



DIRECTOR'S REPORT

to the

National Advisory Council on Drug Abuse

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Nora D. Volkow, M.D.
Director
National Institute on Drug Abuse

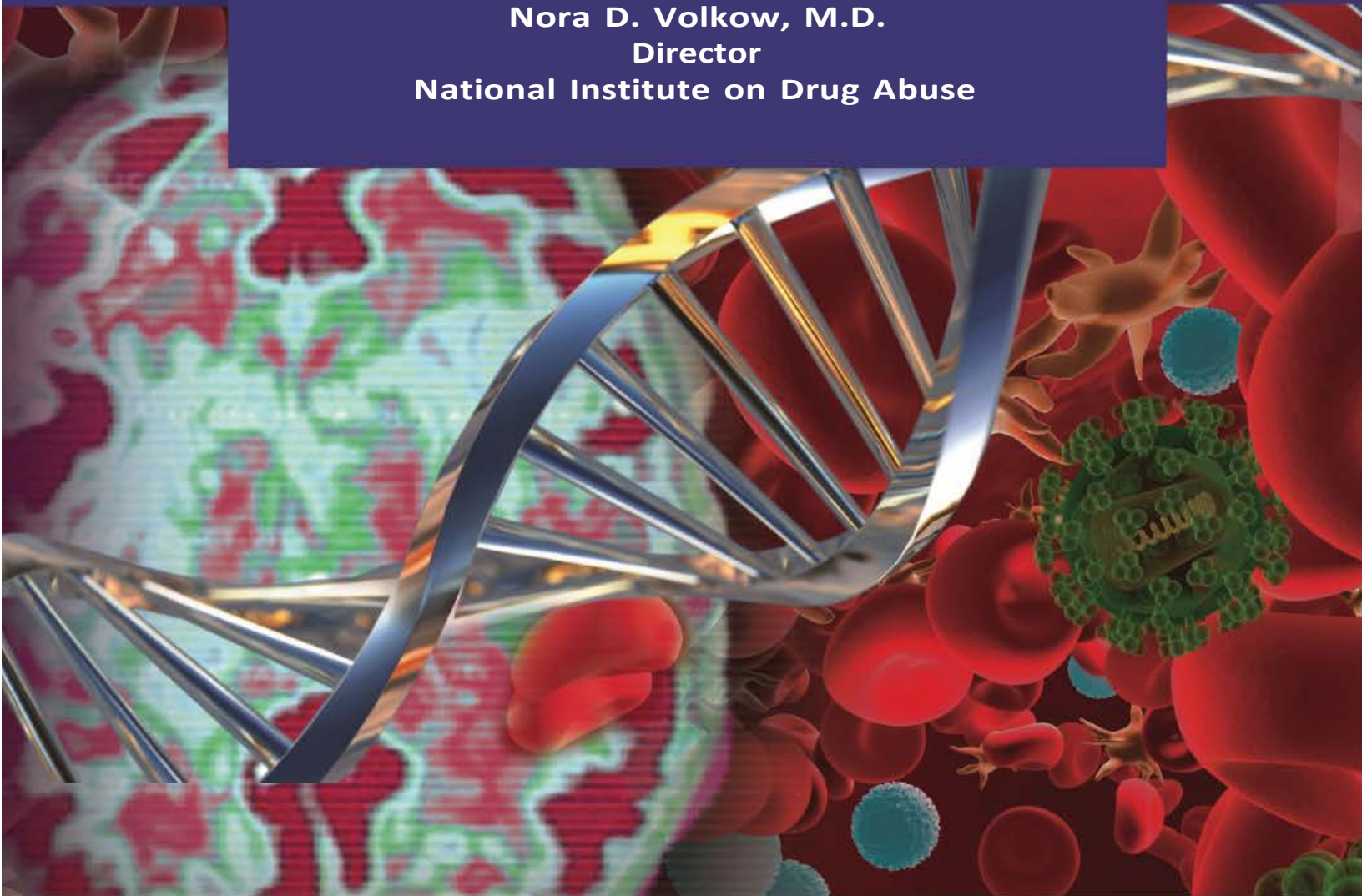


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RESEARCH HIGHLIGHTS

BASIC AND BEHAVIORAL RESEARCH

Modulation Of 5-HT Release By Dynorphin Mediates Social Deficits During Opioid

Withdrawal Pomrenze MB, Pinto DFC, Neumann PA, Llorach P, Tucciarone JM, Morishita W, Eshel N, Heifets BD, Malenka RC. *Neuron*. 2022; 110(24): 1-19.

Social isolation during opioid withdrawal is a major contributor to the current opioid addiction crisis. We find that sociability deficits during protracted opioid withdrawal in mice require activation of kappa opioid receptors (KORs) in the nucleus accumbens (NAc) medial shell. Blockade of release from dynorphin (Pdyn)-expressing dorsal raphe neurons (DR^{Pdyn}), but not from NAc^{Pdyn} neurons, prevents these deficits in prosocial behaviors. Conversely, optogenetic activation of DR^{Pdyn} neurons reproduced NAc KOR-dependent decreases in sociability. Deletion of KORs from serotonin (5-HT) neurons, but not from NAc neurons or dopamine (DA) neurons, prevented sociability deficits during withdrawal. Finally, measurements with the genetically encoded GRAB_{5-HT} sensor revealed that during withdrawal KORs block the NAc 5-HT release that normally occurs during social interactions. These results define a neuromodulatory mechanism that is engaged during protracted opioid withdrawal to induce maladaptive deficits in prosocial behaviors, which in humans contribute to relapse.

