aston-Jones

PI Name: Gary Aston-Jones

Binge eating disorder is the most common eating disorder and the neuronal mechanisms involved in this maladaptive behavior are not well known. Given the links of the orexin/hypocretin system to both reward processing and food intake, this study examined its contribution to binge-like eating in female rats. In addition, behavioral and molecular adaptations induced by eating disorders share commonalities with those involved in addiction. Separate groups were given intermittent (12h) or continuous (24h) access to 10% sucrose or 0.4% saccharin and food over 28 days. Only groups with intermittent access to either sucrose or saccharin displayed excessive intake (i.e., binge eating). DREADDs (Designer Receptors Exclusively Activated by Designer Drugs) were used to inhibit orexin projections from the lateral hypothalamus (LH) towards the ventral tegmental area (VTA) in an orexin-Cre+ rat model using the ligand Clozapine-N-Oxide. Interestingly, all groups exhibited increased numbers of orexin A neurons compared to the group with limited access to food only. In parallel, different doses (10, 20 or 30mg/kg) of an orexin 1 receptor antagonist, SB334867, reduced binge-like intake in groups with intermittent access to sucrose or saccharin but not in rats with continuous access to sucrose. Inhibition of orexins projections (LH->VTA) using DREADDs also led to a decrease binge-like intake in both sucrose and saccharin groups. We then assessed whether binge-like intake alters economic demand for cocaine in females. Only intermittent access groups exhibited increased demand for cocaine. 10 and 30mg/kg doses of SB334867 as well as inhibition of orexins projections using DREADDs decreased demand for cocaine in all groups compared to controls with food only. Interestingly, pre-exposure to cocaine increased saccharin bingeing and daily intake. Altogether, our findings indicate that sucrose and saccharin bingeing alter the orexin system similarly to drugs of abuse. Hence, our results broaden the understanding of neural alterations associated with binge eating pointing towards addictive-like properties of palatable foods.

Poster #4

Effect of acute ethanol on prefrontal cortical excitatory-inhibitory microcircuit interactions

Authors: Esther Ko, and Molly Saunders

PI Name: Rafiq Huda

Acute alcohol intoxication impairs cognitive function in part by affecting neuronal activity in the prefrontal cortex (PFC), but the effect of alcohol on in-vivo microcircuit dynamics remains understudied. Here, we used two-photon calcium imaging in the anterior cingulate cortex (ACC) to examine how varying doses of ethanol impact the activity of vasoactive intestinal polypeptide (VIP)-expressing GABAergic interneurons in mice. Our results show different effects of alcohol on single neuron and network-level activity. Although increasing doses of ethanol decrease VIP neuron activity, pairwise correlation between neurons increases.

Poster #5

Suvorexant co-treatment prevents development of negative affect with chronic oxycodone while preserving analgesia

Authors: Kimberly Newman, Samad Arastu, and Gary Aston-Jones

PI Name: Gary Aston-Jones

Prescription opioids are commonly used to treat chronic pain but can lead to withdrawal and negative affect following dependence, and to development of opioid use disorder (OUD). We developed a rodent model of prescription opioid-associated negative affect, showing that 3wk of oxycodone (oxy) treatment is associated with hyperalgesia and anhedonia-, anxiety-, and depressive-like behavior in acute abstinence. Compared to saline-treated controls, oxy rats had increased numbers of orexin-expressing neurons. Here, we tested whether attenuation of orexin signaling during chronic oxy treatment would prevent negative affect while preserving the analgesic properties of prescription opioids. Male Long Evans rats (n=5/group) were injected with Freund's Complete Adjuvant in the hindpaw (s.c) and given 2wk of twice-daily saline or oxy (3mg/kg, i.p.), in conjunction with daily oral vehicle (veh) or the dual antagonist suvorexant (suvo). During acute abstinence, rats were evaluated on the von Frey test (hyperalgesia), saccharin preference test (anhedonia), elevated plus maze (anxiety-like behavior), and forced swim test (depressive-like behavior). Rats were also tested for mechanical analgesia in a Freund's adjuvant pain model with von Frey 15min following acute oxy. We found that increased negative affect seen in oxy+veh compared to saline+veh rats ($p=0.058$) tended to reverse in oxy+suvo rats (saline+veh vs. oxy+suvo, $p=0.98$), indicating that co-treatment with suvo reversed the increased negative affect produced by the chronic oxy. In pain model rats, acute oxy induced mechanical analgesia as expected (oxy+veh compared to sal+veh rats, p<0.05), and suvo co-treatment did not significantly affect this analgesic action of oxy (von Frey thresholds between oxy+veh and oxy+suvo rats, $p=0.75$). Together, these results indicate that daily co-treatment with suvo prevents oxy-associated negative affect development but does not affect analgesia induced by oxy. Current experiments are repeating these experiments for a larger sample size, evaluating whether daily suvo co-treatment prevents other indices of OUD after chronic oxy (including

