Sunday, June 16, 2024

3:30 P.M. - 4:45 P.M.

LATE-BREAKING ORAL SESSION

Av. Duluth, 2nd Floor

EVALUATION OF THE RECOVERY INCENTIVES PROGRAM: CALIFORNIA'S CONTINGENCY MANAGEMENT BENEFIT

Presenter: Darren Urada*, UCLA Integrated Substance Abuse Programs*

Darren Urada[1], Howard Padwa[1], Valerie Antonini[1], Celine Tsoi[1], Liliana Gregorio[1], Freese Thomas[1], Beth Rutkowski[1], Richard Rawson[1], Anne Lee[1], Brittany Bass[1], Dhruv Khurana[1], Carissa Loya[1], Madelyn Cooper[1], Marylou Gilbert[1], Edward Zakher[1]

[1]*UCLA Integrated Substance Abuse Programs*

Drug Category: Stimulants
Topic: Treatment
Abstract Detail: Other
Abstract Category: Original Research

Aim: To provide a brief overview of the Recovery Incentives Program: California's contingency management benefit, and the first data to emerge from this program. This new benefit, created as part of California's Section 1115 Demonstration project, is the largest Medicaid-funded effort to implement contingency management in history. These results have ramifications for other states and countries considering contingency management as a tool to address stimulant poisonings.
Methods: Descriptive results will be presented from 1) cross-sectional surveys of over 500 clients and 100 treatment providers (supervisors, coordinators, and counselors of both sexes). 2) Follow-up interviews, purposively sampled based on survey responses, and 3) and urinalysis results from the state's Incentive Manager software.
Results: Treatment providers expressed very positive ratings on the effectiveness of the program, provided high ratings the program's implementation, and reported that various anticipated problems turned out to be rare. Clients reported that the program helped them stop using stimulants and improved their lives in a variety of domains. They also provided high satisfaction ratings and recommended the program for others.
Conclusions: Systematic reviews have concluded that contingency management is very effective treatment for stimulant use disorders. The emergence of the what has been referred to as the fourth wave of the overdose epidemic, i.e. accelerating stimulant-related deaths, both with and without fentanyl, along with the lack of an FDA-approved medication for stimulant use, makes contingency management a crucially important tool for the field. These data suggest contingency management can successfully implemented at scale.
Financial Support: California Department of Health Care Services, Interagency Agreement

HARM REDUCTION SUPPLY DISTRIBUTION VIA VENDING MACHINES: 6-MONTH OUTCOMES FOR A CALIFORNIA VETERANS AFFAIRS HEALTH CARE SYSTEM

Presenter: Tessa Rife-Pennington*, San Francisco Veterans Affairs Health Care System*

Tessa Rife-Pennington[1], Michael Douglas[2], David Pennington[1], Sree Sinha[1], Thao Vu[1], Donna Dare[1]

[1]*San Francisco Veterans Affairs Health Care System,* [2]*University of California, San Francisco*

Drug Category: Other, Harm Reduction
Topic: Harm Reduction
Abstract Detail: Other

Abstract Category: Original Research
Aim: To evaluate 6-month outcomes of harm reduction supply distribution via vending machines for a California Veterans Affairs Health Care System Harm Reduction Program.
Methods: Fourteen harm reduction vending machines were installed August through September 2023: two at a Veterans Affairs Medical Center, seven in Veterans Affairs community-based outpatient clinics, and five in Veterans supportive housing. A Veterans Affairs Research Electronic Data Capture survey was used to collect Veteran registration for vending machine access and demographics. VendNovation web-based software was used to collect vending machine dispensing data: machine accessed, date/time, and number/type of items dispensed. Descriptive statistics were used to evaluate results.
Results: Between August 2023 to January 2024, 207 Veterans registered for vending machine access, and 162 (78.3%) accessed ≥1 vending machine item. Most items were dispensed at two supportive housing buildings and one outpatient clinic. Vending machines located in Veterans Affairs settings were most accessed (96.0%) during business hours, whereas machines in housing buildings were most accessed (64.3%) outside regular business hours. Common items dispensed included hygiene kits (n=231), wound care kits (n=224), alcohol swabs (n=152), ascorbic acid powder (n=139), extra-large condoms (n=112), lubricant (n=112), mouthwash (n=106), safer snorting kits (n=97), 31-gauge syringes (n=95), and assorted condoms (n=95). Among Veterans who completed demographics question(s), age was 59.7±14.6 years. Veterans most commonly identified as male gender (n=168, 81.2%). The two most common racial/ethnic identities were White/Caucasian (n=91, 44.0%), and Black/African American (n=48, 23.2%).
Conclusions: Over 78% of Veterans who registered for access utilized the harm reduction vending machine(s). Co-location in settings serving Veterans with housing needs facilitated access, particularly outside regular business hours. Supplies to support basic human needs and safer snorting, injection drug use, and sex were most accessed. Evaluation of staff/Veteran feedback on the machines, harm reduction supplies, use experience, and impact on health outcomes and quality of life is ongoing.
Financial Support: Benioff Homelessness and Housing Initiative (BHHI) Resource Allocation Program (RAP) Grant

AGE DIFFERENCES IN CANNABIS USE PATTERNS AND PROBLEMATIC USE AMONG PATIENTS WITH CANCER

Presenter: Kanya Nesbeth*, Howard University Hospital*

Kanya Nesbeth[1], Margaret Fahey[2], Aimee McRae-Clark[2], Richard Schottenfeld[3], Erin McClure[2]

[1]*Howard University Hospital,* [2]*Medical University of South Carolina,* [3]*Howard University College of Medicine*

Drug Category: Cannabis/Cannabinoids
Topic: Substance Use Disorder
Abstract Detail: Clinical - Epidemiology
Abstract Category: Original Research
Aim: As cannabis use rates continue to rise among adults, including for medical purposes, it is critical to understand the scope of disordered use and the potential impact of age on its development. No research to date has explored age-group differences in the risk of developing cannabis use disorder among cancer patients using cannabis.
Methods: This cross-sectional survey study was conducted at a National Cancer Institute-designated center in a state without legalized access to cannabis. Measures included prevalence of any cannabis/cannabinoid product use following diagnosis, the Brief Cannabis Use Disorder Identification Test Short-Form (CUDIT-SF), interest in reducing cannabis use, and self-reported cannabis addiction. Chi-squared and ANOVA analyses were employed to examine age group differences [younger adults (18-44 years, n=123), middle-aged adults (45-65 years, n=389), and older adults (65+ years, n=524)] in these measures.
Results: Younger adult participants exhibited a higher prevalence (47%) of cannabis use compared to middle-aged (33%) and older adults (20%) ($p > .001$). There were significant age-group differences in CUDIT-SF scores ($p=.044$), with younger adults having higher scores, on average (M=1.5, SD=0.4), compared to middle-aged adults (M=0.8, SD=1.6) and older adults (M=0.6, SD=1.2). Among younger adults using cannabis,

approximately 33% screened positive for a cannabis use disorder, compared to 18% of middle-aged adults, and 16% of older adults. No age group differences were found in interest in quitting/reducing cannabis or in self-reported cannabis addiction.
Conclusions: Findings indicate that, following a cancer diagnosis, younger adults used cannabis more frequently and had greater rates of problematic use. Despite variations in prevalence and risk across age groups, age did not influence individuals' motivation to quit or reduce cannabis use, nor their perception of addiction severity. These results emphasize the importance of considering age as a critical factor when assessing cannabis use behaviors and interventions among cancer patients.
Financial Support: None