Structure-Based Design Of Bitopic Ligands For The M-Opioid Receptor Faouzi A, Wang H, Zaidi SA, DeBerto JF, Che T, Qu Q, Robertson MJ, Madasu MK, Daibani AE, Varga BR, Zhang T, Ruiz C, Liu S, Xu J, Appourchaux K, Slocum ST, Eans SO, Cameron MD, Al-hasani R, Pan YX, Roth BL, McLaughlin JP, Skiniotis G, Katritch V, Kobilka BK, Majumdar S. *Nature*. 2022; 613(7945): 767-774.

Mu opioid receptor (μ OR) agonists like fentanyl have long been used for pain management, but are considered a major public health concern due to their adverse side effects, including lethal overdose. To design safer therapeutics, we report a conceptually novel approach targeting conserved sodium (Na^+) binding site, observed in μ OR and many other class A GPCRs, by bitopic fentanyl derivatives functionalized via a linker with a positively charged guanidino group. Cryo-EM structures of the most potent bitopic ligands in complex with μ OR highlight the key interactions between the ligand's guanidine and the key Asp residue in the Na^+ site. While the lead bitopics maintain nanomolar potency and high efficacy at G_i subtypes, they show strongly reduced arrestin recruitment, one also shows the lowest G_z -efficacy among the panel of μ OR agonists, including partial and biased, morphinan and fentanyl analogs. In mice, the best bitopic ligand displayed μ OR dependent antinociception with attenuated adverse effects supporting the μ OR Na^+ site as a potential target for the design of safer analgesics. In general, our study suggests that bitopic ligands engaging the Na^+ pocket in class A GPCRs can be designed to control their efficacy and functional selectivity profiles for $G_{i/o/z}$ subtypes and arrestins, thus modulating their in vivo pharmacology.

Behavioral And Dopaminergic Signatures Of Resilience Willmore L, Cameron C, Yang J, Witten IB and Falkner AL. *Nature*. 2022; 611(7934): 124-132.

Chronic stress can have lasting adverse consequences in some individuals, yet others are resilient to the same stressor. Susceptible and resilient individuals exhibit differences in the intrinsic properties of mesolimbic dopamine (DA) neurons after the stressful experience is over. However, the causal

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links between DA, behaviour during stress and individual differences in resilience are unknown. Here we recorded behaviour in mice simultaneously with DA neuron activity in projections to the nucleus accumbens (NAc) (which signals reward) and the tail striatum (TS) (which signals threat) during social defeat. Supervised and unsupervised behavioural quantification revealed that during stress, resilient and susceptible mice use different behavioural strategies and have distinct activity patterns in DA terminals in the NAc (but not the TS). Neurally, resilient mice have greater activity near the aggressor, including at the onset of fighting back. Conversely, susceptible mice have greater activity at the offset of attacks and onset of fleeing. We also performed optogenetic stimulation of NAc-projecting DA neurons in open loop (randomly timed) during defeat or timed to specific behaviours using real-time behavioural classification. Both open-loop and fighting-back-timed activation promoted resilience and reorganized behaviour during defeat towards resilience-associated patterns. Together, these data provide a link between DA neural activity, resilience and resilience-associated behaviour during the experience of stress.

[A Neuromarker For Drug And Food Craving Distinguishes Drug Users From Non-Users](#)

Koban L, Wager TD, Kober H. Nat Neurosci. 19 Dec 2022; Online ahead of print

Craving is a core feature of substance use disorders. It is a strong predictor of substance use and relapse and is linked to overeating, gambling, and other maladaptive behaviors. Craving is measured via self-report, which is limited by introspective access and sociocultural contexts. Neurobiological markers of craving are both needed and lacking, and it remains unclear whether craving for drugs and food involve similar mechanisms. Across three functional magnetic resonance imaging studies ($n = 99$), we used machine learning to identify a cross-validated neuromarker that predicts self-reported intensity of cue-induced drug and food craving ($P < 0.0002$). This pattern, which we term the Neurobiological Craving Signature (NCS), includes ventromedial prefrontal and cingulate cortices, ventral striatum, temporal/parietal association areas, mediodorsal thalamus and cerebellum. Importantly, NCS responses to drug versus food cues discriminate drug users versus non-users with 82% accuracy. The NCS is also modulated by a self-regulation strategy. Transfer between separate neuromarkers for drug and food craving suggests shared neurobiological mechanisms. Future studies can assess the discriminant and convergent validity of the NCS and test whether it responds to clinical interventions and predicts long-term clinical outcomes.

[Ptchd1 Mediates Opioid Tolerance Via Cholesterol-Dependent Effects On \$\mu\$ -Opioid Receptor Trafficking](#) Maza N, Wang D, Kowalski C, Stoveken HM, Dao M, Sial OK, Giles AC, Grill B, Martemyanov KA. Nat Neurosci. 2022; 25(9): 1179-1190.