increased demand for opioids), and determining if suvo co-treatment attenuates the increase in orexin cell numbers seen with chronic oxy. These experiments support the adoption of suvo as an adjunct to oxy treatment for chronic pain to prevent OUD development.

Poster #6

Lateral Habenula Inhibition Suppresses Nociception and Future Fentanyl Seeking

Authors: Olivia DePasquale, Chris O'Brien, Juju Han, Simrun Sobti, Dhruvi Desai, Hayden Kenny, Roshni Vemireddy, and David Barker

PI Name: David Barker

Stress is a primary risk factor in the development of mental illness and substance use disorders. Our previous research has shown that footshock stress induces learned helplessness and can alter reward value, affect, and nociception. Moreover, we discovered that these features can predict future fentanyl preference. We therefore predicted that identifying a neural substrate associated with all of these factors could aid in the development of a successful pharmacotherapy. Recently, the Lateral Habenula (LHb) has gained attention for its role in pain, stress, depression, and reward processing. In this study, we investigated whether chemogenetic inhibition of VGlut2 neurons in the LHb during footshock stress could reduce stress-induced opioid susceptibility. Consistent with our previous findings, we observed that stress produced changes in negative valence behaviors, nociception, and oral opioid self-administration following footshock stress. However, we also discovered that chemogenetic inhibition of the LHb could prevent many of these behavioral changes, including future fentanyl preference. Our results indicate that inhibiting the LHb during stress could help mitigate stress-induced susceptibility to fentanyl misuse. Future studies might therefore focus on developing LHb-specific pharmacotherapies.

Poster #7

Auditory Cocaine Conditioning (AuCC) results in sound stimulus control of behavior and neuroplasticity in the auditory system

Authors: Madison Yip, Sarah Rajan, Mark A. Presker Jr., and Kasia M. Bieszczad

PI Name: Kasia M. Bieszczad

Understanding the mechanisms driving cocaine use and dependency is crucial to developing novel treatments to prevent relapse and improve recovery rates. Cocaine affects sensory systems like the auditory brainstem through experience-dependent plasticity, which contributes to behaviors in substance use disorders (SUDs). Prior studies have found that cocaine directly impacts attention-sensation systems in the brain and may divert attention away from learned tasks and toward drug-related behaviors. However, it is still unclear if cocaine-paired sound stimuli alone can cause cocaine-specific changes in auditory brainstem response (ABR) and drive non-drug-seeking behaviors. We hypothesize that even in a drug-free state following cocaine-tone conditioning, ABRs to a previously cocaine-paired sound will differ from pre-conditioning–an indicator of neuroplasticity. We predict that cocaine-associated sounds will increase spontaneous exploration behaviors over learned operant tasks in a learned environment.

Poster #8

Using Active TMS to Enhance N200 Conflict Monitoring Signals During Probabilistic Selection Task

Authors: Daniel Robles, Nicole Zhang, Nicole Lalta, and Travis Baker

PI Name: Travis Baker

Transcranial Magnetic Stimulation (TMS) has shown considerable promise for future clinical interventions aimed at smoking cessation by targeting neural circuits involved in reward processing and cognitive control. TMS allows for the modulation of dopaminergic neuronal activity associated with cognitive functions during reward processing. In this study, subjects participated in an EEG experiment where TMS was applied to the dorsolateral prefrontal cortex (dlPFC) to target mid-cingulate regions, known for their role in cognitive control and decision-making. A robotic arm was used for precise targeting of the dlPFC. Participants were assigned to an active 10 Hz condition or a sham condition, where the coil was flipped. Participants completed a Probabilistic Selection Task (PST). We employed an independent one-tailed t-test to compare the N200 signals during non-reward feedback. The t-test showed a significant increase in N200 amplitude in the active condition relative to the sham, $t(156) = 3.52$, $p = .001$, indicating a robust effect of the active TMS condition. The application of TMS led to a reliable increase in N200 amplitude in the active condition compared to the sham. This increase is associated with enhanced cognitive control during reward processing in the PST task. The results suggest that TMS could be effectively integrated into smoking cessation programs by augmenting cognitive control mechanisms, thereby offering a potential new avenue for treatment in addiction therapy.