APP-BASED CONTINGENCY MANAGEMENT TO REDUCE HEAVY DRINKING DAYS AMONG SMOKERS RECEIVING VARENICLINE: FINDINGS FROM A WITHIN-SUBJECT A-B-A DESIGN TRIAL

Presenter: Andre Miguel*, Washington State University*

Andre Miguel[1], Sterling McPherson[2]

[1]*Washington State University,* [2]*Washington State University Elson S. Floyd College of Medicine*

Drug Category: Polydrug (i.e. concurrent use two or more drugs)
Topic: Behavioral Pharmacology
Abstract Detail: Clinical - Experimental
Abstract Category: Original Research
Aim: Roughly 60–70% of tobacco smokers binge drink or frequently consume dangerous amounts of alcohol, and over 75% of people with an alcohol use disorders (AUD) are smokers. The combined effects of drinking alcohol and smoking cause more illness and is the leading cause of morbidity and mortality in the world. Despite the severe consequences related to alcohol and tobacco co-addiction, smokers with an AUD rarely seek alcohol treatment largely because they do not want to stop drinking. The aim of this pilot study was to evaluate the feasibility and signaling of efficacy of a phone-based Contingency Management (CM) intervention targeting heavy drinking days in combination with varenicline to treat smoking and AUD concomitantly.
Methods: Within-subject analog trial with an ABA design that lasted 9 weeks. The two A phases consisted of varenicline plus non-contingent CM and the B phase consisted of varenicline plus CM.
Results: Participants (n = 14) found the CM intervention easy to understand and the remote CM procedure quick and easy to perform. A total of 2998 samples were submitted (68% of all expected samples) and all 5 daily samples were submitted in 78% of all study days. A total of 10 participants (71%) completed the study, 7 participants (50%) were taking varenicline at the end of the study, and 3 participants (21%) achieved a 7-day abstinence rate at the end of the trial. Days of drinking or heavy drinking did not differ significant during the ABA phases.
Conclusions: Our study suggests that varenicline treatment in combination with a phone-based CM intervention targeting heavy drinking is feasible and may be an effective strategy to promote smoking cessation and AUD treatment for treatment-seeking heavy drinking smokers.
Financial Support: The WSU Alcohol and Drug Abuse Research Program

ACUTE BEHAVIOURAL EFFECTS OF LOW-DOSE CANNABIDIOL IN HEALTHY VOLUNTEERS

Presenter: Lucy Chester*, Universite de Montreal Faculty of Medicine*

Lucy Chester[1], Francois-Olivier Hébert[2], Pamela Lachance-Touchette[2], Amani Mahroug[1], Anita Abboud[1], Stéphanie Marsan[2], Didier Jutras-Aswad[2]

[1]*Universite de Montreal Faculty of Medicine,* [2]*Centre de Recherche du Centre Hospitalier de l'Université de Montréal*

Drug Category: Cannabis/Cannabinoids
Topic: Behavioral Pharmacology
Abstract Detail: Clinical - Experimental
Abstract Category: Original Research
Aim: Evidence for psychoactive effects driven by cannabidiol (CBD) is sparse and inconsistent. Despite this, many CBD products are marketed in Canada as health supplements with mood-modulating effects. This study aims to characterise the effects of acute doses of CBD on subjective and clinician-rated behavioural measures, affect, and anxiety in healthy volunteers.
Methods: In this triple-blind crossover trial, 70 occasional cannabis users of both sexes were randomized to pre-determined dosing sequences of placebo, 20, 50, 100 or 200mg CBD, with minimum one-week washout between experimental visits. The following assessments were performed at multiple timepoints during each visit: Drug Effects Questionnaire (DEQ); Clinician-Administered Dissociative States Scale (CADSS), Cannabis Experiences Questionnaire (CEQ), Positive and Negative Affect Schedule (PANAS), and State-Trait Anxiety Inventory (STAI). Outcomes were assessed using repeated measureANOVA, including baseline scores and CBD dose as within-subjects factors.
Results: Results remain blinded until all other study outcomes have been analysed, estimated 30th April 2024 or earlier. For the primary outcome, DEQ item 3, 'Are the drug effects pleasant?', study drug 'B' was associated with significantly higher peak scores compared to all other CBD doses (B vs. A, EMM difference: +5.3 [95% CI: 0.7–9.9], p=0.023; B vs. C, +5.5 [0.9–10.1], p=0.018; B vs. D, +6.7 [2.1–11.3], p=0.005; B vs. E, +7.2 [2.6–11.7], p=0.002). Significant effects for study drug ($p > 0.05$) were also found for DEQ items 4, 6, 15, 18, 19 and 21, peak PANAS positive scores, and CEQ positive experiences scores. No significant drug effects were found for other outcome assessments.
Conclusions: Our study addresses the scarcity of knowledge regarding CBD's psychoactive effects in the context of widespread cannabis use in Canada. Initial results suggest that certain doses of CBD may produce acute subjective effects. This information can support evidence-based practices for safer consumption and inform more effective public policies and regulations.
Financial Support: The study was funded by Direction Générale de la Santé Publique (DGSP) and Ministère de la Santé et des Services Sociaux (MSSS).

