SUNDAY, JUNE 18, 2023

ORAL COMMUNICATION: ISGIDAR: AGAIN?
Grand Ballroom I

SUVOREXANT, AN FDA-APPROVED DUAL OREXIN RECEPTOR ANTAGONIST, EFFECTIVELY REDUCES OXYCODONE SELF-ADMINISTRATION AND CONDITIONED REINSTATEMENT IN MALE AND FEMALE RATS

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Aim: Amid the opioid crisis, effective strategies to prevent prescription opioid use disorder (OUD) are urgent. The orexin (Orx) system is recruited by drugs of abuse and blockade of Orx receptors (OrxR) prevents drug-seeking behaviors. This study sought to determine whether repurposing suvorexant (SUV)-- a dual OrxR antagonist marketed as Belsomra® (Merck) for insomnia treatment-- can treat two features of prescription OUD: exaggerated consumption and relapse.
Methods: Wistar rats (males and females; n=16/group) were trained to self-administer oxycodone (0.15 mg/kg, i.v., 8h/day) in the presence of a discriminative stimulus (SD). The capacity to decrease self-administration with SUV (0-20 mg/kg, p.o.) was tested. Next, the rats underwent extinction training and the effect of of SUV (0 and 20 mg/kg, p.o.) to prevent SD-induced reinstatement of oxycodone-seeking behavior was tested. Repeated measures ANOVAs analyzed self-administration and reinstatement data. Withdrawal scores were analyzed with Friedman nonparametric tests.
Results: Males ($F(14,196)= 7.09$, $p< 0.001$) and females ($F(1,13)= 74.80$, $p< 0.001$) acquired oxycodone self-administration and exhibited physical signs of opioid withdrawal (males: $Fr= 36.23$, $p< 0.001$; females: $Fr= 37.24$, $p< 0.001$). Females consumed twice as much oxycodone (48.55 ± 5.01 mg/kg) vs. males (22.49 ± 4.83 mg/kg). At 20 mg/kg SUV decreased oxycodone self-administering during the first hour in males ($F(2,26)= 5.05$, $p< 0.05$) and females ($F(2,26) = 4.77$, $p < 0.05$). The oxycodone SD reinstated oxycodone-seeking behavior with more efficacy in females ($t(9)= 4.10$, $p < 0.01$). Suvorexant reversed oxycodone seeking in males to extinction level (Bonferroni $p> 0.05$ vs. EXT; $F(3,35)= 6.72$, $p< 0.01$). In females while a reduction was measured, a substantial reinstatement persisted (Bonferroni $p < 0.01$ vs. 0 mg/kg; $F(3,13)=10.15$, $p< 0.001$).
Conclusions: The findings support targeting OrxR for the treatment for prescription OUD and repurposing SUV as pharmacotherapy for prescription OUD.
Financial Support: This work was supported by The National Institute on Alcohol Abuse and Alcoholism (grant no. AA006420, AA026999, AA028549, and T32 AA007456) and the National Institute on Drug Abuse (grant no. DA053443).

EFFECTS OF BENZODIAZEPINE RECEPTOR POSITIVE ALLOSTERIC MODULATORS ON MIDAZOLAM SELF-ADMINISTRATION IN RHESUS MONKEYS

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Drug Category Sedative/Hypnotics
Topic Behavioral Pharmacology
Aim: We have previously shown that benzodiazepine (GABAA) receptor antagonists induce parallel rightward shifts in the dose-response functions for benzodiazepine self-administration under a progressive ratio (PR) schedule. However, we had yet to investigate the effects of pretreatments with GABAA receptor positive allosteric modulators ("modulators") on benzodiazepine self-administration.
Methods: In the present study, rhesus monkeys (n=4) were trained under a PR schedule of intravenous midazolam delivery, and dose-response functions were determined for midazolam after pretreatments with vehicle or the non-selective benzodiazepine modulator lorazepam. Because benzodiazepines induce

sedative-motor effects at high doses via α1 subunit-containing GABAA receptor (α1GABAAR) mechanisms, we also investigated the effects of pretreatments with the partial modulator TPA023B, a compound lacking activity (i.e. antagonist) at α1GABAARs, on midazolam self-administration. As an additional control, the effects of both lorazepam and TPA023B were evaluated on food-maintained responding.
Results: Our results show that lorazepam induced downward shifts in the midazolam dose-response functions. TPA023B, on the other hand, induced rightward and downward shifts in the midazolam dose-response functions for 3 monkeys and downward shifts only for the 4th monkey. Lorazepam, but not TPA023B, blocked food-maintained responding.
Conclusions: The non-selective full modulator lorazepam attenuated midazolam self-administration at doses that also inhibited food-maintained behavior. TPA023B, a benzodiazepine receptor partial modulator with no efficacy at α1GABAARs, selectively blocked midazolam self-administration without altering operant responding for food. The effects of TPA023B, but not of lorazepam, on midazolam self-administration could be partially surmounted by increasing midazolam dose. These findings support a role for α1GABAARs in the reinforcing effects of benzodiazepine-type ligands, although partial blockade by TPA023B suggests a non-antagonist role for other subtypes (e.g., GABAA subtypes with α2 or α3 subunits).
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ASSOCIATION OF DOPAMINE D2-LIKE AND D3 RECEPTOR FUNCTION WITH INITIAL SENSITIVITY TO COCAINE REINFORCEMENT IN RHESUS MONKEYS

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Drug Category Stimulants
Topic Behavioral Pharmacology
Aim: Identification of neurobiological characteristics that increase risk for developing of cocaine use disorder would be of great value in prevention efforts. Brain dopamine receptors are logical candidates for investigation because of their importance in mediating the abuse-related effects of cocaine.
Methods: We re-analyzed data from two recently published studies (PMID: 33865211, 36001440) that characterized availability of dopamine D2-like receptors (D2R) with [11C]raclopride PET imaging and dopamine D3 receptor (D3R) sensitivity with quinpirole-induced yawning in cocaine-naïve male rhesus monkeys who then acquired cocaine self-administration and completed a cocaine self-administration dose-effect curve. The present analysis examined measures of initial sensitivity to cocaine in light of D2R availability in several brain areas and characteristics of quinpirole-induced yawning.
Results: D2R availability in the caudate nucleus was negatively correlated with the ED50 of the cocaine self-administration curve, although the significance of this relationship was driven by an outlier. No significant associations were observed between D2R availability in any other brain area and measures of cocaine reinforcement. A second PET scan conducted just after completion of the cocaine self-administration dose-effect curves showed no change from baseline D2R availability. Regarding D3R sensitivity, there was a significant negative correlation between the ED50 of the quinpirole-induced yawning curve and the dose at which monkeys acquired cocaine self-administration.
Conclusions: These data suggest the utility of D3R sensitivity, but not D2R availability, as a biomarker for vulnerability and resilience to cocaine use disorder. Moreover, results indicate that the well-established relationships between dopamine receptors and cocaine reinforcement in cocaine-experienced humans and animals may require and result from extensive cocaine exposure. Support: DA 039953.
Financial Support: DA 039953

INFLUENCE OF 5HT1B ACTIVATION ON THE REINFORCING EFFECTS OF INTRAVENOUS COCAINE

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Drug Category Stimulants
Topic Behavioral Pharmacology
Aim: Despite strides in our understanding of the neurobiological underpinnings of cocaine addiction in preclinical models, a limited amount of research has translated those findings into clinical populations. Such translation is crucial to identify neurobiological circuits that contribute to the problems posed by cocaine use disorder and to guide treatment based on those clinical neuroscience findings. Cocaine potently inhibits the reuptake of serotonin (5-HT). 5-HT1b receptors play a particularly important role in preclinical cocaine effects with rodent data showing that zolmitriptan, a commercially available selective 5-HT1b agonist migraine medication, selectively attenuates the reinforcing and other abuse-related effects of cocaine. The overarching goal of this project is to advance these promising preclinical findings into humans, thereby demonstrating that the 5-HT1b system plays a key role in the reinforcing effects of cocaine in clinical populations. We hypothesize that zolmitriptan will reduce cocaine self-administration.
Methods: To date, 7 non-treatment seeking participants (4 women) with cocaine use disorder have completed this ongoing within-subject human laboratory study. Participants are maintained on 0, 2.5, 5 and 10 mg oral zolmitripan/day in random order. After at least 3 days of maintenance on each target dose, participants complete experimental sessions in which the reinforcing effects of 0, 10 and 30 mg/70 kg of intravenous cocaine are determined. Mixed-effects analyses (Prism 9, GraphPad) were used to analyze data.
Results: Cocaine functioned as a reinforcer, producing significant (i.e., $p<0.05$), dose related increases in self-administration. Zolmitriptan did not affect cocaine self-administration.
Conclusions: Data indicate that activating the serotonin 5-HT1b system through zolmitriptan maintenance fails to change cocaine intake, in contrast with preclinical findings. Future work should more closely align preclinical and human laboratory methods to better determine the translatability between these approaches.
Financial Support: R01 DA 052203 and UL1TR001998

ORAL COMMUNICATION: SEXUAL MINORITY HEALTH
Plaza Ballroom A

THE FAMILIAR TASTE OF POISON: A QUALITATIVE STUDY OF MULTI-LEVEL MOTIVATIONS FOR STIMULANT USE IN SEXUAL MINORITY MEN LIVING IN SOUTH FLORIDA

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Drug Category Stimulants
Topic Infectious Disease (e.g., HIV, HCV)
Aim: Stimulant use is associated with a 3-6 times greater rate of HIV seroconversion in sexual minority men (SMM) than in those who do not use stimulants. Annually, 1 in 3 SMM who HIV seroconvert will be persistent methamphetamine (meth) users. The primary objective of this qualitative study was to explore experiences of stimulant use in SMM living in South Florida.
Methods: The sample included 25 SMM who use stimulants, recruited via targeted ads on social networking apps. Participants completed one-on-one semi-structured qualitative interviews, conducted from July 2019 through February 2020. A general inductive approach was used to identify themes relating to experiences, motivations, and overall relationship with stimulant use.
Results: Mean age of participants was 38.8, ranging from 20-61 years old. Participants were 44% White, 36% Latino, 16% Black and 4% Asian. Most participants were born in the US, self-identified as gay, and preferred meth as their stimulant of choice. Themes included: 1) stimulants as cognitive enhancements for focus or task completion, including transitioning to meth after first using prescription psychostimulants; 2) unique South Florida environment where participants could be open regarding their sexual minority status while also being influential on their stimulant use; 3) stimulant use as both stigmatizing and a coping mechanism for stigma. Participants anticipated stigma by family and potential sexual partners due to their stimulant use. They also reported using stimulants to cope with feeling of stigma due to their minoritized identities.

Conclusions: This study is among the first to characterize motivations for stimulant use in SMM living in South Florida, a high priority region for the Ending the HIV Epidemic initiative. Results highlight both the risk and protective factors of the South Florida environment, psychostimulant misuse as a risk for meth initiation, and the role of anticipated stigma on stimulant use in SMM.
Financial Support: National Institute on Drug Abuse (R34- DA046367; Carrico and Grov, PIs)

ASSOCIATIONS BETWEEN GEOSOCIAL SEXUAL NETWORKING APP USE AND DRUG USE, PARTNER TYPE, AND SEXUAL BEHAVIORS AMONG SEXUAL MINORITY MEN DURING THE FIRST SHELTER-IN-PLACE ORDER OF THE CORONAVIRUS PANDEMIC IN TEXAS

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Drug Category Alcohol
Topic Behavior
Aim: Changes in drug use and sexual behaviors among sexual minority men since the coronavirus pandemic have been documented and associated with geosocial sexual networking app use (GSNAU). There is no adequate literature focusing on the state of Texas. This study aimed to determine associations between drug use, sexual behaviors, and GSNAU among sexual minority men who completed the COVID-19 and You Survey conducted between May 2020 to July 2020, during the first shelter-in-place order of the Coronavirus pandemic in Texas.
Methods: Descriptive statistics (n, frequency, and percent) were determined for all measures and their bivariate associations with the continuation or start of GSNAU since shelter-in-place using Chi-Square tests. Significant bivariate associations were determined significant at alpha level 0.05. Adjusted associations with GSNAU were determined using logistic regression adjusting for age, race and ethnicity, education level, citizenship/immigration status, sexual orientation, and HIV-positive status. Adjusted odds ratio and 95% confidence intervals are reported.
Results: Of the 406 sexual minority cisgender men who completed the survey and answered questions about GSNAU, the majority identified as white (72.7%) and gay/same-gender-loving (89.4%). Over a third continued or started GSNAU since shelter-in-place (36.2%). After adjustment, age, relationship status, relationship type, last sexual intercourse, ever engaged in sex work, condoms use, and sexual activity frequency were significantly associated with the continuation or start of GSNAU since shelter-in-place.
Conclusions: These findings contribute to the limited literature in Texas documenting behaviors of sexual minority men impacted by COVID-19, including GSNAU.
Financial Support: The University of Texas at Austin, Office of the Vice President of Research

COMING OUT TO TREATMENT: CHARACTERIZING EXPERIENCES OF SEXUAL AND GENDER MINORITIZED INDIVIDUALS IN SUBSTANCE USE DISORDER TREATMENT BEFORE AND DURING THE COVID-19 PANDEMIC

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Drug Category Opiates/Opioids
Topic Disparities
Aim: Sexual and Gender Minority (SGM) individuals are disproportionately impacted by substance use disorders vs. their non-SGM counterparts. SGM individuals face more barriers to treatment access due discrimination, internalized stigma, and marginalization due to their sex and gender minority statuses. There is a paucity of research relevant to the experience of SGM in Opioid Use Disorder (OUD) treatment settings. This study employs secondary data analysis and a mixed methods approach to (1) describe the population of SGM enrolled in an OUD treatment program, and among a subset (2) identify factors impacting treatment engagement and retention using interviews/ additional measures, and (3) better understand the impact of COVID-19 on treatment in this sample.

Methods: Participants were N=49 SGM enrolled in BRITER at REACH, a substance use treatment facility in Baltimore, MD. Secondary data included demographic and psychosocial variables, program participation, and HIV risk measures. Descriptive statistics were run to characterize SGM BRITER program participants at baseline. The subset of individuals needed for Aims 2 and 3, are currently being recruited from the larger sample, with N=3 individuals recruited thus far to participate, with a goal of N=10-15.
Results: The sample was predominantly Black (60%) Cisgender, Sexual Minority Women (80%) with a mean age of 41.94 yrs. 100% diagnosed with OUD with 85% also meeting for Tobacco Use Disorder and 75% for PTSD. Time in treatment varied from 3 days to over 10 years. Additional results from secondary data will be presented. Results from Aims 2 and 3 are pending. However, themes from initial interviews suggest a perceived influence of discrimination on treatment accessibility prior to program involvement. Additional themes related to treatment engagement will be presented.
Conclusions: Additional research is warranted to understand the factors that impact treatment engagement among SGM individuals. Additional interviews will be conducted to further explore the subjective experiences of SGM in treatment for OUD.
Financial Support: This research was supported by SAMHSA Grant TI080619 and the VCU institute for women's health.

IDENTIFYING THE NEED FOR BRIEF POLYDRUG USE INTERVENTIONS AMONG BLACK AND HISPANIC SEXUAL MINORITY MEN IN THE U.S.

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Aim: Identify the need for brief polydrug use interventions among Black and Latino sexual minority men (SMM) in the U.S.
Methods: Data come from the PrEP and Substance Use National Survey, a study of Black and Latino SMM living in the U.S. Participants were recruited between March and August 2020 via national networks, social media, and mailing lists. Participants were eligible if they were between 18 and 29 and reported sex with another man in the past 12 months. Participants (N = 930) completed an online survey that assessed sociodemographic characteristics and the Alcohol Smoking and Substance Involvement Screening Test (ASSIST). ASSIST scores were used to identify the need for brief intervention for cannabis, cocaine, methamphetamine, inhalants, sedatives, hallucinogens, opioids, and sex drugs. Binary and multinomial logistic regression examined the associations between sociodemographic characteristics and the need for brief intervention for cannabis use only versus brief interventions for cannabis use and another drug.
Results: ASSIST scores suggested that approximately 54.6% of the sample did not need a brief intervention for any substance, 30.0% needed a brief intervention for cannabis use only, and 15.4% needed a brief intervention for cannabis use and another drug. Participants who needed a brief intervention for cannabis use had higher odds of requiring a brief intervention for cocaine (AOR = 3.07, 95% CI = 1.67, 5.64), methamphetamine (AOR = 8.62, 95% CI = 3.78, 19.65), inhalants (AOR = 4.75, 95% CI = 2.95, 7.65), sedatives (AOR = 3.72, 95% CI = 2.06, 6.78), hallucinogens (AOR = 4.95, 95% CI = 2.65, 9.25), and sex drugs (AOR = 3.70, 95% CI = 1.94, 7.08). Participants who identified as Hispanic, not Black and Black, not Hispanic had lower odds than participants who identified as both Black and Hispanic of needing brief interventions for cannabis use and another drug than brief intervention for cannabis use only.
Conclusions: Black and Hispanic SMM who need of brief interventions for marijuana use are likely to need brief polysubstance use interventions. Polysubstance use screening and provision of brief interventions are recommended in healthcare settings.
Financial Support: T32DA031099 (Hasin) K01DA047918-04 (Watson)

ORAL COMMUNICATION: GAPAPENTIN: FRIEND OR FOE?
Governor's Square 15

EFFECTS OF GABAPENTINOIDS ON HEROIN SELF-ADMINISTRATION IN MALE AND FEMALE RATS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavioral Pharmacology
Aim: A growing body of epidemiological evidence suggests increasing misuse of gabapentin, (a calcium channel inhibitor used to treat some neuropathic pain conditions) in people with opioid use disorder. Over the past decade, gabapentinoids have become increasingly prevalent in opioid overdose deaths. Despite these trends little research has evaluated interactions related to misuse (e.g., reinforcing effects) between gabapentin and opioids. The aim of this study was to determine the effects of gabapentin on heroin self-administration in male and female rats.
Methods: Eight male and female Sprague-Dawley rats were trained to self-administer heroin (0.01 mg/kg) under a progressive ratio schedule of reinforcement. Dose-effect curves for heroin (0.0032-0.1 mg/kg/infusion) were determined following pretreatment with gabapentin (1-32 mg/kg; i.v.) or saline. Control dose-effect curves for heroin following saline pretreatment were compared across sexes, while the effects of gabapentin pretreatment were determined by comparing heroin dose-effect curves determined following gabapentin pretreatment to the control dose-effect curve for heroin within each sex.
Results: Male and female Sprague-Dawley rats self-administered heroin in a dose-dependent manner, with the greatest number of infusions (~8) earned at a unit dose of 0.032 mg/kg in both males and females. No sex differences were observed in the self-administration of heroin under control conditions. The number of infusions earned of low doses (0.0032 and 0.01 mg/kg/infusion) of heroin was significantly increased (by ~2 infusions) following pretreatment with 10 and 32 mg/kg gabapentin in male rats. Pretreatment with gabapentin did not alter heroin self-administration in female rats at any dose.
Conclusions: Gabapentin enhanced the reinforcing effects of low doses of heroin in male rats. Interestingly, gabapentinoids did not alter heroin self-administration in female rats. These findings are consistent with epidemiological data suggesting gabapentinoid co-use with opioids is more prevalent in males. Future studies will confirm the selectivity of this enhancement for opioids and further investigate sex-differences in the behavioral effects of gabapentinoids.
Financial Support: Welch Foundation AQ-0039, Texas Research Society on Alcoholism John P. McGovern Fellowship

THE IMPACT OF FENTANYL ON TREATMENT OUTCOMES DURING AN OUTPATIENT BUPRENORPHINE TAPER WITH ADJUNCT GABAPENTIN

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Drug Category Opiates/Opioids
Topic Treatment
Aim: We previously reported that adjunct gabapentin (GBP) had no significant impact on craving, withdrawal, opioid use or the proportion of participants with a history of prescription opioid use disorder who completed a 10-day buprenorphine (BUP) taper in a randomized, placebo (PLA)-controlled clinical trial. Given that fentanyl (FEN) use – currently the primary driver in opioid overdoses – became common part-way through trial enrollment, this study reports on findings from a subset of individuals who underwent urine toxicology test during screening that included FEN to determine the potential impact of recent FEN use on these outcomes.
Methods: Fifty-six participants with a fentanyl (FEN) screening result participated in the detoxification portion of a randomized, double-blind, placebo-controlled trial. During this 3-week phase, participants attended clinic 5-6 days per week to receive study medications, attend weekly therapy, and complete assessments, including thrice-weekly urine toxicology screens. Participants were inducted onto 12 mg buprenorphine daily by day 2 of week 1 and randomized to PLA or GBP (800 mg BID) starting on day 3 of week 1. A 10-day BUP taper began on day 3 of week 2, with the final dose administered on day 5 of week 3. Participants returned on day 1 of week 4 to complete assessments and potentially start oral (naltrexone) NTX induction and transition to Vivitrol.

Results: Of the 56 participants with a FEN screening result at intake, 42 (75%) had a positive FEN screening result. Of the 36 (64.3%) that completed BUP taper, 33.3% had a positive FEN result. Although FEN result did not differentially impact opioid use between GPB/PLA groups, participants with a negative FEN screening result had significantly lower rates of opioid-positive urines than those with a positive FEN screen result (-2.1884, $p < 0.0001$).
Conclusions: FEN- positive drug screens might be associated with poorer outcomes during a BUP-assisted taper.
Financial Support: This work is supported by NIDA grant R01DA036544 and authors have no disclosures.

GABAPENTIN UTILIZATION AMONG BUPRENORPHINE-PRESCRIBED INDIVIDUALS WITH OPIOID USE DISORDER AND ASSOCIATED RISK OF OVERDOSE

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Aim: Gabapentin prescriptions have drastically increased in the United States due to off-label prescribing in multiple settings such as opioid use disorder (OUD) treatment, to manage a range of symptoms and comorbid conditions. While recent reports have highlighted the potential role and risk of gabapentin in opioid overdoses, there is little information on the prevalence, purpose, and associated risks of off-label gabapentin prescribing in OUD treatment.
Methods: Administrative claims data from IBM MarketScan (2006-2016) were used to investigate initiation of gabapentin within 60 days of buprenorphine initiation in persons (n=109,407) diagnosed with OUD. Analyses included prevalence of, and characteristics/conditions associated with, gabapentin initiation, as well as the estimated risk of hospitalization between days with versus without active gabapentin, buprenorphine, or both prescriptions.
Results: Gabapentin was initiated in 31.9% of persons with OUD prescribed buprenorphine. Gabapentin was significantly less likely to be prescribed to Black or Hispanic patients, and more likely to be prescribed to females, those with co-occurring substance use or mood disorders, and those with comorbid physical conditions (i.e., chronic pain). Days of only gabapentin use was not significantly associated with hospitalization (OR=0.96, 0.88-1.03). However, days with gabapentin and buprenorphine use was significantly associated with a decreased odds of hospitalization (OR=0.66, 0.58-0.75).
Conclusions: Gabapentin is frequently utilized in buprenorphine maintenance of OUD and is associated with a myriad of comorbid conditions. Despite minimal evidence on best practices (i.e., dosages) and outcomes for gabapentin prescribing in OUD treatment, and reports on gabapentin-involved overdoses, these data suggest that gabapentin was not associated with an increased risk of overdose alone, or alongside buprenorphine. More data on the safety profile of gabapentin in OUD settings is urgently needed.
Financial Support: This work was supported by a grant from NIDA (T32: 5T32DA015035-13).

GABAPENTIN PRESCRIBING PATTERNS IN PATIENTS TREATED FOR ALCOHOL USE DISORDER

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Drug Category Alcohol
Topic Treatment
Aim: The use of gabapentin in combination with opioids has become controversial with studies suggesting that gabapentin may enhance the effects of opioids and increase the risk of opioid-related overdose, particularly at high doses. Gabapentin is used to treat alcohol use disorder (AUD) but little is known about gabapentin in this population. Here we present data on gabapentin prescribing to a large population of patients treated for AUD.
Methods: The number of gabapentin prescriptions and mg/day gabapentin prescribed between 1/2017 and 12/2022 were assessed in 6166 consecutive patients; no patients were excluded. Ria treats AUD with

coaching and medications including gabapentin; clinical outcomes of World Health Organization (WHO) risk levels for alcohol consumption (an accepted measure of treatment response) and retention in treatment were assessed.
Results: Gabapentin was prescribed to 3145 Ria patients, with 13,083 prescriptions issued. The median and modal doses of gabapentin were 900 mg/day. Gabapentin was prescribed alone or in combination with naltrexone, baclofen, topiramate or acamprosate; most gabapentin prescriptions were in combination with naltrexone. Of the prescriptions issued only 1 was for more than 3600 mg/day (5400 mg/day X 30 days). Clinical outcomes were good. At 180 days 57.6% of patients were retained in treatment and 58.4% achieved a two level reduction in WHO alcohol risk scores; a clinically meaningful endpoint.
Conclusions: Gabapentin appears safe and effective in patients with AUD. Median and modal doses are relatively low with little evidence of potentially excessive dosing. Although gabapentin may be misused with opioids there is little evidence of misuse in an AUD treatment population. DEA scheduling can increase barriers to prescribing which can decrease access to safe and effective medications. Adding barriers to gabapentin prescribing may have the unintended consequence of harming patients.
Financial Support: Ria Health

ORAL COMMUNICATION: CRIMINAL JUSTICE: DANGERS UPON RELEASE
Plaza Ballroom D

JAIL-BASED MEDICATION FOR OPIOID USE DISORDER AND PATTERNS OF COMMUNITY RE-ENTRY AFTER RELEASE: A SEQUENCE ANALYSIS

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Drug Category Opiates/Opioids
Topic Criminal Justice
Aim: Jail-based medication for opioid use disorder (MOUD) (e.g., methadone, buprenorphine) may support a successful transition to the community and reduce adverse outcomes including hospitalization and return to jail. I. This study aimed to 1) using 3-year post-release recidivism, emergency department visit, and hospitalizations data, define re-entry patterns by applying sequence analysis methods and 2) using marginal multinomial logistic regression, measure the association between in-jail MOUD vs out of treatment (referent) and a pattern defined by rare occurrence of reincarceration and preventable healthcare utilization (= stability pattern) vs patterns defined by instability factors.
Methods: Data came from a retrospective, observational cohort study of 6066 adults with opioid use disorder who were incarcerated in New York City jails and released to the community during 2011-14. We performed propensity score matching to address confounding, considering approximately 25 baseline demographic, clinical, behavioral, housing, and criminal legal characteristics.
Results: Forty-two percent had in-jail MOUD three days before discharge and 58% were out of treatment. Five re-entry patterns were identified: stability (64%), hospitalization (23%), delayed reincarceration (7%), immediate reincarceration (4%), and continuous incarceration (2%). After addressing confounding, 64% of the MOUD group was defined by the stability pattern vs 54% of the out-of-treatment groups. In 2012-14, the prevalence of the stability pattern increased year-by-year with a consistently higher prevalence observed among those with in-jail MOUD.
Conclusions: Sequence analysis helped define post-release stability based on health and criminal legal system involvement, which are both highly relevant to defining successful re-entry. Future studies in other samples that aim to assess how MOUD predicts stability should consider both health and recidivism experiences.
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IDENTIFYING STRUCTURAL RISK FACTORS FOR OVERDOSE FOLLOWING INCARCERATION: A CONCEPT MAPPING STUDY

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Drug Category Opiates/Opioids
Topic Criminal Justice
Aim: To identify perceived factors that impact overdose following release from incarceration among people with lived experience.
Methods: Within a community-based participatory approach to research, we used concept mapping to center the perspectives of people with personal experience with the carceral system or those who work with such individuals. We developed a focused prompt for participants: "What do you think are some of the main things that make people who have been in jail or prison more and less likely to overdose?" Individuals participated in three rounds of focus groups as is standard in concept mapping, which included brainstorming, sorting and rating, and community interpretation. We used the Concept Systems Inc. platform groupwisdom™ for our analyses. We constructed cluster maps to analyze the importance of each of the clusters and factors in relation to the rating questions.
Results: Nine people (ages 33 to 53) from four states consented to participate. For each of the three focus groups, there were a total of 7 attendees. The brainstorming process resulted in 83 unique factors that impact overdose ranging from housing and employment to stigma to conditions of incarceration and self-perception. Commonly, mental health and treatment for other comorbidities were noted as factors. The concept mapping process resulted in 5 clusters that included 1) Community-Based Prevention, 2) Intersection of Drug Use and Incarceration, 3) Resources for Treatment for Substance Use, 4) Carceral Factors, and 5) Stigma and Structural Barriers. Community-based prevention (cluster 1) and stigma and structural barriers (cluster 5) were the largest and most contributory clusters. Resources for treatment for substance use (cluster 3) and intersection of drug use and incarceration (cluster 2) were furthest apart.
Conclusions: Our study provides important insight into community-identified factors associated with overdose following incarceration. These factors should be accounted for during resource planning and decision-making.
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RECENT INCARCERATION, SUBSTANCE USE, OVERDOSE, AND TREATMENT AMONG RURAL PEOPLE WHO USE DRUGS

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Drug Category Opiates/Opioids
Topic Criminal Justice
Aim: Approximately 60% of people in US jails and prisons have an active substance use disorder (SUD) and experience a high risk of overdose death upon release. Little is known about drug use and access to SUD treatment following incarceration in rural communities. We assessed associations between incarceration, substance use, overdose, and treatment with medication for opioid use disorder (MOUD) in a sample of people who use nonprescribed opioids or inject drugs across 65 rural counties.
Methods: Data are from the cross-sectional Rural Opioids Initiative survey (2018-2020). Recent incarceration was defined as at least one night in prison or jail in the last six months. Outcomes included

past 30-day substance use, past six-month opioid overdose, and lifetime and past 30-day treatment with MOUD. Mixed-effects regression models were used to estimate associations between recent incarceration and study outcomes, controlling for study and demographic and substance use-related covariates.
Results: Average age of survey participants (N=2,938) was 36 years, and most were male (57%) and White (85%). Forty-two percent were recently incarcerated. Recent incarceration was more prevalent for men (62%), houseless participants (60%), and persons who inject drugs daily (62%). Recent fentanyl use (aOR = 1.32), methamphetamine use (aOR = 1.46), and overdose (aOR = 1.5) were associated with recent incarceration (all $p < .001$). Lifetime use of MOUD was higher among recently incarcerated participants (aOR = 1.19, $p = .03$) but past 30-day MOUD treatment did not differ between groups.
Conclusions: Among rural people who use illicit opioids or inject drugs, recent incarceration was significantly associated with indicators of greater SUD severity and overdose. While lifetime history of MOUD treatment was higher in the group with recent incarceration, recent treatment was not. These findings demonstrate an urgent need for increased opportunities for treatment, including MOUD, in rural jails and prisons.
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BARRIERS AND OPPORTUNITIES TO LINK PEOPLE RELEASED FROM CLOSED-SETTING REHABILITATION CENTERS TO COMMUNITY-BASED SERVICES IN VIETNAM

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Harm Reduction
Aim: Closed-setting drug rehabilitation is a major governmental response to substance use disorders (SUD) in Vietnam. Long-term closed-setting rehab is associated with negative health, social and economic outcomes. We explored the barriers and opportunities to link people with SUD (PWSUD) released from closed-setting rehabs to pro-recovery services.
Methods: Between Oct. 2021 and Aug. 2022, we interviewed PWSUD returning from or about to leave closed-setting rehabs (n=30), their family members (n=30), and addiction professionals (n=30) in three cities across North, South and the Center of Vietnam. Interviews probed post-release concerns, how the current drug policies met their needs, and recommendations for improving linkage to care.
Results: Lack of outpatient drug treatment services other than methadone made closed-setting rehab the default option to relieve families of PWSUD-related emotional and financial burdens and increased the likelihood of subsequent detention given that relapse was common upon release. Respondents indicated that programmatic support to PWSUD has decreased compared to a decade ago. While current policies emphasize support for job placement as well as access to substance use and HIV treatment, most PSWUD could access health services but find employment support absent or unfriendly and ineffective. The connection between the closed-setting rehabilitation and community-based services and among community-based services was weak. Individual-level factors including stigma and low socioeconomic background contributed to the struggles of PSWUD. Facilitative factors included family support, shorter stay in closed settings, greater accessibility of methadone and HIV services, and peer support.
Conclusions: There exist barriers but also opportunities to support recovery process of PSWUD who are released from closed settings. Specific recommendations include greater options for community-based drug treatment, improving and enforcing current supportive policies, and increased support to their families.
Financial Support: NIH R01DA040510

ORAL COMMUNICATION: UNCERTAINTY AS A DRIVER OF SUDS
Governor's Square 15

RESISTANCE OF COCAINE AND FOOD REINFORCEMENT TO EXTINCTION AND PUNISHMENT UNDER FIXED VS. VARIABLE SCHEDULES IN MALE AND FEMALE RHESUS MONKEYS

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Drug Category Stimulants
Topic Behavioral Pharmacology
Aim: Uncertainty in the time and effort required to obtain a drug may be a significant determinant of the reinforcing effects of illicit substances and in the inability of legal restriction and negative consequences to deter substance use. The goal of this study was to determine whether behavior maintained by a variable-ratio (VR) schedule of cocaine reinforcement would be more resistant to extinction and punishment compared with a fixed-ratio (FR) schedule.
Methods: A group of male (n=5) and female (n=6) rhesus monkeys self-administered cocaine (0.03 or 0.1 mg/kg/infusion) or food (4 pellets/delivery) under a single-lever access, FR or VR 200 schedule of reinforcement. During extinction, saline was substituted for cocaine or food, and during punishment, cocaine (0.03 or 0.1 mg/kg/infusion) or food (4 pellets/delivery) was administered in combination with a known drug punisher (histamine; 0.001-0.1 mg/kg/infusion).
Results: The average number of sessions required to meet extinction criteria were greater during VR compared with FR conditions, particularly with food and the lower cocaine dose. Similarly, resistance to punishment was greater during VR compared with FR conditions, indicated by higher response rates, and the effect was more robust with cocaine than food.
Conclusions: Our findings suggest that uncertainty in the time and effort required to obtain a drug may contribute to perseverative substance use and decreased sensitivity to negative consequences associated with drug seeking and taking. These results support the use of therapeutic efforts aimed at reducing the uncertainty of illicit drugs that exists in the environment, perhaps through an agonist-medication approach.
Financial Support: DA045011 (SLH), DA054177 (SLH), DA039167 (KBF)

PRESERVED NEURAL ENCODING OF SUBJECTIVE VALUATION UNDER UNCERTAINTY IN HUMAN OPIOID ADDICTION

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Drug Category Opiates/Opioids
Topic Neurobiology/Neuroscience
Aim: Opioid use disorder (OUD) is associated with increased risk-taking, which is thought to occur through increased valuation of actions associated with uncertain outcomes. One posited computational mechanism for this increase in valuation is the maladaptive computation and encoding of subjective value (SV) based on individual preferences for uncertainty. Previously, uncertainty preferences have been linked to clinical outcomes in OUD. Here, using functional brain imaging, we examined whether uncertainty preferences in people with OUD reflect a normative, value-based process or a breakdown of value computations in the brain's valuation system.
Methods: Treatment-engaged OUD patients (n=31; 7 females; mean [SE] age=45.7 [2.2] years) and matched controls (n=28; 11 females; age=45.4 [2.8] years) completed a decision-making fMRI task targeting two types of uncertainty, known-risk and ambiguity. A modified utility model parameterizing uncertainty was used to compute trial-by-trial SV of the chosen option. Model-based fMRI analyses were used to identify regions encoding chosen SV and assess the influence of uncertainty preferences on the value circuit.
Results: Behaviorally, most subjects were averse to uncertainty (76%; consistent with previous research), without group differences. Neurally, we found that canonical value areas encode the SV of the chosen option similarly across the OUD and control groups ($p<0.001$; ventromedial prefrontal cortex, $t=4.81$; ventral striatum, $t=4.35$; posterior cingulate, $t=5.09$). In addition, there were no differences in these correlates or between groups when uncertainty was split by type, either known-risk or ambiguity.

Conclusions: Contrary to prevailing assumptions, these results imply that the encoding and computation of SV is preserved in people with OUD. Instead, risk-taking observed in OUD may arise from changes in the subjective integration of variables used to compute value. That is, people with OUD do not have 'faulty' valuation or use different decision strategies, but rather differences emerge from subjective (biased) encoding of decision variables consistent with idiosyncratic preferences.
Financial Support: This work was supported by grants from Busch Biomedical Research Program and the National Institute on Drug Abuse (R01DA053282 to ABK).