Poster #9

The Association Between Cannabis Use and Couple Functioning

Authors: Ekta Patel, Sandra Lee,* Prisha Patel*, Sally Kuo, Erin Lumpe, Jessica Salvatore, and Megan Cooke

PI Name: Jessica Salvatore

The goal of this presentation is to share progress on a planned study regarding cannabis use and couple functioning. We seek to recruit 250 couples (500 total participants), who will complete survey-based measures including an online survey battery, salivary DNA collection, and an online video conference call. Forthcoming analyses led by our team will examine the effects of cannabis use on romantic relationships. We expect that cannabis use will be associated with poorer couple dynamics and overall relationship health. The proposed research is timely given recent increases in the prevalence of cannabis use, and it would be beneficial to study cannabis use in the context of romantic relationships given that substance use both affects and is affected by relationship processes. Finding an association between couple dynamics and harmful cannabis use can be used to create personalized preventative interventions that leverage couple dynamics. Some of our specific interests include studying how cannabis use affects couples in which one partner suffers from a mental illness, and discovering how cannabis use interplays with conflict tactics in relationships. The online survey battery will gather information on several aspects

of participants' lives, including cannabis use habits, medical history, family history, and substance use patterns. The online survey battery will also include measures of participants' emotion regulation patterns and other indicators of mental health (e.g., depressive symptoms and anxiety). Data from the proposed work represents an initial step in a broader program of research to use a dyadic biopsychosocial approach to understand cannabis use patterns and consequences.

Poster #10

Determining the optimal TMS image-based target to modulate reward and control functioning in nicotine users

Authors: Emily Zhang, Nicole Lalta, Daniel Robles, Malte Güth, Ravi D Mill, Andrew Reid, Michael W Cole, and Travis E Baker

PI Name: Travis E Baker

Nicotine use disorder can be conceptualized as a failure in cognitive control, and is thought to arise from abnormalities in the reward and control function of the anterior midcingulate cortex (MCC). In this poster, we provide the optimal TMS method for quantifying and modulating the MCC reward (Aim 1) and control function (Aim 2) in nicotine users. In Aim 1, we show that applying TMS over an diffusion-based connectivity target (left prefrontal cortex – MCC) can boost the reward function of the MCC in nicotine users. In Aim 2, we show that applying TMS over an individualized function connectivity-based target (left prefrontal cortex – MCC) can boost the control function of the MCC in nicotine users. The findings from this study may help to develop more precise and effective MCC stimulation protocols according to patients' structural and functional connectivity profiles and cognitive control deficits.

Poster #11

Intact neural encoding of subjective value under uncertainty in human opioid addiction

Authors: Francesca M LoFaro, Maëlle CM Gueguen, Ananya Kapoor, Emmanuel E Alvarez, Darla Bonagura, Marzieh Babaeianjelodar, Annie Cheng, Robert Kohler, Sarah W. Yip, and Anna B Konova

PI Name: Anna B Konova

Opioid use disorder (OUD) is associated with increased propensity for risk-taking. The computation of a risky reward's subjective value (SV) is modulated by individual idiosyncratic tolerance for uncertainty. Researchers have posited that risky decision-making in OUD could be the result of 'faulty' SV computation. We examined, both cross-sectionally and longitudinally, whether SV computations in the brain's valuation system in people with OUD reflect normative differences due to idiosyncratic tolerances or a 'faulty' process misaligned with choice behavior. Subjects' choices in a risky decision-making fMRI task, completed at a single session (n=33 OUD patients [7 female], n=27 comparison controls [11 female]) or up to 8 sessions (n=10 OUD patients [6 female]; 5.5 sessions/subject, approx. weekly), were modeled with a modified utility model to derive individual uncertainty tolerance parameters. Model-based fMRI analyses used this data to identify regions encoding trial-by-trial SV of uncertain options at each session, assessing for a brain-behavior match. Multivariate analyses also ascertained that SV-related activation

patterns were decodable based on individual uncertainty tolerances. Subjects in both groups demonstrated diverse uncertainty tolerances with a majority (>75%) exhibiting a degree of uncertainty aversion that additionally were stable over time in the longitudinal sample. Neurally, we found that canonical value areas (ventromedial prefrontal cortex, posterior cingulate cortex, ventral striatum) encode SV similarly across the OUD and control groups in both univariate and multivariate decoding analyses. And out longitudinal analyses indicated this representation is likely stable despite changing uncertainty tolerances. Contrary to prevailing assumptions, these results indicate that the encoding and computation of SV is preserved in people with OUD and tracks behavioral choices and preferences.