Repeated exposure to opioids causes tolerance, which limits their analgesic utility and contributes to overdose and abuse liability. However, the molecular mechanisms underpinning tolerance are not well understood. Here, we used a forward genetic screen in *Caenorhabditis elegans* for unbiased identification of genes regulating opioid tolerance which revealed a role for PTR-25/Ptchd1. We found that PTR-25/Ptchd1 controls μ -opioid receptor trafficking and that these effects were mediated by the ability of PTR-25/Ptchd1 to control membrane cholesterol content.

Electrophysiological studies showed that loss of Ptchd1 in mice reduced opioid-induced desensitization of neurons in several brain regions and the peripheral nervous system. Mice and *C. elegans* lacking Ptchd1/PTR-25 display similarly augmented responses to opioids. Ptchd1 knockout mice fail to develop analgesic tolerance and have greatly diminished somatic withdrawal. Thus, we propose that Ptchd1 plays an evolutionarily conserved role in protecting the μ -opioid receptor against overstimulation.

EPIDEMIOLOGY, PREVENTION, AND SERVICES RESEARCH

Non-Prescribed Buprenorphine Preceding Treatment Intake And Clinical Outcomes For Opioid Use Disorder

Williams AR, Mauro CM, Feng T, Wilson A, Cruz A, Olfson M, Crystal S, Samples H, Chiodo L. *J Subst Abuse Treat.* 2022; 139: 108770.

Objective: Successful retention on buprenorphine improves outcomes for opioid use disorder (OUD); however, we know little about associations between use of non-prescribed buprenorphine (NPB) preceding treatment intake and clinical outcomes. Methods: The study conducted observational retrospective analysis of abstracted electronic health record (EHR) data from a multi-state nationwide office-based opioid treatment program. The study observed a random sample of 1000 newly admitted patients with OUD for buprenorphine maintenance (2015-2018) for up to 12 months following intake. We measured use of NPB by mandatory intake drug testing and manual EHR coding. Outcomes included hazards of treatment discontinuation and rates of opioid use. Results: Compared to patients testing negative for buprenorphine at intake, those testing positive (59.6%) had lower hazards of treatment discontinuation (HR = 0.52, 95% CI: 0.44, 0.60, $p < 0.01$). Results were little changed following adjustment for baseline opioid use and other patient characteristics (aHR: 0.60, 95% CI: 0.51, 0.70, $p < 0.01$). Risk of discontinuation did not significantly differ between patients by buprenorphine source: prescribed v. NPB (reference) at admission (HR = 1.15, 95% CI: 0.90, 1.46). Opioid use was lower in the buprenorphine positive group at admission (25.0% vs. 53.1%, $p < 0.0001$) and throughout early months of treatment but converged after 7 months for those remaining in care (17.1% vs. 16.5%, $p = 0.89$). Conclusion: NPB preceding treatment intake was associated with decreased hazards of treatment discontinuation and lower opioid use. These findings suggest use of NPB may be a marker of treatment readiness and that buprenorphine testing at intake may have predictive value for clinical assessments regarding risk of early treatment discontinuation.

Effect Of Police Action On Low-Barrier Substance Use Disorder Service Utilization

Weisenthal K, Kimmel SD, Kehoe J, Laroche MR, Walley AY, Taylor JL. *Harm Reduct J.* 2022; 19(1): 86.

Background: Police action can increase risky substance use patterns by people who use drugs (PWUD), but it is not known how increased police presence affects utilization of low-barrier substance use disorder bridge clinics. Increased police presence may increase or decrease treatment-seeking behavior. We examined the association between Operation Clean Sweep (OCS), a 2-week police action in Boston, MA, and visit volume in BMC's low-barrier buprenorphine bridge clinic. Methods: In this retrospective cohort, we used segmented regression to investigate whether the increased police presence during OCS was associated with changes in bridge clinic visits. We used General Internal Medicine (GIM) clinic visit volume as a negative control. We examined visits during the 6 weeks prior, 2 weeks during, and 4 weeks after OCS (June 18–September 11, 2019). Results: Bridge clinic visits were 2.8 per provider session before, 2.0 during, and 3.0 after OCS. The mean number of GIM clinic visits per provider session before OCS was 7.0, 6.8 during, and 7.0 after OCS. In adjusted segmented regression models for bridge clinic visits per provider session, there was a nonsignificant level increase (0.643 $P = 0.171$) and significant decrease in slope (0.100, $P = 0.045$) during OCS. After OCS completed, there was a significant level increase (1.442, $P = 0.003$) and slope increase in visits per provider session (0.141, $P = 0.007$). There was no significant change in GIM clinic volume during the study period. Conclusions: The increased policing during OCS was associated with a significant decrease in bridge clinic visits. Following the completion of OCS, there was a significant increase in clinic visits, suggesting pent-up demand for medications for opioid use disorder, a life-saving treatment.

Predicting Accidental Drug Overdose As the Cause Of Fatality In Near Real-Time Using The Suspected Potential Overdose Tracker (SPOT): Public Health Implications

Hochstatter KR, Rastogi S, Klein K, Tait-Ozer C, El-Bassel N, Graham J. BMC Public Health. 2022; 22(1): 1311.