COMPUTATIONAL MODELING OF EFFORT-BASED DECISION MAKING IN COCAINE USE DISORDER

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Drug Category Stimulants
Topic Behavioral Economics
Aim: Cocaine use disorder (CUD) is characterized by decision-making impairments that may drive CUD symptoms. We used computational modeling to examine how people with CUD integrate information about reward probability and amount into decisions about exerting effort. Prior research shows that difficulty incorporating information about reward probability and amount into decisions relates to more severe negative symptoms of schizophrenia. Thus, we hypothesized that people with CUD who incorporated less information about reward probability and amount into their decisions would show greater anhedonia and more severe CUD.
Methods: This was a secondary analysis of data from a clinical trial (NCT02773212). Participants (N = 50) with at least moderate CUD completed measures of cocaine use severity (composite amount, frequency and consequences of use), anhedonia (Snaith-Hamilton Pleasure Scale; SHAPS) and the Effort-Expenditure for Rewards Task (EEfRT). We conducted computational modeling of EEfRT choices to produce Bayesian Information Criterion difference scores (ΔBIC) indicating the extent to which participants' decisions were fit by a subjective value model incorporating probability and amount vs. a "bias model" not using this information. We then correlated Δ BIC with SHAPS and CUD severity scores.
Results: The majority (64%) of participants were best fit by the bias model. Correlational analysis indicated no significant relationship between Δ BIC and SHAPS ($r = -0.19$, $p = 0.20$), or CUD severity ($r = -0.17$, $p = 0.24$).
Conclusions: We did not find a significant relationship between anhedonia or CUD severity and use of probability and amount information in effort-based decision-making. However, the low rate at which people with CUD incorporated reward information into decision-making is concerning. Although reward-based contingency management is the most effective CUD treatment, it is still only successful in a minority of patients. Failure to use reward-related information when deciding whether to exert effort could explain low success rates for this treatment.
Financial Support: National Institute on Drug Abuse K08DA040006 to MCW

ACCESS TO NO-COST PHARMACEUTICAL ALTERNATIVES TO ILLICIT DRUGS DURING INTERSECTING COVID-19 AND OVERDOSE HEALTH EMERGENCIES IN BRITISH COLUMBIA, CANADA: A QUALITATIVE STUDY

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Drug Category Opiates/Opioids
Topic Harm Reduction
Aim: In response to anticipated COVID-19-related disruptions to overdose prevention and substance use disorder treatment services, British Columbia, Canada released new prescribing guidelines in 2020 – termed 'risk mitigation guidelines' – to facilitate access to pharmaceutical opioids (hydromorphone, diamorphine) and stimulants (dextroamphetamine, methylphenidate) for people who use drugs (PWUD) outside of a

treatment context as an alternative to an increasingly toxic drug supply characterized by fentanyl and other adulterants. This qualitative study was undertaken to examine dynamics that shaped access to these pharmaceutical alternatives among people who use drugs.
Methods: From February to July 2021, we conducted telephone-based qualitative interviews with 40 people who use drugs recruited from across British Columbia, Canada, who accessed prescription opioids (hydromorphone, diamorphine) or stimulants (dextroamphetamine, methylphenidate) under the risk mitigation prescribing guidelines. Data were imported into NVivo, analyzed thematically, and interpreted by drawing on the risk environment framework and concept of structural vulnerability.
Results: Participants expressed that decisions to access pharmaceutical alternatives were motivated by ongoing changes to overdose risk environment during the COVID-19 pandemic, including disruptions to supervised consumption services and peer support networks due to social distancing and greater unpredictability of drug markets (e.g., fluctuations in drug potency and adulterants, disrupted access to regular dealers). Most participants access prescriptions through primary care practitioners or addiction medicine specialists working in connection with low-threshold services targeting structurally vulnerable PWUD. While this program limited exposure to the illicit drug supply, the uneven distribution of addiction medicine supports across the province and onerous program requirements were not fully responsive to structural vulnerabilities experienced by participants. Common program requirements, such as daily pharmacy pick-up and regular medical appointments, were incompatible with the often precarious survival routines and structural vulnerabilities of participants, including periods of housing vulnerability, geographic distance to pharmacies, and sporadic income generating opportunities. Participants emphasized how these program shortcomings undermined the program's effectiveness, as most participants continued to use illicit drugs when unable to rely on access prescription alternatives.
Conclusions: While prescription alternatives to illicit drugs represent a promising strategy for limiting exposure to an increasingly toxic drug supply, it is crucial that these harm reduction measures are implemented in ways responsive to the structural vulnerabilities that shape access among PWUD. Lower-threshold approaches and complementary structural supports, including take-home dosing, tele-health prescribing, and transportation services, are likely necessary to maximize their benefits.
Financial Support: National Institutes of Health (R01DA044181); Canadian Institutes for Health Research

ORAL COMMUNICATION: ALCOHOL TREATMENT DEVELOPMENT
Plaza Ballroom A

EVALUATION OF CANNABIDIOL (CBD) AS A POTENTIAL MEDICATION FOR ALCOHOL USE DISORDER (AUD) – RESULTS FROM A PRECLINICAL DRINKING MODEL IN BABOONS

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Drug Category Alcohol
Topic Treatment
Aim: The cannabinoid cannabidiol (CBD) is currently under investigation as a pharmacotherapy for alcohol use disorder. The aim of the present study was to examine whether acute and chronic treatment with pure CBD would decrease alcohol seeking and consumption behaviors or alter drinking patterns in male baboons with extensive histories of daily alcohol intake (1g/kg/day).
Methods: Seven male baboons self-administered oral alcohol (4% w/v) under a validated chained schedule of reinforcement (CSR) procedure that modeled periods of anticipation (Component 1), seeking (Component 2), and consumption (Component 3). Alcohol was only available in Component 3. In Experiment 1, pure CBD (5-40 mg/kg) or vehicle (USP, sesame oil) was administered orally 15- or 90-minutes prior to the start of the session. In Experiment 2, oral doses of CBD (10-40 mg/kg) or vehicle were administered for 5 consecutive days during ongoing alcohol access under the CSR. In addition, behavioral observations were conducted to assess potential drug side effects (e.g., sedation, motor incoordination) following chronic CBD treatment immediately after session and 24-hours after drug administration.

Results: Across both experiments, baboons self-administered an average of 1 g/kg/day of alcohol under baseline conditions. Administration of acute CBD at doses that encompassed purported therapeutic range (150 – 1200 mg total CBD dose/day) did not significantly reduce alcohol seeking, self-administration or intake (g/kg) and drinking patterns (i.e., number of drinks/bout, bout duration nor interdrink interval) also were not altered. Chronic CBD treatment also did not significantly reduce alcohol seeking or self-administration behavior, alcohol intake, or pattern of alcohol drinking. There were no observable behavioral disruptions following CBD treatment.
Conclusions: In sum, the current data do not support use of pure CBD as an effective pharmacotherapy in the treatment of alcohol use disorder.
Financial Support: NIH/NIAAA R01AA015971

THE ACTIVE ALKALOID OF KRATOM ALONE AND IN COMBINATION WITH NALTREXONE SUPPRESSES OPERANT ALCOHOL SELF-ADMINISTRATION AND ALTERS CFOS EXPRESSION IN BRAIN REWARD REGIONS

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Drug Category Alcohol
Topic Behavioral Pharmacology
Aim: The leaves of the Mitragyna speciosa (kratom) tree contain the alkaloid mitragynine (MG) that is commonly used for relief from pain and opioid withdrawal. This and other evidence suggest MG's effects are mediated through opioid receptors. Kratom also attenuates alcohol withdrawal and consumption in mice. The mu opioid antagonist naltrexone (NTX) reduces alcohol self-administration. Therefore, we tested MG, NTX, and their combination on operant alcohol self-administration in rats.
Methods: Ten female Sprague Dawley rats trained to lever press for alcohol (10%, w/v) under a fixed ratio 2 schedule of reinforcement were tested in standard operant chambers after MG (0.3-3.0 mg/kg, IP) and NTX (0.3-3.0 mg/kg, IP) alone and in combination. Numbers of active and inactive lever presses, reinforcers earned, head entries, and estimated alcohol consumed were recorded. Four separate groups of rats (n=4 each) were assessed for locomotor activity following MG, NTX, or its combination (3.0 mg/kg) and their brains processed to determine cFos expression using immunohistochemistry.
Results: Alcohol self-administration was suppressed by both MG and NTX alone (P's<0.0001); however, the combination had a greater effect than either drug alone (P's<0.01). MG and NTX combined also enhanced cFos expression in several brain regions more than either drug alone (P's<0.01). No effects on locomotor activity were seen.
Conclusions: Both MG and NTX alone and their combination decreased alcohol reinforcement with the greatest effect occurring with the combined treatment. Similar effects were seen in cFos expression. The decreases in alcohol self-administration were not due to non-specific depression of activity levels. Surprisingly, the mu antagonist, NTX, did not block the suppression of alcohol self-administration by MG that suggests it works through alternative mechanisms potentially through delta opioid receptors.
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TRANSCRANIAL DIRECT CURRENT STIMULATION TREATMENT IN PATIENTS WITH ALCOHOL DEPENDENCE: A RANDOMIZED SHAM-CONTROLLED TRIAL

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Drug Category Alcohol
Topic Treatment

Aim: Craving is a critical symptom of addiction and significantly predictive of relapse. Transcranial direct current stimulation (tDCS) has been implied as a potential approach to reduce craving. This study aimed to investigate the safety and effectiveness of tDCS on craving and substance treatment outcomes in patients with alcohol dependence.
Methods: Patients with alcohol dependence (severe alcohol use disorder) were enrolled in the study. Participants were randomized to two groups after two weeks of detoxification: 1) tDCS, and 2) sham, and received a total of 10 tDCS sessions over two weeks. Demographic data, alcohol and other substance use data were collected. The following data were gathered before (T0: week 0), during (T1: week 1), after (T2: week 2), and at follow-up (T3: week 4) to assess symptoms of craving, motivation, and other emotional symptoms: Visual Analog Scale (VAS), Penn Alcohol Craving Scale (PACS), Severity of Alcohol Dependence Questionnaire (SADQ), Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Alcohol Relapse Risk Scale (ARRS), Obsessive Compulsive Drinking Scale (OCDS), Penn Alcohol Craving Scale (PACS), Alcohol Craving Questionnaire-Short Form-Revised (ACQ-SF-R), and Alcohol Withdrawal Self The Alcohol Abstinence Self-Efficacy Scale (AASE).
Results: 37 patients with alcohol dependence were randomly assigned in 2:1 ratio to 26 in the tDCS group and 11 in the sham group. A total of 2 in the tDCS group and 2 in the sham group dropped out. Using repeated measure ANOVA, significant improvements in VAS, PACS, OCDS, ARRS, BDI, BAI, and AASE scores were found in both the tDCS and sham groups after the intervention, but the differences between the two groups were not statistically significant.
Conclusions: This study revealed that tDCS is a safe brain stimulation method with few adverse effects exclusive of seizures in patients with alcohol dependence. This preliminary study suggest tDCS might have potential as an adjunct to addiction treatment.
Financial Support: This work was supported by grants from Taipei City Government (TPECH-10708107)

USING A CASCADE OF CARE FRAMEWORK TO IDENTIFY GAPS IN ACCESS TO MEDICATIONS FOR ALCOHOL USE DISORDER IN BRITISH COLUMBIA, CANADA

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Drug Category Alcohol
Topic Health Services
Aim: Despite the significant burden of alcohol use disorder (AUD) and availability of safe and effective medications for AUD (MAUD), population-level estimates of access and engagement in AUD-related care are limited. The aims of this study were to generate a cascade of care for AUD in British Columbia (BC), Canada, and to estimate the impacts of MAUD on health outcomes.
Methods: Retrospective cohort study using linked administrative health data. Using a 20% random sample of BC residents, we identified 3,566 people with moderate-to-severe alcohol use disorder (PWAUD; overall prevalence = 0.32%) between 2015-2018. We developed a six-stage AUD cascade (from diagnosis to ≥ 6 months retention in MAUD) among PWAUD. We evaluated trends over time and estimated the impacts of access to MAUD on AUD-related hospitalizations, emergency department visits and death.
Results: Between 2015 and 2018, linkage to AUD-related care was relatively stable (approximately 50%). However, rates of MAUD initiation (24.4% to 39.3%), and retention for ≥1 (15.7% to 26.9%), ≥3 (2.7% to 5.9%), or ≥6 months (0.6% to 1.7%) increased significantly. In adjusted analyses, access to MAUD was associated with reduced odds of experiencing any AUD-related adverse outcomes, with longer retention in MAUD showing a trend to greater odds reduction: Adjusted Odds Ratio (95% Confidence Interval) ranging from 0.23 (0.17–0.29) for MAUD retention <1 month to 0.10 (0.03–0.29) for ≥6 months retention.
Conclusions: Access to MAUD among PWAUD in BC increased between 2015-2018. However, in 2018 >60% of PWAUD were not dispensed MAUD, and <6% were retained in MAUD for ≥3 months. There was a trend between longer retention in MAUD and greater reductions in the odds of experiencing AUD-related adverse outcomes, supporting the need to address disparities in access to and retention in MAUD.
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ORAL COMMUNICATION: PRECLINICAL NEURO EFFECTS OF METHAMPHETAMINE
Plaza Ballroom D

THE IMPORTANCE OF THE PERIRHINAL CORTEX TO THE NUCLEUS ACCUMBENS CIRCUIT FOR NOVELTY DISCRIMINATION IN METHAMPHETAMINE SELF-ADMINISTERING RATS

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Drug Category Stimulants
Topic Neurobiology/Neuroscience
Aim: We hypothesize that the perirhinal cortex (PRH; memory)- nucleus accumbens core (NAc; cue recognition) circuit is a link between meth-induced memory deficits and relapse during abstinence. Our aim is to determine the behavioral relevance of this circuit.
Methods: Long-access (LgA,6 hr, daily) meth self-administration (SA) produces focused responding on a meth-associated lever but short-access (ShA, 1 hr, daily) meth SA results in equal responding on both novel- and meth-associated levers. Male and female Sprague-Dawley rats underwent meth SA for 21 days with 1 week of abstinence. Afterwards, we inactivated or activated the PRH-NAc circuit in ShA and LgA rats, respectively, using a dual-viral chemogenetic approach. Rats were injected with Clozapine-N-oxide (CNO; 10 mg/kg, ip) or vehicle (Veh, saline, ip) prior to access to both novel- and meth-associated levers (ShA-hM4D(Gi)-CNO n=13; ShA-hM4D(Gi)-Veh n=13; LgA-CNO n=8; LgA-Veh n=7).
Results: Inactivation in ShA rats (CNO) increased responding on the meth-lever relative to the novel, whereas Veh resulted in similar responding on both levers. Mixed effects analysis: Injection x Lever [$F(2,35)=4.293$; $p = 0.0215$]; and Lever [$F(2,36)=35.23$; $p < 0.0001$]. Unexpectedly, activation of the circuit in LgA rats (CNO) had no behavioral effect. Mixed effects analysis: Injection x Lever [$F(2,38)=3.690$; $p = 0.0343$]; Injection [$F(1,38)=17.88$; $p = 0.0001$]; and Lever [$F(2,38)=24.33$; $p <0.0001$].
Conclusions: Inhibition of PRH-NAc in a ShA procedure is sufficient to shift behavior, however, activating the pathway in LgA procedure is not sufficient to shift focus from meth associated cues back to novel stimuli.
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NEURAL CIRCUITRY IN OBJECT RECOGNITION MEMORY AND METHAMPHETAMINE ADDICTION

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Drug Category Stimulants
Topic Neurobiology/Neuroscience
Aim: We hypothesize that the reciprocal projection between the perirhinal cortex (PRH) - Prefrontal Cortex (PFC) circuit is important for meth-induced novel object memory deficits. Here, we determined the PRH-PFC is the primary direction of communication involved in this memory process that is suspect to functional changes following chronic methamphetamine.
Methods: Male and female (N=52) rats were used to test the importance of the PRH projection to the PFC in drug-naïve and meth-self-administering rats in 3 separate experiments. 1) First retrograde AAV-GFP virus was infused into the PRH or PFC before performing Novel Object Recognition (NOR), then c-Fos+ and GFP+ cells were counted in the terminal areas. 2) To determine the role of the PRH-PFC circuit in meth-induced memory deficits, we used a dual-viral chemogenetic approach. Rats (N=56) underwent meth SA or were drug naïve. The PRH-PFC was inactivated or activated with Clozapine-N-oxide (CNO). Control

rats received vehicle. 3) To gain a brain-wide understanding of meth-induced memory deficits. Rats (N=8) underwent meth (4 mg/kg x 4 injections, two-hour intervals) or saline, and 7 days later were tested for NOR deficits. The brains were cleared with AdipoClear, and brain-wide c-Fos levels were measured.
Results: First, we found Fos+/GFP+ were increased in the PRH (t-test, $p<0.05$), but not the PFC in response to novel objects. Second, inhibition of the PRH-PFC circuit caused NOR deficits, whereas activation of the PRH-PFC circuit restored meth-induced NOR deficits (t-tests, p's<0.05). Finally, whole-brain c-Fos mapping reveals distinct activation patterns between meth and saline rats.
Conclusions: Our data indicate that the PRH to PFC mediates recognition of novel objects and meth-induced cognitive sequela. However, it is unknown if meth-induced deficits in NOR are due to changes in memory impairment or also involve changes in novelty salience.
Financial Support: NIDA R01 DA033049 (CMR) and NIDA T32 DA007288 (STG)

DIRECT PATHWAY SPINY PROJECTION NEURON INTRINSIC EXCITABILITY IS INCREASED IN THE DORSOLATERAL STRIATUM DURING ACUTE BUT NOT PROTRACTED ABSTINENCE FROM METHAMPHETAMINE SELF-ADMINISTRATION

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Drug Category Stimulants
Topic Neurobiology/Neuroscience
Aim: Methamphetamine (meth) is a potent psychostimulant. Our recent study found that indirect pathway spiny projection neuron (iSPN) excitability in the dorsomedial striatum (DMS) was increased during acute and decreased during protracted abstinence from non-contingent meth administration whereas DMS direct pathway spiny projection neuron (dSPN) excitability was unchanged (Choi et al., Sci Rep. 12(1): 12116, 2022). The goal of the current study was to examine SPN excitability in the dorsolateral striatum (DLS) using a mouse model of meth self-administration (MSA).
Methods: Male mice (>8 weeks) expressing eGFP and tdTomato under Drd2 and Drd1a receptor regulatory elements, respectively, were implanted with jugular vein catheters and allowed to self-administer meth (0.1mg/kg/infusion) for 10 days (2hr/day) on a fixed ratio 1 schedule of reinforcement; saline-yoked control mice were run in parallel. After acute (1-4 days) or protracted (21-24 days) abstinence, DLS iSPN and dSPN intrinsic excitability was assessed using whole-cell patch clamp techniques as previously described (Choi et al., Sci Rep. 12(1): 12116, 2022); current-spike response curves were analyzed using two-way ANOVAs with Fisher's LSD post-hoc analysis.
Results: During acute abstinence from MSA, DLS dSPN intrinsic excitability was increased (current X treatment interaction $F(25,375)=3.730$, $p<0.0001$; post-hoc analysis showed significance at 340-500pA between MSA and saline-yoked dSPNs). After protracted abstinence, DLS dSPN intrinsic excitability returned to control levels. In contrast to DLS dSPNs, DLS iSPN intrinsic excitability was unchanged during acute abstinence.
Conclusions: While our recent report found time-dependent changes in DMS iSPN excitability (Choi et al., Sci Rep. 12(1): 12116, 2022), the current study found transient changes in DLS dSPN excitability in a mouse model of MSA. These data suggest that meth produces anatomically, time-dependent, and cell-type specific SPN membrane plasticity. Further study is needed to determine the consequence of dorsal striatal SPN functional dynamics in maladaptive seeking behaviors.
Financial Support: DA051450

CHRONIC METHAMPHETAMINE ADMINISTRATION TO MALE MICE PRODUCES AXONAL LOSS PRIOR TO SOMATIC LOSS IN NORADRENERGIC LOCUS COERULEUS NEURONS

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Drug Category Stimulants
Topic Neurobiology/Neuroscience
Aim: Methamphetamine (meth) is an addictive and neurotoxic psychostimulant. Meth increases monoamine oxidase (MAO)-dependent mitochondrial stress in axonal but not somatic compartments of noradrenergic

locus coeruleus (LC) neurons and chronic 28-day meth (5mg/kg) results in MAO-dependent LC degeneration (Du et al., Front Cell Neurosci 16:949923, 2022). Given that meth increases axonal stress, we hypothesized that LC axonal loss precedes somatic loss suggesting a dying-back pattern of degeneration.
Methods: Male and female C57BL/6J mice (~8 weeks old) were administered saline or meth (5mg/kg; i.p.) for 14, 21, or 28 days and brain sections (40µm) entailing the LC and motor cortex were collected; LC noradrenergic neurons were stained for tyrosine hydroxylase (TH+) and noradrenergic axons in the motor cortex stained for the norepinephrine transporter (NET+). The number of TH+ neurons in the LC and NET+ axon length in the motor cortex were stereologically quantified by a blinded experimenter. Data analyzed using unpaired t-test comparing saline vs. meth; n=6 mice/group.
Results: In male mice 14- ($p=0.0131$) and 21-day ($p=0.0010$) meth treatment resulted in decreased NET+ axon length without somatic loss, whereas 28-day meth resulted in both axonal ($p<0.0001$) and somatic ($p=0.0002$) loss. However, LC neurons in female mice were resistant to meth-induced axonal and somatic loss.
Conclusions: Chronic meth resulted in axonal loss prior to somatic LC degeneration in male mice whereas LC neurons in female mice were resistant to degeneration. Presented data suggest that chronic meth produces a progressive dying-back pattern consistent with that observed in the LC (Doppler et al., Brain 144(9):2732-2744, 2021) and substantia nigra pars compacta (Kordower et al., Brain 136(8):2419-2431, 2013) in patients with Parkinson's disease, a progressive neurodegenerative disorder for which people with a history of meth abuse are at an increased risk (Curtin et al., Drug and Alcohol Dependence 146:30-8, 2015).
Financial Support: NIDA grants: DA054779 (AP), DA051450 (SMG).

ORAL COMMUNICATION: JUVENILE JUSTICE
Grand Ballroom I

PIPES AND LINES: THE ASSOCIATION OF HARSH SCHOOL PUNISHMENT AND CURRENT SUBSTANCE USE AMONG UNDERREPRESENTED MINORITY JUSTICE-INVOLVED ADOLESCENTS

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Drug Category Other, Substance Use
Topic Racial/Ethnic Differences
Aim: 'School-to-prison pipeline' studies demonstrate underrepresented minority (URM) populations are disproportionately funneled from public schools into the juvenile justice system. URM are more likely to be criminalized for minor school infractions via suspensions or expulsions, which is associated with an increased likelihood of entering the juvenile justice system. Involvement in the juvenile justice system can increase the probability of substance use issues. However, there is limited research on the role of school punishment in predicting substance use rates among URM justice-involved adolescents (JIA). This study examined the association between the number of school suspension(s)/expulsion(s) and rates of substance use in JIA over time.
Methods: Stratified fixed effects logistic regression was employed to examine a statewide dataset of 33,455 JIA from the Florida Department of Juvenile Justice (FLDJJ). The FLDJJ sample consisted of both male and female JIA who were arrested and administered the Positive Achievement Change Tool (PACT) intake assessment over three successive occasions, each approximately 90 days apart. Rates of school suspensions and expulsions, current substance use, and demographics were obtained from self-reported PACT data and state records.
Results: Black and Latinx JIA were most likely to experience a school suspension or expulsion than their White counterpart. Compared to those without a suspension or expulsion, Latinx JIA were the only racial/ethnic group to demonstrate statistically higher odds of current substance use if the student had one suspension/expulsion ($OR = 2.38$, $p = .01$), 2 or 3 suspensions/expulsions ($OR = 3.14$, $p < .05$), and more than 3 suspensions/expulsions ($OR = 9.11$, $p < .001$).
Conclusions: Harsh school discipline, such as suspensions and expulsions, adversely impacts URM populations. Particularly among Latinx JIA, the increased number of these punishments correlates with higher rates of current substance use. The data support the growing literature suggesting that schools deviate

from punitive discipline. Opting for reinforcement and function-based interventions sensitive to URM may reduce juvenile justice involvement and substance use rates.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). 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 Florida Department of Juvenile Justice.

THE CONSEQUENCES OF MATERNAL AND PATERNAL INCARCERATION ON ADOLESCENT ALCOHOL AND CANNABIS USE: ASSESSING RACIAL DIFFERENCES

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Drug Category Alcohol
Topic Racial/Ethnic Differences
Aim: Failure to assess the association between parental incarceration and adolescent substance use means we're missing an important opportunity to prevent substance use among adolescents and to reduce further exposure to incarceration among this group. This study estimated the relationship between maternal and paternal incarceration and adolescent alcohol and cannabis, and effect modification by race using longitudinal data.
Methods: Respondents included 14-19 year-olds (N=4,898) from the longitudinal cohort study Fragile Families and Child Wellbeing Study (1998 to 2017). Survey constructed, direct and indirect measures of parental incarceration were used to construct binary lifetime maternal and paternal incarceration variables. Youth reported past-year alcohol and cannabis use (binary). Race was classified as non-Latine White and non-Latine Black. Modified-Poisson regression models were adjusted for parental socioeconomic status, parental depression and alcohol use, youth physical abuse, and externalizing behaviors in childhood.
Results: Adolescents of mothers who were incarcerated in their lifetime had an increased risk of past-year alcohol (relative risk [RR]=1.54, 95% CI=1.17-2.03) and cannabis (RR=1.25, 95% CI=1.01-1.55) use. Exposure to lifetime maternal incarceration was associated with an increased risk of past-year alcohol and cannabis use among both non-Latine Black and White adolescents'. Adolescents of fathers who were incarcerated in their lifetime had an increased risk of past-year alcohol (RR=1.42, 95% CI=1.11-1.81), and cannabis use (RR=1.37, 95%CI=1.10-1.69). Specifically, lifetime paternal incarceration was associated with an increased risk of past-year alcohol (RR=1.77, 95% CI=1.13-2.77) and cannabis (RR=1.41, 95% CI=1.03-1.91) use among non-Latine Black adolescents, and a decreased risk of past-year alcohol (RR=0.78, 95% CI=0.44-1.37) and cannabis use (RR=0.68, 95% CI=0.35-1.30) among non-Latine White adolescents.
Conclusions: Evidence from the current study shows that both maternal and paternal incarceration are associated with increases in adolescent alcohol and cannabis use. Racial differences may be important from a clinical and public health perspective, as the direction of the associations were different by race.
Financial Support: NIDA Substance Abuse Epidemiology Training Grant T32DA031099 (PI: Deborah Hasin)

A STRUCTURAL EQUATION MODELING ANALYSIS OF ANTI-SOCIAL BEHAVIOR, SUBSTANCE MISUSE, TRAUMA, AND IRRITABILITY AMONG JUSTICE-INVOLVED ADOLESCENTS

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Drug Category Other, substance misuse problems
Topic Criminal Justice
Aim: Justice-involved adolescents (JIA) are more likely to be exposed to trauma, like violence and adverse childhood experiences, than general adolescent populations. Traumatic exposure can lead to irritability (i.e., aggression, irascibility) and substance use among adolescents, increasing the risk for justice involvement. While research indicates overlap between these constructs, the relationships between trauma, irritability, and

substance misuse on JIA's anti-social behavior are unclear. The current study investigates if substance misuse mediates relationships between trauma, irritability, and JIA's anti-social behavior.
Methods: Structural equation modeling was used to examine a statewide sample of 79,570 JIA from the Florida Department of Juvenile Justice. The model considered JIA's anti-social behavior as an outcome of three latent constructs: trauma, irritability, and substance misuse. Anti-social behavior and latent constructs were measured with ordinal variables derived from the Positive Achievement Change Tool assessment.
Results: Goodness-of-fit indices indicated that the model acceptably fit the data. The covariance between trauma and irritability was statistically significant (B= .67, p <.00). The direct path between irritability and antisocial behavior was statistically significant (B= 1.2, p <.00). The effect of trauma on antisocial behavior was significantly mediated through its indirect effect on substance misuse (B= .08, p <.00). Likewise, the effect of irritability on antisocial behavior was significantly mediated through its indirect effect on substance misuse (B= .20, p <.00).
Conclusions: Findings demonstrated significant and interrelated relationships between trauma and substance misuse on JIA's anti-social behavior. Irritability had the strongest influence on anti-social behavior, both directly and indirectly. Irritability and trauma were also strongly related. This finding could provide valuable insight for juvenile justice behavioral programs and substance misuse treatment. Juvenile justice programs often do not account for the heterogeneity of trauma and substance misuse among JIA. Trauma-informed practices in juvenile justice settings would be beneficial to mitigate persistent substance misuse and anti-social behavior among JIA.
Financial Support: The National Institute on Drug Abuse supported this research under award numbers 1K01DA052679 (Dr. Micah E. Johnson, PI), R25DA050735 (Dr. Micah E. Johnson, PI), R25DA035163 (Dr. Micah E. Johnson, Sub-PI), and U01DA051039 (Dr. Micah E. Johnson, USF-PI). 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 Florida Department of Juvenile Justice.

THE EFFECTIVENESS OF A VOLUNTARY, PRE-ARREST, DRUG DIVERSIONARY PROGRAM IN LAKE COUNTY, IL

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Drug Category Opiates/Opioids
Topic Epidemiology
Aim: The A Way Out (AWO) program is a Lake County, IL-based, voluntary, pre-arrest drug diversion program designed to help individuals initiate substance abuse treatment and access recovery support services. AWO is administered by the Lake County Health Department with substantial involvement of police municipalities, and support from the state attorney's office, a county opioid overdose prevention group, and other county-based partners. This project aims to assess AWO participants' rates of completion of initial and follow-up treatment placements and possible mediating variables.
Methods: Male and female participants (n=144) entering the AWO program from February 2021 to September 2022 were included in this evaluation. Data collected include demographics, preferred placement, actual placement, attendance of appointments, and placement outcomes. Data were analyzed using Microsoft Excel (2016) and SPSS (version 28).
Results: The program placed 87% of participants in treatment, which 73% completed. Program participants were primarily non-Hispanic White (72.9%), cis-gendered males (67.4%). Their mean age was 38 years. Participants who attended their treatment appointment (n=125) were more likely to successfully complete their initial treatment (r=0.464, p<0.001) as well as follow-up treatment (r=0.344, p=0.006). Successful completion rates were consistent across race/ethnicity ($\chi 2$=0.231, p>0.05) and gender ($\chi 2$ =0.363, p>0.05). Age correlated positively with initial treatment success ($\chi 2$=0.071, p=0.042).
Conclusions: Current findings demonstrate the AWO program is effective for helping individuals with a substance use problem access treatment. Most participants were provided and successfully completed their initial treatment program. This evaluation found no difference in treatment success based on ethnicity. However, the small number of Latino/a/x and LGBTQ participants suggest the continuing need for outreach to these populations.
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ORAL COMMUNICATION: E-CIGARETTES: THAT'S NOT A THUMB DRIVE, MOM!
Grand Ballroom I

SELECTIVE REDUCTION OF SOCIOECONOMIC DISPARITIES IN THE EXPERIMENTAL TOBACCO MARKETPLACE: EFFECTS OF CIGARETTE AND E-CIGARETTE FLAVOR RESTRICTIONS

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Drug Category Nicotine/Tobacco
Topic Behavioral Economics
Aim: Cigarette smoking accounts for >30% of the socioeconomic gap in life expectancy. Flavored restrictions claim to promote equity; however, no previous studies have compared the effect of cigarette and e-cigarette flavor restrictions among individuals who smoke with lower and higher socioeconomic status (SES).
Methods: In a between-group within-subject design, individuals with lower (n=155) and higher (n=125) SES completed hypothetical purchasing trials in the Experimental Tobacco Marketplace (ETM). Conditions were presented in a 2x2 factorial design (cigarette flavors restricted or unrestricted and e-cigarette flavors restricted or unrestricted) with increasing cigarette prices across trials. Analyses investigated (1) differences in purchasing under the current policy (unrestricted) across SES groups; (2) how new restrictions impact purchasing in each group; and (3) whether differences in purchasing across groups persisted or changed under the new restrictions.
Results: Results show 1) SES differences in cigarette (ps<0.010), e-cigarette (p<0.001), and NRT (p=0.026) purchases under current policies, with lower SES showing higher cigarette demand and lower e-cigarette and NRT substitution than higher SES, 2) cigarette restrictions decreased cigarette (ps<0.001) and increased NRT (p=0.008) purchases among lower SES, but no significant changes among higher SES, 3) decreased SES differences in cigarette demand (p=0.008) under cigarette restrictions, but persistence under e-cigarette restrictions (p=0.001) or their combination (p=0.001), 4) persistence of SES differences in e-cigarette purchases when all restrictions were enforced (all ps<0.001), and 5) waning of SES differences in NRT purchasing under all restrictions (all ps>0.05).
Conclusions: Flavor restrictions differentially affected individuals based on SES. Within-group comparisons demonstrated restrictions significantly impacted lower SES, but not higher SES. Between-group comparisons showed SES differences in cigarette purchasing decreased under cigarette restrictions but persisted under e-cigarette-restrictions or their combination. Additionally, SES differences in NRT substitution decreased under flavor restrictions. These findings highlight the utility of the ETM to investigate SES disparities.
Financial Support: This work was supported by the National Cancer Institute at the National Institutes of Health (grant number 5P01CA217806 and 5P01CA200512) and the Fralin Biomedical Research Institute at Virginia Tech Carilion.

IDENTIFYING E-CIGARETTE CONTENT ON TIKTOK: USING BERT TOPIC MODELING APPROACH

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Drug Category Nicotine/Tobacco
Topic Prevention
Aim: E-cigarette content on social media is pervasive, however, there is limited understanding of e-cigarette content that exists on TikTok, which is one of the most popular social media platforms used by young people. To analyze the complex and voluminous amount of data on TikTok, this study aimed to use the novel machine learning approach (i.e., Bidirectional Encoder Representations from Transformers [BERT] topic modeling) to identify the e-cigarette content that exists on TikTok.
Methods: We used an unsupervised machine learning technique, BERTopic modeling, which is based on Google's neural network-based technique that uses natural language processing pre-training to identify the most common e-cigarette topical themes on TikTok. We used 14 unique hashtags related to e-cigarettes (e.g., #vape, #vapelife, #vapenation) for data collection and analyzed 13,573 posts. BERT models were fine-tuned through an iterative corpus-pruning process involving tobacco research experts, in which non-relevant keywords were removed from the dataset. Topics were cross-referenced to determine the most frequently occurring topics and qualitatively labeled by two reviewers.
Results: We identified 18 topics. These topics included vape tricks (e.g., "cloud", "inhales"), specific vape tricks (e.g., "lasso"), vape shops (e.g., "store"), vape shops and tobacco shops (e.g., "smoke"), names of vape brands, vape flavors, mods (e.g., "coil", "wires"), vaping and girls, vape community (e.g., "family"). Identified topics also included non-e-cigarette-related, but styles seen on TikTok (e.g., "comedy", "skit" and "lip", "sync") and hashtags that are frequently used on social media (e.g., "viral" and "trending"). We also identified 3 topics that are in non-English (e.g., French, Romanian and Spanish).
Conclusions: We found predominant e-cigarette-related topics on TikTok including names of e-cigarette brands and stores, themes that appeal to youth such as vape tricks, and that are not suitable for youth such as e-cigarette modifications. Continuous surveillance and regulation are needed on social media platforms to prevent youth access to this content.
Financial Support: The research reported in this publication was supported by grant number R01DA049878 from the National Institute on Drug Abuse (NIDA) and U.S. Food and Drug Administration (FDA) Center for Tobacco Products (CTP)

WORKING MEMORY ALTERATIONS PREDICT ADOLESCENT E-CIGARETTE USE AND POSITIVE OUTCOME EXPECTANCIES VIA ALEXITHYMIA

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Drug Category Nicotine/Tobacco
Topic Neurobiology/Neuroscience
Aim: E-cigarette use remains high among adolescents. Extant literature links working memory (WM) alterations with adolescent substance use (SU), including nicotine. Yet, mechanisms linking WM to SU remain unclear. Alexithymia has been linked with altered activity in the frontal cortices and superior temporal gyrus (STG), which are also engaged during WM. Difficulty describing feelings (DDF), a characteristic of alexithymia, predicts e-cigarette use. Here, we examined the interrelations between WM-related brain activity, task performance, DDF, and e-cigarette use and expectancies.
Methods: Adolescents (n=137; Mage=14.9) from a longitudinal study completed a WM task (n-back) during fMRI scanning at Wave-1. Given associations with alexithymia, the dorsolateral prefrontal cortex (dlPFC; a region activated during WM) and the STG (a region deactivated during WM) were examined. D-prime (3-back) quantified WM task performance and the Toronto Alexithymia Scale at W1 measured DDF. At W2 (~15 months later), an item from the PATH study quantified use days and the Adolescent E-cigarette Consequences Questionnaire quantified use expectancies (e.g., negative affect reduction). Four models estimated the influence of dlPFC/STG activity on e-cigarette use/use expectancies via task performance and DDF.
Results: Across the models, there was no support for serial mediation. However, there was support for simple mediation via DDF. Less dlPFC activity during WM was associated with more DDF, and more DDF predicted more e-cigarette use days (indirect effect=0.25, CI[0.03,0.563]) and positive outcome expectancies (indirect effect=0.01, CI[0.002,0.021]). Less STG deactivation during WM was associated with more DDF,

and more DDF predicted more e-cigarette use days (indirect effect=-0.223, CI[-0.568,-0.027]) and positive outcome expectancies (indirect effect=-0.01, CI[-0.02,-0.001]).
Conclusions: These outcomes highlight alexithymia as a factor linking WM alterations with e-cigarette use and expectancies. Adolescents with alterations in WM-related brain regions may be more prone to experience difficulty communicating emotions and in turn use nicotine to modulate emotions or connect socially.
Financial Support: This work was supported by the National Institute on Minority Health and Health Disparities (U54-MD012393 [subproject 5378], PIs: Trucco, Sutherland) and the National Institute on Drug Abuse T32 Ruth L. Kirschstein National Research Service Award Institutional Research Training Grant (T32DA043449, PI: Pelham).