Poster #12

Understanding Racial/Ethnic Differences in Key Precursors to E-Cigarette Use Among Early Adolescents: Findings from the Adolescent Brain Cognitive Development (ABCD) Study

Authors: John Tarantino, Tammy Chung, Shawn Latendresse, Margret Powell, and Carolyn Sartor,

PI Name: Carolyn Sartor, PhD

Escalating rates of e-cigarette use among adolescents, particularly among Black and Latinx youth, underscore the urgent need for targeted prevention strategies. Identifying precursors to e-cigarette use in pre- to early adolescence is key to informing such strategies. Expectancies about the effects of substances, which predate actual use, are robust predictors of initiation and progression of substance use. This study examined variations among Black, Latinx, and White youth in precursors to e-cigarette use, with a focus on positive and negative e-cigarette outcome expectancies, and explored the potential role of family environment, socioeconomic status, and neighborhood disadvantage in those variations. Data from the Adolescent Brain Cognitive Development (ABCD) Study's 3-year follow-up (mean age=12.9) was analyzed. The ABCD study is an ongoing national 21-site longitudinal study that recruited 11,875 youth aged 9 to 10 (47.8% female; 17.2% Black, 23.2% Latinx, or 59.6% White) at baseline. Youth reported on e-cigarette positive and negative outcome expectancies and other precursors to e-cigarette use, including perceived peer disapproval of e-cigarette use and perceived risk of regular use; Parents reported on their educational attainment and household income (socioeconomic status indicators) and home environment (e.g., parent e-cigarette use). Neighborhood disadvantage scores were derived from geocoded census tract data. Positive and negative outcome expectancy scores were tested for measurement equivalence with respect to race/ethnicity, sex assigned at birth (and their intersection) and adjusted for bias. Multilevel models accounting for sampling design tested for differences by race/ethnicity, and explored other precursors as well as socioeconomic status, neighborhood, and home environmental factors as predictors of positive and negative e-cigarette outcome expectancies. Analyses revealed that, among the six precursors examined: positive and negative expectancies, perceived risk of regular e-cigarette use, perceived friend disapproval of cigarette use, and curiosity about trying e-cigarettes examined, Black youth exhibited the highest frequency of being classified in the "high risk" group (four instances), followed by Latinx youth (two instances) and White youth (one instance). Notably, Black and Latinx, relative to White, youth demonstrated higher levels of negative outcome expectancies, a protective factor against e-cigarette use. Although statistically significant, differences between groups were minimal. Furthermore, after controlling for indicators of socioeconomic status and neighborhood disadvantage, which are

commonly linked to race/ethnicity, race/ethnicity itself was not significantly associated with positive outcome expectancies (Black vs. White: p = 0.749; Latinx vs. White: p = 0.817). However, youth living in the most disadvantaged neighborhoods showed significant associations with both positive (p = 0.043) and negative (p = 0.021) e-cigarette expectancies compared to those in the most advantaged neighborhoods. Differences by race/ethnicity in expectancies and, importantly, the observation that they were accounted for by socioeconomic status, provide insights into the complexity of factors that elevate risk for early adolescent e-cigarette use. In addition, the consistent association of neighborhood disadvantage with positive and negative e-cigarette expectancies underscores the significant role of community-level environmental factors in e-cigarette risk and suggests that factors such as targeted e-cigarette advertising could be counteracted with tailored prevention messaging to reduce environmental risk. Future research can build upon these findings to develop effective interventions for early adolescents.