ENHANCING HIV PREVENTION AND SUBSTANCE USE DISORDER TREATMENT: ADAPTIVE APPROACHES AND HEALTH ECONOMICS INSIGHTS FROM A RECENT SEQUENTIAL MULTIPLE ASSIGNMENT RANDOMIZED TRIAL (SMART)

Presenter: Kathryn McCollister*, University of Miami Miller School of Medicine*

Kathryn McCollister[1], Erminia Fardone[2], Don Ekanayake[2], Leah Davis Ewart[3], Adam Carrico[3]
[1]University of Miami Miller School of Medicine, [2]Miller School of Medicine, University of Miami, [3]Florida International University Robert Stempel College of Public Health & Social Work

Drug Category: Stimulants

Topic: Prevention
Abstract Detail: Other
Abstract Category: Original Research
Aim: Adaptive HIV clinical trials tailor treatment strategies based on individual responses to treatment protocols. One such study, The Positive Reinforcement Intervention and Sustained Motivation (PRISM) trial, demonstrated this tailored approach, focusing on adaptive telehealth motivational enhancement interventions in sexual minority men (SMM). This study is a Sequential Multiple Assignment Randomized Trial (SMART) that combines elements of Contingency Management (CM) and Motivational Interview (MI) across three intervention stages to support initiation and retention in the PrEP care continuum. An economic analysis was conducted to understand the costs of the different strategies that emerged through the trial based on participant responsiveness.
Methods: Seventy SMM using stimulants with non-reactive HIV results, not on PrEP were randomized to 2-session MI intervention focusing on PrEP and risk behavior or CM intervention with financial incentives ($50 each) for completing PrEP clinical evaluation and filling a PrEP prescription. At the 3-month follow-up,

participants who had not filled a prescription for PrEP were randomized to switch intervention (i.e., MI+CM or CM+MI) or continue assessments only. The costs included total intervention costs and participant incentives payments, while research-related expenses like recruitment and assessment surveys were excluded.
Results: Six different strategies were identified during the trial. Start-up costs totaled $31,766 comprised mostly of training activities. Total intervention costs over the 6-month period ranged from $3,053 for CM-only (non-responders) to $7,913 for MI-only (responders). Non-responders that switched interventions had higher odds of PrEP use, lower methamphetamine use severity, and decreased odds of condomless anal sex at six months.
Conclusions: Despite the high initial startup expenses, the overall costs of the intervention, including participant incentives, were relatively modest. Economic data is important for providers that may be considering the adoption of more customized HIV prevention strategies to expand reach to SMM and other vulnerable populations.
Financial Support: Supported by the Center for Health Economics of Treatment Interventions for Substance Use Disorder, HCV and HIV (CHERISH) (P30DA04500)

DEPRESSION AND ANXIETY MODERATE CANNABIS USE DISORDER TREATMENT EFFECTS: A RANDOMIZED CLINICAL TRIAL WITH YOUNG ADULTS

Presenter: Michael Mason*, University of Tennessee*

Michael Mason[1], Douglas Coatsworth[1], Nathaniel Riggs[2], Jeremy Mennis[3], Nikola Zaharakis[1], Michael Russell[4], Aaron Brown[5]

[1]*University of Tennessee,* [2]*Colorado State University,* [3]*Temple University,* [4]*Penn State,* [5]*University of Kentucky*

Drug Category: Cannabis/Cannabinoids
Topic: Treatment
Abstract Detail: Clinical - Experimental
Abstract Category: Original Research
Aim: U.S. young adults (ages 18-25) have the highest past year prevalence (14.4%) of cannabis use disorder (CUD) as well as major depressive disorder (18.6%; SAMHSA, 2021) and any anxiety disorders (9.6% (men) and 26.7% (women); Gustavson et al., 2018) compared to other age groups. More research is needed to determine if untreated depressive and anxiety symptoms interrupt the effects of CUD treatment. We tested whether the effects of a text-message delivered CUD treatment were dependent on depressive and anxiety symptom severity with 1078 young adults enrolled in a 6-month randomized clinical trial.

Methods: We conducted a large (n= 1078) randomized clinical trial of a 4-week CUD treatment with young adults recruited primarily via social media. Participants were allocated to PNC-txt, a text-message delivered, motivational interviewing treatment within a peer relations framework, or a wait-list control condition and followed for 6 months. We collected THC metabolite samples and survey data. Depressive symptoms were measured with the PHQ-9 and anxiety symptoms with the GAD-7.

Results: Screening for psychiatric symptoms at baseline indicated that 46.6% of the sample met criteria for major depressive disorder and 42.9% met criteria for generalized anxiety disorder. Participants with sub-threshold depression and anxiety scores significantly reduced the number of days they used cannabis across all 6 months of the study compared to those with clinically significant scores. Similarly, participants with sub-threshold depression and anxiety scores reduced the probably of the presence of THC metabolites at 300 ng/ml urinalysis. Cohen's D effect sizes were small ranging from .19 to .27. Participants above the clinical cut-point did not statistically differ from controls.
Conclusions: Results support the importance of simultaneously addressing psychiatric symptoms and cannabis use when treating young adults using text-delivered counseling. As mHealth interventions continue to demonstrate efficacy in addressing substance use disorders, simultaneously attending to mood and anxiety disorders appears warranted.

Financial Support: National Institute on Drug Abuse of the National Institutes of Health under Award Number 5R01DA044206 (Mason and Coatsworth).

EFFECT OF COMORBID PSYCHOLOGIC AND SOMATIC SYMPTOM TRAJECTORIES ON EARLY ONSET SUBSTANCE USE AMONG US YOUTH IN THE ABCD STUDY

Presenter: Carol Boyd*, Center for the Study of Drugs, Alcohol, Smoking and Health, University of Michigan School of Nursing*

Carol Boyd[1], Sarah Stoddard[2], Bingxin Chen[2], Robert Ploutz-Snyder[2], Terri Voepel-Lewis[2]

[1]*Center for the Study of Drugs, Alcohol, Smoking and Health, University of Michigan School of Nursing,* [2]*University of Michigan*