DEVELOPING AN APP TO PROVIDE CBT FOR VAPING CESSATION TO YOUTH E-CIGARETTE USERS

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Drug Category Nicotine/Tobacco
Topic Treatment
Aim: Youth e-cigarette use is common and there are no empirically validated interventions for youth vaping cessation. The current study describes the development of a "Kick-Nic©" App that uses Cognitive Behavioral Therapy (CBT) to help youth stop using e-cigarettes.
Methods (Optional): Qualitative interviews with 60 adolescents (13-20 years), and adaptation of materials from an established smoking cessation manual developed for youth, were used to develop the CBT content. The CBT content was further adapted into the format of a computer-delivered CBT intervention (called CBT4CBT), which uses movies and interactive exercises to deliver content and has shown efficacy in reducing substance use among adults. The design and format of the Kick-Nic© App was developed using qualitative interviews with 10 youth e-cigarette users.
Results (Optional): Qualitative interviews identified e-cigarette specific content related to reasons for use and quitting, barriers to quitting, and quitting experiences that were included with CBT skills (preparation to quit, recognizing and handling cues/withdrawal/negative emotions, assertiveness, decision-making, long term planning) in the App. The Kick-Nic© App uses seven digital modules that teach CBT skills through a) guidance and educational narrations provided by moderators, b) role-modeling exercises and personal experiences provided by peers that teach and model effective use of coping skills, and c) animations, quizzes, and other interactive exercises that reinforce the use of coping skills and the development of personalized quitting plans.
Conclusions: The Kick-Nic© App is designed to teach CBT skills for vaping cessation to youth through a media-rich interactive format. Qualitative and clinical testing of the App will be discussed.
Financial Support: Funded by the American Heart Association ENACT grant 20YVNR35460041.

ORAL COMMUNICATION: COCAINE SCIENCE IN HUMANS
Plaza Ballroom A

NEUROCHEMICAL CHANGES IN GLUTAMATE AND GABA AND COGNITIVE FUNCTION IN COCAINE DEPENDENT INDIVIDUALS DURING EARLY WITHDRAWAL

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Drug Category Other, Cocaine
Topic Imaging
Aim: Cocaine use disorder (CUD) and its remission has been associated with changes in the homeostasis of glutamate and GABA in the reward-seeking area like the dorsal anterior cingulate cortex (ACC). However, there is a gap in knowledge in understanding the disturbance of the neurochemical homeostasis during acute withdrawal from cocaine. We hypothesized that there would be a significant increase in glutamate and

GABA concentrations in the cocaine-dependent individuals compared to the healthy control group from baseline to day 3 of withdrawal. Second, we predicted that glutamate and GABA concentrations would stabilize over the 21-day withdrawal period. Finally, we predicted that changes in glutamate and GABA over the 21 days of the study were associated with observable behavioral changes.
Methods: Thirty-eight cocaine users and five healthy control volunteers completed a baseline screening assessment. A total of nine (9) cocaine users and five (5) age-matched healthy controls completed behavioral assessment and 3T proton magnetic resonance spectroscopy (1H MRS) at baseline, day 3, day 7, and day 21. The behavioral measures included mood state for depression and anxiety, cocaine craving questionnaire (CCQ), cognitive testing with Stroop color test, and Trails A and B. The neurochemical variables analyzed included the ratio of GABA/NAA, Glu/NAA, and GABA/Glu.
Results: We applied a linear mixed model analysis to quantify the group differences in the neurochemical variables. We found the group's significant main effect differences for the Glu/NAA ratio ($t=3.416425$, $p<0.0001$) and GABA/Glu ($t= -4.478608$, $p<0.0001$) without any significant interaction effects of time and group in the cocaine-dependent group compared to the healthy controls. Overall, the Glu/NAA remained lower and GABA/Glu remained higher in the cocaine-dependent individuals compared to controls throughout the 21-day withdrawal period. On the other hand, GABA/NAA ratio was not significantly different ($t= 0.0315213$, $p= 0.97503$) in the two groups. Finally, change in the GABA/NAA ratio from baseline through 21 days was correlated with a negative trend with Trails A and B cognitive domains of attention and switching in the cocaine-dependent group ($F=4.305$, $p=0.0647$); there were no behavioral changes in healthy controls.
Conclusions: We conclude that glutamate and GABA homeostasis and cognitive function may take longer than 21 days of abstinence to return to normal concentrations, suggesting that acute treatment strategies should extend beyond 3-4 weeks as is often done.
Financial Support: The work was supported by 1R21 DA036047 (SEL) and T32 DA015036 (SEL).

"ARRESTED DEVELOPMENT"? COCAINE PATIENTS WITH GENETICS LINKED TO OVER-RESPONSE OF THE STRESS (CORTISOL) SYSTEM SHOW AN "IMMATURE" PATTERN OF POSITIVE, RATHER THAN INVERSE, AMYGDALA RESTING FUNCTIONAL CONNECTIVITY WITH THE VMPFC

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Drug Category Stimulants
Topic Imaging
Abstract Detail Clinical - Experimental
Abstract Category Original Research
Aim: We recently demonstrated that adult cocaine or opioid patients carrying a genetic variant known to increase stress (cortisol) reactivity have heightened cue-triggered limbic brain responses, a relapse-relevant phenotype in addiction – and heightened (positive) resting amygdala functional connectivity (rsFC) with the VMPFC. Here, we tested the specificity of our genetic effects in cocaine patients by imaging amygdala rsFC in a demographically-similar adult cohort without a cocaine use history.
Methods: Using BOLD fMRI, we obtained resting state scans (5 minutes) in stabilized, treatment-seeking male cocaine inpatients, and in a control cohort recruited for demographic similarity to our cocaine patients. After pre-processing (standard SPM 12 pipeline), we compared (2x2 ANOVA, thresholded $4<t<10$) amygdala rsFC between the cocaine patients (n=27) and controls (n=19), and for carriers of the minor vulnerability allele (TG, GG) for rs800373 of FKBP5 (n=24), vs. TT homozygotes (n=22). Our anatomical focus was connectivity of the amygdala with VMPFC and with other nodes of the mesocorticolimbic circuitry important in motivation, and in its regulation.
Results: As compared to the controls, cocaine patients had heighted positive rsFC between the amygdala and limbic (amygdalae, insula, midbrain, v. pallidum, putamen) regions. In addition, there was a significant group x allele interaction: for cocaine patients, but not controls, G-carriers had heightened positive rsFC connectivity between the l. amygdala, the VMPFC and insula.
Conclusions: Cocaine patients' heightened (positive) rsFC between the amygdala and limbic regions, including VMPFC, may be a brain marker for difficulty in regulating both appetitive (e.g., drug) and

aversive (e.g., anxiety) motivational states -- and genetic variation in fKBP5 may contribute to this vulnerability. A pattern of (positive) amygdala rsFC with VMPFC is characteristic of still-developing adolescent brains; this pattern in cocaine patients may evidence "arrested development". Developmental cohorts will help determine whether this brain endophenotype predates, and predicts, future drug or mood problems.
Financial Support: Commonwealth of Pennsylvania CURE Addiction Center of Excellence: Brain Mechanisms of Relapse and Recovery (Childress); NIDA U54 DA039002 Cocaine Cooperative Medication Development Center (Kampman, Center PI; Childress, PI Imaging Project); NIDA R01DA039215 (Childress, PI); NIDA UG1DA050209 Clinical Laboratories with Integrated Neuroscience (Kampman and Childress MPI).

ADVANCED CHARACTERIZATION OF ON-BODY ELECTROCARDIOGRAPHIC (ECG) SENSORS' DISCRIMINATORY POWER IN A HUMAN LABORATORY COCAINE SELF-ADMINISTRATION (SA) PARADIGM

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Drug Category Stimulants
Topic Technology (e.g., mHealth)
Aim: Our group has established the ability of on-body ECG sensors to discriminate cocaine use from other sympathomimetic conditions. These analyses attempt to further test whether the discriminatory power is mainly driven by heart rate differences. We also assess for the first time the discriminatory power of the ECG sensors in distinguishing the period immediately preceding cocaine SA from daily living.
Methods: Eleven cocaine users wore the Zephyr BioHarness™ 3 chest band during 1) laboratory, intravenous cocaine SA, 2) methylphenidate's administration, 3) aerobic exercise, 4) tobacco use (N = 7), 5) hour preceding cocaine SA, and 6) inpatient daily living. ECG derived measurements included 1) RR interval (i.e., a reflection of heart rate), 2) ECG proxies (i.e., PR, QS, QT and QTc intervals), and 3) full ECG waveforms. Within subjects analyses selected ECG segments with matched heart rates for all discriminations, except for that between the hour preceding cocaine SA and daily living.
Results: ECG proxies and waveforms exhibited high discriminatory power in distinguishing cocaine use from other sympathomimetic conditions, with mean area under the receiver operating characteristics (AUROC) values ranging from 0.87 to 0.99, and least squares means values significantly higher than 0.5 among all subjects and smokers. On the contrary, the RR approach exhibited poor discriminatory power (i.e., AUROC values from 0.49 to 0.5). In distinguishing the period foregoing cocaine SA, all three ECG features exhibited high discriminatory power, with AUROC values ranging from 0.77 to 0.96.
Conclusions: Our results suggest that the discriminatory power of wearable ECG sensors in cocaine use detection is based on nuances in ECG data beyond mere changes in heart rate. Results also indicate the potential for on-body ECG sensors to recognize changes underscoring the anticipation of cocaine use. Replication of these findings may aid in the monitoring of cocaine use treatment and the advancement of personalized medicine.
Financial Support: Supported by: R01 DA03373301 and CTSA grant number UL1 RR024139

EVALUATING CLAVULANIC ACID FOR TREATMENT OF COCAINE USE DISORDER

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Drug Category Stimulants
Topic Treatment
Aim: Characterize the effects of clavulanic acid (CLAV) on brain network functional connectivity and regional glutamate (Glu) levels in subjects with cocaine use disorder.

Methods: As a glial glutamate transporter, CLAV shows efficacy in animal models of cocaine addiction. We hypothesize that CLAV will induce changes in cocaine craving, brain Glu, and functional connectivity. Subjects with cocaine use disorder were studied as inpatients (n=12). Participants received CLAV (n=9, 500 mg/day-days 1-3, 750 mg/day-days 4-6, and 1,000 mg/day-days 7-10) for 10 days. MRI scans were obtained during 5 sessions. Resting state functional magnetic resonance imaging (rsfMRI) and magnetic resonance spectroscopy (MRS) in the anterior cingulate cortex (ACC) were performed. A group independent component analysis was used to identify brain resting state networks (RSN) common to all participants and sessions. Dual regression was used to identify changes in RSN connectivity between sessions.
Results: The CLAV group demonstrated an inverse relationship between changes in network connectivity and baseline Glu levels in 3 addiction-associated RSNs, the executive control (ECN), nucleus accumbens–orbitofrontal (NAC) and anterior frontal pole (AFP) networks. Connectivity change at day 10 was inversely correlated with baseline Glu in the ECN (r=-.67, p=.050) and NAC (r=-.75, p=.02). Connectivity change at day 6 was inversely correlated with baseline Glu in the AFP (r=-.82, p=.007). Also, higher ACC Glu at day 10 was associated with lower cocaine craving (r=-0.90, p = 0.001).
Conclusions: The inverse relationship between connectivity and baseline Glu suggests that individuals with lower baseline ACC Glu levels respond to repeated CLAV treatment with stronger increases in functional connectivity in some RSNs. For the ECN and AFP this connectivity change suggests improved executive control after CLAV. CLAV participants who achieve a higher Glu level also experience less cocaine craving. These findings support the development of CLAV for cocaine use disorders.
Financial Support: NIH U02 DA048517

ORAL COMMUNICATION: NOVEL STIMULANTS AND MECHANISMS
Plaza Ballroom D

ORGANIC CATION TRANSPORTER 3 (OCT3) IS CRUCIAL FOR THE REINFORCING EFFECTS OF AMPHETAMINE

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Drug Category Stimulants
Topic Behavioral Pharmacology
Aim: Stimulant misuse and overdose deaths involving stimulants have risen. Given that there are no FDA-approved pharmacotherapies for stimulant use disorders, uncovering novel treatment targets is of utmost importance. We recently showed that organic cation transporter 3 (OCT3), a low affinity, high capacity (uptake-2) monoamine transporter, is an important player in the neurochemical and rewarding (measured by conditioned place preference) actions of amphetamine. Here, using self-administration, we tested the hypothesis that OCT3 is necessary for the reinforcing effects of amphetamine.
Methods: Male and female wild-type (OCT3+/+) and knockout (OCT3-/-) mice were trained to respond for the presentation of a 25-µl cup of sweetened liquid food under a fixed ratio 1 schedule of reinforcement. Upon acquisition of stable responding, mice were implanted with a catheter in the left femoral vein. Following recovery from surgery, mice responded for intravenous infusions of amphetamine (0.0032-0.32 mg/kg/inf) or cocaine (0.032-1 mg/kg/inf). A separate cohort of OCT3+/+ and OCT3-/- mice were administered the OCT3 inhibitor decynium-22 (D22) intraperitoneally one hour prior to responding for doses of amphetamine and cocaine that produced maximal self-administration.
Results: There were no differences in acquisition of lever responding for food between genotypes or sexes. Relative to OCT3+/+ mice, responding for amphetamine in male and female OCT3-/- mice was dramatically attenuated, with these mice making significantly more inactive lever presses. In both males and females, peak responding for cocaine in OCT3-/- mice occurred at a half-log higher dose versus OCT3+/+ mice. Treatment with D22 reduced responding for amphetamine in OCT3+/+ mice to parity with knockouts and only modestly reduced cocaine self-administration, regardless of condition.
Conclusions: Data indicate OCT3 is important for the reinforcing effects of amphetamine across sex and show that OCT3 could be a promising target for pharmacological treatments against misuse of amphetamine and its congeners. Future directions will use other schedules of reinforcement (e.g., progressive ratio) to assess and compare motivation to respond for amphetamine using conditional OCT3 knockout approaches.

Financial Support: 5R21-DA049044-02

COMPARISON OF BEHAVIORAL EFFECTS OF NOVEL DESIGNER DRUGS IN MALE RODENTS

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Drug Category Stimulants
Topic Behavioral Pharmacology
Aim: The purpose of these studies was to evaluate novel designer drugs for their ability to stimulate locomotor activity (LMA); to test for substitution for methamphetamine in a drug discrimination (DD) assay; and to determine the potency and efficacy of these compounds relative to methamphetamine.
Methods: 4F-methylphenidate, ethylphenidate, 3F-phenmetrazine, 1,2-diphenyl-2-(1-pyrrolidinyl)-ethanone (α-D2PV), N-cyclohexyl methylone, and N-cyclohexyl butylone were each tested for their ability to stimulate LMA in male Swiss-Webster mice. The discriminative stimulus effects of these designer drugs were assessed in male Sprague-Dawley rats that were trained to discriminate methamphetamine (1 mg/kg) from saline.
Results: Locomotor stimulant effects of 4F-methylphenidate (ED50 = 2.62 mg/kg), ethylphenidate (ED50 = 16.46 mg/kg), 3F-phenmetrazine (ED50 = 4.69 mg/kg), α-D2PV (ED50 = 4.58 mg/kg), N-cyclohexyl methylone (ED50 = 2.63 mg/kg), and N-cyclohexyl butylone (ED50 = 2.80 mg/kg) were observed within 10 min following injection and lasted from 20 to 180 min. In addition, N-cyclohexyl methylone also resulted in dose- and time-dependent depression of locomotor activity at lower doses (1 and 2.5 mg/kg). The maximal motor stimulant actions of all the tested drugs were equivalent to that of methamphetamine. A range of potencies was observed, with 4-fluoromethylphenidate and N-cyclohexyl butylone being the most potent and ethylphenidate being the least potent of the tested drugs. All drugs substituted for the discriminative stimulus effects of methamphetamine in rats, except N-cyclohexylmethylone, which produced only 55% drug-appropriate responding. Clonic convulsions were observed in animals tested with 10 mg/kg of N-cyclohexylmethylone (n=1) and with 25 mg/kg of α-D2PV (n = 1).
Conclusions: The behavioral profiles of these compounds confirmed the potential of abuse of these drugs when used as substitutes for methamphetamine. However, abuse with N-cyclohexylmethylone may be unlikely due to its weak stimulant and discriminative stimulus effects. In addition, N-cyclohexylmethylone and α-D2PV produced convulsions, therefore pose additional dangers for recreational use.
Financial Support: Supported by DEA contract DOJ 15DDHQ19A00000016.

BEHAVIORAL ASSESSMENTS AND NEUROCHEMICAL ASSAYS DIFFERENTIATE THE EFFECTS OF 1-(1-BENZOFURAN-5-YL)-2-(METHYLAMINO) PROPAN-1-ONE HYDROCHLORIDE (BK-5-MAPB) ENANTIOMERS

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Drug Category Stimulants
Topic Behavioral Pharmacology
Aim: This study characterized the locomotor stimulant and discriminative stimulus effects of 1-(1-benzofuran-5-yl)-2-(methylamino) propan-1-one hydrochloride (BK-5-MAPB) enantiomers and differentiated their pharmacokinetics and neurochemical actions.
Methods: Drug discrimination methods were employed to characterize S- and R-BK-5-MAPB (0.32, 0.64, 1.27 mg/kg IP) in 16 male Sprague-Dawley (SD) rats trained to discriminate 1.5 mg/kg MDMA from saline. Locomotor activity was assessed in three separate cohorts of male SD rats (N=6) following a single injection of saline or each enantiomer; doses (0, 0.32, 0.64, 1.27 mg/kg IP) were assessed once per week in ascending order. In a separate set of experiments, monoamine release and uptake inhibition at SERT, DAT, and NET were assayed using rat synaptosomes and [3H]5-HT or [3H]MPP+ as substrate. In separate cohorts of male SD rats (N=4), plasma concentrations were assayed after 1.27 and 3.81 mg/kg IP and pharmacokinetics were estimated.

Results: S-¬BK-5-MAPB produced dose-dependent increases in MDMA-lever responses and full substitution at 0.64 and 1.27 mg/kg; R-BK-5-MAPB produced less than 30% MDMA-lever responding. Both enantiomers increased distance traveled in a dose-dependent manner that was statistically significant compared to saline-treated controls (P= 0.0001). Both enantiomers were substrate-type releasers at all three transporters. The S-enantiomer displayed an MDMA-like profile with greater potency at SERT than DAT (DAT/SERT ratio of 0.6), while R-BK-5-MAPB had a typical stimulant profile (DAT/SERT ratio of 18). Both enantiomers had higher potency at DAT than NET (DAT/NET ratios of 2.7 and 1.9 for the S- and R-enantiomer, respectively). Pharmacokinetics differed between the enantiomers, with R-BK-5-MAPB showing a lower Cmax and higher clearance than the S-enantiomer.
Conclusions: S- and R- BK-5-MAPB produce behavioral and neurochemical actions similar to MDMA and stimulants, likely through monoamine transporters. Because they have reduced potency at NET, these novel substances may have utility in elucidating the contributions of NET to MDMA-like and typical stimulant effects.
Financial Support: Tactogen

THE ACTIVITIES OF THE ENANTIOMERS OF A SLOW ONSET DOPAMINE REUPTAKE INHIBITOR

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Drug Category Stimulants
Topic Chemistry
Aim: CTDP-30,476, a methylphenidate analog, blocks the reuptake of synaptic dopamine (DA) and norepinephrine (NE). It has been shown to have a slow onset of at least 20 minutes; that naïve rats will not self-administer it; that experienced rats will take reduced levels, but by 2 or 3 weeks will reduce their self-administration to the same level as vehicle. The compound may be useful for the treatment of cocaine abuse since it raises DA slowly and would avoid the euphoria associated with cocaine. The purpose of this study is to resolve the enantiomers of the compound and test their activities in animal models.
Methods: The compound was resolved, and chiral chromatography showed that each enantiomer had little or no contamination by the other enantiomer. The enantiomers, ATDP-34,209 and -34,210, were submitted to the Addiction Treatment Discovery Program (ATDP) of NIDA for testing in biogenic amine transporter assays and in in vivo locomotor assays.
Results: Surprisingly, both enantiomers had similar activities in the biogenic amine transporter and mouse locomotor assays. ATDP-34,209 and -34,210 had DA uptake IC50s of 13.0 ± 2.6 nM and 9.8 ± 2.3 nM. On the mouse locomotor assays, the ED50s were 3.3 mg/kg and 3.1 mg/kg based on a linear regression against log10 doses of the compounds. This differs from methylphenidate where only one enantiomer has activity.
Conclusions: Our studies suggest that the absence of a polar ester group such as in cocaine and methylphenidate allow a compound to bind to the reuptake site with different structures and give it a slow onset. Other compounds that have slow onsets are consistent with this. This information is useful for the design of novel stimulants with slow onsets.
Financial Support: The biogenic amine transporter and in vivo locomotor assays were performed by the ATDP program of NIDA.

MONDAY, JUNE 19, 2023

ORAL COMMUNICATION: NOVEL STRATEGIES FOR PAIN THERAPEUTICS: STILL TRYING
Plaza Ballroom A

RESPIRATORY DEPRESSING EFFECTS OF THE FLUORINATED FENTANYL ANALOGS, NFEPP, AND RR-49

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Aim: This study aimed to compare the relative respiratory depressing effects of two novel fluorinated fentanyl analogs (FFAs), RR-49 and NFEPP, to fentanyl in male and female Sprague-Dawley rats and to determine if these effects could be reversed with naltrexone pretreatment. The present report provides insight into the potential for these FFAs to produce analgesia with fewer CNS-mediated side effects, such as respiratory depression, compared to traditional opioids.
Methods: In this study, male and female Sprague-Dawley rats (n=8) were used to examine the RD effects of the leading FFAs, NFEPP and RR-49, and fentanyl using whole-body plethysmography. Compounds were administered intravenously in a cumulative dosing series, and minute volume (MV) was measured. Subsequently, test sessions were repeated with naltrexone pretreatment to determine if observed respiratory effects were opioid-mediated. One-way ANOVAs were used to compare respiratory effects of each drug to each subject's pre-injection baseline.
Results: All compounds significantly decreased MV, but NFEPP and RR-49 were less potent than fentanyl. The minimum doses required to produce changes in MV were 0.18 mg/kg ($p= 0.0254$) for RR-49, 0.32 mg/kg ($p= 0.0127$) for NFEPP, and 0.032 mg/kg ($p= 0.0042$) for fentanyl. The effects of NFEPP and RR-49 on MV were reversed with naltrexone (0.1 mg/kg) pretreatment.
Conclusions: These findings suggest that while RR-49 and NFEPP may represent safer alternatives to traditional opioids, they maintain fentanyl's respiratory depressing effects at doses approximately an order of magnitude greater than fentanyl. However, additional studies are needed to fully define the margin of safety of these compounds relative to traditional opioids in assays of pain.
Financial Support: This work was supported by NIDA grants F30DA057093 to SRE and R01DA039167 to KBF.

CHARACTERIZING BIASED MU-OPIOID RECEPTOR AGONISTS, PZM21 AND SR17018 IN SELF-ADMINISTRATION, AND WHOLE-BODY PLETHYSMOGRAPHY IN RATS

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Aim: Prior reports suggest PZM21 and SR17018 produce antinociceptive effects with reduced adverse side effects due to characteristics associated with biased mu-opioid receptor (MOR) agonists. However, other reports suggest that PZM21 and SR17018's favorable effects are due to partial efficacy at MOR. The current study compared PZM21 and SR17018 to full and partial MOR agonists in self-administration and whole-body plethysmography (WBP) in Sprague-Dawley rats.
Methods: In the self-administration study, six cohorts of two male and two female rats each self-administered MOR agonists (oxycodone, fentanyl, buprenorphine, butorphanol, PZM21, and SR17018) under a progressive ratio schedule of reinforcement. The highest completed ratio irrespective of dose for each agonist was translated to maximum infusion (Imax) and used to quantify relative reinforcing efficacy. In the WBP test, doses for each agonist were administered to three male and four female rats, within-session, in a quarter-log series using a cumulative-dosing procedure. Maximum respiratory depression (RDmax) was calculated by inversing minute ventilation and used for relative efficacy comparison.
Results: In self-administration, all agonists functioned as reinforcers in a dose-dependent manner. The rank order for Imax was fentanyl > oxycodone > PZM21 > buprenorphine > butorphanol > SR17018 > vehicle. Multiple comparisons test detected significant difference among oxycodone ($p = 0.0149$) and fentanyl ($p < 0.0001$) to vehicle. No significant difference was detected among vehicle and other agonists. In WBP, the rank order for RDmax was fentanyl > oxycodone > butorphanol > PZM21 > vehicle > SR17018 > buprenorphine. Multiple comparisons test detected no significant difference.
Conclusions: The results thus far indicate that biased MOR agonists, in terms of in vivo efficacy, do not uniformly cluster within the effect range encompassing prototypical full and partial MOR agonists.

Differences in in vivo efficacy between biased MOR agonists may be due to factors other than signaling bias (e.g., unidentified effects particular to chemical class).
Financial Support: Supported by F31-DA056209 to LMTP and R01-DA039167 to KBF

A HIGHLY G PROTEIN-BIASED MU OPIOID RECEPTOR AGONIST, SR-17018, HAS LOW IN VIVO EFFICACY IN PRIMATES

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Aim: SR-17018 was identified as a G protein-biased mu opioid peptide (MOP) receptor agonist with the highest bias factor and lacked MOP agonist-associated adverse effects in mice. The aim of this study was to determine the functional profile of spinal and systemic delivery of SR-17018 in non-human primates.
Methods: In vivo effects of SR-17018 were compared with those of MOP agonists in different intrinsic efficacies, DAMGO, morphine, heroin, and buprenorphine, in a series of behavioral assays established in rhesus monkeys (Macaca mutatta) (n=4 per study endpoint). Nociceptive, itch/scratching, and operant behavior were measured by experimenters blinded to the dosing conditions.
Results: Following intrathecal administration, SR-17018 (30-300 ug), buprenorphine (3-10 ug), morphine (10-30 ug), and DAMGO (1-3 ug), dose-dependently attenuated capsaicin-induced thermal allodynia ($p < 0.05$). However, unlike DAMGO and morphine eliciting robust itch-scratching activities, intrathecal SR-17018 and buprenorphine only elicited mild scratching activities, indicating that SR-17018 has low efficacy for activating MOP receptors. In the intravenous drug self-administration assay, heroin (0.3-10 ug/kg/infusion) produced a higher reinforcing strength (abuse liability) as compared to lower reinforcing strengths by SR-17018 (3-30 ug/kg/infusion) and buprenorphine (1-10 ug/kg/infusion) in primates under the progressive-ratio schedule of reinforcement ($p < 0.05$).
Conclusions: The intrathecal opioid-induced itch scratching and intravenous drug self-administration have been documented to distinguish MOP receptor agonists with different intrinsic efficacies in primates. Our findings reveal that in vivo apparent low efficacy of SR-17018 is similar to that of a MOP partial agonist buprenorphine measured by the non-human primate assays with translation relevance. Such a low intrinsic efficacy explains its improved side-effect profile of a highly G protein-biased MOP agonist, SR-17018, in primates.
Financial Support: This study was supported by the US-PHS grants DA049580, DA053343, and DA044775.

CHANGES IN ANALGESIC AND ABUSE-RELATED EFFECTS OF CANNABIS WITH REPEATED ADMINISTRATION IN HUMANS

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Drug Category Cannabis/Cannabinoids
Topic Tolerance/Dependence
Aim: Despite most medical cannabis patients citing pain relief as the primary reason for use, little is known about how daily cannabis use affects therapeutic utility relative to its effects on abuse liability. Our objective is to characterize cannabis' analgesic efficacy and abuse-related effects during repeated administration and upon abrupt abstinence.
Methods: Heavy cannabis users participated in this within-subject inpatient study (N = 4 to date). Participants smoked 2 cannabis cigarettes 3x/day, but the strength varied across days: Day 1: active cannabis (7% THC); Day 2-8: inactive cannabis (<0.01% THC); Day 9-15 active cannabis (7% THC). We assessed the effects of abrupt abstinence and repeated cannabis use on experimental pain (Cold Pressor Test; CPT) and abuse liability ('high').

Results: Data are preliminary. On the first day of inactive cannabis administration (Day 2), there was a 31% decrease in pain tolerability relative to active cannabis (Day 1), suggesting hyperalgesia; this resolved by the seventh day of inactive cannabis administration. Upon active cannabis reinstatement (Day 9), there was a 65% increase in pain tolerability relative to Day 1, indicative of analgesia; this returned to baseline within seven days. Ratings of 'high' were 53% greater when active cannabis was reinstated on Day 9 (80.3 ± 9.6 mm) vs. Day 1 (43.0 ± 9.6 mm), indicating that existing tolerance to abuse-related effects was lost following 7 days of abstinence.
Conclusions: There is considerable public health significance in understanding the impact of daily cannabis use and abrupt abstinence. Our findings suggest that (1) abrupt abstinence increases pain sensitivity; (2) analgesic tolerance develops within seven days but can be reversed following abstinence; and (3) tolerance develops to the abuse-related effects of cannabis, which also resolves upon abstinence. Data collection is ongoing.
Financial Support: This study is supported by NIDA DA050752.

ORAL COMMUNICATION: NICOTINE REINFORCEMENT
Plaza Ballroom D

REWARD-ENHANCEMENT DRIVES NICOTINE SELF-ADMINISTRATION IN FEMALE SPRAGUE-DAWLEY RATS

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Drug Category Nicotine/Tobacco
Topic Behavioral Pharmacology
Aim: Enhanced nicotine use vulnerability amongst women is attributed to greater sensitivity to environmental factors maintaining nicotine intake. One such factor is nicotine enhancement of environmental stimuli and rewards. This reward-enhancement facilitates nicotine intake, evidenced in rats by delivery of nicotine with a weakly reinforcing visual stimulus (VS) that nicotine enhances dramatically increasing nicotine self-administration. Only one study has examined the role of reward-enhancement in female rats' nicotine intake, finding a greater role for females. The present study sought to replicate and extend this work.
Methods: Female Sprague-Dawley rats were assigned to intravenously self-administer 0.03 mg/kg/infusion nicotine (n=12) or saline (n=12) on a Variable Ratio-3 schedule in two, ten session phases. Rats began in an Infusion Only phase, responding for only their assigned infusion. All rats then progressed to the Infusion+VS Phase, now responding for their assigned infusion and a 30-second VS. We conducted a three-way mixed ANOVA on Infusions Earned during sessions, examining Phase (Infusion Only vs. Infusion+VS), Drug (Nicotine vs. Saline), and Session (1-10).
Results: Infusions earned did not differ between nicotine and saline rats during the Infusion Only phase ($p=.112$). Nicotine intake dramatically increased during the Infusion+VS phase such that nicotine rats earned 107% more infusions than saline rats ($p=.004$).
Conclusions: Infusions of 0.03 mg/kg nicotine alone were not reinforcing, but delivering nicotine with a VS drastically increased nicotine intake in female rats. We replicated and extended prior research by adding a saline control, allowing researchers to assess the effects of experimental manipulations on VS reinforcement value and its synergistic effects when delivered with nicotine. Given the large role of reward-enhancement in female rats' nicotine intake, future studies should use this expanded behavioral model to examine the effects of female and women-specific factors potentially involved in women's enhanced nicotine use vulnerability.
Financial Support: Research supported by NIH R01-DA034389. RAB partially supported by DA046109.

DIET-INDUCED CHANGES IN NICOTINE VAPOR SELF-ADMINISTRATION AND METABOLIC MARKERS IN C57BL/6J MICE

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Drug Category Nicotine/Tobacco
Topic Behavior
Aim: Studies investigating the relationship between diets and drug use suggest that individuals who consume high-calorie, fat-rich foods are likely to depend on other substances, such as nicotine. Irrespective of this evidence, few studies have explored the pathophysiology of diet-induced obesity and nicotine vapor self-administration. Therefore, our objective was to investigate if diet impacts nicotine intake and, in parallel, examine glucose and insulin levels.
Methods: Adult male and female C57/BL6J mice were used in nicotine e-vape® self-administration (EVSA) assays after being maintained on a low-fat diet (LFD; n=9) or HFD (n=8) for 6 weeks. Weight and amount of food consumed were recorded weekly. After the EVSA schedule, plasma glucose and insulin levels were analyzed with an ELISA kit.
Results: HFD-assigned mice exhibited a significant increase in body weight ($p < 0.0002$), which correlated positively with glucose ($R2=0.2119$; $p = 0.2510$) and negatively with insulin levels ($R2=0.05207$; $p = 0.6226$). There was a significant increase in kcals of food consumed by HFD mice ($p < 0.0001$). LFD mice exhibited increased nicotine EVSA during low-effort responding (FR1 schedule; $p = 0.5654$). Conversely, HFD mice exhibited reduced reinforcing-related behavior (FR3 schedule; $p = 0.0023$) and motivation-related behavior (PR schedule; $p = 0.0153$). Physiologically, there was a negative association between glucose levels and nicotine vapor delivery in the HFD mice ($R2=0.1513$; $p = 0.3410$). Conversely, HFD mice showed a positive correlation between insulin levels and nicotine vapor delivery ($R2=0.4846$; $p = 0.0823$). Overall, there was no significant change in glucose ($p = 0.1976$) and insulin levels ($p = 0.8243$) in both LFD and HFD mice.
Conclusions: The results gathered from our experiment suggest that diet-induced nicotine intake may be due to a decrease in glucose and a parallel increase in insulin levels. Furthermore, these data support previous findings on smoking and insulin resistance. This experiment is clinically relevant to understanding the pathophysiology of diet-induced obesity and nicotine addiction.
Financial Support: This research was supported by the National Institute of General Medical Sciences of the National Institutes of Health under Award Number P20GM121299-01A1 through a pilot grant from the Joan C Edwards School of Medicine COBRE-ACCORD.