Background: Effective responses to the worsening drug overdose epidemic require accurate and timely drug overdose surveillance data. The objectives of this paper are to describe the development, functionality, and accuracy of the Suspected Potential Overdose Tracker (SPOT) for predicting accidental drug overdose as the cause and manner of death in near real-time, and public health implications of adopting the tool. Methods: SPOT was developed to rapidly identify overdose deaths through a simple and duplicable process using data collected by death investigators. The tool assigns each death a ranking of 1 through 3 based on the likelihood of it being an unintentional drug overdose, with 1 representing the highest likelihood that the death will be confirmed as an unintentional drug overdose and 3 representing the lowest. We measured the accuracy of the tool for predicting overdose deaths by comparing potential overdose deaths in New York City from 2018–2020 that were identified using SPOT to finalized death certificates. We also calculated the proportion of death certificate-confirmed overdoses that were missed by the SPOT tool and the proportion of type 1 errors. Results: SPOT captured up to 77% of unintentional drug overdose deaths using data collected within 72 h of fatality. The tool predicted unintentional drug overdose from 2018 to 2020 with 93–97% accuracy for cases assigned a ranking of 1, 87–91% accuracy for cases assigned a ranking of 2, and 62–73% accuracy for cases assigned a ranking of 3. Among all unintentional overdose deaths in 2018, 2019, and 2020, 21%, 28%, and 33% were missed by the SPOT tool, respectively. During this timeframe, the proportion of type 1 errors ranged from 15%-23%. Conclusions: SPOT may be used by health departments, epidemiologists, public health programs, and others to monitor overdose fatalities before death certificate data becomes available. Improved monitoring of overdose fatalities allows for rapid data-driven decision making, identification of gaps in public health and public safety overdose response, and evaluation and response to overdose prevention interventions, programs, and policies.

References To Evidence-Based Program Registry (EBPR) Websites For Behavioral Health In U.S. State Government Statutes and Regulations

Lee MJ, Maranda MJ, Magura S, Greenman G 2nd. J Appl Soc Sci (Boulder). 2022; 16(2): 442-458.

Background and aim: U.S. state governments have the responsibility to regulate and license behavioral healthcare interventions, such as for addiction and mental illness, with increasing emphasis on implementing evidence-based programs (EBPs). A serious obstacle to this is lack of clarity or agreement about what constitutes "evidence-based." The study's purpose was to determine the extent to which and in what contexts web-based Evidence-based Program Registries (EBPRs) are referenced in state government statutes and regulations ("mandates") concerning behavioral healthcare. Examples are: What Works Clearinghouse; National Register of Evidence-based Programs and Practices; Cochrane Database of Systematic Reviews. Methods: The study employed the Westlaw Legal Research Database to search for 30 known EBPR websites relevant to behavioral healthcare within the statutes and regulations of all 50 states. Results: There was low prevalence of EBPR references in state statutes and regulations pertaining to behavioral healthcare; 20 states had a total of 33 mandates that referenced an EBPR. These mandates usually do not rely on an EBPR as the sole acceptable source for classifying a program or practice as "evidence-based." Instead, EBPRs were named in conjunction with internal state or external sources of information about putative program effectiveness, which may be less valid than EBPRs, to determine what is "evidence-based." Conclusion: Greater awareness of scientifically - based EBPRs and greater

understanding of their advantages need to be fostered among state legislators and regulators charged with making policy to increase or improve the use of evidence-based programs and practices in behavioral healthcare in the U.S.

TREATMENT RESEARCH

Effects Of Daily Methocinnamox Treatment On Fentanyl Self-Administration In Rhesus Monkeys Maguire DR, France CP. J Pharmacol Exp Ther. 2022; 382(2): 181-187.

Methocinnamox (MCAM), a long-acting μ -opioid receptor antagonist, attenuates the positive reinforcing effects of opioids, such as heroin and fentanyl, suggesting it could be an effective treatment of opioid use disorder (OUD). Because treatment of OUD often involves repeated administration of a medication, this study evaluated effects of daily injections of a relatively small dose of MCAM on fentanyl self-administration and characterized the shift in the fentanyl dose-effect curve. Rhesus monkeys (3 males and 2 females) lever-pressed for intravenous infusions of fentanyl (0.032-10 μ g/kg infusion) or cocaine (32-100 μ g/kg infusion) under a fixed-ratio 30 schedule. MCAM (0.032 mg/kg) or naltrexone (0.0032-0.032 mg/kg) was administered subcutaneously 60 or 15 minutes, respectively, before sessions. When administered acutely, naltrexone and MCAM decreased fentanyl self-administration, with effects of naltrexone lasting less than 24 hours and effects of MCAM lasting for up to 3 days. Daily MCAM treatment attenuated responding for fentanyl, but not cocaine; effects were maintained for the duration of treatment with responding recovering quickly (within 2 days) following discontinuation of treatment. MCAM treatment shifted the fentanyl dose-effect curve in a parallel manner approximately 20-fold to the right. Naltrexone pretreatment decreased fentanyl intake with equal potency before and after MCAM treatment, confirming sensitivity of responding to antagonism by an opioid receptor antagonist. Although antagonist effects of treatment with a relatively small dose were surmountable, MCAM produced sustained and selective attenuation of opioid self-administration, supporting the view that it could be an effective treatment of OUD.

SIGNIFICANCE STATEMENT: Opioid use disorder and opioid overdose continue to be significant public health challenges despite the availability of effective treatments. Methocinnamox (MCAM) is a long-acting μ -opioid receptor antagonist that blocks the reinforcing and ventilatory depressant effects of opioids in nonhuman subjects. This study demonstrates that daily treatment with MCAM reliably and selectively decreases fentanyl self-administration, further supporting the potential therapeutic utility of this novel antagonist.