Poster #13

Examining Product Features for Promoting Top-selling Cannabis Vape Products in an Online Retail Environment

Authors: Kathryn La Capria, Siyan Meng, Rosanna Mazzeo, Neha Vijayakumar, Kristina Jackson, and Julia Chen-Sankey

PI Name: Julia Chen-Sankey

Cannabis vape products (CVPs) are vape pens and vape cartridge/disposable products designed specifically to vaporize cannabis extracts. There has been tremendous growth in CVP use in the past few years in the U.S. CVP commercial marketing exposure may be a contributing factor for CVP use, but little is known about the content and types of product features detailing the functionalities or benefits of use in CVP promotion. This study examined the product features commonly used for marketing CVPs from a large cannabis retailer website. Product descriptions from a sample of 343 CVPs of top-selling brands were obtained from Jane Technologies, a top-trafficked online cannabis retail website. The sample of CVPs selected for content coding included CVPs with the highest customer ratings and recent reviews (<2 years) on the website. Using a codebook developed by top-down and bottom-up process, the descriptions of these CVPs were coded based on the content of product features (e.g., psychoactive effects, flavor names or descriptors, social facilitation). The most frequent category of product features was flavor profile and sensation (74.1%), which included content of general and specific flavor descriptors including specific flavor names (e.g., fruit flavors), and flavor sensation profile (e.g., sweet, spicy). Reduced harm/product quality (49.6%) was found in about half of the descriptions. Descriptions in this category indicated that the product was safe, chemical-free (suggesting reduced harm), or included descriptors that suggested product quality (high-quality, purity, and natural). Psychoactive effects appeared in 47.5% of the descriptions, which detailed the potency of the products or the effects on the user such as feeling high, stoned, or buzzed. Other main product feature categories were mood enhancement (33.8%), relaxation/tension reduction (23.9%), therapeutic effects (18.1%), focus/creativity (16.6%), convenience/discreetness (11.1%), social facilitation (6.7%), and physical performance enhancement (6.1%). The commonly promoted product features of CVPs appearing on cannabis retailer websites may shape product perceptions and use interests among new and existing consumers. Some of these product

features, such as flavor profile and sensation, and psychoactive effects, may be especially appealing to young consumers for recreational use. Some other frequently used product features, such as reduced harm/product quality, may mislead consumers to perceive the products as healthy or less harmful to use, which may also increase product misuse. More research is greatly needed to understand the impact of promoting those product features in commercial CVP advertisements on CVP-related perceptions and use behaviors among priority populations.

Poster #14

Qualitative Exploration of Drinking Consequences Reported during MI Sessions With Underrepresented Young Adults Engaging In Heavy Drinking

Authors: Maria Eugenia Contreras Perez, Eric Wagner, Michelle M. Hospital, Staci L. Morris, Kristina Jackson, and Molly Magill

PI Name: Kristina Jackson

Members of underrepresented racial and ethnic groups face stressors resulting from stigma, prejudice, racism, toxic environments, and discrimination, which heighten their susceptibility to substance use and its consequences. Motivational Interviewing (MI) is widely used to address alcohol use, but evidence of its efficacy with underrepresented minoritized clients is inconsistent. This poster will present preliminary results regarding the drinking consequences reported in 19 MI sessions with clients from underrepresented racial and ethnic groups. Data from an NIH-funded R01 MI RCT were analyzed using Thematic Analysis. No distinct patterns by race or ethnicity emerged; participants primarily cited negative consequences (e.g., hangover symptoms, accidents, injuries, and situations in which their school or work was affected by their drinking) and positive consequences (e.g., socialization, mood, and performance enhancement), aligning with their developmental stage. Findings suggest that factors beyond race or ethnicity, such as developmental transitions and interpersonal influences, may be more salient in the drinking motives of emerging adults.

Poster #15

Marketing of Derived Psychoactive Cannabis Vapes: A Content Analysis

Authors: Siyan Meng, Kathryn La Capria, Rosanna Mazzeo, Neha Vijayakumar, Matthew Rossheim, and Julia Chen-Sankey

PI Name: Julia Chen-Sankey

Derived psychoactive cannabis products (DPCPs) are sold in most states, regardless of their cannabis laws. They are often marketed as naturally derived or hemp-based, despite being chemically synthesized and able to induce a “high” similar to cannabis. The use of DPCPs is associated with health risks, such as mental illness, respiratory problems, injuries, and poisoning. DPCPs are commonly sold as vapes, referred to as derived psychoactive cannabis vapes (DPCVs). Commercial marketing of DPCVs might influence consumers’ using behavior, but there is limited knowledge about the specific marketing including product features, functionalities, and alleged benefits. This descriptive study explored the marketing content on