INTERACTION OF CIGARETTE NICOTINE DOSE AND DOSE EXPECTANCY IN HEALTH PERCEPTIONS AND BEHAVIORAL ECONOMIC DEMAND

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Drug Category Nicotine/Tobacco
Topic Behavioral Pharmacology
Aim: Prospective regulatory efforts to reduce public health harms of tobacco use may focus on mandates of cigarette nicotine content. Few studies have examined specifically how the interaction of (a) expectations of nicotine content and (b) actual nicotine content may affect consumer response and subsequent regulatory success (e.g., reduced abuse liability). The purpose of this within-subject, human laboratory study was to evaluate reduced nicotine expectancy effects using a balanced placebo design.
Methods: Participants who smoke daily (N=18; 44.4% female) completed four experimental sessions (random order, 2X2) manipulating expectancy (label of "average" nicotine versus "very low" nicotine) and nicotine dose (15.8 mg/g versus 0.4 mg/g). Participants first smoked a cigarette of that session's assigned condition with measurement of puff topography and cigarette subjective/health effects. Participants then completed an incentivized purchase task to measure behavioral economic demand for experimental cigarettes. Analyses evaluated main and interactive effects of dose expectancy and nicotine dose.
Results: Significant main effects of expectancy ($p<.001$) and dose ($p=.03$) were observed for estimated nicotine content with perceived lower nicotine in reduced nicotine expectancy and reduced nicotine dose conditions. Full nicotine cigarettes significantly increased heart rate relative to reduced nicotine regardless of expectancy ($p=.005$) indicating that pharmacological relevant doses were measured. Significantly lower

demand intensity (consumption at free price) was observed for reduced nicotine cigarettes in both expectancy conditions. Trends towards lower health harm attributed to reduced nicotine expectancy regardless of actual nicotine dose was observed (p=.08). No effects on puff topography were observed.
Conclusions: These data suggest that actual nicotine content may alter the reinforcing and physiological effects of cigarettes independent of dose expectancy while dose expectancy may alter the perceived health harms of cigarettes independent of actual nicotine dose. Future chronic exposure designs are needed to explore the durability of these effects to inform impacts on regulatory efforts.
Financial Support: Support was provided by the National Institute on Drug Abuse (NIDA) of the National Institutes of Health (R03 DA054098; T32 DA07209).

EXAMINING RACIAL DIFFERENCES IN SMOKING-RELATED OUTCOMES IN HUMANS DURING EARLY ABSTINENCE AND AFTER INTRAVENOUS NICOTINE INFUSION

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Drug Category Nicotine/Tobacco
Topic Substance Use Disorder
Aim: There are significant racial disparities in the prevention, pathophysiology, and treatment of smoking-related diseases, with minoritized populations carrying a heavier burden of smoking-related morbidity and mortality. While an enormous amount of smoking-related research exists, most studies investigating smoking-related illnesses have been conducted in racially-mixed or White-only samples, and minoritized populations remain under-represented. This study investigated racial differences between Black and White smokers in self-report, physiological, and biochemical smoking-related outcomes following confirmed overnight abstinence and subsequent IV nicotine infusion.
Methods: The sample consisted of 206 smokers (N=103 Black, N=103 White). Smoking-related baseline characteristics as well as outcome measures were separately analyzed with repeated-measures mixed-models.
Results: In terms of baseline demographics, Black smokers had lower rates of nicotine metabolism compared to White smokers (0.30 vs 0.44 3HC/cotinine, p<.0001), assessed with the nicotine metabolite ratio (NMR), and were more likely to smoke mentholated cigarettes than White smokers (99 vs 62 percent of sample, p<.0001). Black smokers experienced more negative drug effects, as measured by responses to the Drug Effects Questionnaire (DEQ), in response to nicotine after overnight abstinence ($F(2, 205.9)=3.48$, p=0.02), whereas White smokers reported no variation in subjective drug effects. Compared to Black smokers, White smokers had higher levels of negative affect ($F(1, 201.4)=4.48$, p=0.04), as measured by responses to the Positive and Negative Affect Scale (PANAS), after abstinence and nicotine infusion. No racial differences in withdrawal, cravings, or physiological outcomes were observed.
Conclusions: These findings suggest differences across race in nicotine's pharmacologic effects, which may stem from differences in the rate of nicotine metabolism and motivations to smoke. Greater insight into these differences may improve treatments for smoking-related illnesses for minoritized groups who smoke.
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ORAL COMMUNICATION: SEX AND GENDER DIFFERENCES IN SUDS
Grand Ballroom II

CHRONIC PROGESTERONE TREATMENT REDUCES NICOTINE CONSUMPTION AND ACCUMBENS MICROGLIAL MORPHOMETRICS IN A SEX-SPECIFIC FASHION

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Drug Category Nicotine/Tobacco
Topic Sex/Gender Differences
Aim: Craving and relapse to smoking appear to vary as a function of biological sex. In women, increases in 17β-estradiol (E2) and progesterone (P4) are associated with addiction vulnerability and resilience, respectively. P4 has been examined clinically as a smoking cessation agent and shows some promise for women. However, studies incorporating men have shown unclear or limited to no efficacy. As well, steroid hormones including P4 exert anti-inflammatory properties, which may underlie sex-specific effects on nicotine-related outcomes. We have previously found that neuroimmune signaling within the nucleus accumbens core (NAcore) is driven by nicotine seeking and consumption in a sex-specific fashion, whereby female rats are more susceptible to nicotine-induced neuroimmune consequences as compared to males. To date, there are no studies evaluating the neurobiological mechanisms by which P4 may yield sex-specific efficacy, and no studies have evaluated P4 in a preclinical nicotine rodent model.
Methods: 60 male and female Long Evans rats underwent nicotine or saline self-administration (SA) for 10 sessions (0.06 mg/kg/infusion), followed by 15 sessions in which rats received either P4 (1.75 mg/kg in 0.1 mL sesame oil, SC) or vehicle (sesame oil, SC) 15 min prior to sessions. Females were vaginally swabbed for cytology to track estrous cycle, and all rats were perfused immediately following the 25th session. Nucleus accumbens core (NAcore) tissue was then dissected for immunohistochemistry, confocal microscopy, and microglial morphometrics using the automated analysis program 3DMorph.
Results: Daily P4 treatment decreased nicotine consumption in gonad-intact female (but not male) rats (0.06 mg/kg/infusion; LME, $p<0.05$), and nicotine SA resulted in a phagocyte-like morphological structure of microglia. Surprisingly, we found that chronic, systemic P4 enhanced nicotine-induced NAcore microglial proliferation and phagocytic structure as compared to vehicle only in female rats, measured by significant reductions in ramification index (RI) and number of endpoints (LME, p's<0.05). Reductions in RI are associated with decreases in normal immune surveillance by microglia. As well, P4 treatment also increased the number of microglia present following chronic nicotine SA only in females (LME; $p<0.05$), which may indicate that P4 rescues microglia from definitive cell death induced by chronic nicotine use with sex specificity.
Conclusions: Together, we show that P4 may exert glioprotective effects on microglia and may reduce nicotine consumption in females through modulating NAcore microglia. Translationally, this neurobiological mechanism may underlie the sex-specific efficacy of P4 as a smoking cessation treatment. Given that P4 does not reduce smoking in men, our results may also justify examination of other possible therapeutics that have anti-inflammatory properties for smoking cessation, which may yield higher efficacy across both biological sexes.
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SEX DIFFERENCES IN GABA REGULATION OF DOPAMINE RELEASE IN THE NUCLEUS ACCUMBENS AND ITS ROLE IN COCAINE USE DISORDER

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Drug Category Stimulants
Topic Substance Use Disorder
Aim: While sex differences in the pervasiveness and prognosis of neuropsychiatric disorders have long been known to exist, there are few instances where approaches to pharmacological treatment of these disorders differ between the sexes, which likely contributes to ineffective treatments in women. In substance use disorder (SUD), women exhibit increased propensity to use drugs, a faster transition to addiction from first use, greater problems maintaining abstinence, and relapse at a higher rate than men. At the center of sex-differences in addiction vulnerability is the mesolimbic dopamine system. While work has focused on sex differences in the anatomy of dopamine neurons and relative dopamine levels, an important characteristic of dopamine release from axon terminals in the nucleus accumbens (NAc) is that it is rapidly modulated by local regulatory mechanisms independent of somatic activity. GABA released from local microcircuitry in

the NAc has been shown to play a critical role in regulating dopamine release at the terminals through ionotropic GABA-A and Gi-coupled GABA-B receptors and has also been implicated in cocaine-induced processes. Here we define basal sex differences in dopamine release regulation via GABA in the NAc and show how this is dysregulated by chronic cocaine exposure.
Methods: To dissociate dopamine terminal regulation from somatic regulation, we utilize ex vivo fast scan cyclic voltammetry and optogenetics in striatal brain slices. Dopamine release was evoked from terminals, and GABA receptor modulation of this signal was determined via bath application of picrotoxin (GABA-A antagonist), muscimol (GABA-A agonist), saclofen (GABA-B antagonist), and baclofen (GABA-B agonist) to slices. This was done at baseline in both males and females as well as after chronic cocaine exposure. For statistical analysis, we utilized two-tailed t-tests for all pairwise comparisons, and for all experiments with two categorical variables we utilized two-way ANOVA analysis.
Results: First, we found that both GABA-A and GABA-B receptors modulate dopamine release on a rapid time scale directly at the terminals in the NAc. There were sex differences in this regulation, with enhanced GABA-A-mediated inhibition observed in females and greater GABA-B-mediated inhibition observed in males. Additionally, GABAergic modulation of dopamine release was blunted in males following chronic cocaine exposure.
Conclusions: The results of these studies will contribute to the understanding of how sex fits into the comprehensive framework for dopamine release regulation and how dysregulation of these processes influences the trajectory of CUD in both males and females.
Financial Support: Funding was provided by startup funds from V.U. School of Medicine, Department of Pharmacology and the National Institutes of Health (NIH) (to E.S.C.). Funds from the National Institute of Drug Abuse (NIDA) DA042111, DA048931, DA056221, the Brain and Behavior Research Foundation, Whitehall Foundation, and the Edward J Mallinckrodt Jr. Foundation (E.S.C) also supported this work.

SEX DIFFERENCES IN THE BEHAVIORAL PHARMACOLOGY OF FENTANYL IN RATS

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Drug Category Opiates/Opioids
Topic Sex/Gender Differences
Aim: Fentanyl (FEN), a synthetic opioid and highly effective mu-opioid receptor agonist, is a major contributor to the growing rates of opioid-related overdoses and deaths. Sex differences in behavioral responses to morphine (MOR) have been reported previously. We now examine whether there are sex differences in behavioral responses to FEN. Findings would provide evidence of a potential driver of FEN addiction vulnerability in women.
Methods: Separate sets of male and female Sprague-Dawley rats were tested for: 1) analgesic responses in hot plate and tail flick tests; 2) locomotor activity in an open field (30-m); and 3) schedule-controlled responding under a fixed-ratio 15 (FR15) schedule of food pellet delivery (30-m). Analgesia responses and locomotor activity were assessed 30-m after administration of saline, 0.05 and 0.1 mg/kg (SC). Several doses of both FEN (0.003- 0.1 mg/kg) and morphine (0.3-10 mg/kg) were assessed in the schedule-controlled responding study 30-m after administration.
Results: Analgesic responses showed significant Sex, Dose, and Sex X Dose effects for both tail flick and hot plate tests ($P's < 0.01$). Latencies were lower in females compared to males across FEN doses but no differences were seen at baseline. No sex differences were found in distance traveled. Schedule-controlled responding rates decreased across FEN and MOR doses but there were no sex differences.
Conclusions: While FEN has a high analgesic potency, females uniquely showed increased analgesic responses compared to males. Yet, FEN did not alter activity effects differently between the sexes. These results mirror those reported from MOR behavioral responses in rats. Further analysis of the lever pressing and drug seeking for oral FEN self-administration is ongoing to assess whether there are sex differences in persistence of responding for FEN.
Financial Support: Office of the Assistant Secretary of Defense for Health Affairs through the Alcohol and Substance Abuse Research Program under Award No. W81XWH-18-2-0044 to CNH.

DO OVARIAN HORMONES MODULATE THE EFFECT OF DELTA-9-TETRAHYDROCANNABINOL (THC) ON INHIBITORY CONTROL IN WOMEN?

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Drug Category Cannabis/Cannabinoids
Topic Sex/Gender Differences
Aim: Cannabis and its main psychoactive constituent, delta-9-tetrahydrocannabinol (THC), impair cognitive processes, including the ability to inhibit inappropriate responses. However, there is a great deal of variability in responses to cannabinoid drugs, and little is known about the factors that influence the risk for adverse effects. One potential source of variation in response to cannabinoids in women is circulating ovarian hormones such as estrogen (E) and progesterone (P). Preclinical studies indicate that E levels are positively related to cannabinoid receptor density in limbic brain regions and increase behavioral sensitivity to cannabinoids. It is not known whether the effects of THC on inhibitory performance in women depend on levels of circulating E. Here, we investigate whether levels of estrogen during the follicular phase of the menstrual cycle modulate the effect of THC on inhibitory control in healthy women.
Methods: Healthy female occasional cannabis users (N = 60) participated in three sessions during which they received THC (7.5 mg and 15 mg, oral) and placebo during the follicular phase, when estrogen levels varied from low to high. They completed a Go/No Go (GNG) task at the time of peak drug effect. We hypothesized that higher levels of estrogen would impair GNG performance and worsen THC-induced impairment.
Results: THC (15 mg) increased response time and errors of commission/false alarms and decreased accuracy on the GNG task, relative to placebo. GNG task performance was not related to estrogen levels, either after placebo or THC.
Conclusions: These results suggest that variations in estrogen levels during the follicular phase do not alter GNG performance or the effect of THC on inhibitory control.
Financial Support: NIDA F31DA049391 (PI: Elisa Pabon); NIDA R01DA002812 (PI: Harriet de Wit)

ORAL COMMUNICATION: CANNABIS POLICY AND REGULATION
Governor's Square 15

STATE CANNABIS LEGALIZATION AND INCREASES IN CANNABIS USE DISORDER IN THE U.S. VETERANS HEALTH ADMINISTRATION, 2005 TO 2019

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Aim: Cannabis use disorder (CUD) is increasing among U.S. adults, but few national studies examined the role of medical and recreational cannabis laws (MCL, RCL) in these increases. We examined the role of MCL and RCL enactment in increases in CUD prevalence among Veterans Health Administration (VHA) patients, 2005-2019.
Methods: Patients age 18-75 with ≥1 VHA primary care, ED or mental health visit and no hospice/palliative care within a given calendar year (n=3,234,382 to 4,579,2994) were analyzed using electronic health record ICD-9-CM or ICD-10-CM CUD diagnoses. Staggered-adoption difference-in-difference analyses estimated MCL and RCL effects on CUD prevalence, using linear binomial regression with fixed effects for state, year, time-varying MCL/RCL status, state-level sociodemographic covariates, and patient age-group, sex, race and ethnicity.
Results: From 2005-2019, adjusted CUD prevalences increased from 1.38% to 2.25% in no-CL states; 1.38% to 2.54% in MCL-enacting states, and 1.39% to 2.56% in RCL-enacting states. Enacting MCL led to a 0.054% (0.045-0.064) increase in CUD prevalence, i.e., that 4.7% of the increase in CUD prevalence in MCL-enacting states could be attributed to MCL, while enacting RCL led to a 1.115% (95% CI=0.098-

0.131) increase in CUD prevalence, i.e., that 9.8% of the increase in CUD prevalence in RCL-enacting states could be attributed to RCL. RCL effects were strongest in patients aged 65-75, with an increase of 0.147% (95% CI=0.129-0.166) in CUD prevalence due to RCL, i.e., 18.6% of the increase in CUD prevalence in that age group.
Conclusions: MCL and RCL contributed to higher CUD prevalence in VHA patients, particularly older ones. Consistent with household surveys, effects were relatively small, suggesting that laws affected cannabis diffusely across the country, or that other factors played a larger role in the overall increases. Results underscore the need to screen for cannabis use and CUD, and treat CUD when it is present.
Financial Support: R01DA048860; New York State Psychiatric Institute; Veterans Health Administration (VHA)

CHANGES IN STATE-LEVEL MEDICAL AND RECREATIONAL CANNABIS LAWS AND CANNABIS USE OUTCOMES BY SEXUAL IDENTITY AND GENDER FROM 2015-2019

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Drug Category Cannabis/Cannabinoids
Topic Policy
Aim: Prevalence of cannabis use (CU) and cannabis use disorder (CUD) is higher among sexual minoritized adults versus heterosexuals and, in cross-sectional studies, is higher for sexual minority adults in states with t medical cannabis laws (MCL) versus without MCL. To explore if these differences were attributable to cannabis laws, we examined associations between changes in state MCL and recreational cannabis law (RCL) status and CU outcomes by sexual identity and gender.
Methods: We used 2015-2019 National Survey on Drug Use and Health data on sexual identity (heterosexual, gay/lesbian, bisexual) and CU outcomes among adults (n≈51,000 annually). For descriptive analyses of CU outcomes, states were categorized using 2019 MCL/RCL status. For time-varying MCL/RCL exposure, we compared individual interview dates with state MCL/RCL operationalization dates; people interviewed after MCL/RCL were considered exposed. We used multilevel logistic regression controlling for state, year, and individual/state characteristics to generate predicted prevalences of past-year daily CU (300+ days) and CUD among those with past-year CU by time-varying MCL/RCL status. Adjusted odds ratios compared changes in daily CU/CUD prevalence after-MCL versus before-MCL and after-MCL/after-RCL versus after-MCL/before-RCL by sexual identity and gender.
Results: In 2019, daily CU was 27.6%-78.0% higher for bisexual versus heterosexual women across all states. Daily CU was higher among heterosexual women in MCL-only (22.8%) and MCL/RCL states (16.8%) versus never MCL/RCL states (13.9%). There were no differences in past-year CUD prevalence. Adjusted odds of daily CU decreased only among heterosexual women after-MCL/after-RCL versus after-MCL/before-RCL (aOR=0.67[0.50-0.90]), but not when comparing after-vs-before MCL. Policy changes were not associated with CUD changes for any gender or sexual identity subgroup.
Conclusions: Past-year daily CU decreased among heterosexual women after RCL, but not among gay/lesbian or bisexual women or among men from 2015-2019. Bisexual women's already elevated prevalence of daily CU may limit the impact of state cannabis laws.
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CANNABINOID-INVOLVED EXPOSURES, ED VISITS AND HOSPITALIZATIONS BEFORE AND AFTER ARKANSAS MEDICAL MARIJUANA LAW ENACTMENT: INITIAL TRENDS

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Aim: Medical marijuana laws (MMLs) have been enacted in most U.S. states and have been associated with negative consequences, included increased illicit cannabis use, rates of cannabis use disorder, unintentional childhood exposure, and impaired driving. Given the 2019 MML enactment in Arkansas, this study examined initial trends regarding several health outcomes from 2017 to 2020 or 2021(as data are available).

Methods: Cannabinoid exposure data were obtained from the UAMS Poison Center. Emergency department (ED) visits and hospitalizations that included a diagnostic code for marijuana and/or emesis were obtained from the Arkansas Department of Health Hospital Discharge Data System. Given the first medical marijuana dispensary opened in May of 2019, poison regression analyses determined any longitudinal changes in number of cannabinoid exposures from 2017-2018 to 2020-2021 (cannabinoid exposures) or 2017-2018 to 2019-2020 (ED visits, hospitalizations). Pairwise comparisons between years with unadjusted and Tukey adjusted p-values were also performed.
Results: The number of cannabinoid exposures in 2020 and 2021 were significantly higher than in 2017 and 2018 ($p<0.0001$). The number of marijuana-involved ED visits increased significantly each year from 2017 to 2019 ($p<0.0001$), with no significant difference between 2019 and 2020 ($p=0.84$). ED visits involving marijuana and emesis increased significantly from 2017 to 2019 ($p<0.002$) and from 2017 to 2020 ($p<0.001$), with the number being higher in 2020 than in 2019 ($p<0.0001$) or 2018 ($p<0.001$). Hospitalizations involving marijuana significantly increased every year from 2017 to 2020 ($p<0.0001$). Changes in the number of hospitalizations involving marijuana and emesis were significantly greater from 2019 to 2020 than 2017 to 2018 ($p=0.0074$) and the number hospitalized in 2020 was significantly greater than in 2017-2019 ($p<0.0001$).
Conclusions: As elsewhere, MML enactment in Arkansas is associated with initial negative health outcomes. Continued monitoring is vital in order to inform public awareness/prevention and policy in the state.
Financial Support: Supported by SAMHSA grants H79TI083287 and 6H79SP080990 to Arkansas Department of Human Services/Division of Aging, Adult, and Behavioral Health Services

DOSE-DEPENDENT EFFECTS OF SMOKED CANNABIS ON SIMULATED DRIVER PERFORMANCE: PRELIMINARY FINDINGS

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Drug Category Cannabis/Cannabinoids
Topic Other
Aim: Epidemiological and laboratory data show that cannabis can impair driving-related skills and increase the risk of collision involvement. We used established driving simulator parameters to examine the relationships between driving performance and dose.
Methods: 36 adults (19 females; 17 males) aged 19 to 36 years (mean 25.5) who used cannabis 1-5 days/week participated in a randomized, double-blinded, placebo-controlled, within-subjects study. A range of smoked cannabis doses (0.0%, 6.25%, 12.5%, 22.0% THC) were examined using an ad libitum smoking procedure. Measures of vital signs, subjective effects (visual analogue scales [VAS]), and cognition were analyzed. Participants drove 30 and 90min after smoking cannabis. Peak change from baseline scores were analyzed using linear mixed-effect models.
Results: At 30 and 90 minutes, standard deviation of lateral position in all active doses significantly differed from placebo in both the full attention ($p < 0.001$) and cognitive load ($p < 0.01$) tasks. Standard deviation of speed (SDSP) in all active doses significantly differed from placebo in both full attention ($p < 0.01$) and cognitive load ($p < 0.05$) with the high dose producing a higher SDSP than other doses for the full attention task. For reaction time (RT), we saw a strong dose effect ($p < 0.0001$) with medium and high doses producing longer RT than placebo ($p < 0.0001$), while the low dose was similar to placebo. The models indicated that the dose effect was similar at 30 and 90 minutes. There were significant main effects of dose for all VAS measures and significant main effects of time for some VAS measures ($p < 0.05$).
Conclusions: Preliminary findings suggest some dose-dependent effects of cannabis on driving performance measures and that there may be divergence between observed effects on driving performance and RT that is inconsistent with when drivers subjectively perceive they are impaired.
Financial Support: Public Safety Canada

ORAL COMMUNICATION: PREP AMONG DRUG USERS
Governor's Square 15

EXPLORATION OF HIV RISK BEHAVIORS AND ATTITUDES TOWARDS PREP AMONG PEOPLE WHO INJECT DRUGS BY GENDER AND SEXUAL ORIENTATION

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Drug Category Opiates/Opioids
Topic Behavior
Aim: Decreasing new HIV infections in the US by 90% by 2030 is the goal of the federal Ending the HIV Epidemic initiative. People who inject drugs (PWID) are at increased risk for acquiring HIV, however uptake of Pre-Exposure Prophylaxis (PrEP) in this group has been extremely limited in the US and globally. This study evaluated interest and concerns around both oral and injectable PrEP among PWID across different gender and sexual orientations.
Methods: Cross-sectional analysis of survey data from 8 different sites assessing attitudes and interest in PrEP were collected at a single post-treatment study visit during HERO, a pragmatic clinical trial of models of hepatitis C virus (HCV) treatment delivery among people who had injected drugs in the past 90 days. Demographics, HIV risk behaviors and attitudes towards PrEP are described overall as well as by the following self-identified gender and sexual orientation categories: heterosexual men, heterosexual women, men who have sex with men (MSM), women who have sex with women (WSW), transgender male to female (MtF); no female to male transgender participants enrolled. Interest in and barriers to PrEP were compared across categories using Chi-square tests.
Results: 283 participants completed the survey between Sept 2016 and Aug 2018. The mean (±SD) age was 44 (±11) years. Gender and sexual orientation were reported as follows: heterosexual men 65%, heterosexual women 23%, MSM 4%, WSW 6%, and MtF 1%. 42% reported receptive injection equipment sharing and 41% had overlap of sex and injecting partners during the past 3 months. Self-perceived HIV risk scores (0-10) were low overall, mean (±SD) 2.3 (±2.0). Interest in injectable PrEP (49.6%) was substantially higher than interest in daily oral PrEP (19.6%). Interest in injectable PrEP was significantly different across the groups; heterosexual men reported the lowest interest (43.8%), compared to heterosexual women (59.6%), MSM (58.3%), WSW (76.5%) and MtF (100%) (p=0.003 across groups). The most commonly cited concerns were medication side effects (52%) and interactions with other medications (39.4%). Perceived HIV risk and PrEP barriers were not significantly different among the gender/sexual orientation categories.
Conclusions: Despite ongoing risk factors for HIV, this cohort of PWID who had been treated for HCV had low self-perceived HIV risk. There was higher interest in injectable PrEP, and the top concerns about PrEP were related to side effects and medication interactions. These results suggest high acceptability of injectable PrEP among PWID, particularly among women and gender/sexual minority groups who may have overlapping sex and drug risk factors, and the need for education around PrEP candidacy and side effects.
Financial Support: PCORI Research Grant

FACTORS ASSOCIATED WITH ACTIVE AMPHETAMINE-TYPE STIMULANT USE AMONG MALAYSIAN TRANSGENDER WOMEN

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Sex/Gender Differences
Aim: Aims. The use of illicit amphetamine-type stimulants (ATS), including methamphetamine and MDMA (3,4-methylenedioxy-methamphetamine) has greatly increased over the last decade. The use of ATS is associated with several adverse health outcomes, including HIV transmission. Evidence suggests that ATS use has expanded rapidly among key populations affected by HIV in Malaysia, including transgender women. This study explores the drivers of active ATS use among transgender women in Malaysia.
Methods: Methods. Data are from a 2017 cross-sectional survey of 361 transgender women regarding their attitude towards PrEP knowledge and use for HIV prevention. The present study aimed to evaluate the factors associated with active ATS use, defined as the use of methamphetamine or MDMA within the previous 30 days. Data were analyzed using logistic regression to determine factors associated with active ATS use.
Results: Results. Most participants were between 25-40 years old (57.3%), ethnically identified as Malay (75%), and single (67.6%). Active ATS use was reported by 10.2% of participants. In the multivariable analysis, active ATS use was significantly associated with active hormone therapy use (aOR = 0.364; 95% CI = 0.169, 0.784) and having a history of drug related arrests (aOR = 4.604; 95%CI = 1.813, 11.691).
Conclusions: Conclusions. Our findings show a high prevalence of active ATS use among transgender women in Malaysia, in addition to its correlation to other health-related factors. Interestingly, we found that trans women who were actively using hormone therapy, were less likely to engage in active ATS use. This relationship should be explored further along with the relationship between incarceration history. In addition, further prevention strategies and efforts are needed to decrease ATS use among transgender women in Malaysia.
Financial Support: Supported by (funding source). This research was supported by a grant from the Yale Bates Summer Fellowship, the Yale Global Health Seed Funding Award, and Yale Global Health Studies Scholarship.

HIV PRE-EXPOSURE PROPHYLAXIS PROGRAMMATIC PREFERENCES AMONG PEOPLE WHO INJECT DRUGS: A DISCRETE CHOICE EXPERIMENT

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Infectious Disease (e.g., HIV, HCV)
Aim: To elicit preferences for HIV pre-exposure prophylaxis (PrEP) programmatic characteristics and assess differences by sex assigned at birth among people who inject drugs (PWID), who, despite an increased burden of HIV, have very low PrEP uptake.
Methods: From January-December 2022, we conducted a discrete choice experiment, a market-based research technique, with 238 PWID in San Diego, California. Participants viewed 18 different programmatic scenarios in sets of three and chose their preferred scenario in each set. Scenarios consisted of the following characteristics: PrEP modality (injectable, implant, oral), frequency of use (annual, bi-monthly, daily), service setting (community-based organization, clinic, telemedicine), prescription access (on-site service setting, street outreach, mail), and adherence support (social support, outreach worker, text reminder). We modeled choice overall and by sex assigned at birth using multinomial logistic regression to estimate part-worth utility scores (PWUS; which reflect relative preferences for specific characteristics) and relative importance scores (RIS; which reflect the influence of characteristics on program choice).
Results: Most participants were assigned male at birth (71.84%). Overall, frequency of use (RIS: 52.70) and modality (RIS: 31.96) had the greatest impact on choice. Relative to daily use, participants preferred annual (PWUS: 1.54) and bi-monthly (PWUS: 0.663) use. Relative to no PrEP, participants preferred oral (PWUS: 0.96) and injectable PrEP (PWUS: 0.459) over PrEP implants (PWUS: 0.024). Participants did not indicate strong preferences for specific service setting, prescription access, or adherence support characteristics. Results by sex assigned at birth mirrored the overall sample, but adherence support had a slightly greater impact on choice than service setting or prescription access for females, and preferences for oral over injectable PrEP were stronger for males.

Conclusions: PrEP modalities with less frequent use requirements may support PrEP uptake and persistence among PWID. Programmatic modifications may be needed to optimize PrEP implementation for specific subgroups of PWID.
Financial Support: This work was supported by the San Diego Center for AIDS Research (National Institute of Allergy and Infectious Diseases, grant P30AI036214) with additional support from the National Institute on Drug Abuse (grants R01DA049644-S1, R01DA049644-02S2, K01DA043412, T32DA023356, and 3K01DA043412-04S1), and NIH NRSA T32 DA023356.

IMPACT OF IMPAIRED COGNITIVE FUNCTIONING AMONG PERSONS ON MEDICATION FOR OPIOID USE DISORDER

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Drug Category Opiates/Opioids
Topic Infectious Disease (e.g., HIV, HCV)
Aim: Persons with opioid use disorder (OUD) often exhibit mild to moderate cognitive impairment that disrupts treatment adherence and retention in care. This also reduces the ability for people with OUD to retain and apply HIV prevention knowledge over time. We aimed to investigate whether impaired cognitive functioning impacts the accrual of Pre-Exposure Prophylaxis (PrEP) -related adherence knowledge and motivation in the context of a bio-behavioral intervention.
Methods: A sample of 168 people on medication for OUD in New Haven, CT completed a 4-week evidence-based PrEP-focused HIV prevention intervention. All participants were stabilized on medication for opioid use disorder (MOUD) in the context of outpatient drug treatment and were newly started on PrEP. Using a cognitive dysfunction risk score, participants were categorized into two groups: Impaired or Intact cognitive functioning. Data were analyzed using t-tests to determine if there were between-group differences in PrEP-related adherence knowledge and motivation at a 3-month follow-up point.
Results: Participants with Impaired cognitive functioning displayed lower retention of PrEP knowledge ($p=0.037$) and lower levels of motivation to adhere to PrEP ($p=0.013$) compared to participants with Intact cognitive functioning 3-months after completing the intervention.
Conclusions: The opioid epidemic has led to increases in HIV transmission among people who inject drugs and people with OUD. PrEP can serve as a key HIV prevention tool but requires high levels of adherence. Results from this study provide evidence of predictors of PrEP adherence, as persons with impaired cognitive functioning displayed significantly impeded PrEP-related adherence knowledge and motivation. These results have implications for an array of fundamental outcome variables, including motivation to stay in drug treatment. Future studies should develop/test strategies to compensate for cognitive dysfunction in this patient population in order to enhance key outcomes, such as PrEP adherence.
Financial Support: This research was funded by the National Institute of Drug Abuse (NIDA) via grant R01-DA044867 to Dr. Michael Copenhaver.

TUESDAY, JUNE 20, 2023

ORAL COMMUNICATION: SUD AND PREGNANCY
Grand Ballroom II

USE OF CLUSTER ANALYSIS TECHNIQUES TO EXPLORE ICD-10-CM CODE DATA IN A LONGITUDINAL BIRTHING PERSON-CHILD LINKED SURVEILLANCE SYSTEM OF PREGNANCIES COMPLICATED BY OPIOID USE DISORDER

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Center, [5]University of Utah, [6]Boston Medical Center, [7]Center for Health Research, Kaiser Permanente Northwest, [8]University of South Florida Health, [9]University of Rochester Medical Center, [10]Friends Research Institute
Drug Category Opiates/Opioids
Topic Artificial Intelligence
Aim: The MATernaL and Infant NetworK to Understand Outcomes Associated with Medication for Opioid Use Disorder (OUD) during Pregnancy (MAT-LINK) conducts linked surveillance of birthing person and child dyads using electronic health records from seven U.S. clinical sites. Few resources exist for understanding ICD-10-CM code data in the context of a longitudinal surveillance system with linked dyads. Traditional approaches such as descriptive statistics limit the ability to identify patterns or meaning within large unstructured data. This analysis explored unsupervised machine learning techniques to investigate patterns in ICD-10-CM code data for pregnancies complicated by OUD.
Methods: The ICD-10-CM code data were categorized using the Clinical Classifications Software Refined (CCSR) reference list. K-means and hierarchical clustering analyses were performed using Python to identify clusters and explore similarity among dyads based on CCSR category patterns. Summary tables and data visualizations were employed to assess analysis results.
Results: By applying k-means and hierarchical clustering, we identified three main clusters of dyads. The most common CCSR comorbidities varied by cluster as follows: Cluster 1 (N: 2,603), personal/family history of disease (mean comorbidity count per dyad in the cluster: 3.4, SD: 5.6); Cluster 2 (N: 496), tobacco-related disorders (mean: 19.5, SD: 17.0); and Cluster 3 (N: 9), stimulant-related disorders (mean: 29.9, SD: 89.7). Heat maps and scatterplots identified comorbidity patterns, including a higher occurrence of neurodevelopmental disorders and stimulant disorders in Cluster 2.
Conclusions: K-means and hierarchical clustering identified patterns in ICD-10-CM code data for birthing person-child linked longitudinal data that will inform future modeling efforts, particularly where literature on potential relationships among prenatal exposures, comorbidities, and child health outcomes are limited. These methods are customizable and can be applied to other datasets involving unstructured data to discover patterns that would otherwise require time-intensive manual review or may be missed by observation.
Financial Support: None

PREVALENCE OF PSYCHOSOCIAL ISSUES AMONG PREGNANT WOMEN WHO DO AND DO NOT USE ILLICIT SUBSTANCES

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Drug Category Alcohol
Topic Disparities
Aim: During pregnancy, psychosocial issues like smoking, depression, and inadequate health care, can contribute to adverse birth outcomes. It is generally believed that pregnant women who use illicit substances are more likely to experience these issues compared to pregnant women who don't. However, the prevalence of these psychosocial issues has rarely been calculated and compared using nationally-representative data.
Methods: The American College of Obstetricians and Gynecologists recommends pregnant women be screened for 10 different psychosocial issues. We calculated the weighted prevalence of six of them using representative variables in the National Survey on Drug Use and Health (NSDUH 2015-2019), comparing pregnant women who did vs. did not report past-month illicit substance use. More specifically, we examined tobacco use (current cigarette smoking), alcohol use (past-month alcohol use), depression (serious past-month distress), barriers to care (no health insurance), nutrition (receiving food stamps), and unstable housing (moved 3+ times in past year).
Results: Women pregnant at the time of survey (n=3,657) who reported past-month illicit substance use (6.3%) had higher rates of all psychosocial issues examined, including current cigarette smoking (44.9% vs. 6.5%; age-adjusted odds ratio (AOR)=7.14 (95% CI 4.98, 10.20), p<.001); past-month alcohol use (36.1% vs. 7.8%; AOR=6.80 (4.69, 9.86), p<.001); serious past-month distress (23.0% vs. 5.0%; AOR=4.99 (3.07, 8.11), p<.001); lack of health insurance (11.7% vs. 6.2%; AOR=1.79 (1.07, 2.99), p=.03); and receipt of food stamps (45.0% vs. 24.0%; AOR=2.26 (1.55, 3.29), p<.002). Housing instability trended in the same

direction but was compatible with there being no difference between groups (10.6% vs. 5.5%; AOR=1.59 (0.95, 2.66), p=.08).
Conclusions: All the psychosocial issues examined were more pervasive among pregnant women reporting recent illicit substance use, most by a factor of 2 or more. These results underscore the importance of multidisciplinary efforts to engage them in care and improve maternal and perinatal health outcomes.
Financial Support: R01DA047867

PSYCHOSOCIAL FACTORS ASSOCIATED WITH PRENATAL MARIJUANA USE

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Drug Category Cannabis/Cannabinoids
Topic Prenatal/Perinatal
Aim: Prenatal cannabis use has increased in the past few years among young women. This study examines the psychosocial factors associated with prenatal cannabis use in a sample of young women and hypothesizes that depression will be associated with prenatal cannabis use.
Methods: Pregnant individuals were recruited from several prenatal clinics and an antepartum unit in the Pittsburgh area. Participants (N=359) aged 13-21 (M = 19.5) completed an online survey that measured frequency and quantity of marijuana use before and during pregnancy. The survey also assessed multiple facets of psychosocial health including depressive symptoms, stress, intimate partner violence (IPV), reproductive coercion, and satisfaction with living situation.
Results: Participants were 66.9% Black, 20.6% White, 9.7% Bi-racial, 2% other, and 0.6% Asian. Before pregnancy, 224 (62.3%) participants used marijuana at least yearly and 96 (26.7%) continued use after pregnancy recognition. Bivariate analyses showed that being older ($r = .17$ $p < .001$), identifying as Black ($r_{pb} = -.11$, $p = .04$), stress ($r = .17$, $p < .001$), having experienced IPV ($r_{pb} = .12$, $p = .03$), and depressive symptoms ($r = .22$ $p < .001$) were significantly correlated with prenatal cannabis use. After controlling for age, race, and pre-pregnancy cannabis use, depressive symptoms was the only significant psychosocial predictor of prenatal cannabis use ($b^* = .18$, $p = .01$) in a hierarchical regression model ($F (6, 325) = 26.27$, $p < .001$, $R2 = .33$).
Conclusions: The relationship between depression and prenatal cannabis use indicates that interventions to reduce cannabis use may be more effective if designed to address depression. As rates of both depression and cannabis use have increased in recent years, more research examining this dynamic is needed. Finally, integration of mental health care in obstetric settings could contribute to a wide variety of positive outcomes for both mother and child.
Financial Support: National Institute of Health, R01DA046401, PI: De Genna

TIME-VARYING EFFECTS OF SUBSTANCE CRAVING ON SUBSTANCE USE AMONG PREGNANT WOMEN IN SUBSTANCE USE DISORDER TREATMENT

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Drug Category Other, Substance use broadly
Topic Other
Aim: Substance use during pregnancy confers a wide range of risks to both the mother and the developing fetus. We conducted a 4-week ecological momentary assessment (EMA) study of pregnant women (n = 32) in substance use disorder treatment who had a history of trauma (Sanjuan et al., 2019) to uncover the risk and protective factors for substance use at the momentary level. Using multilevel modeling, we found positive within-subject associations between posttraumatic stress disorder symptoms and substance craving, which in turn was associated with increased substance use (Sanjuan et al., 2020). These prior analyses assume the associations between these variables are constant over time.
Methods: In the present study, we conducted a Time-Varying Effect Model (TVEM; Li et al., 2015) to determine if the association between substance craving and substance use changes as a function of

gestational weeks. We fit the model using the P-spline method; the best model fit had six splitting points ("knots") based on AIC.
Results: Consistent with our hypothesis, we found that the positive association between substance craving and substance use diminished over time such that substance craving was a significant risk factor for substance use earlier in the pregnancy (i.e., from weeks 18 to 25), but was largely non-significant later in the pregnancy (i.e., from weeks 25 to 38). Given the gestational age range in the present study (at baseline, M = 26.8 weeks, SD = 5.29, range = 18 - 35), we had very low precision in the substance craving-substance use relationship later in pregnancy (i.e., after 28 weeks).
Conclusions: Future research is needed to examine these associations earlier in pregnancy (e.g., during the first trimester). Further, additional research is needed to explore plausible biological and psychological mechanisms for these changing associations.
Financial Support: U54MD004811 (MPIs: Brave Heart, Cacari Stone, Sanchez, Verney)
K23AA025094 (PI: Sanjuan)
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ORAL COMMUNICATION: MINOR CANNABINOIDS: MILD HIGH?
Plaza Ballroom A

THE EFFECTS OF CANNABICHROMENE (CBC) ON CISPLATIN-INDUCED NEUROPATHY AND REWARD IN MICE

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Drug Category Cannabis/Cannabinoids
Topic Behavioral Pharmacology
Aim: Cannabichromene (CBC) has demonstrated anti-nociceptive properties against acute pain and against chronic inflammatory pain. This research examined whether CBC could attenuate cisplatin-induced tactile allodynia without rewarding effects.
Methods: To evaluate the effects of CBC on cisplatin-induce neuropathy (CIN), male mice were given 6 doses of 2.3 mg/kg cisplatin intraperitoneally on alternating days to produce tactile allodynia, which was quantified using an electronic Von Frey (eVF). On test day, mice were administered either vehicle or 3.0 mg/kg oxycodone or 10.0, 25.0, 50.0, 75.0 mg/kg CBC IP and tactile responses were measured on the eVF 30 min later. To determine if analgesic doses of CBC produced reward, mice were enrolled in the condition place preference paradigm (CPP). Mice received 4 drug/no-drug conditioning trials using 3.0 mg/kg oxycodone as a positive control.
Results: Cisplatin produced robust tactile allodynia that was attenuated by 3.0 mg/kg oxycodone, 25.0, 50.0, and 75.0 mg/kg CBC but was not affected by vehicle or 10.0 mg/kg CBC. In CPP, the doses of CBC that produced anti-nociception against CIN showed neither reward nor aversion.
Conclusions: These findings suggest CBC could be an effective treatment for neuropathic pain without signs of aversion or an abuse liability. These data build on previous findings that CBC is efficacious against acute pain- particularly thermal, inflammatory, and acid-induced pain. Future studies should examine whether prophylactic treatment of CBC can prevent the onset of chemotherapy-induced neuropathy, as this would significantly increase the quality of life for cancer patients. These results suggest CBC as potential analgesic in pain management.
Financial Support: University of Mississippi Center of Biomedical Research Excellence in Natural Products Neuroscience (P30GM122733).