PPL-103: A Mixed Opioid Partial Agonist With Desirable Anti-Cocaine Properties Cippitelli A, Zribi G, Toll L. Prog Neuropsychopharmacol Biol Psychiatry. 2022; 119: 110599.

Cocaine use disorder (CUD) is a persistent public health problem for which no effective medications are available. PPL-103 is an opioid receptor ligand with partial agonist activity at μ , κ and δ opioid receptors, with a greater efficacy for κ and low efficacy at μ receptors. Because chronic cocaine use induces changes in the κ opioid receptor/dynorphin system, we hypothesized that a κ partial agonist, such as PPL-103, would attenuate the aversive properties of the upregulated κ system, resulting in effective treatment approach for CUD. We tested the effects of PPL-103 on cocaine self-administration models that recapitulate core aspects of CUD in humans. We found that PPL-103 reduced both long and short access cocaine self-administration, motivation to respond for cocaine, and binge-like cocaine taking, in rats. Operant responding for food, fentanyl and locomotor behavior were not altered at doses that decreased cocaine infusions. Repeated PPL-103 treatment did not lead to tolerance development. PPL-103 also reduced both priming- and cue-induced reinstatement of cocaine seeking, being more effective in the former.

Surprisingly, PPL-103 reduced self-administration parameters and reinstatement in rats previously treated with the long-acting kappa receptor antagonist JDTC more potently than in non-JDTC treated animals, whereas naltrexone injected to rats subsequent to JDTC administration increased self-administration, suggesting that the partial mu agonist activity, rather than kappa agonism is important for reduction in cocaine taking and seeking. However, partial kappa activation seems to increase safety by limiting dysphoria, tolerance and addiction development. PPL-103 displays a desirable profile as a possible CUD pharmacotherapy.

Recovery Of Dopaminergic System After Cocaine Exposure And Impact Of A Long-acting Cocaine Hydrolase Deng J, Zhang T, Zheng X, Shang L, Zhan CG, Zheng F. *Addict Biol.* 2022; 27(4): e13179.

Dysregulation of dopamine transporters (DAT) within the dopaminergic system is an important biomarker of cocaine exposure. Depending on cocaine amount in-taken, one-time exposure in rats could lead to most (>95% of total) of DAT translocating to plasma membrane of the dopaminergic neurons compared to normal DAT distribution (~5.7% on the plasma membrane). Without further cocaine exposure, the time course of striatal DAT distribution, in terms of intracellular and plasma membrane fractions of DAT, represents a recovery process of the dopaminergic system. In this study, we demonstrated that after an acute cocaine exposure of 20 mg/kg (i.p.), the initial recovery process from days 1 to 15 in rats was relatively faster (from >95% on day 1 to ~35.4% on day 15). However, complete recovery of the striatal DAT distribution may take about 60 days. In another situation, with repeated cocaine exposures for once every other day for a total of 17 doses of 20 mg/kg cocaine (i.p.) from days 0 to 32, the complete recovery of striatal DAT distribution may take an even longer time (about 90 days), which represents a consequence of chronic cocaine use. Further, we demonstrated that a highly efficient Fc-fused cocaine hydrolase, Coch5-Fc(M6), effectively blocked cocaine-induced hyperactivity and DAT trafficking with repeated cocaine exposures by maintaining a plasma Coch5-Fc(M6) concentration $\geq 58.7 \pm 2.9$ nM in rats. The cocaine hydrolase protected dopaminergic system and helped the cocaine-altered DAT distribution to recover by preventing the dopaminergic system from further damage by cocaine.

Development Of A Highly Efficient Long-Acting Cocaine Hydrolase Entity To Accelerate Cocaine Metabolism Zheng F, Jin Z, Deng J, Chen X, Zheng X, Wang G, Kim K, Shang L, Zhou Z, Zhan CG. *Bioconjug Chem.* 2022; 33(7): 1340-1349.

It is particularly challenging to develop a truly effective pharmacotherapy for cocaine use disorder (CUD) treatment. Accelerating cocaine metabolism via hydrolysis at cocaine benzoyl ester using an efficient cocaine hydrolase (CocH) is known as a promising pharmacotherapeutic approach to CUD treatment. Preclinical and clinical studies on our first CocH (CocH1), in its human serum albumin-fused form known as TV-1380, have demonstrated the promise of a general concept of CocH-based pharmacotherapy for CUD treatment. However, the biological half-life of TV-1380 ($t_{1/2} = 8$ h in rats, associated with $t_{1/2} = 43-77$ h in humans) is not long enough for practical treatment of cocaine dependence, which requires enzyme injection for no more than once weekly. Through protein fusion of a human butyrylcholinesterase mutant (denoted as Coch5) with a mutant (denoted as Fc(M6)) of Fc from human IgG1, we have designed, prepared, and tested a new fusion protein (denoted as Coch5-Fc(M6)) for its pharmacokinetic profile and in vivo catalytic activity against (-)-cocaine. Coch5-Fc(M6) represents the currently most efficient long-acting cocaine hydrolase with both the highest catalytic activity against (-)-cocaine and the longest elimination half-life ($t_{1/2} = 229 \pm 5$ h) in rats. As a result, even at a single modest dose of

3 mg/kg, CocH5-Fc(M6) can significantly and effectively accelerate the metabolism of cocaine in rats for at least 60 days. In addition, ~70 nM CocH5-Fc(M6) in plasma was able to completely block the toxicity and physiological effects induced by intraperitoneal injection of a lethal dose of cocaine (60 mg/kg).