three major DPCP retailer websites. 491 DPCV descriptions were gathered from the three top-visited websites selling DPCPs, as identified by a digital market intelligence platform that monitors website traffic. Using a codebook developed through a combination of top-down and bottom-up methods, these DPCV descriptions were analyzed and categorized according to various content of product descriptions, including product composition, flavor names or descriptors, and quality descriptions. The most frequently mentioned product feature was product design (97.6%), which included aspects such as color, shape, long-lasting batteries, Bluetooth functionality, and the use of cartridges or pods. Also frequently mentioned were Cannabinoids (97.4%), including cannabidiol (CBD) and the level of Delta-9-tetrahydrocannabinol (THC), as well as product composition (92.2%) including the ingredients of a product and manufacturing processes. Flavor description (64.5%) was presented to detail specific flavors like strawberry and mint, as well as flavor concepts such as sour diesel. Lab testing (62.5%) was mentioned to describe products' quality or that the products were lab-tested or verified by a third party. Warnings (51.2%) were included to emphasize potential side effects of the product (e.g., warning that consumption could expose users to chemicals that cause cancer, birth defects, or other reproductive harm). Hemp-derived content was noted in 45.3% of the descriptions, indicating that the product was made from or contained hemp. Psychoactive effects were mentioned in 41.8% of the descriptions, emphasizing the products' potency or their psychoactive effects on the user, such as feeling high, stoned, or buzzed. Other descriptions included an emphasis on product quality (38.4%) and compliance with the 2018 Farm Bill (32.7%). We found several main categories of product description content for promoting DPCVs on top-visited DPCP retail websites. Some of the descriptions may promote product use for recreational reasons among young people (e.g., appealing packages including shapes and colors, product technology, flavor variety, flavor sensory). Content related to hemp-based products, lab testing process, product quality, and compliance with the 2018 Farm Bill may reduce consumers' harm perceptions towards using those products. Warnings, the only content to potentially increase harm perceptions and reduce use intentions were only found in half of the product descriptions. More research is needed to investigate the influence of these various types of product descriptions on consumers' perceptions and use of DPCVs.

Poster #16

Close-loop TMS-EEG Modulation of Reward-Related ERPs

Authors: Yifan Gao, Daniel Robles, Emily Zhang, Malte Güth, Drew Headley, and Travis Baker

PI Name: Travis Baker

Substance use disorder is associated with impairments in cognitive control and is thought to arise from anterior midcingulate cortex (MCC) dysfunction. In this study, we present a novel closed-loop system capable of tracking reward-related MCC activity, the frontal midline theta (FMT) oscillations, in real-time and using that information to control TMS delivery to modulate reward-related MCC activity. In particular, we delivered a single pulse of TMS targeting either the peak or trough phase of feedback-related FMT during a reward task. Since TMS generates unique artifacts in the EEG, a processing pipeline for TMS artifact removal in the ERP was presented. Our results show that FMT trough stimulation blunted

the reward positivity, an EEG signal associated with MCC reward function. This approach potentially offers bidirectional treatments that are spatially, temporally, and cognitively precise.

Poster #17

Emergency Department Medication for Opioid Use Disorder Quality Metric

Authors: Brittany Simon, Alexis LaPietra, Michael Litterer, Elliott Liebling, Reyna Maybloom, and Jessica Perez-Ng,

PI Name: Alexis LaPietra

The executive leadership team at RWJBarnabas Health Emergency and Hospitalist Medicine service line, in partnership with the RWJBH Institute for Prevention and Recovery, developed the 2023 Emergency Department Medication for Opioid Use Disorder quality metric incentive linked to buprenorphine prescribing for nonfatal-naloxone-reversed overdose patients seen and discharged from the ED. The purpose of the quality metric is to increase the number of patients administered or prescribed buprenorphine in the ED. The quality metric incorporates the entire site and the initiative includes a system-wide physician lead, dedicated education at each hospital site, collaboration with ED nursing, information technology support, clinical pharmacy, and the 24/7 hospital-based Peer Recovery Program employed by the system. Since the inception of the ED MOUD quality metric, the number of ED patients administered or prescribed buprenorphine post-naloxone reversal has continued to trend upwards and buprenorphine administrations and prescriptions have increased for non-naloxone-reversed ED patients as well. The adoption of a systemwide ED MOUD quality metric incentive is associated with a greater proportion of patients being administered or prescribed buprenorphine.

Poster #18

Maternal Health through the Peer Recovery Program

Authors: Brittany Simon, Angela Cicchino, Reyna Maybloom, and Sasha Condas

PI Name: Angela Cicchino

Utilizing a peer recovery approach, PRP-Maternal Health partners with hospital- and community-based organizations in Middlesex County to implement evidence-based interventions that strengthen perinatal and postnatal support services for patients with substance use disorder, connect patients with peer recovery specialists who are cross-trained as doulas, address social determinants of health and reduces deaths among perinatal and postpartum patients.