TERPENE AND CANNABINOID PROFILE PREFERENCES AND CANNABIS USE PRACTICES IN MEDICAL CANNABIS PATIENTS WHO USE CANNABIS FOR PAIN AND ANXIETY

Ekaterina Fedorova[*1], Janna Ataiants[1], Jim Seaberg[1], Maddy Finkelstein[1], Victoria Ryan[1], Jon Cohn[2], Stephen Lankenau[1]*

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Aim: Pain and anxiety are the two most common qualifying conditions among medical cannabis patients (MCPs) in Pennsylvania, and the majority of MCPs with pain as a qualifying condition also report having anxiety. There has been a growing interest in the therapeutic potential of different terpene profiles in cannabis products, though certain terpenes that alleviate pain might also exacerbate anxiety symptoms. We analyzed data from a baseline survey of MCPs to understand how cannabis use practices, including preferences for terpenes and cannabinoids, differ between MCPs who use cannabis to relieve pain, or anxiety, or both.
Methods: The analytic sample (n=341) consisted of participants who self-reported using cannabis in the past 90 days to relieve physical pain only (n=44, 12.9%), to relieve feeling uptight/anxious only (n=91, 26.7%), or to relieve both conditions (n=206, 60.4%). For cannabis practices (CBD use, cannabis forms, days and amount, time of the day, primary strain, terpenes, cannabinoids) that were associated with use for pain and/or anxiety at $p<0.05$ level in bivariate analysis (Chi-square or Kruskal-Wallis tests), we further examined associations in adjusted models with use for anxiety only as a reference group.
Results: MCPs who used cannabis for both pain and anxiety were more likely to report CBD use ($p<0.01$); use cannabis any time of the day or night ($p<0.01$); use topicals/creams ($p<0.001$); and prefer Myrcene, Caryophyllene, and CBG ($p<0.001$) compared to those who used cannabis for anxiety only. Furthermore, those seeking to relieve both conditions reported that terpene ($p<0.001$) and cannabinoid ($p<0.01$) profiles influence strain choice.
Conclusions: MCPs who use cannabis for pain and anxiety demonstrated cannabis practices and terpene and cannabinoid preferences distinct from those who use cannabis either for pain or anxiety alone. Further qualitative and controlled studies of cannabis strains with terpene and cannabinoid profiles suitable for simultaneous pain and anxiety relief are warranted.
Financial Support: Verano

WITHIN-SUBJECT, DOUBLE-BLIND HUMAN LABORATORY EVALUATION OF CANNABIDIOL ON OPIOID-INDUCED ANALGESIA AND SUBJECTIVE EFFECTS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavioral Pharmacology
Aim: Preclinical studies support the coadministration of cannabinoids with opioid agonists to reduce the amount of opioids required for analgesia. However, human laboratory studies on the opioid-sparing properties of cannabinoids are fewer in number and less promising. This double-blind, randomized human laboratory study evaluated the acute effects of cannabidiol (CBD; Epidiolex) on opioid induced analgesia and subjective effects among healthy adults.
Methods: Participants (n = 27) completed 5, 8-hour sessions in which they received: (1) placebo + placebo, (2) 4 mg hydromorphone + placebo, (3) 4 mg hydromorphone + 50 mg CBD, (4) 4 mg hydromorphone + 100 mg CBD, and (5) 4 mg hydromorphone + 200 mg of CBD. To assess analgesic effects, participants completed the cold pressor task (CPT) in which they immersed their hand into cold water (10 +/-1 degree C) until no longer tolerable. CPT-related outcomes include elapsed time (seconds) until pain first detected/reported by participant (pain threshold) and elapsed time (seconds) at which participant withdrawals hand from water (pain tolerance). The CPT was collected prior to drug administration and at +60, +120, +180, and +240 min after study drug administration. Participants completed drug effect questions on a visual analogue scale (range: 0-100) prior to drug administration and every hour for 6 hours after dosing.
Results: Pain threshold was significantly greater with hydromorphone combined with 200 mg of CBD relative to hydromorphone alone. Pain tolerance was significantly greater with hydromorphone combined with 50, 100, and 200 mg of CBD relative to hydromorphone alone. Hydromorphone combined with 100

and 200 mg of CBD produced significantly greater "Drug" and "Bad" effects compared to hydromorphone alone.
Conclusions: This trial suggests a range of CBD doses enhance opioid-induced analgesia, but higher doses are associated with stronger "Drug" and "Bad" effects which could limit its utility.
Financial Support: R01DA040644

EFFECT OF CANNABIDIOL ON SUBJECTIVE INDICES OF MORPHINE ABUSE LIABILITY

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[1]Wayne State University
Drug Category Cannabis/Cannabinoids
Topic Drug Interactions
Aim: Prescription opioids are used to treat nearly 20% of chronic pain cases in the United States and their misuse has contributed to an opioid epidemic. Although cannabis has emerged as a potential adjunctive medication, it has been shown to potentiate some abuse liability effects of oxycodone. Cannabidiol (CBD), a non-psychoactive component of cannabis, also is being studied as a potential adjuvant to opioid medication, but it remains unclear whether CBD modulates opioid abuse liability. The current study aims to examine the potential effects of cannabidiol on morphine abuse liability.
Methods: Nine participants (mean age=27 yrs, 77.8% female) have completed an ongoing double-blind, placebo-controlled, within-subject crossover study, where they self-administered vaporized CBD (0.5g cannabis containing 0.003% THC and 0.00% CBD [bout 1] vs 9.7% CBD [bout 2], cumulative within-session dosing) combined with oral morphine (0mg, 15mg, and 30mg in three separate sessions). Subjective measures of abuse liability (e.g. liking, desire to take drug again) are assessed within each session at baseline, post-morphine, post-morphine + CBD placebo, and post-morphine + CBD. Linear regressions were used to test whether slope of the group-mean curve across time points within each morphine condition (reflecting combined CBD + morphine effects) significantly exceeds zero.
Results: CBD is potentiating morphine "liking" in the 30mg condition, $r2=.92$, $F(1,2)=21.65$, $p=.043$; and 15mg condition, $r2=.94$, $F(1,2)=30.63$, $p=.031$; but not the placebo condition, $r2=.65$, $F(1,2)=3.69$, $p=.195$. CBD is potentiating "desire to take again" in the 30mg morphine condition, $r2=.99$, $F(1,2)=13596$, $p<.0001$; at trend-level in the 15mg condition, $r2=.83$, $F(1,2)=9.65$, $p=.090$; but not the placebo condition, $r2=.71$, $F(1,2)=4.82$, $p=.159$.
Conclusions: Results suggest co-administration of CBD and morphine may dose-dependently increase subjective indices of morphine abuse liability. These findings contribute to an emerging literature that seeks to inform the clinical use of CBD in conjunction with opioids.
Financial Support: NIH R21 DA047662 (LHL), Gertrude Levin Endowed Chair in Addiction and Pain Biology (MKG), Michigan Department of Health and Human Services (Lycaki/Young Funds)

ORAL COMMUNICATION: COCAINE IN CONTEXT
Plaza Ballroom D

CONCURRENTLY AVAILABLE NEGATIVE REINFORCEMENT DECREASES COCAINE SELF-ADMINISTRATION IN RATS

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Drug Category Stimulants
Topic Behavioral Pharmacology
Aim: Drug-taking despite negative consequences is a prevalent behavioral characteristic of addiction. However, few studies have examined behavioral allocation between concurrently available self-administered drug or escaping/avoiding an aversive stimulus (i.e., negative reinforcement). The goal of this study was to establish a cocaine-vs-negative reinforcement choice procedure in male and female rats and determine sensitivity to environmental and pharmacological manipulations.

Methods: Under a discrete-trial cocaine-vs-negative reinforcement choice procedure, Sprague-Dawley rats (total n=21; 10F/11M) lever-pressed for either negative reinforcement (foot shock escape or avoidance, 0.7mA) under a fixed-ratio (FR1) schedule or intravenous cocaine infusions (0.32 – 1.8mg/kg/inf) under an FR3 schedule. After establishing baseline cocaine-vs-negative reinforcement choice behavior, choice was re-assessed following environmental (shock intensity (0 – 0.7mA), response requirement (FR1-16)) and pharmacological (acute diazepam (0.32 – 10mg/kg, ip), 10 days of extended access cocaine self-administration) manipulations.
Results: Negative reinforcement (foot shock escape/avoidance) was consistently chosen over all cocaine doses. Decreasing shock intensities decreased escape/avoidance trials completed; however, cocaine trials did not significantly increase. Increasing the response requirement for negative reinforcement only increased omitted trials. Acute diazepam pretreatment failed to alter behavioral allocation between negative reinforcement and cocaine up to doses that eliminated operant responding. Extended cocaine access increased daily cocaine intake to ~96 mg/kg but failed to significantly alter choice between negative reinforcement and cocaine.
Conclusions: Concurrent availability of negative reinforcement decreased cocaine self-administration across a range of doses that we have previously shown were chosen over nondrug positive reinforcers (i.e., food, social interaction). The lack of behavioral allocation between the two reinforcers in response to environmental manipulations suggest that cocaine and negative reinforcement may be economic independents. Lastly, the failure of extended cocaine access to increase cocaine choice does not provide empirical evidence for the theory of drug-taking despite negative consequences. Future studies will investigate neural mechanisms underlying interactions between concurrently available positive and negative reinforcers.
Financial Support: P30DA033934, T32DA007027

A SOCIAL PEER RENEWS COCAINE SEEKING: POTENTIAL ROLE OF THE NUCLEUS ACCUMBENS

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[1]University of Kentucky
Drug Category Stimulants
Topic Behavior
Aim: The purpose of this study was to determine if cocaine seeking is renewed in an ABA renewal paradigm by a social context (peer) and to examine a potential role of the nucleus accumbens (NAc) within this paradigm.
Methods: Young adult male/female Sprague-Dawley rats (N=22) were trained in a dual-compartment operant conditioning chamber to self-administer cocaine using a 2-lever procedure in the presence of a same-sex/age peer (Context A). Following 21 days of self-administration using a terminal FR5 schedule, rats underwent 10 extinction sessions with the peer (Context A) or without the peer (Context B). Renewal of cocaine seeking was tested by reintroducing the peer (Context A). All rats (both AAA and ABA groups) were perfused 30 min with 4% PFA after exposure to either Context A or Context B. Brains were removed for immunohistochemical (IHC) analysis.
Results: During acquisition, active lever presses were significantly higher than inactive presses beginning at session 8 (FR3), $t(28 = 4.567, p<0.0001)$, and at FR5, $t(28 = 9.436, p<0.0001)$. Both ABA and AAA rats decreased responding across extinction sessions ($F(9.180) = 25.37, p<0.0001$), with ABA rats having less overall responding than AAA rats ($F(1,20) = 4.585, p<0.05$). ABA rats renewed cocaine seeking when reintroduced to their cocaine-associated peer (Context A) compared to extinction in context B, $F(1,20) = 13.03, p<0.001$); 95% CI [-46.34, -7.234] $p<0.01$, and compared to AAA rats, $t(15) = 4.882, p<0.001$. ABA rats that were perfused following exposure to Context A had a higher number of cFos-immunopositive cells within the NAc compared to ABA rats perfused following exposure to Context B, ($t(13) = 2.290, p<0.05$).
Conclusions: Social peers serve as powerful stimuli to trigger drug seeking and engender activity of cells within the NAc.
Financial Support: Supported by NIH grants R21 DA041755, R01 DA053070, and T32 DA035200.

THE EFFECT OF NICOTINE ON COCAINE REINFORCEMENT IN A NONHUMAN PRIMATE MODEL OF COCAINE ABUSE

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavioral Pharmacology
Aim: Because there are no FDA-approved treatments for cocaine use disorders (CUD), a great deal of research has focused on the behavioral and neuropharmacological effects of cocaine in animal models, with the goal of identifying novel interventions. While the majority of people with CUD also smoke cigarettes, most preclinical cocaine research does not include the co-use of nicotine. This study examined the effects of adding nicotine to cocaine under several conditions of intravenous drug self-administration in monkeys.
Methods: In experiment 1, 3 individually housed male rhesus monkeys were implanted with indwelling venous catheters and trained under a progressive ratio schedule of reinforcement. In experiment 2, 13 socially-housed cynomolgus monkeys (7 females and 6 males) were implanted with indwelling venous catheters and allowed to choose between food pellets and a cocaine dose (saline, 0.003-0.1 mg/kg/injection) during daily 1 hour sessions. Following cocaine vs food choice dose-effect curve determinations, nicotine (0.01-0.056 mg/kg/injection) was added to the cocaine solution starting with the highest dose of cocaine where food was preferred. The effect of delaying the drug reinforcer was also studied using this paradigm.
Results: In all monkeys, adding nicotine shifted the cocaine dose-response curve to the left; in one monkey, it also increased the breakpoint, suggesting an increase in reinforcing strength. Adding nicotine shifted the cocaine dose-response curve to the left in most monkeys, with no evidence of sex or social rank differences. Delaying the preferred drug reinforcer, the co-use of nicotine and cocaine required significantly larger delays compared with cocaine alone.
Conclusions: These results suggest that the co-use of nicotine + cocaine is not simply changing the potency of cocaine, but rather changing a fundamentally different condition that should be utilized to understand better the neuropharmacology of CUD and the evaluation of potential treatments.
Financial Support: RO1: DD017763-15

A BEHAVIORAL ECONOMIC ANALYSIS OF POLYSUBSTANCE USE: STUDIES WITH COCAINE, FENTANYL, AND COCAINE–FENTANYL MIXTURES IN MALE AND FEMALE SPRAGUE-DAWLEY RATS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavioral Economics
Aim: The current study sought to investigate the reinforcing effects of cocaine-fentanyl mixtures using behavioral economic demand analyses to help ascertain which factors may promote polysubstance use in humans.
Methods: The current study used a multiple component schedule of drug self-administration to assess economic demand for cocaine (0.032, 0.1, 0.32, 1.0 mg/kg/inf), fentanyl (0.0032, 0.01, 0.032, 0.1 mg/kg/inf), and mixtures of cocaine:fentanyl (in 10:1, 3:1, 1:1, 1:3, 1:10, relative to the dose ranges above) in rats. Available unit-doses of drug increased across 4, 20-min drug components, with increases in the response requirement (fixed ratio) occurring across sessions. Demand curves for cocaine, fentanyl, and their respective mixtures were generated by normalizing consumption (number of infusions earned) to Q0 (estimate of unconstrained demand) and plotted as a function of standardized price (FR X Q0). Elasticity coefficients (α) generated from demand curve analyses were used to assess the relative value of each drug and mixture preparation.
Results: The elasticity coefficient of fentanyl was greater than that of cocaine (i.e., cocaine had a greater "essential value"). Similarly, demand for the 10:1 mixture of cocaine + fentanyl was found to be greater than demand for fentanyl alone but comparable to cocaine. Mixtures of 1:3 and 1:10 cocaine + fentanyl produced alpha values that were greater than that of cocaine but not that of fentanyl, further suggesting that interactions may be strictly additive in respect to their reinforcing effects.

Conclusions: Results from the current study compliment reports from nonmedical opioid users who combine opioids with stimulants to "enhance the high". Together, the co-use of cocaine and fentanyl may increase the risk for developing a substance use disorder. Additionally, treatment targeting opioid use may be less effective in individuals who co-use stimulants such as cocaine with opioids. Future studies are warranted to assess how opioid dependence and withdrawal may impact the reinforcing effectiveness of cocaine-fentanyl mixtures compared to either drug alone.
Financial Support: This research was funded by the National Institutes of Health (R01 DA039146) and NIH/NIDA T32 (DA031115) postdoctoral research fellowship.

ORAL COMMUNICATION: TELEHEALTH: UNIFORM STILL REQUIRED
Grand Ballroom II

IDENTIFYING LATENT CLASSES OF EMERGENCY DEPARTMENT PATIENTS RECEIVING TELEHEALTH PEER RECOVERY COACH SERVICES FOR SUBSTANCE USE DISORDER AND ASSESSING CLASS PREDICTORS AND OUTCOMES

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Drug Category Other, The study looks at a wide range of substance use types.
Topic Health Services
Aim: Examine latent classes, peer follow-up engagement, and subsequent emergency department (ED) encounters among patients admitted to the ED for substance use disorders (SUD) and medical problems and who received telehealth peer recovery coach (PRC) services.
Methods: Data are drawn from the PRC telehealth hub services database and the Indiana Network for Patient Care (INPC). Patients are identified based on having an admitting diagnose code related to SUD and/or information provided during the encounter. Primary diagnosis, primary drug at admission, naloxone administration, and prior/post ED utilization were used to define latent classes. Distal outcomes included number of ED visits in year following accepted PRC services and participant's acceptance of a post-visit PRC contact. Multinominal regression and multivariate analysis of factors associated with distal outcomes was conducted.
Results: 2,953 total patients were approached by a PRC at the index ED visit. Five latent classes (LC) were defined; 1) alcohol related; 2) psychiatric disorder; 3) co-occurring SUD and medical condition(s); 4) opioid use disorder and/or overdose; and 5) medical condition(s). Patients within LC1 - alcohol related (OR: 0.38; 95% CI 0.24, 0.51; $p < 0.05$) had lower odds of having 1-5 ED visits in the post year period, whereas patients in LC 4- OUD/OD (OR: 3.29; 95% CI 2.16, 4.41; $p < 0.05$) had higher odds of having 1-5 ED visits in the post year period, compared to patients with no ED visits. Patients in LC 4 – OUD/OD (OR: 0.60; 95% CI 0.36, 0.84; $p < 0.05$) had lower odds of accepting peer recovery coach follow-up, compared to patients who do not accept PRC follow-up.
Conclusions: ED-based telehealth PRC may be an opportunity to connect SUD patients with needed services and reduce future ED visits. Intervention outcomes could be improved by targeting the collection of information regarding unique patient circumstances to guide recovery supports.
Financial Support: National Institute on Drug Abuse R21/R33DA045850

DEPRESSION SCREENING AMONG PERINATAL PATIENTS WITH AND WITHOUT SUBSTANCE USE DISORDERS FOLLOWING IMPLEMENTATION OF A COLLABORATIVE CARE PROGRAM

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Drug Category Other, substance use disorders
Topic Prenatal/Perinatal
Abstract Detail Clinical - Epidemiology

Abstract Category Original Research
Aim: The Perinatal Behavioral Health Integration initiative (PBHI) is a telehealth-based collaborative care program implemented within a large integrated healthcare system. Aims of PBHI included: increasing depression screening rates among all perinatal patients and improving access to care for patients with mental health (MH) conditions, particularly for high-risk subgroups such as those with substance use disorder (SUD). The purpose of this study was to compare changes in screening rates pre- vs. post-implementation and to examine potential differences in screening rates related to history of MH and SUD diagnosis.
Methods: Patients who were pregnant or up to 1 year postpartum were eligible for screening using standardized depression screening tools (e.g., PHQ-9); screening was conducted as part of routine care. We examined screening rates between 1/1/2019-3/31/2020 (i.e., pre-implementation) and 4/1/2020-12/31/2021 (i.e., post-implementation). Using ICD-10 diagnostic codes, patients were grouped into 4 groups: 1) without MH or SUD, 2) MH only, 3) SUD only, and 4) MH and SUD. A total of 24,456 perinatal patients who had delivery between 2019 and 2021 were included. Adjusted prevalence ratios (aPRs) and 95% CIs were estimated by logistic regression to compare screening rates in the pre- and post-implementation time periods.
Results: Depression screening increased after implementing PBHI. Patients with MH or SUD had higher depression screening prevalence pre-implementation (35%-50%) compared to those without MH or SUD (13%-50%). Adjusting for sociodemographic factors, depression screening increased by 91% post-implementation among patients without MH or SUD (aPR = 1.91, 95% CI: 1.79-2.04). Screening increased by 46% among those with SUD, and increased by 12% among those with both MH and SUD.
Conclusions: The PBHI initiative increased depression screening rates among perinatal patients. Patients with MH or SUD had higher rates of depression screening pre- and post-implementation compared to those without a diagnosis. Findings have implications for universal screening and identification among perinatal patients.
Financial Support: Ethel and James Flinn Foundation

RETENTION IN TELEHEALTH TREATMENT FOR OPIOID USE DISORDER AMONG PREGNANT PEOPLE

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Drug Category Opiates/Opioids
Topic Prenatal/Perinatal
Aim: Pregnant people with opioid use disorder (OUD) face numerous barriers to treatment, but telehealth has the potential to increase access to care for this population. We assessed retention in care and buprenorphine positivity among pregnant people receiving treatment for OUD through telehealth.
Methods: This was a retrospective cohort study of pregnant patients enrolled in a harm-reduction-based telehealth OUD treatment program. Participants met the following inclusion criteria: 1) age 18 years or older; 2) attended a medical appointment via telehealth between June 6, 2021 through June 5, 2022; 3) use of ICD 10 billing code for pregnancy; and 4) received a clinical diagnosis of OUD. Outcomes were percent who attended visits and percent who were positive for buprenorphine at 1-, 3-, and 6-months follow-up. Analyses were descriptive and, due to the paucity of data on telehealth OUD outcomes among pregnant people, there were no prespecified hypotheses about the extent to which they would be retained in care. Due to limited data, delivery and fetal health outcomes were not able to be assessed.
Results: Throughout the study period, 50 individuals met inclusion criteria and had the following characteristics: 100% female, mean age 32.3 years (standard deviation 4.5); 82% Medicaid, and 74% urban. Among a subsample with additional characteristics, 87% identified as heterosexual, 67% were unemployed/disabled, and 63% were partnered. At 1-, 3-, and 6-months follow up, 80.0%, 76.0%, and 72.0% of patients were retained in care, respectively. At 1-, 3-, and 6-months follow up, 76.0%, 68.0%, and 70% were positive for buprenorphine, respectively.
Conclusions: Telemedicine is an effective approach for treating OUD among pregnant people, with high retention and adherence. Telehealth policies should be extended in order to maximize accessibility to effective treatment for OUD among pregnant people.
Financial Support: The authors are employed by Workit Health. Although Workit Health is an SBIR recipient, this study was not supported by external funding.

TELEMEDICINE FOR UNHEALTHY ALCOHOL USE FOR ADULTS LIVING WITH HIV IN ALABAMA, USING COMMON ELEMENTS TREATMENT APPROACH (TALC)

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Drug Category Alcohol
Topic Treatment
Aim: Unhealthy alcohol use among people living with HIV remains a substantial barrier to achieving and maintaining optimal viral load values and engagement in care. Integrated screening and intervention to address common behavioral and mental health comorbidities can help patients reduce their alcohol use and improve HIV clinical and quality of life outcomes. Further, telemedicine provides an opportunity to engage patients in rural settings in mental health and substance use treatment. Telemedicine for Unhealthy Alcohol Use for Adults Living with HIV in Alabama using Common Elements Treatment Approach (TALC) aims to test the effectiveness of Common Elements Treatment Approach (CETA) in reducing unhealthy alcohol use among patients receiving HIV care at one of six Ryan-White funded community clinics in Alabama.
Methods (Optional): CETA is a transdiagnostic treatment approach designed for lay people to administer to peers in low-income countries, however, will be employed in Alabama by Medical/Clinical Psychology doctoral students through telehealth. Participants will be randomized to either receive brief intervention (BI) for alcohol use, or BI plus CETA, and program analyses will assess group differences in alcohol use and secondary outcomes (i.e., mental health, HIV clinical data) across a 12-month study period. Dried blood spots will be collected from participants at baseline, 6-, and 12-months post enrollment, to measure the level of Phosphatidylethanol (PEth) in the blood. Validity of our findings will be strengthened through the concurrent collection and analyses of PEth, an objective measure of alcohol intake, and scores on the Alcohol Use Disorders Identification Test.
Results (Optional): Preliminary results on patient and clinic engagement, feasibility, and mental health and substance use data will be presented.
Conclusions: Implications include evidence to support integrated substance use treatment among HIV clinics and the potential ability for telehealth to bridge disparities in access to mental health and substance use treatment in rural communities.
Financial Support: 1 P01 AA029540-01

ORAL COMMUNICATION: BEHAVIORAL ECONOMICS
Plaza Ballroom A

CHRONIC THC EXPOSURE DURING ADOLESCENCE PRODUCES PERSISTENT ECONOMIC DEMAND ABNORMALITIES IN ADULT NONHUMAN PRIMATES

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Drug Category Cannabis/Cannabinoids
Topic Behavioral Economics
Aim: Chronic cannabis use during adolescence can impair complex behavioral processes. However, the extent to which such deficits persist into adulthood is currently not well understood. Recent research in our laboratory has begun to address this knowledge gap with longitudinal studies examining the impact of chronic exposure during adolescence to delta-9-tetrahydrocannabinol (THC) on cognitive function during adulthood via a battery of touchscreen-based tasks.
Methods: Female and male squirrel monkeys (n=23) were treated daily for 6 months during late adolescence with either vehicle, a low dose (0.32 mg/kg), or a high dose (3.2 mg/kg) of THC. Approximately 6 months after THC administration was discontinued, a touchscreen-based economic demand procedure was used to examine reward sensitivity by evaluating the extent to which these subjects, now adult, would defend consumption of a palatable food reinforcer in the face of escalating response requirements. In addition, sensitivity to different reinforcer magnitudes was evaluated.

Results: All subjects learned to engage in the task and exhibited demand functions that were well characterized by well-validated exponential equations. In drug-free control subjects, increasing reward magnitude produced orderly decreases in elasticity (alpha) that were well characterized by a simple linear regression (R2=0.94). However, this fundamental magnitude/elasticity relationship was dose-dependently disordered in subjects treated with THC during adolescence (R2 values =0.75 and 0.37 in, respectively, low and high dosage groups).
Conclusions: Chronic THC treatment during adolescence produced reward sensitivity deficits that persisted into adulthood, as assayed by a touchscreen-based economic demand procedure. Ongoing studies employing other cognitive tasks are examining the selectivity of these deficits. The present data are of particular concern in view of the ubiquitous role that basic reward processes play in everyday life.
Financial Support: Supported by R01-DA047575

LOSS AVERSION PREDICTS CIGARETTE SMOKING STATUS ACROSS GENDER AND SOCIOECONOMIC LEVELS

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Drug Category Nicotine/Tobacco
Topic Behavior
Aim: Loss aversion refers to the tendency for choices to be more sensitive to potential losses relative to similar gains. Low loss aversion is associated with risk for cigarette smoking as well as use of several other harmful substances. Previous studies of loss aversion and cigarette smoking controlled for the potentially confounding influence of important sociodemographic variables (age, gender, educational attainment, income). The present study examined associations between low loss aversion and smoking risk within levels of sociodemographic risk factors for smoking.
Methods: Participants (N=769) were recruited using standard crowdsourcing methods and completed items on sociodemographics, a hypothetical gamble task measure of loss aversion, and a monetary choice measure of delay discounting, a decision-making bias referring to the rate at which reward lose value with increasing delay to receipt.
Results: Low loss aversion was observed among individuals that endorsed current cigarette smoking and this was not influenced by reported age, educational attainment, income, or gender, $F(1, 758) = 20.77$, $p < .0001$, $\eta 2 = .009$. Higher delay discounting rate was also observed across sociodemographic categories, $F(1, 758) = 6.59$, $p = .010$, $\eta 2 = .008$. Importantly, loss aversion and delay discounting remained significantly associated with smoking status when accounting for the other suggesting an independent contribution of each decision-making factor to smoking risk.
Conclusions: Sociodemographic and decision-making vulnerabilities may intersect to influence risk for smoking and other substance use. The findings emphasize the importance of accounting for sociodemographic variables when comparing decision-making factors associated with risk for unhealthy behavior. The association of low LA with cigarette smoking was consistent across levels of educational attainment, income, and gender. The results provide additional support for loss aversion as an important decision-making factor associated with risk for cigarette smoking and other substance use.
Financial Support: NIH grants K01-DA044456, U54-DA036114, and P20-GM103644

OPIOID DEMAND AND PAIN-RELATED MEASURES FOLLOWING TRAUMA SURGERY

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Drug Category Opiates/Opioids
Topic Behavioral Economics
Aim: Prescription opioid use following trauma surgery is associated with increased risk of future opioid misuse. Various opioid risk assessments are available, but all have limitations. The current pilot study examined associations and changes in opioid demand, a behavioral economic measure of reward and abuse liability, following trauma surgery.

Methods: Participants (N = 60) were trauma surgery patients discharged with an opioid prescription for their pain. Web-based, follow-up assessments of opioid demand, pain, and opioid use were conducted at 7-, 30-, and 90-days following discharge from the hospital.
Results: Acceptability and feasibility were promising, with 60 out of 71 initial candidates consenting to be a part of the study. Follow-up completions rates were 73%, 67%, and 68% for the 7-, 30-, and 90-day follow-ups, respectively. Generally, opioid demand characteristics (Q0, essential value, Omax, Pmax, breakpoint) were found to be statistically associated with self-reported, pain-related measures, but the particular pain-related measures changed over time. Specifically, demand characteristics were most likely to be significantly associated with past 7-day opioid use and injury related stress/anxiety at the 7-day follow-up. At 30- and 90-day follow-up assessments, opioid demand characteristics were most likely to be associated with average past 7-day pain and need for additional treatment services. Q0 (intensity of demand) exhibited the most frequent significant associations with pain-related measures at all time points. Results from GLMM showed decreases from day 7 to 90 for all demand characteristics (PP% = 83-98) and pain-related measures (PP% = 88-99).
Conclusions: Results from the current pilot study demonstrated positive feasibility and acceptability of assessing opioid demand and pain-related measures following trauma surgery. These findings establish a promising foundation for assessing both initial opioid misuse risk as well as changes in risk over time.
Financial Support: McGovern Medical School Pilot Grant

THE BLINDED-DOSE PURCHASE TASK: ASSESSING HYPOTHETICAL DEMAND BASED ON COCAINE, METHAMPHETAMINE, AND ALCOHOL ADMINISTRATION

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavioral Pharmacology
Aim: Behavioral economic drug purchase tasks quantify the reinforcing value of a drug (i.e., demand). Although widely used to assess demand, drug expectancies are rarely accounted for and may introduce variability across participants given diverse drug experiences. Three experiments validated and extended previous hypothetical purchase tasks by using blinded drug dose as a reinforcing stimulus and determined hypothetical demand for experienced effects while controlling for drug expectancies.
Methods: Across three double-blind, placebo controlled, within-subject experiments, cocaine (0, 125, 250 mg/70 kg; n = 12), methamphetamine (0, 20, 40 mg; n = 19), and alcohol (0, 1 g/kg alcohol; n = 25) were administered and demand was assessed using a novel Blinded-Dose Purchase Task. Participants answered questions regarding simulated purchasing of the blinded drug dose across increasing prices. Demand metrics, subjective effects, and self-reported real-world monetary spending on drugs were evaluated.
Results: Data were well modeled by the demand curve function, with significantly higher intensity (purchasing at low prices) for active drug doses compared to placebo for all experiments. Unit-price analyses revealed more persistent consumption across prices (lower alpha) in the higher compared to lower active dose condition for methamphetamine (a similar non-significant finding emerged for cocaine). Significant associations between demand metrics, peak subjective effects, and real-world spending on drugs also emerged across all experiments.
Conclusions: Orderly demand curve data revealed differences across drug and placebo conditions, and associations with real-world measures of drug spending, and subjective effects. Unit-price analyses enabled parsimonious comparisons across doses. Results lend credence to the validity of the Blinded-Dose Purchase Task, which allows for control of drug expectancies.
Financial Support: We gratefully acknowledge that this research was supported in part by National Institute on Drug Abuse (NIDA) grants R21DA032717 (MWJ), R01DA032363 (MWJ), R01DA035277 (MWJ). Support for MSB, GPN, and PSJ was provided by the National Institute on Drug Abuse Grant T32DA007209.