Drug Category: Polydrug (i.e. concurrent use two or more drugs)
Topic: Comorbidities, Psychologic symptoms and adolescent substance use
Abstract Detail: Preclinical - In Vivo
Abstract Category: Original Research
Aim: We examined associations between comorbid psychologic and somatic symptom trajectories (C-PSST) from late childhood (ages 9-10yrs) to early adolescence (13-14yrs) and early onset substance use (SU).
Methods: We used multi-variable, latent-class growth analyses to differentiate C-PSST among youth without SU at baseline in the Adolescent Brain Cognitive Development study (v.5.1). C-PSST were derived from anxiety, depression, pain, somatic, and sleep symptom scores over 5 years (Child Behavior Checklist and Sleep surveys). Regression analyses examined the association between C-PSST and Lifetime SU by study year 5 (i.e., any self-reported alcohol [≥ full drink], tobacco [≥ full cigarette/e-cigarette], marijuana [GREATER THAN puff] or other drug use). Models accounted for demographics, parental SU and mental health, household income, expectancies about substance effects, and random family effects.
Results: Four C-PSST were identified in 8311 youth from age 9.97±0.74 to 13.57±0.88years; Asymptomatic (n=2311, 27.8%), Low/stable (n=3245, 39%), Moderate (n=2101, 25.3%) and High/worsening (n=654, 7.9%). Lifetime SU (mean reported onset 12.4 years) was lowest for the Asymptomatic (n=180, 7.8%) and Low/stable (n=291, 9%) groups, compared to Moderate (n=251, 11.9%) and High C-PSST groups (n=94, 14.4%). Usage trends were similar across C-PSST for individual drug classes (e.g., marijuana 2.3%, 2.6%, 3.8%, 5.5%). Adjusted for effects of covariates, youth with High C-PSST were at least twice as likely as the Asymptomatic group to report use of any substance (adj.OR 2.08 [95% CI 1.34, 3.22], alcohol (2.82 [1.51, 5.29]), tobacco (2.23 [1.27, 3.92]), marijuana (2.36 [1.29, 4.31]) and polysubstance use (2.37 [1.27, 4.41]. Baseline clinical range anxiety and depression symptoms increased the risk for later SU by 37 and 51%, respectively.
Conclusions: Higher C-PSST was associated with an increased likelihood of early onset SU in this national sample. Recognition and early intervention for comorbid symptoms in late childhood may be warranted to mitigate SU behaviors during adolescence.
Financial Support: NIDA R01DA052310

EXPERIENCING AND NAVIGATING THE EXPANDING PRESENCE OF XYLAZINE WITH FENTANYL: A QUALITATIVE STUDY

Presenter: Danielle German*, Johns Hopkins Bloomberg School of Public Health*

Danielle German[1], Julie Evans[1], Adrian Guta[2], Renee Johnson[1], Johannes Thrul[1], Becky Genberg[1]

[1]*Johns Hopkins Bloomberg School of Public Health,* [2]*University of Windsor*

Drug Category: Polydrug (i.e. concurrent use two or more drugs)
Topic: Harm Reduction
Abstract Detail: Clinical - Epidemiology
Abstract Category: Original Research

Aim: Xylazine with fentanyl has raised alarms across North America for its role in overdose and severe wounds, but physiological implications have received less attention. This qualitative study aimed to understand how people who use drugs (PWUD) experience and navigate the expanding presence of xylazine within their local drug supply.
Methods: From December 2023 through March 2024, we conducted in-depth interviews with 61 PWUD (any gender) across 18 counties in Maryland, USA. Eligible respondents reported past 6-month use of opioids and stimulants. We searched transcripts for xylazine mentions and identified themes that emerged from the data.
Results: Participants described xylazine as a common local drug supply contaminant, often referring to regular use of "fentanyl and xylazine". They indicated differences in acute effects ("It knocks you out, still wake up feeling like you need to use dope"), increased tolerance ("Regular stuff doesn't do it anymore"), more severe and unique withdrawal symptoms ("it feels way different" and is "way harder to get off of") and compromised MOUD effectiveness ("methadone isn't working the same"). Many described concerns about or experiences with skin wounds ("It eats holes in your body") and expressed fear and uncertainty about xylazine overdose implications. Some participants noted that they try to avoid xylazine, but also said that "it's everywhere". Participants said they try to avoid xylazine by buying from dealers they know, and a few reported using xylazine test strips.
Conclusions: This study highlights that effective public health response to xylazine requires attention to the unique high and withdrawal profile of fentanyl with xylazine and related clinical implications, in addition to expanded harm reduction resources. One case of unexpected cardiovascular response during detox and the resulting emergency department care experience highlights an urgent need for stigma reduction in medical settings and the advancement of emergency department best practices for withdrawal management.
Financial Support: Centers for Disease Control and Prevention R01CE003467; National Institutes of Drug Abuse R21DA060056

CHARACTERIZATION OF THE PHARMACOLOGICAL EFFECTS OF TIANEPTINE

Presenter: Jenny Browning*, DHHS/NIH/NIDA*

Jenny Browning[1], Jane Acri[2], Carol Hubner[2], Matthew Seager[3], David White[2]

[1]*DHHS/NIH/NIDA,* [2]*National Institute of Drug Abuse, National Institutes of Health,* [3]*National Institute on Drug Abuse/NIH*

Drug Category: Opiates/Opioids
Topic: Behavior
Abstract Detail: Preclinical - In Vivo
Abstract Category: Original Research
Aim: Tianeptine is an antidepressant approved in other countries but not in the U.S. It acts as an atypical tricyclic antidepressant and has known mu-opioid agonist activity. In the U.S., tianeptine is sold over-the-counter and popularly referred to as "gas station heroin," because it is often sold in gas stations. The FDA has issued warnings of abuse liability and dangerous side-effects; however, its use is on the rise. The purpose of this study was to evaluate the effects of tianeptine in vitro and in cocaine- and opioid-related behavioral models and assess its abuse liability.
Methods: Through NIDA's Addiction Treatment Discovery Program (ATDP), tianeptine was tested in a variety of in vitro and behavioral models (e.g., precipitated opioid withdrawal, locomotor activity, drug discrimination, intracranial self-stimulation, and reinstatement of drug seeking) alone and in combination with cocaine and morphine.
Results: In addition to opioid receptors, tianeptine was found to act at COX-1 and COX-2. In vivo, tianeptine significantly reduced cocaine-prime reinstatement. It also produced morphine-like discriminative effects, consistent with its mechanism of action. Following repeated administration, tianeptine produced opioid withdrawal-like symptoms. Modest increases in frequency-rate responding were observed in intracranial self-stimulation at mid-range frequencies, indicating that tianeptine may have abuse potential.
Conclusions: The results suggest that in a pre-clinical model, tianeptine may have therapeutic potential for cocaine use disorder, but its abuse potential would limit therapeutic use. Additional testing is currently underway to further elucidate its behavioral effects.

Financial Support: This work was supported by the National Institute on Drug Abuse.

Monday, June 17, 2024

2:15 P.M. - 3:30 P.M.