Poster #19

Kratom (Mitragyna speciosa) alkaloids effects on hemodynamic and pulmonary measures in obese mice

Authors: Nicholas T. Bello, Spencer E. Fields, Harsh Shah, Arul Elango, Elif Ece Akgun, Emma Bernstein, James E. Simon, and Qingli Wu

PI Name: Nicholas T. Bello

Kratom (Mitragyna speciosa) is an evergreen tree indigenous to Southeast Asia. Kratom leaves contain >40 unique alkaloids with opioidergic and adrenergic actions and has been used in traditional botanical medicine to manage pain and opioid withdrawal. Kratom products are widely available in the US, but these products are not regulated by state or federal agencies. As such, the safety of these products are not well-characterized. Recently, kratom products have been marketed for appetite suppression and weight loss. Our goal was to examine whether chronic oral dosing of a standardized alkaloid enriched-kratom extract (KE) prevented weight gain in high fat diet (HFD; 45% fat) fed mice. In addition, we examined whether acute human equivalent doses of KE and the major alkaloid, mitragynine (MTG), differentially influence cardiopulmonary measures in normal weight or obese male mice. Kratom powder was standardized to a KE with 62.5 ± 1.2 mg/g of MTG. For obesity prevention, male C57BL/6J mice (8 weeks old; n=24) received daily oral doses of vehicle, KE 50 mg/kg (or KE 150 mg/kg coincident with a HFD switch). On days 26- 30, mice were assessed for hemodynamic parameters using a non-invasive CODA® tail-cuff system. For acute dosing, normal weight (n = 16) or diet-induced obese (>13 weeks on HFD; n=14) mice received an oral dose of vehicle, 290-500 KE, or 18-31.3 mg/kg MTG prior to hemodynamic or DSI® whole body plethysmography assessments. For chronic obesity prevention, there were no differences in body weight gain, but there was a blood-pressure lowering effect in systolic, diastolic, and mean blood pressures (all p< 0.05) with KE 50 mg/kg compared with vehicle (p<0.05 for all). For acute dosing, there was a dose lowering effect (p< 0.05) with the 31.3 mg/kg MTG dose in normal weight compared with the obese mice. There were dose suppressive effects with 18 mg/kg MTG and 290 mg/kg KE on breaths per minute (both doses p<0.0001) and ventilation rate in the obese group only (both doses p<0.05). Our preliminary findings do not support the use of KE in diet-induced obesity prevention but do suggest a differential effect of kratom products on hemodynamic measures related to weight gain in mice.

Poster #20

Synaptojanin1 maintains dopamine D2 autoreceptor at release sites

Authors: Ping-Yue Pan, Elnaz Khezerlou, and Justin Cai

PI Name: Ping-Yue Pan

Dopamine D2 receptors (DRD2) are essential for dopamine (DA) signaling in the basal ganglia, however, its molecular regulation remains poorly understood. In this study, we report that a presynaptic endocytic molecule and Parkinson's disease gene, Synaptojanin1 (Synj1), facilitates the maintenance of D2 receptor short isoform (D2S) at boutons. We show a significant impairment of D2-mediated behavioral inhibition in Synj1 haploinsufficient (Synj1+/-) male, but not female mice. In cultured Synj1+/- neurons, dopamine release sites exhibit an overall enhanced release and a reduction in D2-induced release inhibition measured by GRABDA2m. Furthermore, using a newly engineered pH sensitive optical sensor, pHmScarlet-D2S, we demonstrate that repeated exposure to dopamine resulted in a greater loss of D2S at the surface of Synj1+/- ventral midbrain neuronal boutons compared to those in wildtype neurons. Thus, our work employing state-of-art imaging strategies and behavioral pharmacology identified a novel role of Synj1 in shaping dopamine signaling via maintaining presynaptic DRD2. Our study provides important insight for synaptic dysfunction in SYNJ1 mutation associated parkinsonism.