[Acute Glucagon-like Peptide-1 Receptor Agonist Liraglutide Prevents Cue-, Stress-, And Drug-induced Heroin-Seeking In Rats](#) Douton JE, Acharya NK, Stoltzfus B, Sun D, Grigson PS, Nyland JE. *Behav Pharmacol.* 2022; 33(5): 364-378.

Substance use disorder is challenging to treat due to its relapsing nature. In the last decade, opioid use disorder has been a threat to public health, being declared an epidemic by the Centers for Disease Control and Prevention. This is a tragic situation, considering there currently are only three effective, yet not ideal, treatments to prevent relapse to opioids. Recent research has shown that hormones that modulate hunger and satiety also can modulate motivated behavior for drugs of abuse. For example, the short-acting analog of glucagon-like peptide-1 (GLP-1), an incretin hormone that regulates homeostatic feeding, has been shown to reduce responding for rewarding stimuli such as food, cocaine, heroin, and nicotine when administered over several days or weeks. This may serve as an effective adjuvant during treatment; however, whether it would be effective when used acutely to bridge a patient between cessation of use and onset of medication for the treatment of an opioid addiction is unknown. Here, we tested the acute effects of the longer acting GLP-1 analog, liraglutide, on heroin-seeking. In rats with heroin self-administration experience, we found that subcutaneous administration of an acute dose of 0.3-mg/kg liraglutide was effective in preventing drug-seeking after exposure to three major precipitators: drug-associated cues, stress (yohimbine-induced), and the drug itself. Finally, we confirmed that the reduction in drug-seeking is not due to a locomotor impairment, as liraglutide did not significantly alter performance in a rotarod test. As such, acute use of GLP-1 analogs may serve as a new and effective nonopioid bridge to treatment.

[Metabolism Of Speciociliatine, An Overlooked Kratom Alkaloid For Its Potential Pharmacological Effects](#) Kamble SH, Berthold EC, Kanumuri SRR, King TI, Kuntz MA, León F, Mottinelli M, McMahon LR, McCurdy CR, Sharma A. *AAPS J.* 2022; 24(5): 86.

Speciociliatine, a diastereomer of mitragynine, is an indole-based alkaloid found in kratom (*Mitragyna speciosa*). Kratom has been widely used for the mitigation of pain and opioid dependence, as a mood enhancer, and/or as an energy booster. Speciociliatine is a partial μ -opioid agonist with a 3-fold higher binding affinity than mitragynine. Speciociliatine has been found to be a major circulating alkaloid in humans following oral administration of a kratom product. In this report, we have characterized the metabolism of speciociliatine in human and preclinical species (mouse, rat, dog, and cynomolgus monkey) liver microsomes and hepatocytes. Speciociliatine metabolized rapidly in monkey, rat, and mouse hepatocytes (in vitro half-life was 6.6 ± 0.2 , 8.3 ± 1.1 , 11.2 ± 0.7 min, respectively), while a slower metabolism was observed in human and dog hepatocytes (91.7 ± 12.8 and > 120 min, respectively). Speciociliatine underwent extensive metabolism, primarily through monooxidation and O-demethylation metabolic pathways in liver microsomes and hepatocytes across species. No human-specific or disproportionate metabolites of speciociliatine were found in human liver microsomes. The metabolism of speciociliatine was predominantly mediated by CYP3A4 with minor contributions by CYP2D6.

Characterizing Cannabis Use Reduction And Change In Functioning During Treatment: Initial Steps On the Path To New Clinical Endpoints

Borodovsky JT, Sofis MJ, Sherman BJ, Gray KM, Budney AJ. Psychol Addict Behav. 2022; 36(5): 515-525.

Reduction-based cannabis use endpoints are needed to better evaluate treatments for cannabis use disorder (CUD). This exploratory, secondary analysis aimed to characterize cannabis frequency and quantity reduction patterns and corresponding changes in psychosocial functioning during treatment. We analyzed 16 weeks (4 prerandomization, 12 postrandomization) of data (n = 302) from both arms of a randomized clinical trial assessing pharmacotherapy for CUD. Cannabis consumption pattern classes were extracted with latent profile modeling using self-reported (a) past-week days used (i.e., frequency) and (b) past-week average grams used per using day (i.e., quantity). Changes in mean Marijuana Problem Scale (MPS) and Hospital Anxiety and Depression Scale (HADS) scores were examined among classes. Urine cannabinoid levels were examined in relation to self-reported consumption as a validity check. Two-, three-, four-, and five-class solutions each provided potentially useful conceptualizations of associations between frequency and quantity. Regardless of solution, reductions in MPS scores varied in magnitude across classes and closely tracked class-specific reductions in consumption (e.g., larger MPS reduction corresponded to larger frequency/quantity reductions). Changes in HADS scores were less pronounced and less consistent with consumption patterns. Urine cannabinoid levels closely matched class-specific self-reported consumption frequency. Findings illustrate that frequency and quantity can be used in tandem within mixture model frameworks to summarize heterogeneous cannabis use reduction patterns that may correspond to improved psychosocial functioning. Going forward, similar analytic strategies applied to alternative metrics of cannabis consumption may facilitate construction of useful reduction-based clinical endpoints.