ORAL COMMUNICATION: NICOTINE CLINICAL TREATMENTS
Plaza Ballroom D

THE INFLUENCE OF E-CIGARETTE REDUCTION ON COMBUSTED CIGARETTE SMOKING AMONG DUAL USERS: A PILOT RANDOMIZED CONTROLLED TRIAL

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Drug Category Nicotine/Tobacco
Topic Behavior
Aim: E-cigarettes are less harmful than combusted cigarettes, but 40-50% of US adults who start using e-cigarettes continue to smoke cigarettes (i.e., dual users). Cutting down on e-cigarette use is common but little is known about how e-cigarette reduction affects cigarette smoking.
Methods: This trial randomized 77 adult dual users with no intention to quit either product in the next month to (A) switch to e-cigarettes with 40% less nicotine (n=26), (B) reduce their number of full nicotine e-cigarettes by 40% (n=25), or (C) continue e-cigarettes as usual (n=26) during a 4-week study period. We provided no instruction regarding cigarette smoking. Primary outcomes included compliance with study e-cigarettes (i.e., feasibility) and cigarettes per day (CPD) at the end of the study period.
Results: Self-reported compliance with the assigned type and number of e-cigarettes was high (Mean compliance=89.3%, SE=3.1) and did not differ between conditions (all $p>0.1$). After controlling for baseline CPD, participants assigned to reduce number of e-cigarettes reported smoking marginally significantly more CPD (Mean=9.4, SE=0.7) than those assigned to continue e-cigarette use as usual (Mean=7.4, SE=0.7; $p=0.050$). Participants assigned to switch to e-cigarettes with less nicotine reported a Mean of 8.6 CPD (SE=0.7), which did not significantly differ from the other two conditions (both $p>0.1$). Across all conditions, there was a negative correlation between percent change in e-cigarette use and percent change in CPD during the study period (Spearman $r = -0.24$, $p=.049$) demonstrating that e-cigarette reduction was associated with increased cigarette smoking.
Conclusions: To the best of our knowledge, this pilot randomized controlled trial is the first to test the impact of e-cigarette reduction on cigarette smoking. Though effect sizes were small, findings suggest that e-cigarette reduction could result in increased cigarette smoking among dual users. Future research is needed to replicate results in a larger sample.
Financial Support: Supported by National Institute on Drug Abuse (NIDA) and U.S. Food and Drug Administration (FDA) grant U54DA036114, T32 DA007242 from NIDA as well as P20GM103644 from National Institute of General Medical Sciences (NIGMS).

REDUCED SMOKING AND BEHAVIOR CHANGE MECHANISMS ASSOCIATED WITH A GENETICALLY-INFORMED SMOKING CESSATION INTERVENTION: A FULLY-REMOTE RANDOMIZED CONTROLLED TRIAL

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Drug Category Nicotine/Tobacco
Topic Mechanisms of Action
Aim: Genetic variation in nicotinic receptor subunits explains differences in smoking behaviors and risk of smoking-related diseases. Despite promising findings in proof-of-concept testing, it remains unknown whether returning genetic risk results can motivate smoking cessation and personalize treatment. We aimed to investigate the potential mechanisms of behavior change and extent to which a genetically-informed smoking cessation intervention can reduce smoking.
Methods: In a fully-remote randomized controlled trial, we enrolled 148 adult participants who smoke. Participants completed genetic testing via 23andMe, received a genetically-informed risk feedback tool (RiskProfile) or active comparator (brief cessation advice) via Zoom, and completed assessments at 30-day and 6-month follow-up. RiskProfile uses a participant's smoking-specific genetic information to calculate, categorize, and communicate personalized risks for lung cancer and recommendations for treatment and

cessation. We conducted effect size estimations and significance testing using repeated-measures ANOVA controlling for baseline cigarettes per day (CPD).
Results: At 30-day follow-up, there was very little reduction in average CPD (partial eta-squared=.01, small effect size; p=.281). However, at 6-month follow-up, we found clinically meaningful and statistically significant reductions in CPD of 4.54 in the RiskProfile intervention group versus 1.99 in the active comparator group (partial eta-squared=.04, small-to-medium effect size; p=.027). Participants receiving the RiskProfile were nearly twice as likely as those receiving the active comparator to use smoking cessation medications (22% versus 12%) at 30-day follow-up. Increases in perceived importance of tobacco treatment, as well as higher personal relevance and systematic processing with RiskProfile versus the active comparator, appear to be promising mechanisms of behavior change.
Conclusions: In this fully-remote trial, we significantly reduced access-related barriers to participation, yielding high retention rates of 89% at 6-month follow-up. The genetically-informed RiskProfile intervention appeared to influence hypothesized mechanisms of behavior change leading to reduced cigarette smoking. These promising efficacy findings can pave the way for effectiveness testing in pragmatic settings.
Financial Support: NIDA R34DA052928; NIDA K12DA041449; NCI P50CA244431; NCI R01CA268030; NIDA R01DA056050

EVALUATING THE FEASIBILITY AND PRELIMINARY EFFICACY OF A REAL-TIME SMOKING INTERVENTION USING WEARABLE TECHNOLOGY

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Drug Category Nicotine/Tobacco
Topic Technology (e.g., mHealth)
Aim: Cigarette smoking is the leading cause of preventable death, and treatment innovations are critically needed. Wearable technology has the potential to enhance tobacco treatment by allowing for passive, automatic identification of smoking behavior that can be used to trigger a real-time intervention.
Methods: We enrolled n=58 adults from an outpatient tobacco treatment center (age M=55.9, SD=9.8, 57% female, race/ethnicity: 16% Hispanic, 57% White, 31% Black, 9% Other, 3.4% Multiracial) who smoked daily (M=15.9, SD=10.1 cigarettes per day). Participants were randomly assigned to a control group (standard treatment including smoking cessation counseling and pharmacotherapy, n=29) or experimental group (standard treatment plus real-time smartband intervention for 8 weeks, n=29).
Results: Results provide support for the feasibility and acceptability of the smartband technology providing passive real-time smoking monitoring. Participants in the experimental group wore the smartband 70% of the days during treatment. After improvements were made to the software, the experimental group reported improved ratings of satisfaction and perceived helpfulness of the smartband, and there were promising differences observed between groups in changes in smoking behavior during the 8-week treatment, although no group differences reached statistical significance. Similar rates of biochemically confirmed 7-day point-prevalence abstinence were observed (11% experimental, 5% control group). However, those in the experimental group had a larger reduction in cigarettes smoked per day (CPD) from baseline to Week 8 (mean change in CPD=10.2, SD=12.2 vs. control (n=20) mean change in CPD=7.7, SD=6.5, cohen's d=.26), and the experimental group reported nearly double the percent days smoke-free during the 8-week period (M=12.4%, SD=27.2% vs. control M=6.9%, SD=14.6%, cohen's d=.26).
Conclusions: Findings support the use of smartband technology for passive smoking monitoring in adults seeking to quit smoking and provide initial evidence that this technology may improve cessation efforts above and beyond standard tobacco treatment. Additional large-scale clinical trials are needed.
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SPONTANEOUS CHANGES IN CIGARETTE SMOKING FOLLOWING PSILOCYBIN-ASSISTED TREATMENT FOR ALCOHOL USE DISORDER

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Drug Category Nicotine/Tobacco
Topic Treatment
Aim: Emerging research suggests psilocybin-assisted psychotherapy (PAP) may be efficacious for smoking cessation. However, it is unclear if PAP may spontaneously facilitate smoking cessation in other patient populations with different therapeutic targets such as alcohol use disorder (AUD) and major depression.
Methods: This study examined pre-to-post treatment changes in a subsample of male and female tobacco smokers (n=22) and marijuana user (n=19) from a double-blind, placebo-controlled PAP trial in patients with AUD (n=93). The timeline followback interview was used to assess daily tobacco smoking and cannabis use, yielding estimates of the percentage of days that each drug was used during the double-blind follow-up period (8 1-month periods after first medication session). Mixed models for repeated measures (MMRMs, one for tobacco and one for cannabis) evaluated the effects of treatment (psilocybin versus active placebo control), time, the time-by-treatment interaction, and pre-treatment use of the respective substance on post-randomization use of tobacco and cannabis.
Results: For tobacco smoking, the MMRM identified a trending main effect of treatment ($p=0.060$), with significant group differences at 4 months ($p=0.038$) and 5 months ($p=0.022$) post-treatment. Paired samples t-tests showed a reduction in percent days smoking for the psilocybin group ($p=0.032$), but not the placebo group ($p=0.660$). The effect of time and the time-by-treatment interaction were not significant. No significant effects of treatment or time were observed for marijuana use. Pre-treatment use of tobacco and marijuana were strong predictors of post-treatment use of tobacco and marijuana ($p<0.001$).
Conclusions: Findings suggest psilocybin may elicit spontaneous reductions in tobacco smoking in patients undergoing PAP for AUD. Studies with larger sample sizes are needed to confirm these findings, compare efficacy with PAP targeted toward smoking cessation, and determine if findings generalize to other clinical populations.
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WEDNESDAY, JUNE 21, 2023

ORAL COMMUNICATION: METHAMPHETAMINE SCIENCE IN HUMANS
Plaza Ballroom A

ADOLESCENTS' STIMULANT THERAPY FOR ADHD AND LATER COCAINE AND METHAMPHETAMINE USE DURING YOUNG ADULTHOOD: A NATIONAL LONGITUDINAL STUDY

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Drug Category Stimulants
Topic Substance Use Disorder
Aim: To examine the longitudinal transitions from use and misuse of stimulant therapy for ADHD in adolescence to cocaine and methamphetamine use during young adulthood.
Methods: National longitudinal multi-cohort panels (baseline years 2005–2017) of US 12th graders (N=5034) were surveyed via self-administered questionnaires at baseline and followed to age 24. The

sample is 52.0% female, 59.7%, White, 11.7% Black, and 15.1% Hispanic. Design-based logistic regression models were fitted to test associations between history of stimulant therapy at baseline and later illicit stimulant use (cocaine and methamphetamine incidence and prevalence), controlling for relevant covariates.
Results: At baseline, 10.2% of adolescents reported stimulant therapy for ADHD (including 6.4% with no history of prescription stimulant misuse [PSM] and 3.8% with a history of PSM), 14.6% reported PSM only (i.e., those reporting PSM and not treated with stimulants for ADHD), and 75.2% did not report stimulant therapy for ADHD or PSM (i.e., population controls). Stimulant therapy for ADHD at baseline was not associated with significantly increased adjusted odds of transitioning to incident or prevalent use of cocaine or methamphetamine use during young adulthood, compared to population controls. In contrast, adolescents engaged in PSM only at baseline had significantly higher adjusted odds of transitioning to later cocaine and methamphetamine use during young adulthood, compared to population controls (adjusted odds ratios ranged from 1.9 to 4.7). Approximately one-third of adolescents who reported PSM ten or more times at baseline later reported past-year cocaine or methamphetamine use at ages 19–24.
Conclusions: Adolescents who reported stimulant therapy for ADHD did not have a significantly increased risk of later cocaine or methamphetamine use during young adulthood compared to population controls. Monitoring adolescents for PSM is warranted because this behavior offers a strong signal for subsequent cocaine or methamphetamine use during young adulthood.
Financial Support: Supported by a research award 75F40121C00148 from the Food and Drug Administration and research awards R01DA001411, R01DA016575, R01DA031160, R01DA036541, UH3DA050252, and R01DA043691 from the National Institute on Drug Abuse and the National Institutes of Health.

NATIONAL TRENDS IN METHAMPHETAMINE-RELATED PSYCHIATRIC HOSPITALIZATIONS IN THE UNITED STATES, 2015-2019

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Drug Category Stimulants
Topic Epidemiology
Aim: To compare U.S. trends in psychiatric hospitalizations with and without methamphetamine (MAMP).
Methods: We use data from the National Inpatient Sample to study patients 18 years and older with a psychiatric hospitalization from October 2015 to December 2019. The primary outcome was quarterly psychiatric hospitalization rates by substance use group. We classified substance use groups using International Classification of Diseases codes, Tenth Revision which included: 1) MAMP +/- other substances, 2) MAMP alone (no cocaine or opioids), 3) MAMP + cocaine (no opioids), 4) MAMP + opioids (no cocaine), 5) MAMP + cocaine + any opioid, 6) any opioid or cocaine (no MAMP) relative to 7) psychiatric hospitalizations without substances (cocaine, opioids, or MAMP). We used Joinpoint regression to identify temporal trends.
Results: Our cohort included 6,573,198 total psychiatric hospitalizations. The total number of psychiatric hospitalizations remained relatively unchanged by quarter from Q4 2015 to Q4 2019 (range 340,033 in Q4 2015 to 399,970 in Q4 2019). The rate of psychiatric hospitalizations increased by 58% from 1.23% (95% confidence interval [CI] 1.20, 1.27) to 1.94% (95% CI 1.90, 1.99) in the MAMP +/- other substances group, increased by 58% from 0.84% (95% CI 0.80, 0.87) to 1.33% (95% CI 1.29, 1.36) in the MAMP alone group, increased by 57% from 0.23% (95% CI 0.21, 0.24) to 0.36% (95% CI 0.35, 0.38) in the MAMP + opioids group, and decreased by 16% from 0.55% (95% CI 0.53, 0.58) to 0.46% (95% CI 0.35, 0.38) in the opioid and/or cocaine group. There was no change in the MAMP + cocaine or no substances groups. Joinpoint regression analysis did not identify interval time points in which MAMP-related psychiatric hospitalization trends changed significantly over the study period.
Conclusions: MAMP-related psychiatric hospitalizations increased steadily from 2015 to 2019. Psychiatric hospitalizations without substances remained stable.
Financial Support: National Institute on Drug Abuse [K01DA051684 and DP2DA051864 to JAB] and [K08DA049905-03 to SLC].

DIFFERENCES IN PSYCHOSTIMULANT INTAKE LEVELS DO NOT NECESSARILY CORRESPOND TO DIFFERENCES IN MOTIVATION FOR THE DRUG

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Drug Category Stimulants
Topic Behavioral Pharmacology
Aim: In preclinical research, subjects can self-administer high or low levels of psychostimulants, with the idea that the high takers may represent more motivated (addicted) subjects than the low takers. However, it is not clear that high and low takers represent different motivations for drugs.
Methods: Male Sprague Dawley rats self-administered different doses of cocaine. Median split analysis was employed at every dose to determine the consistency of the designations of high and low takers. Behavioral economic analysis, with price as dose of drug being administered, was employed to estimate Q0 (cocaine consumption at zero price) and α (motivation to consume cocaine despite increases in prices). Normal mixtures clustering analysis was performed to determine if there were different groups of subjects based on Q0 and α. The groupings via normal mixtures clustering and via median split analysis were compared.
Results: Normal mixtures clustering of Q0 and α revealed two groups designated groups low Q0 (LQ0) and high Q0 (HQ0) with differences in Q0 but no differences in α. These groups corresponded 100% to groups identified by median split analysis at cocaine doses = 0.3 and 0.56 mg/kg/infusion, but not at other doses. Interestingly, Q0 was unrelated to α, suggesting that the identified groups of high and low takers (normal clustering, median split analysis) did not represent different motivations for cocaine.
Conclusions: Designating cocaine-consuming subjects as high and low takers of cocaine does not necessarily correspond to differences in motivation for the drug.
Financial Support: Department of Health and Human Services/National Institutes of Health/National Institute on Drug Abuse/Intramural Research Program, Baltimore, MD, USA

OBJECTIVE AND SUBJECTIVE SLEEP DURING LISDEXAMFETAMINE TREATMENT OF ACUTE METHAMPHETAMINE WITHDRAWAL: NEW MEASUREMENT PARADIGM

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Drug Category Stimulants
Topic Other
Aim: Sleep disturbance is common during methamphetamine (MA) use and withdrawal. To date, questionnaire-based sleep assessments have primarily been used to assess sleep disturbance in clinical trials involving this population. Actigraphy is a well-established, non-invasive measure of sleep-wake cycles with good concordance with polysomnographic sleep studies in healthy sleepers. This is the first study to investigate the feasibility and utility of using actigraphy and sleep diaries to investigate sleep during MA withdrawal.
Methods: We conducted a feasibility and utility study of actigraphy and sleep diaries during a clinical trial of a 5-day tapering-dose regimen of lisdexamfetamine for the treatment of MA withdrawal. Participants were inpatients for 7 days and continuously wore an actigraph (Philips Actiwatch 2) and completed a modified Consensus Sleep Diary each morning. Participants were interviewed between days 3-5.
Results: 10 participants (mean age 37 years, 90% male) were enrolled in the pilot study. Participants interviewed (n=8) reported that the actigraph was not difficult or distracting to wear or completion of daily sleep diary onerous. No participants removed the device prematurely. Actigraphic average sleep duration over 7 days was 568 minutes, sleep onset latency (SOL) 22.4 minutes, wake after sleep onset (WASO) 75.2 minutes and sleep efficiency 83.6%. Sleep diaries underreported sleep compared with actigraphy (sleep

duration was 56 minutes less (p=0.008) and WASO 47 minutes less (p<0.001)). Participants rated their overall sleep quality at 4.4 on a nine-point scale.
Conclusions: Continuous actigraphy is feasible to measure sleep-wake cycles in people withdrawing from MA, with low participant burden, and could be trialled in long-term outpatient monitoring. We found important differences in self-reported and actigraphic sleep, which need to be explored in more detail. Accurate sleep measurement is essential to better understand stimulant use and withdrawal given the potential role of sleep disturbance in maintaining substance use.
Financial Support: This study was funded by the National Centre for Clinical Research on Emerging Drugs (NCCRED). NCCRED is funded by the Australian Government Department of Health and Aged Care.

ORAL COMMUNICATION: EMERGING DRUGS: AS IF THERE WEREN'T ENOUGH ALREADY
Governor's Square 15

XYLAZINE: AN ADULTERANT DRUG OF CONCERN

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Other
Aim: To assess the scope and risks associated with the use of xylazine, we reviewed its pharmacology and epidemiology.
Methods (Optional): We conducted a systematic review of the scientific literature on PubMed, and Embase, using a combination of keywords to identify pharmacological and epidemiological studies reporting measures of abuse and related exposures involving xylazine through September 22, 2022.
Results (Optional): Xylazine is an alpha-2 receptor agonist approved for veterinary use for its sedative and short-acting analgesic properties. Xylazine has been available for veterinary use since the early 1970s. However, in the last decade it has emerged in the illicit market as an adulterant of known drugs of abuse, such as opioids. The scientific literature, data from NPDS cases from calls to poison centers, and postmortem case reports indicate that: 1) xylazine is usually found in combination with fentanyl, fentanyl analogues, and heroin; 2) xylazine-associated intoxication and overdose cases are increasing; and that 3) xylazine use is associated with clinically significant harms. These harms may include 1) a potential delay in the management of polysubstance overdose, as the signs and symptoms of xylazine toxicity may appear like that of opioids, but may not be reversed by naloxone; 2) development of severe necrotic skin lesions with repeated injection of xylazine, often in areas of the body away from the site of injection; and 3) repeated use of the drug may lead to physical dependence and withdrawal upon abrupt discontinuation, which is not managed by standard treatment.
Conclusions: Our review indicates that the exposure to xylazine in combination with other drugs of abuse is increasing and is associated with serious health consequences among people who inject drugs. These findings prompted FDA to issue a safety communication informing healthcare professionals about these risks and their management.
Financial Support: N/A

XYLAZINE REDUCES INTRAVENOUS FENTANYL CONSUMPTION BUT DOES NOT IMPAIR LEVER DISCRIMINATION IN MALE AND FEMALE RATS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Substance Use Disorder
Aim: Opioid use disorder (OUD) is a leading public health crisis in the United States. The current surge in overdose-related deaths is attributed to a rapid increase in the use of fentanyl, a synthetic μ-opioid receptor

agonist. Recent urine screens of fentanyl-positive individuals have found positive for xylazine, which is an adrenergic α2a receptor (A2aR) agonist that is commonly used as a veterinary anesthetic. Users of this drug combination, termed "tranq dope", report that xylazine prolongs the "high" of fentanyl as well as the onset of fentanyl withdrawal. Users of tranq dope also display heightened resistance to naloxone. Despite this rising and problematic pattern of polysubstance use, the impacts of xylazine on the neurobehavior of fentanyl use remain unknown, and no studies to date have established a preclinical model with exposure to xylazine during fentanyl self-administration (SA). Thus, the current study determined whether the consumption of intravenous fentanyl during SA in the presence of xylazine is altered as a function of biological sex.

Methods: Long Evans male and female rats (N=16/sex) underwent fentanyl (2.5 µg/kg/infusion, FR1) or saline SA for 10 sessions (2 hrs in length). Rats then underwent 8 days of fentanyl or saline SA with either xylazine (2.5 mg/kg, i.p.) or vehicle (saline, i.p.) pretreatment. A separate cohort (N=12) is currently underway to determine somatic signs of withdrawal induced by chronic xylazine treatment (10 consecutive days, same injection protocol) which is being examined at 0, 24, 48, 120, and 240 hrs post-xylazine or saline pretreatment.

Results: In the acquisition phase, all rats acquired fentanyl SA (consumption >25 µg/kg/day and >66.67% active lever discriminability for 5 consecutive sessions). During the treatment phase, fentanyl consumption was significantly reduced following xylazine injections as compared to pre-treatment acquisition (LME; $p<0.05$). Fentanyl consumption was also decreased in animals receiving xylazine pretreatment as compared to vehicle (LME; $p<0.05$), although this effect appeared to be more pronounced in males as compared to females. There was no decrease in lever discrimination from pre- to post-treatment (within-subject), and no differences in lever discrimination between treatment groups ($p's>0.05$).

Conclusions: Xylazine exposure during fentanyl SA reduces fentanyl consumption, although this effect may be greater in males as compared to females. Together, this is the first preclinical study to evaluate the effects of xylazine on intravenously self-administered fentanyl as a function of biological sex. Ongoing studies are examining (1) xylazine's effects in combination with or independent from fentanyl, (2) the unique impacts of intravenously delivered xylazine as an adulterant in fentanyl infusions on the fentanyl dose-response curve, and (3) how neurobiological alterations induced by xylazine/fentanyl co-use may induce naloxone resistance.

Financial Support: This work was funded by grants DA046526, DA055879, DA044479, DA045881, DA049130 (to CDG), and a pilot from the Substance Use Research Priority Area at UK (to CDG and SNK).

PHARMACOLOGICAL EFFECTS OF 2-BENZYLBENZIMIDAZOLE OPIOIDS EMERGING IN CLANDESTINE DRUG MARKETS WORLDWIDE

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Drug Category Opiates/Opioids

Topic Mechanisms of Action

Aim: Illicitly manufactured fentanyl plays a major role in the current opioid crisis, but non-fentanyl mu-opioid receptor (MOR) agonists are emerging in drug markets worldwide. Synthetic 2-benzylbenzimidazole opioids, also known as "nitazenes", are examples of non-fentanyl MOR agonists linked to human fatalities. Limited information is available about the structure-activity relationships for nitazene analogs.

Methods: We characterized the pharmacological effects of nitazenes with differing alkoxy chain length: metonitazene (methyl), etonitazene (ethyl), protonitazene (propyl), isotonitazene (isopropyl), and butonitazene (butyl). Effects of the analogs were tested in assays measuring in vitro MOR binding and MOR-mediated inhibition of cAMP formation. The antinociceptive, locomotor, and body temperature effects of subcutaneously (s.c.) administered drugs were examined in male C57Bl/6J mice (N=5-6 mice per dose).

Results: Nitazenes displayed higher affinity for MOR (Ki range=3.6-53.1 nM) over delta- and kappa-opioid sites and increasing alkoxy chain length decreased MOR affinity. Nitazenes were agonists in the cAMP assay, but potency varied (EC50 range=0.03-0.50 nM). In the cAMP assay, the ethyl, isopropyl, and propyl analogs were more potent than fentanyl (EC50=0.10 nM) and morphine (EC50=1.22 nM). Nitazenes induced antinociception (ED50 range=0.01-1.4 mg/kg), locomotor stimulation, and hypothermia. In the hot

plate assay, the ethyl, isopropyl, and propyl analogs were more potent than fentanyl (ED50=0.15 mg/kg) and morphine (ED50=10.19 mg/kg).
Conclusions: Our findings reveal that nitazenes are potent MOR agonists in vitro and in vivo, whereby the ethyl, isopropyl, and propyl chain lengths provide optimal pharmacological activity. Nitazenes may pose serious risks to human users.
Financial Support: Funded by IRP, NIDA, NIH

EFFECTS OF UNSCHEDULED BENZODIAZEPINES IN A MIDAZOLAM DISCRIMINATION ASSAY

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Drug Category Sedative/Hypnotics
Topic Behavioral Pharmacology
Aim: Forensic laboratory databases have reported increased encounters of 'designer' benzodiazepine substances. These drugs are not approved for use in the USA, and very little is known about their pharmacological effects. We sought to evaluate the discriminative stimulus effects of benzodiazepine drugs provided by the Drug Enforcement Administration (DEA) in rats trained to discriminate midazolam from saline.
Methods: Male rats were trained to discriminate 0.32 mg/kg midazolam from saline using a 2-lever procedure of food-maintained behavior. During training sessions, responses on one lever were reinforced with food pellets following injection of midazolam and responses on the alternative lever were reinforced following saline injection. Drug or saline sessions occurred on a modified double alternation schedule. Once rats reached testing criteria, ≥ 90% correct lever responding on 4 out of 5 consecutive training sessions, test sessions interspersed training days. Test sessions were similar to training sessions except that both levers were active. Full dose-effect functions were generated for nine benzodiazepine compounds – flualprazolam, etizolam, clonazolam, diclazepam, flunitrazepam, flunitrazolam, flubromazolam, adinazolam, and bromazolam - as well as several controls (midazolam, diazepam, alprazolam, methohexital, pentobarbital, morphine and xylazine). Effects of drugs that substituted for midazolam were redetermined following pretreatment with 1 mg/kg flumazenil.
Results: All benzodiazepines except adinazolam increased responding on the midazolam-associated lever, as did methohexital and pentobarbital. Morphine and xylazine did not substitute for midazolam up to doses with rate decreasing effects. No rate effects were observed for the benzodiazepine compounds. Pretreatment with flumazenil fully antagonized doses of the benzodiazepines that substituted for midazolam but did not alter the discriminative stimulus effects of methohexital or pentobarbital.
Conclusions: Eight of nine 'designer' benzodiazepines fully substituted for the discriminative stimulus effects of midazolam, and these effects were antagonized by flumazenil. These data suggest that eight compounds may have abuse-related effects similar to other benzodiazepine drugs.
Financial Support: 15 DDHQ21Q00000835

ORAL COMMUNICATION: ONLINE DRUG MARKETING: DEALING IN THE WORK-FROM-HOME AGE
Grand Ballroom I

EVALUATING INFLUENTIAL FEATURES OF SOCIAL MEDIA POSTS ADVERTISING ILLICIT DRUGS USING CONJOINT ANALYSIS

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Behavior

Aim: Illicit drug sales on social media is a growing public health issue. However, little is known about how users evaluate what features of a post selling drugs convey safety or are attractive. To identify these features, this study uses conjoint analysis, which can determine how people value different attributes (e.g., features) of posts.
Methods: 439 respondents were recruited from Amazon Mechanical Turk (MTurk). Respondents were selected based on whether they self-reported having ever purchased or used a prescription drug recreationally or a controlled substance. 48 mock social media posts advertising the sale of a controlled substance were created testing the following attributes: packaging of drugs; drug offerings; profile of seller; payment info provided; and use of emojis. Mock posts had every possible combination of tested attributes and were based on prior work detecting illicit controlled substance sales. Respondents were shown 1 post at a time and asked to evaluate how safe it would be to purchase from the user of the post. A multinomial logistic regression with a hierarchical Bayesian application was used to calculate preference scores for the tested features.
Results: Packaging was ranked the most influential tested attribute by a large margin (Average Importance =43.68; Drug offering=14.94; Profile=13.86; Payment=14.11; Emoji=13.41). Of the specific options tested, posts that include drugs displayed in official pill bottles were assessed as the most safe, as well as posts that advertised multiple drugs, had a blank profile, included payment info, and included emojis.
Conclusions: Users who self-reported online purchasing of drugs expressed preference for posts with official packaging, but also those with multiple controlled drugs and payment options, with the later features indicating risk as it is illegal to purchase controlled substances online. Identifying features of posts that are most likely to elicit a drug purchase can aide interventions and needed online content moderation.
Financial Support: This research was supported by the National Institute on Drug Abuse (Award 1R21DA050689-01) and Sawtooth Software.

MONITORING ONLINE ILLICIT DRUG MARKET DURING THE COVID-19

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Epidemiology
Aim: Matanga is an online platform selling illicit drugs in a number of countries in Europe. We aimed to examine trends in illicit drug sales on Matanga's Georgian (country) segment during the COVID-19.
Methods: We used a locally developed software to monitor and record transactions. To estimate transactions, the following variables were used: name of the item, name and code of the seller, count of units, volume of the unit (grams or number of tablets and blotters), unit cost. Data were collected through March 2020-April 2021.
Results: Despite COVID-19 related restrictions, the Matanga platform was actively used to purchase illicit drugs. Over 12 months of monitoring the 171 unique vendors offered 21 categories of illicit drugs, there were more than 46,756 sale transactions, and total revenues exceeded $8.2 million. Cannabis products accounted for the largest volume of sales, both in terms of a number of transactions and in terms of revenues generated and were followed by cocaine. Daily offers and daily sales were vastly equal throughout the studied period. It was unclear why unit cost of a specific substance increased over the studied period, and for others have not.
Conclusions: Drug supply through online drug market did not seem to be seriously affected during the lock-down period. Online shops were able to follow the demand, at least to some extent. Continuous monitoring of online platforms for illicit drug sales can provide useful data to better understand the dynamics of illicit drug market and can be an important source of data for a national early warning system.
Financial Support: This stud was implemented in the framework of the EU4Monitoring Drugs project, funded by the European Union (Contract number: CT.20.EU4MD.0028.1.0).

CANNABINOID CONTENT AND LABEL ACCURACY OF VARIOUS HEMP-DERIVED COSMETIC AND FOOD/BEVERAGE PRODUCTS AVAILABLE ONLINE AND AT NATIONAL RETAIL STORES

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Drug Category Cannabis/Cannabinoids
Topic Behavioral Pharmacology
Aim: To evaluate the label accuracy of cannabidiol (CBD) within cannabinoid-infused cosmetic and food/beverage products.
Methods: Inclusion criteria included designation as hemp beauty/haircare products (i.e., cosmetics) or food/beverages advertised to contain CBD. Products were purchased from retail stores in Baltimore, Maryland, and online. Actual CBD content was measured using gas chromatography mass-spectrometry. Percent deviations between labeled and actual CBD concentrations were determined. References to the Food and Drug Administration (FDA) were quantified.
Results: A total of 96 products were purchased (35 retail, 61 online). Of the 78 products with labeled CBD content, 29 (37%) were over-labeled (i.e., contained >10% less CBD than advertised) and 37 (47%) were under-labeled (i.e., contained >10% more CBD than advertised). Of the 29 over-labeled products, 12 (41%) contained no CBD. The median (range) percentage deviation between actual and labeled CBD was 23% (-100% to 4,468%) and -14% (-100% to 1,407%) for retail and online products, respectively. The median (range) percentage deviations were 16% (-100% to 1,011%) for beauty products, -53% (-100% to 30%) for haircare, and -1% (-100% to 4,468%) for food/beverages. Several beauty/haircare products made therapeutic (e.g., “prevents hair loss”) or cosmetic claims (e.g., “promotes youthful-looking appearance”), and 57 (59% of total) noted that products/claims were not regulated/evaluated by the FDA.
Conclusions: In a case series of cosmetic and food/beverage cannabinoid products purchased from retail stores and online, most CBD labels were highly inaccurate, and several products contained no CBD. Additionally, many made therapeutic/cosmetic claims, but roughly a third did not include disclaimers that the products/claims had not been evaluated by the FDA. Moreover, it is unclear whether these disclaimers accurately convey that therapeutic/cosmetic claims in many cases have not been empirically substantiated. These findings highlight the need for proper regulatory oversight of cannabinoid-infused/hemp products to ensure established standards for quality assurance are met.
Financial Support: This research was supported by the Substance Abuse and Mental health Services Administration.

IDENTIFICATION AND CHARACTERIZATION OF CANNABIS PRODUCTS ON THE DARK WEB

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Drug Category Cannabis/Cannabinoids
Topic Policy
Aim: States have enacted different cannabis legalization, licensing, and control policies. However, unregulated access can be found on the dark web through a shadow economy that specializes in the trading of illicit goods and services. In this study, we identify and characterized cannabis products found on the dark web.
Methods: We collected content using data mining approaches and keyword search queries related to common cannabis product keywords (e.g. “vape”, “cartridges”, “e-liquid”, “disposable”, “pods”, “THC”) to identify specific dark web markets and selling listings. Next, we applied content coding to identify type of products, price, and payment methods.
Results: We identified four dark web markets (Archetyp. Incognito, Royal and Wethenorth) that yielded a total of 3059 selling posts. An assortment of products comprised of both cannabis related products and other prescription and illicit drugs were confirmed through manual annotation. The 3 most common products being marketed on dark web marketplace listings reviewed included THC vape products, (1498, n=48.9%), followed by edibles (733, n=23.9%), and different types of illicit drugs (synthetic opioids, heroin, and ecstasy) was being listed (228, n=7.4%). Payment modality being advertised included bitcoin, with an emphasis on discrete transnational, domestic, and international shipping products.

Conclusions: A review of illegal dark web marketplaces found that THC vape products comprised almost half of all selling posts followed by various cannabis edibles. Many of these cannabis products reported high concentrations of THC, likely representing unknown consumer safety risks and including unregulated products. Additional research is needed to identify the health impact of access to dark web cannabis products.
Financial Support: This study was funded from the National Institute on Drug Abuse (Award 1R21DA050689-01), the National Institute on Drug Abuse Small Business Innovation Research Program (award 75N95020C00025), and the University of California Tobacco-related Disease Research Program (award no. T32IP4788.)