Poster #21

Epigenetic mechanisms underlying susceptibility to methamphetamine self-administration in methamphetamine-sired male rats

Authors: Sarah E. Swinford-Jackson, Azadeh Jadali, BaDoi N. Phan, Mateo Sarmiento, Yixiao Zhu, Sharvari Mankame, Samantha J. Worobey, Tyler J. Sacko, Dominick Gangemi, Andreas R. Pfenning, Kelvin Y. Kwan, Ronald P. Hart, and R. Christopher Pierce

PI Name: R. Chris Pierce

Preclinical evidence indicates parental exposure to drugs of abuse alters behavior and physiology of offspring. We previously demonstrated that when male rats self-administered cocaine, their male, but not female, progeny displayed reduced cocaine self-administration. Contrary to our hypothesis, male offspring of methamphetamine-experienced sires self-administered more methamphetamine (0.1 mg/kg/infusion) and were more motivated for methamphetamine than saline-sired conspecifics. There was no difference in methamphetamine self-administration or motivation for methamphetamine in female offspring. Sires self-administered methamphetamine (0.033 mg/infusion) or cocaine (0.25 mg/infusion) and controls received yoked-saline delivery for 60 days and were subsequently mated with naïve females. The gene expression and open chromatin profiles of experimentally-naïve methamphetamine- and saline-sired male offspring were investigated by multiomic single nuclei RNA-sequencing and ATAC-sequencing of the nucleus accumbens from adult male F1 offspring. Differential gene expression was observed primarily in neuronal (dopamine D1 and D2 receptor-containing medium spiny neurons) and glial (especially microglia) subtypes and in pathways associated with neuronal transmission and synapse regulation. Differential transcription factor binding motifs included those that were bidirectionally regulated in cocaine- vs. methamphetamine-sired offspring. These results implicate potential mechanisms for the epigenetic inheritance of cocaine resistance or methamphetamine susceptibility in drug-sired male offspring, and further suggest putative molecular targets for modulating drug intake. Future experiments will functionally validate candidate genes to manipulate drug self-administration and interrogate the epigenetic profile in the sperm of methamphetamine sires for targets that may influence offspring gene expression.

Poster #22

Co-use of Alcohol and Cannabis and HIV Biomedical Intervention Engagement among young Black Sexually Minoritized Men and Transgender Women: An Event-Level Analysis

Authors: **Y**en-Tyng Chen, Ellen Almirol, Justin Knox, Jade Pagkas-Bather, Ella Remund Wiger, Megan E. Marziali, Devin English, Dustin T. Duncan, John Schneider

PI Name: Yen-Tyng Chen

Young Black sexually minoritized and gender expansive groups (YBSGM) are more impacted by HIV and have poorer outcomes than other groups on pre-exposure prophylaxis (PrEP) and antiretroviral therapy (ART) use due to contextual adversity, including substance use. We evaluated whether alcohol and cannabis use, including co-use, were associated with HIV care engagement and outcomes among YBSGM.

Data were drawn from the ongoing Neighborhoods and Networks (N2) Study of 16-34-year-old YBSGM in Chicago, Illinois (n=379) in 2022-2023. Participants completed daily ecological momentary assessment (EMA) surveys on: PrEP use, ART use, alcohol use, and cannabis use for 14 days and an in-person assessment, which included a HIV diagnostic test. Daily substance use was categorized as alcohol use only, cannabis use only, and co-use of alcohol and cannabis. We estimated associations of daily alcohol use, cannabis use, and co-use of alcohol and cannabis with PrEP/ART use, clustered at the individual-participant level. A total of 4,164 daily EMA surveys were completed (78.5% response rate of a maximum of 5,306 daily surveys: 379 participants x 14 days). Overall, among total daily surveys, 5.8% (n=241/4164) involved daily alcohol use only, 35.5% (n=1476/4164) involved daily cannabis use only, 32.0% involved co-use of alcohol and cannabis (n=853/4164), and 34.9% (n=1451/4164) involved no substance use events during the 14-day EMA period. Compared to no daily substance use, substance use was associated with greater daily PrEP or ART use: daily alcohol use only (incidence ratio [IR]=1.26, 95% CI: 1.14-1.39), daily cannabis use only (IR=1.40; 95% CI: 1.25-1.56), and daily alcohol/cannabis co-use (IR=1.34; 95% CI: 1.09-1.77). YBSGM reported high levels of daily cannabis use, including co-use of cannabis with alcohol. Substance use was positively associated with better engagement in HIV care, including daily PrEP and ART use. Our results underscore the need for integrated interventions that target HIV and substance use, which are syndemic among YBSGM, e.g., the inclusion of screening and referrals to substance use treatment services in HIV care.

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