LATE-BREAKING ORAL SESSION

Av. Duluth, 2nd Floor

PRELIMINARY FINDINGS IN THE DEVELOPMENT OF A CLOSED-LOOP, AUTOMATED MECHANISM FOR OPIOID OVERDOSE REVERSAL

Presenter: James Mahoney*, West Virginia University School of Medicine/Rockefeller Neuroscience Institute*

James Mahoney[1], Shannon Schuetz[2], Ben Pless[2], Dan Baucher[2], Victor Finomore[1], Jennifer Marton[1], Daisy Thompson-Lake[1], Ali Rezai[1]

[1]*West Virginia University School of Medicine, Rockefeller Neuroscience Institute,* [2]*Celero Systems*

Drug Category: Opiates/Opioids
Topic: Technology (e.g., mHealth)
Abstract Detail: Clinical - Experimental
Abstract Category: Original Research

Aim: A high number of opioid overdoses occur when an individual is alone (GREATER THAN 60%). Developing an automated mechanism for opioid overdose reversal has the potential to reduce mortality. Our aim is to develop an ingestible device (Vitals Monitoring (VM) – Pill) to detect respiratory depression during opioid overdose, subsequently triggering the release of an opioid reversal agent (Nalmefene). We initiated a pilot assessing the safety, tolerability, and feasibility of the VM-Pill in participants with opioid use disorder (OUD) and assessing the accuracy of the VM-Pill in measuring physiological functioning including respiratory rate (RR) and heart rate (HR).

Methods: Ten participants receiving residential addiction treatment were enrolled. After ingesting the VM-Pill, breath holding (respiratory depression) sessions were recorded. Data capture was completed while awake and sleeping and transferred wirelessly from the VM-Pill to a computer twice daily for ~3 days. Participants also wore an external smart device (Oura ring) to correlate physiological measurements with VM-Pill data. Gastrointestinal (GI) x-rays were performed ~14 days after VM-Pill ingestion to confirm device excretion.

Results: Participants were aged 35.8 [6.6 years] (Mean [SD]), predominantly male (n=9), White (n=9), and used opioids regularly for 14.3 [10.4 years]. There were no adverse events related to the VM-Pill which passed safely through the GI tract. There was indication that the VM-Pill successfully detects respiratory depression, evidenced by a 70% decrease in respiratory signal amplitude during breath holding sessions. VM-Pill recordings of physiological measurements (e.g., HR, temperature) were highly correlated with Oura ring data ($p > 0.05$).

Conclusions: The VM-Pill is safe, well-tolerated and accurately measures RR and HR from within GI tract. Findings across the VM-Pill and the external wearable device were consistent across for RR, HR, temperature and accelerometry. Current development of closed-loop systems with an automated mechanism to release Nalmefene once a threshold of respiratory depression is met is ongoing.

Financial Support: Internal funding from Rockefeller Neuroscience Institute/West Virginia University.

ADVANCING THE PREDICTION OF ADOLESCENT ALCOHOL USE ONSET BY DERIVING POLYEXPOSURE ALCOHOL RISK SCORES (PXARS) USING THE ADOLESCENT BRAIN COGNITIVE DEVELOPMENT (ABCD) STUDY

Presenter: Faith Adams*, Icahn School of Medicine at Mount Sinai*

Faith Adams[1], Yixuan He[2], Iliyan Ivanov[3], Chirag Patel[2], Muhammad Parvaz[1]

[1]*Icahn School of Medicine at Mount Sinai,* [2]*Harvard Medical School,* [3]*Mount Sinai Children's Hospital,*

Drug Category: Alcohol
Topic: Environment/Stress
Abstract Detail: Clinical - Epidemiology
Abstract Category: Original Research

Aim: Early alcohol use onset increases the risk of alcohol dependence. Both genetics and environment plays roles in onset, yet better understanding of non-genetic factors – the exposome – is needed. This study employs an Exposome-Wide Association Study (ExWAS), analogous to genome-wide association study (GWAS), to develop 'PolyeXposure Alcohol Risk Scores (PXARS) for evaluating the aggregate burden of the environment on alcohol use onset.
Methods: We analyzed youth from the Adolescent Brain Cognitive Development cohort (n = 11,235, ages 9-14). First, we used ExWAS to evaluate the associations of 201 quality controlled environmental measures with alcohol use onset. Next, to identify the most robust associations, we used multivariate modelling of the significant independent associations, and computed PXARS, a weighted sum of the final significant variables retained. We also computed family history density (FHD) by taking the weighting for family relatedness (i.e. parent = 0.50, grandparents =0.25). The individual and additive predictive utility of PXARS and FHD were assessed.
Results: Nineteen variables were significantly associated with alcohol use onset. Notably, among these factors, screen media activity, discrimination, and adverse life experiences emerged as significant risk factors for alcohol use onset, while religious beliefs and neighborhood crime served as protective factors. The multivariate model yielded screen media activity, prenatal alcohol exposure, and experiences of discrimination as significant predictors, and contributed to PXARS calculation. Both, PXARS and FHD significantly differentiated alcohol initiators and non-initiators ($p > 0.0001$). Independently, FHD and PXARS effectively discriminated between the groups [C-statistics: 0.581; 95% CI 0.511, 0.677] and [C-statistics: 0.644; 95% CI 0.531, 0.729]. Combining PXARS and FHD improved C-statistic to [0.622; 95% CI 0.529, 0.696], indicating a marginal increase in the predictive power.
Conclusions: This approach assesses the combined impact of diverse environmental exposures, ensuring simplicity and interpretability. Additionally, PXARS improves the prediction of alcohol use onset in youth.
Financial Support: F31AA031437, R61DA056779, R01DA058039

INTERLEUKIN-17A: A TARGET FOR METHAMPHETAMINE USE DISORDER

Presenter: Saadet Inan*, Lewis Katz School of Medicine at Temple University*

Saadet Inan[1], Sonita Wiah[1], Scott Rawls[1]

[1]*Lewis Katz School of Medicine at Temple University*

Drug Category: Stimulants
Topic: Behavioral Pharmacology
Abstract Detail: Preclinical - In Vivo
Abstract Category: Original Research

Aim: We previously reported that blocking IL-17A, a proinflammatory cytokine, using the non-selectiveIL-17A antagonist, cyanidin and IL-17A antibody (Ab) prevented both anxiety- and depression-like effects elicited by MDPV (a psychostimulant) withdrawal and chronic oxycodone use, respectively, in rats (Inan et al., 2023, 2024). Here, we studied whether lack of IL-17A signaling (pharmacological antagonism and genetic) would attenuate behavioral effects of chronic methamphetamine (METH) in adult male and female mice (C57/BLJ6).
Methods: Locomotor activity, withdrawal-induced anxiety- or depression-like effects and rewarding effects of METH were studied. IL-17A Ab (60 µg/100 µl, IP, every 3rd day) and mice lacking IL-17 receptor C (RC, IL-17 A binds) for were used. Mice (n=8-12) received saline or METH (5 mg/kg, IP) once daily for 18 days.