ORAL COMMUNICATION: SUD AND COMORBID ANXIETY
Grand Ballroom II

INDIVIDUALS WITH SUBSTANCE USE DISORDER EXHIBIT HEIGHTENED ANXIETY AND ANTERIOR CINGULATE ACTIVATION DURING FEAR CONDITIONING

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Drug Category Other, General Substance Use Disorder
Topic Substance Use Disorder
Aim: Fear conditioning (FC), or learning from aversive experience, is an important process influencing action-outcome associations. Frontocingulate, insular, and amygdalar regions are: (1) associated with FC; and (2) altered in substance use disorders (SUD). However, it is unclear whether FC processes are specifically disrupted in SUD. This investigation examined the hypothesis that SUD individuals show altered neural processing during FC.
Methods: SUD+ (n=162) and SUD- (n=110) groups from the Tulsa-1000 study underwent Pavlovian FC during functional magnetic resonance imaging. Linear mixed effects models compared group, conditioned stimulus type (CS+, CS-) and time (familiarization: run 1, conditioning: runs 2-3) on: (1) brain activation in frontocingulate, amygdala, and anterior insula (AI) regions of interest; and (2) subjective ratings of valence, anxiety, and arousal.
Results: SUD+ reported greater anxiety symptoms than SUD- ($p<.001$, $g=.52$) but groups did not differ on other demographic characteristics. During conditioning, compared to SUD-, SUD+ showed: (1) lower anxiety rating differentiation between CS+ and CS- ($p=.03$, $g=.28$); and (2) greater dorsal anterior cingulate cortex activation to CS+ ($p=.04$, $g=.26$); Across participants, higher AI activation ($p<.001$, $g=.30$) and negative valence/arousal ratings to CS+ ($p's<.001$, $g=.64/.32$) were also present during conditioning.
Conclusions: In support of hypotheses, SUD was associated with heightened anterior cingulate processing during FC, which may reflect increased conflict detection to stimuli paired with threat. In contrast, SUD individuals did not show altered AI or amygdala processing during FC, suggesting that salience-relevant neural alterations in SUD may depend upon task context (e.g., drug versus non-drug cues, decision-making task demands).
Financial Support: RO1 DA050677

RELATIONSHIP BETWEEN INCREASED POLYSUBSTANCE USE, ANXIETY, AND STRESS DURING THE COVID-19 PANDEMIC: RESULTS FROM THE COVID-19 CANNABIS HEALTH STUDY

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Comorbidities

Aim: Sudden environmental change is a known risk factor for poor mental health (i.e., anxiety, stress), which may be associated with increased substance. Minoritized populations are at disproportionate risk for such outcomes after exposure to abrupt environmental change such as the COVID-19 pandemic. The purpose of this study was to examine the association between (1) anxiety and stress and change in polysubstance use among cannabis users during the COVID-19 pandemic; and (2) how this association differed by race/ethnicity.
Methods: An electronic cross-sectional survey was disseminated via RedCap from March 2020-March 2022 and completed by 2,816 adults who consume cannabis (>18 years; 85% US residents). Participant self-report of increase/decrease/no change in use of tobacco, alcohol, opioids, cocaine, methamphetamines, and psilocybin was collected. Increase of any combination of these substances was compared to no change in use. The general anxiety disorder (GAD-7) score and the Pandemic Stress Index (PSI) collected exposure data. T-tests and logistic regression assessed overall associations, and by race/ethnicity group.
Results: Among the sample (mean age 42 years [15.7], 78.7% non-Hispanic white, 49% female), those who reported increased polysubstance use were significantly younger (38-years vs 44-years, $p<0.001$); disproportionately female (55%, $p=0.004$). Among the entire sample, those who reported increased polysubstance use had higher mean GAD-7 scores than with no change (10.8 vs 8.2, $p<0.001$). After adjusting for demographics and PSI, increased polysubstance use was associated with a 4% increase in GAD-7 scores (OR: 1.06, 95% CI: 1.02-1.06). PSI was not found to be associated with increased polysubstance use; no differences in anxiety or stress by polysubstance use were found by race/ethnicity.
Conclusions: Findings indicate that health care professionals should screen for substance use among patients with anxiety and provide healthy coping strategies for anxiety which has been common over the past several years due to the pandemic.
Financial Support: The presenter is supported by the Research Training Program in Substance Abuse Prevention at Yale University (T32-DA019426). Funding for this research was made possible (in part) by T37MD008647 from the National Institute on Minority Health and Health Disparities.

ANXIETY TRAJECTORIES, WELL-BEING, AND CANNABIS USE IN A COHORT OF PENNSYLVANIA MEDICAL CANNABIS PATIENTS

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Drug Category Cannabis/Cannabinoids
Topic Behavior
Aim: Anxiety disorders are a qualifying condition in only seven of 39 U.S. jurisdictions with legalized medical cannabis, including Pennsylvania; this may reflect controversy surrounding the anxiolytic efficacy of cannabis and a paucity of prospective research among medical cannabis patients. This study aimed to identify longitudinal anxiety profiles and their associations with health outcomes and generalized cannabis use in a cohort of Pennsylvania-based medical cannabis patients (MCP) with varying levels of baseline anxiety.
Methods: The study utilized 5 waves of quarterly data collected over a 12-month span from an ongoing rolling cohort study of PA-based MCP recruited between 2021-2022 (n=363 at baseline, n=71 at 12 months thus far). Anxiety was measured using the Generalized Anxiety Disorder scale (GAD-7); other measures included depression (PHQ-9), severity of dependence (SDS), quality of life (Flourishing scale), self-reported history of health conditions, and cannabis use days in the past 90 days. Latent class growth analysis estimated longitudinal anxiety profiles and outcome trajectories across each profile; missing data were handled using the maximum likelihood estimation.
Results: Two distinct anxiety profiles emerged: “Minimal-to-mild” (61.8%) and “Moderate-to-severe” (38.2%). Women’s gender, younger age, anxiety disorders as a primary qualifying condition, and lifetime diagnosis of PTSD predicted membership in the “Moderate-to-severe” versus “Minimal-to-mild” group. At baseline, “Moderate-to-severe” group had higher levels of depression, cannabis use days, cannabis dependence, and lower quality of life than “Minimal-to-mild” group. By month 12, “Moderate-to-severe” group experienced increased depression and declining quality of life, decrease in cannabis use days, but no changes in anxiety or cannabis dependence levels.

Conclusions: Medical cannabis did not increase anxiety in this sample. However, consistent, elevated level of anxiety was associated with increasing depression and lower quality of life. Further understanding of whether anxiety and comorbid depression are secondary to other health conditions among MCP may assist in devising clinical interventions for this group.
Financial Support: This study was supported by research contract between Verano and Drexel University.

LATINX INDIVIDUALS WHO SMOKE DAILY WITH AND WITHOUT A PROBABLE ANXIETY DISORDER: DIFFERENCES IN SMOKING BEHAVIOR AND BELIEFS ABOUT ABSTINENCE

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Drug Category Nicotine/Tobacco
Topic Disparities
Aim: Latinx smokers represent a tobacco-related health disparities population. While extant work has documented that anxiety disorders impair successful smoking cessation and the maintenance of abstinence from smoking, limited work has expressly focused on Latinx smokers in terms of anxiety symptoms and disorders. The present investigation aimed to explore differences among English-speaking Latinx adults who live in the United States (US) and smoke cigarettes with and without a probable anxiety disorder in terms of cigarette dependence, perceived barriers for quitting, severity of problems when quitting, and smoking abstinence expectancies.
Methods: The sample included 338 adult Latinx daily cigarette smokers (Mage = 35.53 years; SD = 8.65; age range 18-61; 37.3% female) who identified as Latinx and were recruited nationally throughout the US. Seven analysis of covariance models were conducted to evaluate differences in clinically relevant smoking outcomes and beliefs about abstinence among Latinx smokers with and without a probable anxiety disorder.
Results: Results indicated that Latinx persons who smoke with a probable anxiety disorder, compared to those without, were more likely to demonstrate statistically significant higher levels of cigarette dependence, severity of problems when trying to quit, and greater perceived barriers for quitting. These significant effects were small in magnitude, but evident above and beyond the variance associated with relevant covariates. Further, there were significant anxiety-based group differences in terms of smoking abstinence expectancies. Specifically, Latinx persons who smoke with a probable anxiety disorder compared to those without a probable anxiety disorder demonstrated heightened beliefs that smoking abstinence (acutely) would be associated with negative mood, somatic perturbation, and harmful consequences.
Conclusions: The current findings are the first to document probable anxiety disorder status as a clinically relevant factor for a wide range of smoking variables and beliefs about abstinence among Latinx persons who smoke.
Financial Support: None

ORAL COMMUNICATION: IMAGING
Governor's Square 15

AMYGDALA-PREFRONTAL CIRCUIT AS A POTENTIAL MEDIATOR OF REWARD SENSITIVITY IN NON-HUMAN PRIMATES

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Drug Category Other, Natural reward (Food)
Topic Substance Use Disorder
Aim: Individual differences in response to various rewards are thought to be a risk factor for substance use disorder; however, the brain structural mechanisms underlying reward sensitivity are not completely

understood. Here, we investigated whole-brain structural features in grey matter (volume) and white matter (fractional anisotropy) associated with reward sensitivity in non-human primates.
Methods: Adult rhesus monkeys (5 males; 7 females) responded for each of several concentrations of sweetened condensed milk (0, 10, 30, 56%) using a self-administration procedure in which the response requirement for milk delivery increased across sessions in ascending order (i.e. FR 1, 3, 10, 30, 100, etc). Magnetic resonance imaging was used to measure brain region volumes (structural MRI) and white matter microstructure (diffusion MRI). Statistical significance was determined by unpaired t-tests with correction for multiple comparisons using the Holm-Sidak method.
Results: Subjects were divided into high (n=6) or low (n=6) reward sensitivity groups based on differences in essential values ($P<0.01$) determined in behavioral-economic analysis for milk (10, 30, 56%). Subjects in the high sensitivity group had greater volumes in brain regions involved in reward conditioning, including dorsolateral prefrontal cortex (dlPFC, $P=0.05$) and centro-medial amygdaloid complex (ceMA, $P=0.03$), compared to subjects in the low sensitivity group. Further, monkeys in the high sensitivity group had lower fractional anisotropy values in the dorsal cingulate bundle (CBD, $P=0.03$), a white matter tract connecting dlPFC and CeMA, compared to monkeys in the low sensitivity group. Essential value was positively correlated with the volume of reward conditioning-related brain regions [dlPFC ($R=0.64$, $P<0.01$) and CeMA ($R=0.69$, $P<0.01$)], and negatively correlated with mean fractional anisotropy of the CBD ($R=-0.73$, $P<0.01$).
Conclusions: These results suggest that amygdala-prefrontal circuitry is a potential mediator of reward sensitivity, which could serve as predictive biomarkers of vulnerability to substance use disorders.
Financial Support: R01DA048150

COCAINE SELF-ADMINISTRATION BEHAVIOR IS ASSOCIATED WITH SUBCORTICAL AND CORTICAL GRAY MATTER IN INDIVIDUALS WITH COCAINE USE DISORDER

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Drug Category Stimulants
Topic Imaging
Aim: Links between gray-matter macrostructure and cocaine-use behaviors have been reported in animal models of addiction. While cortical and subcortical alterations in gray matter have been reported in individuals with cocaine-use disorder (CUD), little is known regarding potential relationships with direct cocaine-use behaviors.
Methods: Thirty-three individuals with CUD (33% female, 44±6.5 years old) completed a 1-hour laboratory-controlled intravenous cocaine self-administration procedure and high-resolution structural magnetic resonance imaging. The primary outcome was number of responses to receive a cocaine infusion. Gray matter volumes (GMVs) in the putamen, caudate, accumbens, hippocampus, amygdala, as well as average cortical thickness of gyrus rectus, anterior cingulate gyrus/sulcus, orbital gyrus, medial orbital sulcus, and insula gyrus/sulcus, were considered. Regression analyses examined relationships between primary outcomes and total gray matter, age, years of cocaine use, and time since last cocaine use as confounders. Additional models examined potential associations with subjective ratings.
Results: The number of responses to receive cocaine infusions was negatively associated with GMV in the putamen ($\beta=-0.69$, $\sigma=0.32$, $p=0.030$) and amygdala ($\beta=-7.21$, $\sigma=2.56$, $p=0.005$). When subjective ratings were included as covariates, responses were positively associated with thickness of the gyrus rectus ($\beta=6.66$, $\sigma=2.26$, $p=0.003$) and insula ($\beta=1.46$, $\sigma=0.73$, $p=0.046$), and negatively associated with thickness of the anterior cingulate ($\beta=-2.96$, $\sigma=1.36$, $p=0.030$).
Conclusions: Consistent with animal models, gray-matter macrostructure was linked to cocaine-use behavior in people who chronically/regularly used intravenous and/or smoked cocaine. Findings suggest that identified regions may contribute to behaviors linked to reinforcing properties of cocaine or cognitive control over cocaine-seeking, with roles extending beyond the regulation of subjective feelings associated with the drug.
Financial Support: R01DA052454-02 (GA) and T32DA007238 (RK)

FMRI INFORMED TMS TARGET SELECTION FOR FRONTOAMYGDALA CIRCUIT IN PEOPLE WITH METHAMPHETAMINE USE DISORDER

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Drug Category Stimulants
Topic Substance Use Disorder
Aim: A large body of evidence supports the notion that the prefrontal-limbic network plays a major role in cue-induced craving and relapse in substance use disorders. Neuroimaging findings in substance use disorders suggest that TMS over the frontopolar can stimulate the frontoamygdala circuit. However, interindividual variability has not yet been considered such that stimulation of cortical-subcortical circuits could modulate behavioral outcomes across a population. Here, we assessed individualized targeting and dosage of TMS over frontopolar using an fMRI-informed pipeline for modulation of the frontoamygdala circuits.
Methods: fMRI data were acquired from 60 participants with methamphetamine use disorder (MUD) during a drug cue-reactivity task. Craving self-reports were collected before and after the MRI session. Amygdala was among the most activated areas in response to drug cues. To localize cortical regions with significant functional connectivity with the amygdala during cue exposure, we calculated seed-to-whole-brain psychophysiological interaction (PPI). Personalized TMS targets within the right-frontopolar were calculated considering each person's most positive frontoamgdala connection. Using personalized head models, coil orientation was then optimized for each person.
Results: A significant cluster with increased PPI connectivity to the medial amygdala was found in the right frontopolar cortex; 2462 voxels MNI-peak: [25 39 35], $P<0.001$, $Z=4.7$. Interindividual variabilities were found in terms of location (mean±SD MNI coordinate: [18.33 64.8 -0.33] ± [8.7 3.5 11.6] in a cube with a volume of 14.92cm3) and strength (mean±SD: 1.51±0.9 ranges from 0.2 to 5.6) of frontoamygdala PPI connections which were positively correlated with changes in craving ($r=0.4$, $P<0.04$). Personalized coil orientation was determined based on maximizing the strength of the electric field perpendicular to individualized targets (maximum electric field ranges from 0.69 to 1.3 V/m).
Conclusions: We highlighted the importance of inter-individual variability in targeting frontolimbic connectivity via TMS and developed an individualized fMRI-guided pipeline to modulate the frontopolar-amygdala circuits in MUD. The data suggests a wide range of inter-individual variations in location and dose which justifies individualized protocols to optimize and harmonize the intervention across participants.
Financial Support: None

TREATMENT-RELATED CHANGES IN THE TEMPORAL DYNAMICS OF RESTING-STATE BRAIN ACTIVATION IN NICOTINE-DEPENDENT INDIVIDUALS

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Drug Category Nicotine/Tobacco
Topic Neurobiology/Neuroscience
Aim: Resting state functional neuroimaging has identified functional brain networks linked with smoking behaviors. While typically studied using static connectivity methods, these brain networks can be evaluated using coactivation pattern analysis, which identifies momentary brain states with characteristic patterns of temporal coactivation. Given this, we were interested in whether the temporal dynamics of brain states would change in tobacco smoking individuals following treatment for nicotine dependence. Participants received either nicotine replacement therapy (NRT, n=20), or both NRT and non-nicotine containing e-cigarettes (n=27).
Methods: Study visit (pre/post treatment) and treatment group were considered to test for differences in temporal dynamics. We tested the amount of time spent in eight empirically derived brain states, which were identified within a large sample of control subjects. These brain states share substantial overlap with default mode (DMN), frontoparietal (FPN), dorsal attention (DAN), salience (SN), and sensory processing networks.
Results: No differences were found between treatment groups, but time spent in states differed as a function of study visit. Following treatment, individuals spent less time in the frontoinsular-DMN, canonical DMN,

and dorsal attention network states, and more time in the FPN, SN, and sensorimotor-DMN ($p < 0.05$, Bonferroni-corrected).
Conclusions: Findings demonstrate that the time spent in prototypical resting-state brain states can change after treatment for nicotine dependence. This suggests that the brain networks coactivating to form these brain patterns at rest are malleable and responsive to treatment strategies.
Financial Support: Supported by 5K02DA042987(AJ), 5R01DA039135 (AJ), T32DA015036 (TW), and support from the NIDA Intramural Research Program

ORAL COMMUNICATION: OPIOID-STIMULANT INTERACTIONS: SPEEDBALLS AND GOOFBALLS
Plaza Ballroom A

NALOXONE IS LESS EFFECTIVE AT REVERSING THE PHYSIOLOGICAL EFFECTS OF FENTANYL-METHAMPHETAMINE MIXTURES THAN FENTANYL ALONE

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Drug Interactions
Aim: Over the past decade, opioid-related deaths have increased exponentially, however, there is increasing realization that many these deaths involved both opioids and stimulants. Despite these trends, little is known about the toxidrome of mixtures of opioids and stimulants. The current studies aimed to characterize the cardiovascular and respiratory effects of opioids, stimulants, and opioid+stimulant mixtures, and to determine the effectiveness of naloxone to reverse these effects.
Methods: Following venous catheterization, male and female Sprague Dawley rats (n=12/sex) were acclimated to a testing chamber for 1-h prior to intravenous drug administration, after which heart rate and percent oxygen saturation (SPO2) were measured for 30-min using a pulse oximeter. Dose-response curves for the effects of fentanyl (0.0056-0.56 mg/kg), and methamphetamine (0.1-1 mg/kg) on heart rate and SPO2 were generated prior to evaluating a mixture of fentanyl (0.56 mg/kg) and methamphetamine (1 mg/kg). Finally, naloxone (0.01, 0.1, or 1 mg/kg) was administered as a 5-min post-treatment to determine its effectiveness to reverse the cardiovascular and respiratory effects of fentanyl, methamphetamine, and mixtures of fentanyl+methamphetamine.
Results: Fentanyl produced a dose-related bradycardia and reduction in SPO2, whereas methamphetamine produced a dose-related tachycardia and was without effect on SPO2. When co-administered, fentanyl and methamphetamine produced a significant bradycardia and reduction of SPO2. Naloxone rapidly reversed the cardiovascular and respiratory effects of fentanyl but was less effective at reversing the effects of a mixture of fentanyl+methamphetamine.
Conclusions: These studies suggest that concurrent use of opioids (fentanyl) and stimulants (methamphetamine) can result in enhanced cardiovascular and respiratory responses. Additionally, although naloxone produced a rapid and full reversal of the physiological of fentanyl, the fact that it was unable to reverse the effects of a mixture of fentanyl+methamphetamine suggests that alternate strategies are needed to address the growing number of overdoses related to co-use of opioids and methamphetamine.
Financial Support: This work was supported by NIH/NIDA grant R01 DA039146.

USING BEHAVIORAL ECONOMICS TO QUANTIFY HOW PEOPLE WHO USE COCAINE RESPOND TO FENTANYL ADULTERATION

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Drug Category Stimulants
Topic Behavioral Economics
Aim: Overdoses related to fentanyl-adulterated cocaine have recently increased. Yet, research on how people who use cocaine perceive fentanyl adulteration, or who might be at risk of overdose has been limited. In the current pilot study, we used a behavioral economic paradigm, cocaine demand, to better understand

the decision-making processes related to cocaine use that may be adulterated with fentanyl. Specifically, we developed a novel hypothetical cocaine purchasing task to assess cocaine consumption with no chance vs a 1 in 10 chance of fentanyl contamination. We also tested on an exploratory basis whether any individual characteristics predicted continued demand for cocaine despite fentanyl adulteration.
Methods: In this online study, self-reported cocaine purchasers (N = 32) completed measures of demand for fentanyl-adulterated cocaine as well as self-reported demographics and substance use history.
Results: In regard to demand characteristics, mixed effects models showed a significant effect of adulteration on intensity of demand ($B = -6.88$, $SE = 2.20$, $t(31) = -3.13$, $p < 0.01$), such that possible fentanyl adulteration decreased intensity, but not for elasticity ($p = 0.73$). For individual characteristics, opioid co-use ($p = 0.53$), gender ($p = 0.54$), age ($p = 0.33$), income ($p = 0.20$), education ($p = 0.62$), and chronic pain ($p = 0.56$) did not moderate the relationship between adulteration and intensity. However, lack of findings in this area may have been due to a small sample size.
Conclusions: Overall, this small pilot's findings suggested fentanyl adulteration reduced demand for cocaine in some but not all participants. This measure will require additional validation, but thus far results suggest that our adulterated-cocaine purchasing task may be a useful tool for identifying people at greater risk of fentanyl overdose.
Financial Support: This research was supported by a grant from the National Institute on Drug Abuse to Cecilia Nunez (UG1DA049467).

EFFICACY OF EXTENDED-RELEASE INJECTABLE BUPRENORPHINE FOR PATIENTS WITH DUAL OPIOID AND COCAINE USE DISORDER

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Treatment
Aim: To present findings from the first randomised controlled superiority trial of extended-release injectable buprenorphine for opioid use disorder (OUD) with a focus on impact of treatment for patients with dual OUD and cocaine use disorder.
Methods: Oral (trans-mucosal) buprenorphine and oral (liquid) methadone – are the daily standard of care (SOC) partial and full mu-opioid agonist pharmacotherapies for opioid use disorder (OUD), but there is sub-optimal patient adherence, retention, and response, and treatment can be complicated by the dual OUD and cocaine use disorder (OUD-CUD); especially high prevalence in the United Kingdom). Subcutaneously injected, extended-release, subcutaneous injectable buprenorphine (BUP-XR; Sublocade®, Indivior) has superiority potential through better blockade of the reinforcing effect of non-medical opioids, prevention of withdrawal, suppression of craving, and simple monthly dosing, but there has been no efficacy evaluation. The Extended-release Pharmacotherapy for OUD (EXPO study) was a randomised, two-arm, parallel group, open-label, phase III superiority trial at five community treatment centres in England and Scotland. Eligible participants (adults aged ≥18 years; all meeting DSM-5 diagnostic criteria for moderate–severe OUD) were randomised (1:1) to receive continued standard care (i.e. ongoing SOC (choice of daily, trans-mucosal buprenorphine [usual dose 8–24 mg/day] or methadone [usual dose 60–120 mg/day]), or BUP-XR (two monthly injections of 300 mg, then four monthly injections of 100 mg), all over 24 weeks. In the intent-to-treat population, with a 1-week measurement grace period after randomisation, the primary efficacy endpoint was the count of self-reported days abstinent from illicit and non-medical opioids between days 8–168 (i.e. weeks 2–24; 161 days) combined with urine drug screening. Secondary outcomes included retention; craving frequency (Craving Experiences Questionnaire [CEQ-F]), and use of cocaine and non-medical benzodiazepines.
Results: 314 participants were randomly allocated to receive SOC (n=156) or BUP-XR (n=158). At admission, 49% used cocaine in the past month. At the endpoint, participants were abstinent from opioids for a mean of 104·4 days (range: 0–161 days) in the SOC group and 123.4 days (range: 24-161 days) in the BUP-XR group (model adjusted incident rate ratio [IRR] 1·18, 95% confidence interval [CI] 1·05–1·33; p-value 0·004). There was also more complete attenuation of craving for opioids on the CEQ-F among the BUP-XR group (adjusted OR 3·22; 95% CI 1·65–6·36) and reduced craving frequency (adjusted IRR 0·52;

95% CI 0·35–0·81), but BUP-XR did not achieve a statistically significant reduction in craving for cocaine (p-value 0.885) nor an increase in abstinence from cocaine (p-value 0.230).
Conclusions: Together with other findings to be summarised, the EXPO study indicates that Sublocade® is a simple, acceptable, and effective treatment for OUD. but adjunctive pharmacotherapies and psychosocial interventions – to be discussed - are needed to help OUD-CUD patients address cocaine-related problems.
Financial Support: The EXPO study was funded by collaborative research agreement with Indivior.

OPIOID- AND STIMULANT-INVOLVED OVERDOSE DEATHS AMONG BLACK PEOPLE IN ST. LOUIS, MO: EXAMINING SOCIAL DETERMINANTS OF HEALTH

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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Disparities
Aim: Over 75% of U.S. overdose deaths in 2021 involved opioids and approximately 50% involved stimulants as rates co-involved deaths have recently increased. Since 2013, rates of opioid overdose deaths have increased starkly among Black Americans, outpacing those of White Americans. Concurrently, stimulant-involved overdose deaths, driven largely by cocaine, have disproportionately affected Black people compared to other ethnic/racial groups. Despite this emergent health inequity, little is known about the sociodemographic correlates that differentiate stimulant and opioid-involved overdose deaths among Black individuals.
Methods: Data were derived from all drug-involved death records from the medical examiners of St. Louis City and County from 2016-2021. Included records were Black decedents whose cause of death was opioid and/or stimulant involved overdose (N = 1930, 73% male). Multinomial regression estimated type of drugs involved in overdose: stimulant only (SO; reference category), opioid only (OO), or both (SAO). Age, sex, comorbid medical condition at death, and Area Deprivation Index (ADI; derived from 17 census variables including income, education, and housing), based on residence address at death, were independent variables.
Results: Age was significantly associated with OO and SAO relative to SO with younger decedents more likely to be in the former categories (OR = .93-.94, $p < .001$). Decedents with OO and SAO overdose were also more likely to be male relative to SO (OR = 1.91-1.94, $p < .05$). Decedents with OO and SAO overdose were less likely to have medical conditions present relative to SO (OR = .01-.03, $p < .001$). ADI was not significantly associated with OO or SAO.
Conclusions: Findings suggest similar sociodemographic correlates of opioid overdose deaths whether or not stimulants are involved. As residential deprivation was not associated with overdose type, future research should examine social determinants of health characteristic of the injury environment in fatal and nonfatal overdoses among Black individuals.
Financial Support: Substance Abuse and Mental Health Services Administration: (Grant number 1H79TIO80271)

ORAL COMMUNICATION: DIGITAL THERAPEUTICS: HARMFUL IF SWALLOWED!
Plaza Ballroom D

REMOTE CONTINGENCY MANAGEMENT FOR ALCOHOL USE DISORDER: RELATIONSHIP OF TREATMENT OUTCOMES TO INITIAL ABSTINENCE STATUS

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Drug Category Alcohol
Topic Treatment
Aim: Contingency Management (CM) is a highly effective, evidence-based intervention for improving substance use disorder (SUD) outcomes. Prior research primarily among people who use cocaine has found that baseline drug use severity, as measured by submission of cocaine positive samples at study start, can

relate to CM efficacy. This analysis determined if similar effects occur with CM delivered for alcohol outcomes – suggesting either a generalized or drug-specific effect of baseline severity.
Methods: Data are from an ongoing randomized clinical trial in which participants meeting DSM-5 criteria for alcohol use disorder were randomized to receive contingent monetary rewards based on behavioral targets including abstinence from drugs and alcohol (n=69) or research payments for completion of study assessments (n=66).This analysis of data from the first month of the study compares intervention outcomes between participants who submitted any positive test during the week prior to randomization versus those submitting only negative samples.
Results: An overall main effect of entry week test status was observed such that those with a positive test had fewer weeks abstinent in the first month, p=.001. A significant interaction between entry week positive status and intervention group was also observed, p=.04. Among participants with an entry week positive test, abstinence rates were higher for the intervention versus control group (58.3% versus 35.9% weeks abstinent, p=.02, d=0.69). Among participants with negative entry week tests, no differential effect of intervention versus control was observed (75.6% versus 77.3%, p=.80, d=0.05).
Conclusions: These findings provide a conceptual replication showing an interaction between baseline severity and CM treatment response, suggesting generality across specific drug problems. Findings are relevant to beliefs about who should receive CM treatment- suggesting that those who fail to meet initial abstinence goals may benefit more than highly motivated patients with early treatment success.
Financial Support: Support was provided by DynamiCare Health, Inc. and the National Institute on Alcohol Abuse and Alcoholism (R44AA026234).

PARTICIPANT RETENTION IN DIGITALLY-PROVIDED BUPRENORPHINE TREATMENT FOR OPIOID USE DISORDER COMPARED WITH TREATMENT AS USUAL OFFICE-BASED TREATMENT: AN OBSERVATIONAL LONGITUDINAL COHORT STUDY

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Drug Category Opiates/Opioids
Topic Technology (e.g., mHealth)
Aim: During the COVID-19 pandemic, federal agencies permitted telehealth initiation of buprenorphine treatment for opioid use disorder (OUD) without an in-person assessment. It remains unclear how digitally-provided buprenorphine treatment impacts treatment retention when compared with treatment as usual office-based treatment.
Methods: This is an on-going observational longitudinal cohort study. Participants with OUD initiating buprenorphine were recruited from a digital-only treatment provider ("Boulder Care") or treatment as usual (TAU) via a brick-and-mortar setting employing selective telehealth. Eligible participants were early in OUD treatment (<= 45 days) and had internet and phone access. The primary outcome was self-reported buprenorphine retention at 4, 12, 24, and 36 weeks. Logistic generalized estimating equations assessed retention over time. We calculated adjusted odds ratios (OR) to compare odds of retention at each timepoint between digital-only vs. TAU, after controlling for covariates.
Results: Participants (n=100 digital-only group; n=58 TAU) had a mean age of 37.1 years (SD=9.8 years) and included 51.9% women, 83.5% with Medicaid coverage, 80% identified as White, 65.2% unemployed/student, and 19% unhoused. Groups (digital-only vs TAU) differed on gender (56.0% vs 44.8% women, p=.04), employment (61.0% vs 72.45% unemployed/student, p=.09), and housing (14.0% vs 27.6% homeless, p=.06). Overall, there were no differences in retention across timepoints (interaction p=.97). At all follow-up timepoints, TAU had decreased odds of retention compared to digital-only arm, though estimates did not reach statistical significance (week 4 aOR=0.42, 95% CI[0.08, 2.18]; week 12 aOR=0.51, 95% CI[0.11, 2.36]; week 24 aOR=0.36, 95% CI[0.08, 1.63]; week 36 aOR=0.32, 95% CI[0.09, 1.18]).
Conclusions: There were no statistically significant differences in retention between digital-only and TAU delivered treatment. There was signal that participants receiving digital-only treatment had higher odds of retention at weeks 24 and 36. Longer follow-up periods may be required to evaluate the impact of telehealth interventions and improved treatment retention.
Financial Support: NIDA 4 R44 DA 050345-02. This project was funded by the National Institute on Drug Abuse Small Business Innovation Research (SBIR) grant; therefore, by design, has academics and industry

working together. The funder did not participate in the design of the study, nor in the collection, analysis, interpretation of data, or writing of the manuscript. ; NIDA K23 DA053390 (Chan)

PRELIMINARY RESULTS FROM A DECENTRALIZED TRIAL EVALUATING A NOVEL, GAME-BASED DIGITAL THERAPEUTIC FOR OPIOID USE DISORDER

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Drug Category Opiates/Opioids
Topic Technology (e.g., mHealth)
Aim: Clinical trials and real-world observational studies have demonstrated that patients will engage with an FDA-authorized prescription digital therapeutic (PDT) for the treatment of opioid use disorder (OUD). Given the demonstrated relationship between treatment engagement and positive patient outcomes, we hypothesized that a more interactive content delivery platform could further enhance PDT engagement. A game-based version of a PDT for OUD (gDT) was developed utilizing a game economy consisting of virtual and tangible rewards designed to enhance engagement. Both digital therapeutics were evaluated in a two-arm, decentralized, randomized controlled trial.
Methods: Participants (N=52) currently receiving outpatient buprenorphine treatment for OUD and within the first 120 days of treatment initiation were enrolled at two virtual recruitment sites. Eligible, consenting individuals were randomized 1:1 to receive the PDT or the gDT for 12 weeks. Participants attended weekly remote study visits for weeks 1-8 and a final remote study visit at week 12. Outcomes were digital therapeutic engagement (# days of use; % of therapy lessons completed) and retention (% study completers) by treatment arm.
Results: Study participants were 54.9% female (45.1% male); 90.4%% (n=47) White; 7.7%% (n=4) Latino; and had a mean age of 36.8 years (SD 8.26). Mean number of active days for participants randomized to the gDT was 21.5 compared to 31.2 for the PDT. Mean percentage of total lessons completed was 175% for participants randomized to the gDT (representing significant lesson repetition) compared to 55.1% for the PDT. For study retention, 92.0% of participants randomized to the gDT were retained at week 12 compared to 81.5% for the PDT.
Conclusions: Preliminary results demonstrate relatively high digital therapeutic engagement and rates of retention for both treatment arms. Ongoing data analysis, including statistical testing, will be presented to explain and interpret the impact of engagement differences, including skills acquisition, participant satisfaction, and substance use.
Financial Support: This research was supported by the National Institute on Drug Abuse (A Game-Based Intervention for Opioid Use Disorder; 5R44DA042652-03) and Pear Therapeutics (US), Inc.

ORAL COMMUNICATION: SUD AND SUICIDALITY
Grand Ballroom I

HIGH SUICIDALITY PREDICTS OVERDOSE EVENTS AMONG PEOPLE WITH SUBSTANCE USE DISORDER: A LATENT CLASS ANALYSIS

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Drug Category Other, All substance use
Topic Other

Aim: Suicide is the tenth leading cause of death in the US and remains a major public health concern. Suicide risk is heightened among individuals with substance use disorders (SUD) and most prevalent in patients with co-occurring mental health conditions – those most prone to poor substance use related outcomes including overdose. Identifying individuals with SUD who are suicidal, and therefore potentially most at risk of overdose, is an important step to address the "dual epidemic" in the US, represented by suicides and overdose deaths. The current study utilizes latent class analysis to assess whether response patterns to items assessing suicidal propensity and suicidal thoughts can indicate risk for poor substance use related outcomes.
Methods: The study includes 2,541 participants (male and female) with SUD enrolled across 8 randomized clinical trials, conducted in the National Drug Abuse Treatment Clinical Trials Network from 2012 to 2021. Characteristics of individuals in each class are presented, and multivariate regression analyses examine latent class membership as a predictor of 1) overdose and 2) substance use days, controlling for covariates.
Results: Three classes are identified: 1) Minimal Suicidality; 2) Moderate Suicidality; and 3) High Suicidality. Individuals in the High Suicidality class comprise the highest proportions of males, Black/ African American individuals, and those with psychiatric history and baseline depression. Regression analysis reveals that those in the High Suicidality class are more likely to overdose compared with the Minimal Suicidality class ($p=0.04$). Results also show that those in the Moderate Suicidality class were more likely to have more drug use days compared with the Minimal Suicidality class.
Conclusions: Suicidality is an essential factor to consider when building strategies to screen, identify, and address individuals at risk for overdose. The integration of detailed suicide assessment and suicide risk reduction is a critical step to prevent poor outcomes among people with SUD.
Financial Support: This research is supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Numbers UG1DA013720, 2UG1DA049436, U54GM104942, UG1DA013035, 2UG1DA049436 01,75N95019D00013/N01DA-19-2250 (NIDA DSC contract to The Emmes Company, LLC), and 75N95020D00012/N01DA-20-2251 (NIDA CCC contract to The Emmes Company, LLC).

A COLLABORATIVE CARE INTERVENTION TO PREVENT DEATH FROM OPIOID OVERDOSE AND SUICIDE AMONG THOSE WITH CO-OCCURRING DISORDERS

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Drug Category Opiates/Opioids
Topic Health Services
Aim: Individuals with opioid use disorders (OUDs) and co-occurring disorders are at higher risk of attempting and dying from suicide or overdose than individuals with either disorder alone. Collaborative care, an evidence-based service delivery intervention, does not systematically address these risks. This study extends a larger trial, CLARO (Collaboration Leading to Addiction Treatment and Recovery from Other Stresses) and tests the incremental effectiveness of an additional collaborative care module to prevent suicide and overdose. We describe the development of the CLARO+ module.
Methods: We conducted a literature review to identify potential clinical interventions to reduce suicide and overdose and used the Framework for Reporting Adaptations and Modifications-Enhanced (FRAME) to document our decision-making process. Qualitative interviews were conducted with patients (n=4) to evaluate the proposed additions identified by literature review; patient feedback was used to develop the CLARO+ module. The module was beta-tested with eight patient and support person (SP; family, partner, friend) dyads (n=16). Post-session interviews were conducted, and transcripts were analyzed using rapid content analysis.
Results: We documented our development of the CLARO+ module, which included three evidence-based interventions (1) lethal means safety counseling, (2) overdose prevention, recognition, and response training, and (3) Caring Contacts, an evidence-based suicide prevention in which care coordinators mail caring messages to patients. We also added risk assessments, developed a joint patient-SP session to reinforce patient goals and provide OUD/naloxone education to SPs, and developed training to support care

coordinators. Patients felt topics were important and welcomed the joint session. Patient and SP participants spoke to the lack of resources for family members, found the joint session valuable, and offered recommendations that were integrated into the intervention.
Conclusions: The CLARO+ module aims to increase access to evidence-based strategies for overdose recognition and response training and suicide prevention in primary care settings.
Financial Support: This research was supported by a grant to Drs. Watkins and Komaromy (Multiple PIs) from the National Institute of Mental Health/NIMH (U01MH121954).