A Preliminary Investigation Of The Role Of Intraindividual Sleep Variability In Substance Use Treatment Outcomes

Schick MR, Slavish DC, Dietch JR, Witcraft SM, Simmons RO, Taylor DJ, Smith JP, Book SW, McRae-Clark AL, Wilkerson AK. Addict Behav. 2022; 131: 107315.

INTRODUCTION: Poor sleep health is common among individuals in early treatment for substance use disorders (SUDs) and may serve an important role in predicting SUD outcomes. However, sleep parameters have been inconsistently linked with risk of relapse, perhaps because previous research has focused on mean values of sleep parameters (e.g., total sleep time [TST], sleep efficiency [SE], and sleep midpoint [SM]) across multiple nights rather than night-to-night fluctuations (i.e., intraindividual variability [IIV]). The current study assessed sleep across the first week of SUD treatment, with the aim of prospectively examining the relationship between mean and IIV of TST, SE, and SM and treatment completion and relapse within one-month post-treatment. METHODS: Treatment-seeking adults (N = 23, Mage = 40.1, 39% female) wore an actigraph to assess sleep for one week at the beginning of an intensive outpatient program treatment. Electronic medical record and follow-up interviews were utilized to determine treatment outcomes. RESULTS: Greater IIV in TST was associated with higher odds of relapse (OR = 3.55, p = .028). Greater IIV in SM was associated with lower odds of treatment completion, but only when removing mean SM from the model (OR = 0.75, p = .046). DISCUSSION: Night-to-night variability in actigraphy-measured TST is more strongly associated with SUD treatment outcomes than average sleep patterns across the week. Integrating circadian regulation into treatment efforts to improve SUD treatment outcomes may be warranted. Given the small sample size utilized in the present study, replication of these analyses with a larger sample is warranted.

Effect Of TRV130 And Methadone On Fentanyl-vs.-Food Choice And Somatic Withdrawal Signs In Opioid-dependent And Post-opioid-dependent Rats

Townsend EA, Blough BE, Epstein DH, Negus SS, Shaham Y, Banks ML. *Neuropsychopharmacology*. 2022; 47(12): 2132-2139.

The high efficacy mu-opioid receptor (MOR) agonist methadone is an effective opioid use disorder (OUD) medication used exclusively in opioid-dependent patients. However, methadone has undesirable effects that limit its clinical efficacy. Intermediate efficacy MOR agonists may treat OUD with fewer undesirable effects. We compared the effects of methadone with the intermediate efficacy MOR agonist TRV130 (oliceidine) on fentanyl-vs.-food choice and somatic withdrawal signs in opioid-dependent and post-opioid-dependent rats. Male rats (n = 20) were trained under a fentanyl-vs.-food choice procedure. Rats were then provided extended fentanyl (3.2 µg/kg/infusion) access (6 p.m.-6 a.m.) for 10 days to produce opioid dependence/withdrawal. Rats were treated with vehicle (n = 7), TRV130 (3.2 mg/kg; n = 8), or methadone (3.2 mg/kg; n = 5) three times per day after each extended-access session (8:30 a.m., 11 a.m., 1:30 p.m.). Withdrawal sign scoring (1:55 p.m.) and choice tests (2-4 p.m.) were conducted daily. Vehicle, TRV130, and methadone effects on fentanyl choice were redetermined in post-opioid-dependent rats. Vehicle-, TRV130-, and methadone-treated rats had similar fentanyl intakes during extended access. Vehicle-treated rats exhibited increased withdrawal signs and decreased bodyweights. Both methadone and TRV130 decreased these withdrawal signs. TRV130 was less effective than methadone to decrease fentanyl choice and increase food choice in opioid-dependent rats. Neither methadone nor TRV130 decreased fentanyl choice in post-opioid-dependent rats. Results suggest that higher MOR activation is required to reduce fentanyl choice than withdrawal signs in fentanyl-dependent rats. Additionally, given that TRV130 did not precipitate withdrawal in opioid-dependent rats, intermediate efficacy MOR agonists like TRV130 may facilitate the transition of patients with OUD from methadone to lower efficacy treatments like buprenorphine.

Evaluating Cannabis Use Risk Reduction As An Alternative Clinical Outcome For Cannabis Use Disorder

Sherman BJ, Sofis MJ, Borodovsky JT, Gray KM, McRae-Clark AL, Budney AJ.

Psychol Addict Behav. 2022; 36(5): 505-514.