Locomotion was measured on days 1 and 15. The elevated plus maze and forced swim test were used to measure anxiety- and depression-like effects on days 21 and 22, respectively.
Results: METH-induced hyperlocomotion was significantly reduced in IL-17RC KO mice compared to WT. METH abstinence induced depression-like behavior. Immobility time was significantly increased in mice that received saline-METH treatment compared to other groups in both studies. Mice treated with IL-17A Ab-METH had a similar immobility time with controls, suggesting that Ab prevented the development of depression-like effects. Immobility time of IL-17RC KO mice that received METH was significantly lower than WT mice receiving METH, indicating a reduced effect in KO mice. The conditioned place preference test was performed in separate mice. The difference score was significantly higher in mice that received saline-METH compared to control and IL-17A Ab-METH groups, indicating the Ab prevented rewarding effects of METH.
Conclusions: Our data suggest that IL-17A contributes to the pathogenesis of METH-use disorder (MUD) and is a potential target for the treatment of MUD.
Financial Support: R01 DA045499 (SMR)

A RANDOMIZED OPEN-LABEL STUDY COMPARING RAPID AND STANDARD INDUCTIONS TO INJECTABLE BUPRENORPHINE EXTENDED-RELEASE (BUP-XR) TREATMENT

Presenter: Robert Dobbins*, Indivior Inc.*

Rajinder Shiwach[1], Bernard Le Foll[2], Hannu Alho[3], Stephanie Strafford[4], Yue Zhao[4], Robert Dobbins[4]
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Drug Category: Opiates/Opioids
Topic: Treatment
Abstract Detail: Clinical - Experimental
Abstract Category: Original Research
Aim: This multi-center, randomized, open-label sub-study (NCT04995029), evaluated treatment retention using standard induction (SI) vs. rapid induction (RI) onto BUP-XR injection in treatment-seeking participants who frequently inject opioids or use fentanyl/high doses of opioids.
Methods: Participants were randomized at a 2:1 ratio to RI (a single dose of 4 mg transmucosal [TM] buprenorphine [BUP]) or SI (≥7days of TM-BUP) before BUP-XR injection 1. Randomization was stratified by the same-day urine drug screen fentanyl result (78% positive). The primary endpoint, retention rate difference at injection 2 (administered 1 week after injection 1), was estimated by a Bayesian approach. The posterior probability was evaluated for superiority of RI to SI (RI – SI GREATER THAN 0) using a 96% critical value for overall 1-sided Type I error > 10%. Investigator assessed precipitated opioid withdrawal (POW) was reported.
Results: There were 729 randomized participants who initiated treatment with TM-BUP per protocol (255 SI, 474 RI) with 406 males and 323 females, mean age of 41 years, and mean opioid use of 15 years. RI was superior to SI: The difference in retention rates with its 95% highest posterior density intervals and posterior probabilities for RI superior to SI at injection 2 was 11.8% (4.3-19.0%) and 99.9% for the overall population, and 14.8% (6.5-23.7%) and 100.0% for the fentanyl positive subpopulation. The proportion of participants with investigator assessed POW symptoms was 18.0% SI vs. 24.1% RI. In RI, POW did not result in increased discontinuation compared to SI. Between injections 2 and 3, no individual adverse event was observed in ≥5% of participants.
Conclusions: Compared to SI, RI improved treatment retention without significantly increasing POW in this high-risk population. Administration of injection 2 one week after injection 1 was well tolerated. The shorter time necessary for RI may increase retention on BUP-XR treatment.
Financial Support: Indivior Inc.

ASSOCIATION OF DAILY DOSES OF BUPRENORPHINE WITH URGENT HEALTH CARE UTILIZATIONS: THE INFLUENCE OF HIGH DAILY DOSES

Presenter: Bradley Stein*, RAND Corporation*

Bradley Stein[1], Sarah Axeen[2]

[1]*RAND Corporation,* [2]*University of Southern California*

Drug Category: Opiates/Opioids
Topic: Substance Use Disorder
Abstract Detail: Clinical - Epidemiology
Abstract Category: Original Research
Aim: We examined the association between higher doses of buprenorphine (GREATER THAN 24 mg) and subsequent emergency department or inpatient (ED/IP) service use.
Methods: We conducted a retrospective survival analysis using Cox Proportional Hazard models with Optum's de-identified Clinformatics® Data Mart Database (CDM) medical and prescription drugs claim data of patients aged 18 years or older with a diagnosis of opioid use disorder starting buprenorphine treatment and dispensed at least 14 days supply from 2016 to 2021.
Results: We identified 35,451 individuals with an OUD diagnosis who began buprenorphine treatment. 27.3% (n=9669) were in the 1-8 mg tier; 42.9% (n=14802) were in the 8-16mg tier; 29% (n=10329) were in the 16-24mg tier; and 1.8% (n=651) were in the GREATER THAN 24 mg tier. After regression adjustment, patients with GREATER THAN 24 mg had lower rates of ED/IP use than patients in other tiers (16-24 mg: HR 1.300; 95% CI: 1.027 to 1.645; 8-16 mg: HR 1.405; 95% CI: 1.112 to 1.776 and 1-8 mg: HR 1.276; 95% CI: 1.006 to 1.618). Findings were comparable when we examined time to an all-cause ED/IP service, and when we restricted analyses to individuals with no observed ED/IP visit in the 90 days before treatment.
Conclusions: We found those receiving higher maximum doses of buprenorphine (GREATER THAN 24 mg) had significantly lower rates of acute care utilization than their peers receiving FDA-recommended doses (between 1-16 mg). Our findings contribute to the sparse empirical literature regarding potential benefits of higher dose buprenorphine treatment of individuals with OUD. Clinicians should be aware of the potential effects of higher buprenorphine doses on healthcare utilization while policymakers work to ensure equitable access to individuals who could potentially benefit from higher doses.
Financial Support: Supported by the National Institute on Drug Abuse (P50DA046351 and R01DA045800).