PREDICTION OF LIFETIME HEROIN OVERDOSE: INJECTION USE, QUIT ATTEMPTS, SUICIDAL IDEATION, AND HEPATITIS

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Drug Category Opiates/Opioids
Topic Behavior
Aim: Opioid use and its adverse sequelae remain at epidemic levels. Emerging data suggest overlap between opioid overdose and suicidality; however, this relationship is undoubtedly multifactorial and our present understanding is limited. This study examines predictors of lifetime heroin overdose including lifetime suicidal ideation and attempts, substance-use, demographic, and health characteristics.
Methods: This analysis includes 427 regular heroin users who were screened for several opioid pharmacology studies. Participants self-reported demographics including area deprivation index, lifetime and current heroin and other substance-use history (e.g. duration, injection use, frequency and amount, consequences of use including overdose, quit-attempts and seeking treatment), and medical conditions. Following nonparametric bivariate correlation analysis, binary logistic multiple regression was used to predict lifetime heroin overdose.
Results: Logistic regression analysis (group N [percent of sample], standardized beta, Wald F and p values) found that lifetime indices of opioid injection vs. non-injection use (Ns=292 [68.4%] vs. 135; beta=0.13, F=29.23, p<.001), more log10 heroin-quit attempts (beta=2.09, F=8.07, p=.004), suicidal ideation (Ns=77 [18%] positive vs. 350 negative; beta=0.44, F=7.98, p=.005), and hepatitis (Ns=54 [12.6%] positive vs. 373 negative; beta=0.43, F=7.02, p=.008, which correlated with injection use, □2=20.01, p<.001) predicted higher likelihood of heroin overdose (Ns=127 [29.7%] positive vs. 300 negative; Nagelkerke r2=.264, predictive accuracy=73.5%). Other factors examined including sex (301 male, 126 female), race (251 black, 175 white), age, area deprivation index, duration of heroin use, ever seeking heroin treatment (n=308), lifetime suicide attempts (n=27), and other medical problems (e.g. pain, head injury, cardiovascular, respiratory) were unrelated to heroin overdose in the multivariate model.
Conclusions: Lifetime heroin overdose is predicted by injection (more harmful) use, hepatitis infection (likely secondary to injection use), more heroin quit-attempts (problems sustaining abstinence), and suicidal ideation (but not attempts). Understanding the interplay and chronology of these effects is important for developing prevention and treatment programs.
Financial Support: NIH R21 DA015462 (MKG), Gertrude Levin Endowed Chair in Addiction and Pain Biology (MKG), F30 DA052118 (TEHM), Michigan Department of Health and Human Services (Lycaki/Young Funds), and Detroit Wayne Integrated Health Network

SEX DIFFERENCES IN EPIDEMIOLOGY RESEARCH ON NEWLY INCIDENT HEROIN USE AND SUICIDE ATTEMPTS

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Drug Category Opiates/Opioids
Topic Epidemiology
Aim: We are studying co-incident epidemiological trends of United States residents (a) who just started to use heroin among other internationally regulated drugs (IRD) and (b) who show suicide-related behaviors. In this project, focusing on individuals, we aim to estimate the degree to which newly incident users of internationally regulated drugs (IRD) subtypes might be more likely to attempt suicide. We estimate

variations by taking sex differences, studying time trends, and various IRD sub-types. In this abstract, we describe our general research approach and offer bi-annual and meta-analysis summary estimates for subgroups of newly incident heroin users versus expected values for the US population at large.
Methods: After identifying all new heroin initiates (n>800) within US National-Surveys-on-Drug-Use-and-Health, 2008-2019, we derived point estimates and appropriate variances for multi-stage area probability sampling with audio computer-assisted self-interviews (ACASI). The standardized ACASI items measured population parameters for heroin onsets and recent suicide attempts. Our presentation offers bi-annual estimates, meta-analysis summaries, and both Bayesian and frequentist credibility/compatibility intervals (CI).
Results: Among individuals observed within 0-12 months after first heroin use, the frequentist meta-analysis shows that an estimated 2% to 6% of these new initiates made a recent suicide attempt. For comparison, the expected value for the US population is <0.5% (95% CI = 0.0049, 0.006), with an 8-fold heroin-associated excess. Among women, the heroin-associated excess is tangibly larger.
Conclusions: Female-associated excess suicide attempt risk is well-established. Robust evidence also links one's history of long-standing heroin use with a history of making a suicide attempt and with suicide. Our novel evidence focuses on new heroin initiates and suggests that newly incident heroin use warrants attention as a signal of suicide risk. Individuals who self-identify both as female and as newly incident heroin users may deserve special attention in suicide prevention initiatives.
Financial Support: NIDA R25DA051240 (JCA).

ORAL COMMUNICATION: UNDERSTANDING SUD THROUGH NARRATIVE PERSPECTIVES

Plaza Ballroom A

CAREGIVING AND COPING: ALCOHOL USE DURING THE PANDEMIC IN NEW YORK CITY

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Drug Category Alcohol
Topic Racial/Ethnic Differences
Aim: Little is known about caregivers' alcohol consumption during the SARS-CoV-2 (COVID-19) pandemic. The current study examines frequency of alcohol use and associations with COVID-19 exposure among Black and Latine families living in the Bronx, New York.
Methods: A secondary analysis of data from 30 caregivers ($\bar{x}$ age = 40; 46.7% Latine, and 43.3% Black) who participated in a mixed-method study using self-report measures about past month weekly alcohol use and direct or family COVID-19 exposure (e.g., participants or family member(s) were sick with COVID-19), and PhotoVoice, a qualitative data collection method. Three alcohol consumption groups were created: low (0 drinks/month), moderate (1-2/month), and high use (3+/month). Chi-square tests were executed to examine past-month alcohol consumption by exposure to COVID-19. Qualitative data was analyzed using content analysis.
Results: Of those affected by COVID-19, 36.4% reported high alcohol use. Participants affected by COVID-19 reported more alcohol use than expected by chance (i.e., 36% compared to 5.6%). The relationship between COVID-19 exposure (yes/no) and drinking rates (low, moderate, high) was statistically significant ($X2$ (1, N=30) = 8.02), p = .02). Those affected by COVID-19 were more likely than those who were not affected by COVID-19 to report high use of alcohol. The probability of being affected by COVID-19 among the low alcohol use group was lower than expected by chance (9%). Qualitative themes included overall financial distress, loss of jobs and income.
Conclusions: Overall, findings suggest caregivers affected by COVID-19 may engage in high use of alcohol to cope with COVID-19 related stress. Although given financial stress and the overall low rates of alcohol use, participants may have had trouble purchasing alcohol. Clinical interventions should inquire about how caregivers coped with family members (or themselves) being infected by COVID-19 and any changes in their alcohol intake.

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"CATCHING CHARGES SAVED MY LIFE": EXPLORING COMMUNITY PERSPECTIVES ON THE ROLES PLAYED BY THE CRIMINAL LEGAL SYSTEM IN ADDRESSING OPIOID USE DISORDER

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Drug Category Opiates/Opioids
Topic Criminal Justice
Aim: The purpose of this study is to use Photovoice methodology to explore community perspectives on the intersection of the criminal legal system (CLS) and opioid use disorder (OUD) recovery, with a focus on the tensions between public safety and harm reduction.
Methods: As part of the HEALing Communities Study, Photovoice sessions were conducted with eight community groups and two recovery coach groups to understand community concerns related to the opioid epidemic. Photovoice is a participatory action research method that engages community members to photograph areas of strength and concern related to a health issue and then critically analyze in focus-group discussion the causes and solutions. A qualitative content analysis of transcribed sessions identified five groups (n=22 participants) that addressed CLS involvement. Inductive coding of the transcripts was conducted to determine themes surrounding participants' perspectives of the role of the CLS in opioid use treatment and recovery and how CLS involvement supports, coerces, and/or hinders an individual's recovery journey.
Results: One theme from sessions including participants with lived experience of OUD and CLS involvement was the lack of individualized recovery services. For example, participants who had been pregnant while incarcerated discussed experiencing greater stigmatization by CLS and healthcare professionals and the need for recovery services specific to pregnant people. By contrast, participants who are CLS professionals framed CLS involvement more optimistically as a "door to recovery" as they described improvements in CLS capacity to "meet people where they are."
Conclusions: Photovoice promotes in-depth reflection about the CLS involvement as a simultaneous and sometimes contradictory barrier and facilitator of OUD recovery. CLS professionals and people with lived experience perceive different rates of progress toward person-centered treatment, which should be considered in efforts to secure client and staff buy-in for implementing evidence-based interventions in CLS agencies.
Financial Support: This research was supported by the National Institutes of Health and the Substance Abuse and Mental Health Services Administration through the NIH HEAL (Helping to End Addiction Long-termSM) Initiative under award numbers UM1DA049406 (ClinicalTrials.gov Identifier: NCT04111939). This study protocol (Pro00038088) was approved by Advarra Inc., the HEALing Communities Study single Institutional Review Board. We wish to acknowledge the participation of the HEALing Communities Study communities, community coalitions, and Community Advisory Boards and state government officials who partnered with us on this study. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, the Substance Abuse and Mental Health Services Administration or the NIH HEAL InitiativeSM.

WHEN BEST PRACTICES FAIL: NUANCES OF USING NARRATIVES IN DISSEMINATING SUBSTANCE USE RESEARCH TO POLICYMAKERS

Elizabeth Long[*1], Jessica Pugel[1], Leanna Kalinowski[2], Patrick O'Neill[3], Glenn Sterner[1], Charleen Hsuan[1], Rachel Smith[1], Camille Cioffi[4], D. Max Crowley[1], J. Taylor Scott[1]*
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Drug Category Polydrug (i.e. concurrent use two or more drugs)
Topic Policy

Aim: Research can help inform policies that prevent, treat, and reduce harm associated with substance use (SU) and substance use disorders (SUDs). The present study tested narratives to optimize the reach of SU/SUD research to policymakers. We hypothesized that policymakers would engage more with research sent via emails with narratives than without narratives.
Methods: In five rapid-cycle randomized controlled trials, SU/SUD research fact sheets were emailed to state and federal policymakers (Ns = 5,964 – 11,212). We tested the use of narratives on the number of clicks on the fact sheets. In three trials, the narrative was about the sender's own lived experience with SUD. In two trials, the narrative was about someone else's lived experience.
Results: When the narrative was about someone else's experience, the fact sheet was clicked significantly less than the control email without a narrative, regardless of whether the narrative was told in third person (IRR=0.42; p<.001) or first person (IRR=0.32, p<.001), and whether the email body was short (IRR=0.48, p<.001) or long (IRR=0.48, p<.001). When the narrative was about the sender's own lived experience, the fact sheet was clicked significantly more than the control without a narrative (IRR=1.36, p=.041; IRR=1.74, p=.001). However, when the sender researched SU/SUDs and had lived experience with SU/SUDs, the fact sheet was clicked more when the narrative was about why they research SU/SUDs, relative to the control (IRR=1.39, p=.001), while the narrative about their lived experience with SU/SUDs did not differ from the control (IRR=1.10, p=.34).
Conclusions: The benefit of using narratives in emails disseminating SU/SUD research to policymakers is nuanced. Engagement increased when the narrative was about the sender, and when the sender's identity appeared to be congruent with the person's background. This work informs strategies for sharing SU/SUD research with policymakers, which is critical for achieving public health benefits.
Financial Support: William T. Grant Foundation, the Eunice Kennedy Shriver National Institute of Child Health and Human Development (grant P50HD089922), the National Science Foundation (grant 2030660), the Huck Institutes of the Life Sciences at Pennsylvania State University, and the Social Science Research Institute at Pennsylvania State University.

PHOTOVOICE AS A PRISMATIC LENS ON DEFINITIONS OF COMMUNITY AND THEIR IMPLICATIONS FOR STIGMA AND POWER RELATIONS IN ADDRESSING THE OPIOID EPIDEMIC

Margaret McGladrey[*1], Marisa Booty[2], Ramona Olvera[3], Peter Balvanz[4], Hilary Surratt[2], Carrie Oser[2]*
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Drug Category Opiates/Opioids
Topic Other
Aim: There are significant but often under-explored implications of how we use the term "community" in addiction research, especially considering the power differences among community roles that are central in addressing stigmatized health conditions. Typically, people occupying the community roles of citizens/residents, practitioners/service providers, and service users/consumers are considered interchangeably in defining what constitutes the community to be engaged in efforts to address drug misuse. Discussions of what community means to public health are at the heart of Photovoice, a participatory action research method in which participants photograph and critically analyze areas of health strength and concern that has been demonstrated to reduce stigma when focused on substance use. Photovoice involves focus-group discussion about how and why the health issue illustrated in participant photography persists to identify health improvement opportunities. The National Institutes of Health and the Substance Abuse and Mental Health Services Administration sponsored the HEALing Communities Study (HCS) to test the impact of implementing evidence-based practices across healthcare, behavioral health, and justice sectors, paired with community engagement and anti-stigma communication campaigns, on reducing opioid overdose deaths. The Kentucky, Massachusetts, and Ohio sites developed and executed a supplemental Photovoice protocol during HCS Wave 1 allowing for comparison across sectors and roles in relationship to the opioid epidemic.
Conclusions: This presentation will explore how Photovoice implementation by the HCS sites balanced participant involvement with methodological rigor while accounting for differences in power/stigma, commitments, interests, motivations, expectations, and communication needs associated with their distinct community roles – people actively receiving services and people with lived experience of addiction, professionals providing services and treatment, policymakers and advocates, and researchers. Academic and

non-academic participants will reflect on how our positions affected group dynamics, work styles, roles and responsibilities, and impact of the project on participants and exhibit audiences in catalyzing action to address the opioid epidemic.
Financial Support: This research was supported by the National Institutes of Health and the Substance Abuse and Mental Health Services Administration through the NIH HEAL (Helping to End Addiction Long-term) Initiative under award numbers UM1DA049406 (ClinicalTrials.gov Identifier: NCT04111939). This study protocol (Pro00038088) was approved by Advarra Inc., the HEALing Communities Study single Institutional Review Board. We wish to acknowledge the participation of the HEALing Communities Study communities, community coalitions, and Community Advisory Boards and state government officials who partnered with us on this study. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health, the Substance Abuse and Mental Health Services Administration or the NIH HEAL Initiative.

ORAL COMMUNICATION: DELTA-8-THC: MILE HIGH?
Governor's Square 15

REWARDING EFFECTS OF DELTA 8-TETRAHYDROCANNABINOL, CANNABIDIOL, AND A MIXTURE FOLLOWING OF VAPOR EXPOSURE IN MALE RATS

Dustin Stairs[*1], Julia King[1], Darby Durbin[1], Hayden Fitzgerald[1], Emily Cronin[1], Lauren Beringer[1], Harrison Witmer[1], Kianna Nguyen[1], BethAnne Drobny[1], Claire Shinners[1], Keegan Kalkman[1], Abbie Mollison[1], Giorgio Bacchin[1]*
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Drug Category Cannabis/Cannabinoids
Topic Behavioral Pharmacology
Aim: Delta-8-Tetrahydrocannabinol (Delta-8) has the largest growth in sales in the 2021 cannabinoid market, although overall sales still trail cannabidiol (CBD). The current study was designed to determine if exposure to vaporized Delta-8, CBD and a mixture of the two drugs result in rewarding effects using the conditioned place preference (CPP) procedure.
Methods: Forty-eight male Sprague Dawley (PND 56; N=12/drug group) rats were exposed for 10 min to vaporized concentrations of either Delta-8 distillate (10 mg/300 µl), CBD isolate (30 mg/300 µl) and a mixture of CBD/Delta-8 (30mg/10mg per 300 µl) or the vehicle propylene glycol (PG). Using a biased three-chamber CPP design, animals first had a 15 min pretest with access to all three chambers to determine their initial side preference. On the next day, the animals started daily conditioning trials where they received a vaporized exposure of either active cannabinoid drug or PG. Following the 10 min exposure, animals were immediately confined to one of the pairing chambers of the CPP apparatus for a 30 min conditioning trial. Conditioning trials were repeated across 16 daily conditioning trials. After the 8th and 16th conditioning session non-vapor exposed rats were tested for CPP response during a 15 min test session.
Results: Results indicated that relative to a PG only group neither the active concentration of Delta-8, CBD or the mixture of the two drugs results in a significant CPP response after the first 8 conditioning trials. Although, after the 16th conditioning trial, both Delta-8 and the mixture of CBD/Delta-8 resulted in a significant CPP response compared to PG, while CBD alone did not result in a CPP response and a trend towards aversion.
Conclusions: The current results indicate vaporized exposure to Delta-8 THC and Delta-8 THC combined with CBD can result in rewarding effect while CBD alone does not.
Financial Support: Creighton Faculty Fellowship fund

DOSE EFFECTS OF ORAL AND VAPORIZED DELTA-8-THC AND COMPARISON TO DELTA-9-THC IN HEALTHY ADULTS

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Drug Category Cannabis/Cannabinoids
Topic Behavioral Pharmacology
Aim: Characterize the acute effects of oral and inhaled Delta-8-THC, compared with a positive control dose of D-9-THC and placebo, on subjective drug effects, cardiovascular effects, cognitive performance, and pharmacokinetics.
Methods: Healthy adults were recruited to participate in 2 studies, one that evaluated the acute effects of oral delta-8-THC (0 mg, 10 mg, 20 mg and 40 mg) and oral delta-9-THC (20 mg) and the other that evaluated the same doses via vaporization. Both studies used a within-subject crossover design, dose order was randomized, and a minimum of 6 days separated each test session. Vital signs, blood, urine and oral fluid samples, self-reported drug effects and performance on a battery of cognitive tasks were obtained from participants at baseline and for 8 hours after dosing.
Results: To date, 7 participants have completed the oral dosing study and 6 have completed the vaporization study. In the oral dosing study, pharmacodynamic assessments show a dose orderly effect of delta-8-THC on all assessments. The 20 mg delta-9-THC dose showed a qualitatively stronger drug effect than all 3 doses of delta-8-THC on most measures. In the vaporized dose study, pharmacodynamic outcomes were mostly similar across the 3 doses of delta-8-THC. Puff topography data showed that puff volume was lower for the 20 mg and 40 mg doses compared with the 10 mg dose and placebo, suggesting participants were titrating inhalation behavior. Delta-9-THC produced qualitatively higher effects on most outcomes than all doses of delta-8-THC. Pharmacokinetic testing of biological samples is pending.
Conclusions: Acute doses of oral and vaporized delta-8-THC produced pharmacodynamic drug effects that overlap almost completely with the acute drug effects of delta-9-THC. However, delta-8-THC produces significantly lower magnitude of effects compared with delta-9-THC at the same dose, which is consistent with prior research on binding affinity between the 2 isomers.
Financial Support: This study was funded by the Substance Abuse and Mental Health Services Administration.

PREVALENCE AND CHARACTERISTICS OF DELTA-8 THC USE IN U.S. ADULTS

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Drug Category Cannabis/Cannabinoids
Topic Epidemiology
Aim: We aimed to: (1) estimate the prevalence and patterns of delta-8 THC use and (2) assess reasons for delta-8 THC use among adults in the United States.
Methods: A cross-sectional internet-based survey was used to explore self-reported marijuana usage patterns, including frequency, method, and reason for use. Information was collected from 1,100 adults aged 18-59 participating in the Qualtrics® research survey panel service. Independent analysis was performed on the group of self-reported recent cannabis users and the overall sample population.
Results: The prevalence of recent (past 12 month) delta-8 THC use within the study sample was 11.7% (n=118). The primary purpose for delta-8 THC use among recent users included medical, non-medical, and combination medical/non-medical reasons, with anxiety, pain, depression, and sleep disorder relief reported as the main targeted medical reasons for delta-8 THC use.
Conclusions: There is discordance between the prevalence of delta-8 THC use within this study and reports from other studies stemming from the scarcity of research and unclear legislation involving delta-8 THC. The reasons reported for delta-8 THC use are consistent with the reported reasons for cannabis and CBD uses. This study underlines the need for further research surrounding delta-8 THC usage patterns and prevalence.
Financial Support: National Institute on Drug Abuse (K01DA047912; Okafor)

IDENTIFICATION AND CHARACTERIZATION OF UNREGULATED MARKETING AND SALE OF CANNABIS PRODUCTS ON THE MESSAGING SERVICE PLATFORM TELEGRAM

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Drug Category Cannabis/Cannabinoids
Topic Policy
Aim: Unregulated and potentially illegal sales of cannabis-related products have been reported and detected on various web-based platforms, including social media, e-commerce sites, online retailers, and even the dark web. New and interactive instant messaging services that offer end-to-end encryption are also becoming popular among online users and present opportunities for marketing, trading, and selling of various forms of cannabis products with little oversight. This study sought to identify and characterize selling activity on the popular messaging platform Telegram.
Methods: This study was conducted in three phases: (1) identifying keywords related to cannabis products for purposes of detecting Telegram groups and channels; (2) automated data collection from public Telegram channels to identify and characterize selling activity; and (3) manual annotation and classification of posts marketing and selling product to consumers.
Results: We identified four keywords ("Cannabis", "Vape", Nicotine", and "Smoke") that yielded twenty-one Telegram groups. Active subscribers from the groups totaled 262,506. Total volume of posts was 70,884 comprised of 43,959 unique posts that included 3,564 (5.0%) cannabis product marketing/selling posts that were confirmed through manual annotation. Detection of various forms of cannabis products included cartridges, concentrates, edibles, and vapes. Marketing tactics included posting pictures of available product, providing contact information, minimum order size, product reviews, and varying options to pay for product (e.g., cryptocurrencies, etc.). A mix of seller accounts were observed, though most appeared to be individual suppliers. No known age verification process or shipping restrictions to prohibited areas was observed on these channels.
Conclusions: Telegram is a global online messaging application that allows for custom channel creation and global connectivity. Based on our study results, it is also a platform that enables a robust cannabis selling marketplace. As states debate cannabis regulation, easy accessibility and unregulated Internet channels of access must be further studied to assess their public health impact and their enablement of a digital cannabis black market.
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ORAL COMMUNICATION: DECISION-MAKING IN SUDS
Plaza Ballroom D

EFFECTS OF BUSPIRONE PRETREATMENT ON OXYCODONE VS. MILK "CHOICE" SELF-ADMINISTRATION IN NON-HUMAN PRIMATES

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Aim: Clinical reports suggest that the most effective strategies for managing opioid use disorder (OUD) comprise a program of both pharmacological and non-pharmacological approaches. Intravenous drug self-administration procedures in which subjects have concurrent access to drug and non-drug reinforcers – e.g., drug vs. food "choice" procedures - have been utilized to evaluate the impact of alternative reinforcers on the abuse-related effects of drugs and are thought to be highly translational for human drug use. Buspirone, a partial agonist at 5HT1A receptor subtypes and dopamine D3/4 receptor antagonist, has previously been evaluated as a candidate medication for substance use disorder. However, few studies have examined its effects on self-administration of opioids. The present study evaluated the efficacy of acute buspirone on the reinforcing effects of oxycodone in nonhuman primates.

Methods: Three adult female squirrel monkeys with a history of opioid self-administration responded under concurrent second-order FR3(FR5:S);TO45s schedules of reinforcement for intravenous oxycodone (0.01mg/kg/inj) or saline on one lever and 20% sweetened condensed milk on the other during daily 1-hour sessions. When responding was stable, doses of buspirone (0.01-0.1mg/kg) were administered intramuscularly 10-min prior to self-administration sessions.
Results: Results show subjects responded exclusively on the milk lever when saline was available (~70 milk deliveries and 0 saline injections) and exclusively on the drug lever when 0.01 mg/kg oxycodone was available (~25 injections and 0 milk deliveries). Buspirone pretreatment produced a significant and dose-dependent reduction of oxycodone self-administration. Specifically, while 0.01mg/kg buspirone was ineffective, doses of 0.03 and 0.1mg/kg decreased oxycodone self-administration (10 and 0 oxycodone injections, respectively). This reduction in oxycodone self-administration coincided with an increase in responding for milk to baseline levels.
Conclusions: These data indicates that subjects reallocated their behavior from drug to non-drug reinforcers following buspirone and supports further research into buspirone as a potential treatment for OUD.
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AYAHUASCA SELF-ADMINISTRATION USING A TWO-BOTTLE CHOICE PROCEDURE IN MALE MICE

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Drug Category Psychedelics
Topic Behavioral Pharmacology
Aim: Ayahuasca, a hallucinogenic beverage used in traditional Amazonian communities for ritualistic purposes, has been proposed as a treatment for substance use disorders. However, because of its hallucinogenic properties, studies investigating its abuse potential are needed. The aim of the present study was to investigate ayahuasca self-administration in mice using a two-bottle choice procedure.
Methods: Male mice were exposed to two bottles, one of water and one of ayahuasca (0.01, 0.03 or 0.1 mg/ml), for 15 hours at a time (17h00–08h00), under three different protocols: (1) access every other day for 68 days (39 exposures); (2) access every 3 days for 93 days (39 exposures); (3) access every 5 days for 134 days (39 exposures). Animals were then submitted to a 14-day drug-free period, followed by 3 re-exposure sessions, with 7 drug-free days between each session. During re-exposure tests, animals were submitted to the same conditions as during acquisition.
Results: Our findings show that, regardless of ayahuasca concentration, all animals showed a preference for the ayahuasca bottle when exposed to ayahuasca self-administration every other day, both during the acquisition phase and during the re-exposure phase. Extending the days between ayahuasca self-administration sessions changed the acquisition and expression of ayahuasca self-administration, with the longest break (5 days between acquisition exposures) being associated with the development of a preference for the water bottle (i.e. aversion to ayahuasca) at all concentrations.
Conclusions: The frequency of exposure is critical when determining whether mice self-administer ayahuasca using a two-bottle choice procedure. Prolonging the interval between ayahuasca exposures can not only prevent animals from showing a preference for the ayahuasca bottle, but also may lead to aversion to ayahuasca. These findings can help guide therapeutic/ritualistic ayahuasca use.
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ASSESSMENT OF THE SUBJECTIVE VALUE OF SOCIAL CONTEXT IN INDIVIDUALS WHO USE CANNABIS

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Drug Category Cannabis/Cannabinoids

Topic Behavior
Aim: Environmental cues contribute to value calculations that underlie decision-making. This study used a concurrent monetary choice procedure to test the hypothesis that cannabis and social cues would influence decision-making for a non-drug reinforcer.
Methods: Individuals reporting current cannabis use (n=85) and controls (n=98) participated. A cued concurrent choice task presented trials with cannabis, social, cannabis+social, or neutral cues presented side by side followed by concurrent monetary options. Bias was defined as cue choice when monetary values were equal. Participants also completed a Social Anhedonia Scale (SAS) and purchase tasks evaluating demand for access to a party with and without a cannabis "open bar".
Results: An ANOVA revealed a Group x Cue interaction, $F(5,905)=77.2$, $p<0.001$. Compared to controls, participants in the cannabis group presented a bias towards cannabis-cued options compared to neutral-cued and social-cued options. Additionally, the cannabis group was biased towards cannabis+social-cued options compared to neutral-cued and social-cued, and social-cued compared to neutral-cued options, relative to controls. No preference was found between cannabis and cannabis+social-cued options in the cannabis group. Cannabis party demand was more intense $t(137)=3.525$, $p<0.001$ and less elastic $t(137)= -7.53$, $p<0.001$ in the cannabis group compared to controls and elasticity was negatively correlated with choice bias towards cues that included cannabis $r(75)= -0.33$, $p<0.01$. Neither drug-free party demand indices nor pleasure from social situations differed across groups. Social anhedonia was correlated only with choice bias for neutral compared to social cues $r(83)= 0.22$, $p<0.05$
Conclusions: Cannabis and social cues biased monetary choice as a function of cannabis use history and social anhedonia. Similar SAS scores and drug-free party demand across groups, along with bias towards social versus neutral cues and lack of bias between cannabis and cannabis+social cues in the cannabis group, suggest that cannabis use does not devalue social contexts.
Financial Support: T32DA07209, R01DA036550, and pilot funding from the University of Kentucky

ORAL COMMUNICATION: NOVEL TREATMENT TARGETS FOR FENTANYL AND BEYOND
Grand Ballroom II

POSITIVE SEROTONIN 5-HT2A/2C RECEPTOR ALLOSTERIC MODULATORS DERIVED FROM OLEAMIDE COMPOUNDS

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Drug Category Psychedelics
Topic Chemistry
Aim: The 5-HT2 receptor (5-HT2R) family provides intriguing targets of interest for cocaine use disorder (CUD) neurotherapeutics. However, the 5-HT2AR, 5-HT2BR, and 5-HT2CR share homology at the orthosteric ligand binding site for 5-HT and achieving selectivity amongst this family is critically important. We are pioneering efforts to develop positive modulators targeting the conserved extracellular allosteric domain of these receptors. The fatty acid amide oleamide promotes 5-HT receptor signaling promiscuously and, we employed a fragment-based discovery approach to discover novel oleamide analogues as positive allosteric modulators (PAMs).
Methods: Novel oleamide-based molecules were designed, synthesized and screened for efficacy to enhance 5-HT-induced intracellular calcium release in stable cell lines expressing the human (h) 5-HT2AR, h5-HT2BR or h5-HT2CR. Selected compounds were evaluated in in vitro and in vivo drug metabolism and pharmacokinetics followed by behavioral assays directed toward optimizing compound profiles.
Results: We identified selective 5-HT2CR PAMs and dual 5-HT2CR/5-HT2AR PAMs, with subtype selectivity vs. the 5-HT2BR. Compound 13 exhibited the profile of a 5-HT2CR/5-HT2AR PAM with negligible displacement of the orthosteric binding sites of roughly 50 GPCRs and transporters, including 5-HT2AR and 5-HT2CR. Compound 13 exhibited an appropriate CNS MPO value, acceptable in vitro and in vivo PK profile, decent brain penetrability and behavioral efficacy in a spontaneous locomotor activity assay. Thus, 13 maintains favorable drug-like properties as an in vivo probe of allosteric modulation of the 5-HT2CR/5-HT2AR.

Conclusions: Our phased success in the chemical modification of oleamide enriches the 5-HT2R allosteric modulatory library with a novel series of structurally diversified scaffolds. Compound 13 is a first-in-class dual 5-HT2CR/5-HT2AR PAM selected from an extended medicinal chemistry endeavor. Our future objectives are to optimize these 5-HT2CR/5-HT2AR PAMs with favorable drug-like properties and analyze select molecules in proof-of-concept in vivo assays as new pharmacological tools to leverage toward understanding CUD biology and developing effective CUD therapeutics.
Financial Support: R01DA038446, Center for Addiction Research

ALPHA 1 AND 2 NORADRENERGIC RECEPTORS AS TARGETS FOR REVERSING FENTANYL-INDUCED RESPIRATORY DEPRESSION

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Aim: The U.S. Department of Homeland Security (DHS) considers high potency opioids such as fentanyl to be a chemical threat because they can be easily synthesized and delivered as an aerosol to cause a mass casualty event. Unlike morphine, fentanyl causes vocal cord closure and rigidity of the chest wall muscles, an effect known as "wooden chest syndrome", and this effect may not be fully reversed by pure mu opioid antagonists such as naloxone or naltrexone. This study assessed the ability of α1 and α2 noradrenergic drugs to decrease fentanyl-induced locomotor and respiratory depression in rats.
Methods: Male and female Sprague-Dawley rats (n=27) were given saline or fentanyl (200 µg/kg; s.c.) 15 min prior to a second injection of one of the following: (1) vehicle, (2) naltrexone (0.003-0.1 mg/kg; s.c.), (3) α1-noradrenergic agonist phenylephrine (0.1– 10 mg/kg; s.c.), (4) α1-noradrenergic antagonist prazosin (0.1-3 mg/kg; s.c.), (5) α2-noradrenergic agonist clonidine (0.01-0.3 mg/kg; i.p.) or (6) α2-noradrenergic antagonist yohimbine (0.3-10 mg/kg; i.p.). Rats were immediately placed into a locomotor chamber. After 15 minutes, rats were placed into a plethysmography chamber to record ventilatory effort for 30 minutes.
Results: Naltrexone reversed completely the locomotor and respiratory depressant effects of fentanyl compared to saline controls ($F(7, 61) = 5.310$, $p < 0.0001$); $F(7, 61) = 3.209$, $p = 0.0058$). Yohimbine produced a partial (~54%) reversal of the respiratory depressant effect of fentanyl compared to saline control ($F(6, 21) = 2.675$, $p = 0.0435$), but had no effect on fentanyl-induced locomotor depression. No significant reversal effects were obtained with phenylephrine, prazosin or clonidine at the doses tested.
Conclusions: This study suggests that α2-noradrenergic receptors are involved in the respiratory depressant effect of fentanyl and that yohimbine may serve as an effective adjunctive countermeasure agent combined with naltrexone or naloxone to reverse fentanyl-induced respiratory depression.
Financial Support: Supported by: U01 DA051377

THE NOCICEPTIN RECEPTOR ANTAGONIST LY2940094 SUPPRESSES OPIOID SELF-ADMINISTRATION IN MALE RATS

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Aim: The "non-classical" nociceptin receptor (NOPr) binds the endogenous neuropeptide nociceptin, a receptor system well-represented in reward-processing circuits. LY2940094 ('094) exhibits 1,000-fold higher selectivity for NOPr vs. classical opioid receptors and is a selective NOPr antagonist with high receptor occupancy and target engagement in rodents. Initial clinical trials indicated that '094 is safe and well-tolerated in clinical populations and suggest that this NOPr antagonist has the potential to positively alter behavior in those suffering from opioid use disorder. The present studies assess the efficacy of '094 in preclinical models of opioid self-administration, relapse-like behaviors and abuse liability in rodents.
Methods: Male, Sprague-Dawley rats (n=6-18/group) were trained to acquire stable fentanyl (3.2 µg/kg/inf, i.v.) self-administration prior to pretreatment with acute or repeated doses of '094 (0-30 mg/kg, i.p.; 15 min).

Fentanyl intake and responding for fentanyl-associated cues during abstinence were assessed as was the abuse liability of '094 in the fentanyl self-administration assay. The fentanyl vs. saline drug discrimination paradigm was employed to inform mechanisms and assess abuse liability in the context of patterns of self-administration. The impact of '094 on quantifiable physiological responses +/- fentanyl was determined.
Results: '094 dose-dependently suppressed fentanyl intake and fentanyl-seeking with the greatest efficacy evident at 30 mg/kg ($p<0.05$). Repeated treatment with 30 mg/kg of '094 for either two- or three-days during abstinence reduced reinstatement of intake by over 50% ($p<0.05$). '094 did not alter inactive lever presses or latency to respond. '094 did not substitute for fentanyl, but dose-dependently suppressed the stimulus properties of fentanyl in drug discrimination assays. '094 did not alter physiological measures associated with fentanyl-evoked respiratory depression.
Conclusions: Our preclinical data position the NOPr antagonist '094 as a potential therapeutic strategy to mitigate opioid intake and relapse vulnerability without inherent abuse liability and with a limited side effect profile.
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IDENTIFICATION OF A FENTANYL-TARGETING MONOCLONAL ANTIBODY CSX-1004 THAT BLOCKS FENTANYL'S EFFECTS IN SQUIRREL MONKEYS

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Drug Category Opiates/Opioids
Topic Behavioral Pharmacology
Aim: Fentanyl is a synthetic opioid that is routinely abused for its pleasurable psychoactive effects, which can lead to opioid use disorder (OUD) and subsequent overdose. While μ-opioid receptor antagonist-based treatments for fentanyl overdose exist, they can be ineffective and are short-acting. Antibody-based therapeutics have emerged as a new approach to prevent fentanyl overdose. Here, we examined the ability of a novel fentanyl-targeting monoclonal antibody, CSX-1004, to block fentanyl's effects.
Methods: Eight squirrel monkeys were treated with either 10 or 40 mg/kg CSX-1004 via IV infusion and received fentanyl challenge up to 28 days post-infusion to determine the time course and the magnitude of fentanyl antagonism. Respiratory depression was examined using a ventilation chamber in which subjects were exposed to air and an air + 5% CO2 mixture.
Results: Results show that CSX-1004 blocked fentanyl's respiratory depressant effects in a dose- and time-dependent manner. Fentanyl challenge on Day 0 after CSX-1004 resulted in no fentanyl-associated reductions in minute volume, and these effects continued through Day 28, with diminished efficacy starting at Day 14. Subjects that received 10 mg/kg CSX-1004 also showed protection from fentanyl's effects, but efficacy began to diminish at day 7. Both 40 and 10 mg/kg CSX-1004 produced, respectively, a ~14- and ~5-fold rightward shift in the fentanyl dose-response function but did not block the effects of other mu-opioid agonists. CSX-1004's ability to block fentanyl's antinociceptive (warm water tail withdrawal) and behaviorally disruptive (schedule-controlled responding) effects were also determined. Results from these studies show that administration of 40 mg/kg IV CSX-1004 produced a ≥10-fold rightward shift in the dose-response function of fentanyl's antinociceptive and behaviorally disruptive effects, but not other opioids like oxycodone.
Conclusions: Collectively, these studies suggest that CSX-1004 could be a promising treatment in preventing fentanyl overdose while not disrupting the efficacy of prescription opioids used for pain management.
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