CANNABIS AND TOBACCO CO-USE AND ITS ASSOCIATION WITH STRIATAL BRAIN MORPHOMETRY: LEVERAGING DATA FROM THE ENIGMA ADDICTION WORKING GROUP

Presenter: Zac J. S. Yeap*, McGill University*

Zac J. S. Yeap[1], Anthony Juliano[2], Devarshi Pancholi[2], Francesca Filbey[3], Hugh Garava2[4], Murat Yucel[4], Valentina Lorenzetti[5], Nadia Solowij[6], Rocio Martin-Santos[7], Albert Batalla[8], Janna Cousijn[9], Edythe London[10], Xiaochu Zhang[11], Rachel Rabin[1]

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Drug Category: Cannabis/Cannabinoids
Topic: Neurobiology/Neuroscience
Abstract Detail: Other
Abstract Category: Original Research
Aim: The striatum is posited to play a central role in the pathophysiology of addiction, and shows altered gray matter volume (GMV) in individuals with addiction. Cannabis and tobacco are frequently used addictive substances and daily co-use is common. Studies show that cannabis use is associated with greater striatal GMV, while others show that tobacco use is associated with lower striatal GMV. However, the effects associated with their combined use on striatal GMV remain unclear. Therefore, we investigated whether daily

cannabis and tobacco co-use was associated with different patterns of striatal GMV compared to either substance alone or no substance use.
Methods: Pooling T1-weighted MRI scans from 10 ENIGMA Addiction sites yielded a sample of N=273. Males and females, aged 18-45, were parsed into 4 groups according to their current cannabis and tobacco use: individuals with co-use (CT, n=45), cannabis-only use (CAN, n=28), tobacco-only use (TOB, n=60), and no use (controls, n=140). Participants in the cannabis groups used ≥0.5 joints/day and those in the tobacco groups used ≥5 cigarettes/day. Using Freesurfer, GMV in the nucleus accumbens, caudate nucleus, and putamen were extracted. We employed 2x2 ANCOVAs controlling for age, sex, site, and alcoholic drinks/day. Since years of cannabis use differed between CT and CAN, and years of tobacco and daily tobacco use differed between CT and TO, these were also controlled for in the analyses. False-discovery-rate correction was applied to control for multiple comparisons.
Results: In the right nucleus accumbens, there was a significant interaction between cannabis and tobacco use (p=0.042). The main effects for cannabis (p=0.06) and tobacco use (p=0.39) were not significant. Post-hoc comparisons revealed higher GMV in CAN compared to CT (p=0.045), TOB (p=0.028), and controls (p=0.001); no other group differences emerged.
Conclusions: Among individuals with cannabis use, tobacco co-use may suppress cannabis-induced GMV increases in the nucleus accumbens.
Financial Support: None

LIBRARY-DELIVERED TELEHEALTH TO INCREASE BUPRENORPHINE TREATMENT USE AMONG UNSTABLY HOUSED PATRONS USING OPIOIDS: PRELIMINARY RESULTS OF A PILOT RANDOMIZED CONTROLLED TRIAL

Presenter: Lianne A. Urada*, San Diego State University School of Social Work*

Lianne A. Urada[1], Carla Marienfeld[2], Megan Partch[3], Richard S. Garfein[4], Steffanie A. Strathdee[2], Jordan Jump[5], Ashley Weitensteiner[1], Melanie J. Nicholls[1], Peter Davidson[2], Eileen V. Pitpitan[1]

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Drug Category: Opiates/Opioids
Topic: Treatment
Abstract Detail: Clinical - Experimental
Abstract Category: Original Research
Aim: Accessing opioid use disorder (OUD) treatment is difficult for homeless individuals. This population often uses public libraries for computer and internet access, which could provide telehealth access to OUD treatment. We developed a novel 12-week telehealth intervention called "Bupe by the Book" (BBB) that uses library resources to facilitate initiation and retention in OUD treatment with buprenorphine.
Methods: We conducted a pilot randomized controlled trial of BBB in San Diego, California, to evaluate treatment acceptance and retention among individuals reporting homelessness and OUD (with or without other substance use). Library patrons were recruited via flyers, screened for eligibility, and referred to a nearby treatment program for in-person intake. Those who attended intake were enrolled in the study and randomized to BBB (i.e., follow-up telehealth visits using library internet access) or treatment as usual (i.e., follow-up visits in person or by phone). We examined the feasibility and acceptability of the BBB intervention on 1) self-reported measures (e.g., substance use, mental health, quality of life) at 1-,2-,4-,8-, and 12-weeks; 2) clinic visits; 3) weekly urine drug screenings; and 4) prescription pick-ups.
Results: To date, of 130 individuals who were screened, 28 were enrolled (pilot target=40). Barriers to enrollment included challenges related to mental health that made it difficult to attend the first intake visit. Overall, 71% of enrolled participants were retained over the 12-week trial; self-report data showed 94% had at least one pharmacy pickup, and 81% took buprenorphine. Among protocol-adherent participants (n=16), those randomized to BBB (n=8) were 3 times more likely to attend GREATER THAN 1 treatment visit and to test positive for buprenorphine in urine screens.

Conclusions: Preliminary data suggest BBB is a feasible and acceptable strategy to leverage public library resources for telehealth to engage and retain unstably housed people with OUD in buprenorphine treatment.
Financial Support: National Institute on Drug Abuse

CLATHRIN NANOPARTICLES WITH DAT-ANTIBODY TARGETED BDNF TO DOPAMINE BRAIN REGIONS, REGENERATED NEURONS AND RESTORED MOUSE BRAIN FUNCTIONS BY REVERSING METHAMPHETAMINE AND/OR HIV-TAT INDUCED NEUROTOXICITY

Presenter: Gordana Vitaliano*, McLean Hospital, Harvard Medical School*

Gordana Vitaliano[1], Yasaman Razavi[1], Christopher Adam[2], Jing Liu[1], Corvens Depaliste[2], Franco Vitaliano[3]

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Drug Category: Stimulants
Topic: Treatment
Abstract Detail: Preclinical - In Vivo
Abstract Category: Original Research
Aim: Methamphetamine (MA) use disorder is prevalent among individuals infected with HIV-1 and can lead to neurodegeneration of dopaminergic (DA) system and Parkinsonism. Brain-derived Neurotrophic Factor (BDNF) plays a critical role in cell survival, growth and synaptic plasticity, and has been identified as a potent therapeutic for neuropsychiatric disorders. However, BDNF has poor blood-brain barrier penetrability which limits its use in medicine. Our goal was to target BDNF to DA neurons using clathrin-nanoparticles (NPs) and ameliorate neurotoxic effects of MA and HIV-Transactivator of transcription (Tat) protein.
Methods: NPs were synthesized by conjugating dopamine-transporter (DAT) antibody and BDNF to clathrin triskelia using PEG-linkers. iTat mice (N=74) were treated daily for 7 days with saline (Tat-) or doxycycline (100mg/kg/d i.p.) that induces HIV-Tat expression (Tat+). Concurrently, mice received nasal NPs (BDNF-0.3mg/kg) or saline (40µl). On day 6, mice received 4 binge doses of MA (4 mg/kg/i.p) or saline. On day 7, mice were tested with open field, grip strength and rotarod tests. Brains were collected. DA-cell numbers and fiber density were determined in the substantia nigra (SN) and striatum (STR) using Tyrosine hydroxylase (TH) as a marker.
Results: NP targeted BDNF to DA-neurons. NPs vs. saline increased numbers of DA-neurons in SN of Tat+($p=0.0086$), MA($p=0.0011$) and MA/Tat+($p=0.0052$) mice and enhanced TH+ fiber density in STR of Tat+, MA and MA/Tat+ mice ($p > 0.0001$ in all groups). NPs improved rotarod performance in Tat+($p=0.0026$), MA($p=0.0085$) and MA/Tat+($p=0.024$) mice, and increased grip strength in Tat+($p=0.0249$), MA($p=0.0322$) and MA/Tat+($p=0.0051$) mice. In OF, NPs lowered hyperactivity in MA mice($p=0.0319$) and increased activity in MA/Tat+mice ($p=0.0158$).
Conclusions: Our innovative approach delivered BDNF to DA neurons and ameliorated neurodegenerative effects of MA and/or HIV-Tat protein. Using highly efficient clathrin-NPs this noninvasive nanotechnology may be able to enhance neuronal regeneration and synaptic plasticity and restore brain functions more quickly and completely than existing treatment methods.
Financial Support: NIDA R44DA044050 and K08DA037465 awards

SUICIDE ATTEMPTS AMONG PATIENTS PRESENTING TO EMERGENCY DEPARTMENTS FOR A CONFIRMED OPIOID OVERDOSE: A MULTICENTER STUDY

Presenter: Rachel Culbreth*, American College of Medical Toxicology*

Rachel Culbreth[1], Alyssa Falise[1], Kim Aldy[1], Jeffrey Brent[2], Paul Wax[1], Alex Krotulski[3], Shao Li[1], Sharan Campleman[1], Barry Logan[3], Stephanie Abston[1], Adrienne Hughes[4], Rob Hendrickson[4], Alexandra Amaducci[5], Bryan Judge[6], Joseph Carpenter[7], Michael Levine[8], Diane Calello[9], Christopher Meaden[9], Jennie Buchanan[10], Joshua Shulman[11], Evan Schwarz[8], Alex Manini[13]

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Drug Category: Opiates/Opioids
Topic: Substance Use Disorder
Abstract Detail: Clinical - Epidemiology
Abstract Category: Original Research

Aim: Suicide attempts via overdose (OD) are a major cause of morbidity and mortality for emergency department (ED) patients. This study investigated patients' sociodemographic and toxicological predictors associated with intentionality for confirmed opioid ODs. This study also compared medical interventions for opioid ODs associated with suicide attempts compared to unintentional ODs.
Methods: This analysis is based on the Toxicology Investigators Consortium (ToxIC) Fentalog Study, an ongoing prospective cohort of patients presenting to one of ten participating EDs for a suspected opioid OD. The Center for Forensic Science Research and Education tested patients' residual serum samples for over 1100 drugs and novel psychoactive substances using liquid chromatography quadrupole time-of-flight mass spectrometry. Chart reviews were conducted to determine the patients' intentions for opioid OD (suicide attempt vs. unintentional overdose) and medical interventions (intubation, CPR, ICU admission). Multivariable regression analyses computed odds ratios for associations between predictors (sociodemographic variables and detected analytes) and OD intentionality. This study was approved by a central IRB (WCGIRB) with waiver of consent.
Results: Among patients who were screened as of February 12, 2024 (N=6371), a total of 1809 patients were included (N=1588 had completed laboratory analysis), and 1259 patients presented with a confirmed opioid OD related to either suicide attempt (6.4%) or unintentional overdose (93.6%). In the multivariable analysis, prescription opioids only (without illicit opioids) were associated with suicide attempts compared to unintentional overdose (OR: 1.27; 95% CI: 1.21, 1.34). Presenting after suicide attempt was not associated with increased odds of intubation, CPR, or ICU admission.
Conclusions: In this large multicenter cohort of patients presenting to emergency departments after opioid OD, suicide attempts were associated with prescription opioids rather than illicit opioids. Additionally, those with suicide attempts had no differences in clinical severity measures compared to those who presented after unintentional overdoses after adjusting for other detected analytes and medical center.
Financial Support: Research reported in this publication was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Number R01DA048009 (PI: Alex Manini). Supplemental funding is provided by the Centers for Disease Control and Prevention (Award Number 3R01DA048009-04S1) to increase the project's testing capacity. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Centers for Disease Control and Prevention.

IMPACT OF VANILLA FLAVOR ON NICOTINE TASTE, INTAKE, AND SEEKING BEHAVIORS

Presenter: Deniz Bagdas*, Yale Department of Psychiatry*

Deniz Bagdas[1], Andy Z. Ma[1], Lilley Harris[1], Karina Minanov[1], Jaysen Lara Jimenez[1], Nii A. Addy[1]

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Drug Category: Nicotine/Tobacco
Topic: Behavioral Pharmacology
Abstract Detail: Preclinical - In Vivo
Abstract Category: Original Research

Aim: Electronic delivery systems and smokeless tobacco products often contain flavors that impact nicotine product use. We aimed to investigate the impact of vanillin, the principal chemical of vanilla flavor in tobacco products, on nicotine taste and use behaviors.
Methods: To explore the long-term effects of early exposure to sweetened vanillin, we utilized a combined model of two-bottle free-choice paradigm (2BC) and intraoral self-administration (IOSA). In 2BC, rats were

exposed to sweetened vanillin. We later assessed nicotine taking and seeking behaviors in the presence or absence of unsweetened vanillin. To quantify the liking and disliking taste responses to oral nicotine with or without vanillin, we conducted a taste reactivity test (TRT). Additionally, we determined the effects of commercial vanilla flavor on nicotine intake in an operant vapor self-administration (VSA) model. We used nicotine concentrations of 10 μg/ml for oral and 6 mg/ml for inhalation studies. While vanillin (10 - 100 μg/ml) was used for oral studies and a vanilla commercial e-liquid was used for inhalation studies. Female and male Sprague Dawley young adult rats (n=7-11/sex/group) were used in separate studies. Data were analyzed using mixed-model ANOVA.

Results: Vanillin alone and the combination of vanillin plus nicotine led to greater IOSA compared to water. However, females self-administered vanillin plus nicotine more than their male counterparts. Vanillin also increased nicotine-seeking only in females. Vanillin reversed nicotine aversion by increasing ingestive taste responses and blocking nicotine's aversive taste responses to high concentration of nicotine, in both sexes. Vanilla flavor did not alter nicotine vapor intake at tested concentrations in VSA.

Conclusions: The results indicate that vanilla flavor can increase oral nicotine intake and seeking and can also increase liking and decrease disliking of nicotine's taste. The impact of vanilla flavor on nicotine use behaviors is dependent on concentration, sex, and administration route.

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