OBJECTIVE: Abstinence is rarely achieved in clinical trials for cannabis use disorder (CUD). Cannabis reduction is associated with functional improvement, but reduction endpoints have not been established, indicating a need to identify and validate clinically meaningful reduction endpoints for assessing treatment efficacy. **METHOD:** Data from a 12-week double-blind randomized placebo-controlled medication trial for cannabis cessation (NCT01675661) were analyzed. Participants (N = 225) were treatment-seeking adults, M = 30.6 (8.9) years old, 70.2% male, and 42.2% Non-White, with CUD who completed 12 weeks of treatment. Frequency (days of use per week) and quantity (grams per using day) were used to define high-, medium-, and low-risk levels. Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale and cannabis-related problems were assessed using the Marijuana Problems Scale. General linear models for repeated measures tested associations between the magnitude of risk reduction and functional outcomes from baseline (BL) to end-of-treatment (EOT). **RESULTS:** Cannabis risk levels were sensitive to reductions in use from BL to EOT for frequency- ($\chi^2 = 19.35$, $p = .004$) and quantity-based ($\chi^2 = 52.06$, $p < .001$) metrics. Magnitude reduction in frequency-based risk level was associated with magnitude decrease in depression ($F = 2.76$, $p = .043$, $\eta^2 = .04$), anxiety ($F = 3.70$, $p = .013$, $\eta^2 = .05$), and cannabis-related problems ($F = 8.95$, $p < .001$, $\eta^2 = .12$). Magnitude reduction in quantity-based risk level was associated with magnitude decrease in anxiety ($F = 3.02$, $p = .031$, $\eta^2 = .04$) and cannabis-related problems ($F = 3.24$, $p = .023$, $\eta^2 = .05$). **CONCLUSIONS:** Cannabis use risk levels, as operationalized in this study, captured reductions in

use during a clinical trial. Risk level reduction was associated with functional improvement suggesting that identifying risk levels and measuring the change in levels over time may be a viable and clinically meaningful endpoint for determining treatment efficacy.

[Effects Of Methadone, Buprenorphine, And Naltrexone On Actigraphy-based Sleep-like Parameters In Male Rhesus Monkeys](#)

Berro LF, Zamarripa CA, Talley JT, Freeman KB, Rowlett JK. *Addict Behav.* 2022; 135: 107433.

Opioid use disorder (OUD) has been associated with the emergence of sleep disturbances. Although effective treatments for OUD exist, evidence suggests that these treatments also may be associated with sleep impairment. The extent to which these effects are an effect of OUD treatment or a result of chronic opioid use remains unknown. We investigated the acute effects of methadone, buprenorphine, and naltrexone on actigraphy-based sleep-like parameters in non-opioid-dependent male rhesus monkeys (*Macaca mulatta*, n = 5). Subjects were fitted with actigraphy monitors attached to primate collars to measure sleep-like parameters. Actigraphy recordings were conducted under baseline conditions, or following acute injections of vehicle, methadone (0.03-1.0 mg/kg, i.m.), buprenorphine (0.01-1.0 mg/kg, i.m.), or naltrexone (0.03-1.0 mg/kg, i.m.) in the morning (4 h after "lights on") or in the evening (1.5 h before "lights off"). Morning and evening treatments with methadone or buprenorphine significantly increased sleep latency and decreased sleep efficiency. The effects of buprenorphine on sleep-like measures resulted in a biphasic dose-response function, with the highest doses not disrupting actigraphy-based sleep. Buprenorphine induced a much more robust increase in sleep latency and decrease in sleep efficiency compared to methadone,

HIV RESEARCH

[Raman Spectroscopy Based Molecular Signatures Of Methamphetamine And HIV Induced Mitochondrial Dysfunction](#)

Chean KT, Aalinkeel R, Abbasi S, Sharikova AV, Schwartz SA, Khmaladze A, Mahajan SD. *Biochem Biophys Res Commun.* 2022; 621: 116-121.

METH and HIV Tat treatment results in increased oxidative stress which affects cellular metabolism and causes DNA damage in the treated microglia. Both, METH ± HIV Tat impair mitochondrial respiration, leading to dysfunction in bioenergetics and increased ROS in microglial cells. Our data indicate that mitochondrial dysfunction may be key to the METH and/or HIV Tat-induced neuropathology. METH and/or HIV Tat induced changes in the protein, lipid and nucleotide concentration in microglial cells were measured by Raman Spectroscopy, and we speculate that these fundamental molecular-cellular changes in microglial cells contribute to the neuropathology that is associated with METH abuse in HIV patients.

[HIV Integration In the Human Brain Is Linked To Microglial Activation and 3D Genome Remodeling](#)

Plaza-Jennings A, Valada A, O'Shea C, Iskhakova M, Hu B, Javidfar B, Hutta GB, Lambert T, Murray J, Kassim B, Chandrasekaran S, Chen BK, Morgello S, Won H, Akbarian S. *Molecular Cell.* 2022; 82(24): 4647-4663.

To explore genome organization and function in the HIV infected brain, we applied single nuclei transcriptomics, cell-type specific chromosomal conformation mapping, and viral integration site sequencing (IS-seq) to frontal cortex from individuals with encephalitis (HIVE) and without (HIV+). De-repressive changes in 3D genomic compartment structures in HIVE microglia were linked to transcriptional activation of interferon (IFN) signaling and cell migratory pathways, while transcriptional downregulation and repressive compartmentalization of neuronal health and signaling genes occurred in both HIVE and HIV+ microglia. IS-seq recovered 1,221 brain integration sites showing distinct genomic patterns as compared to peripheral lymphocytes, with

enrichment for sequences newly mobilized into a permissive chromatin environment after infection. Viral transcription occurred in a subset of highly activated microglia comprising 0.003% of all nuclei in HIV brain. Our findings point to disrupted microglia-neuronal interactions in HIV and link retroviral integration to remodeling of the microglial 3D genome during infection.

[Spatial Accessibility To HIV Testing, Treatment, And Prevention Services In Illinois And Chicago, USA](#) Kang JY, Farkhad BF, Chan MS, Michels A, Albarracin D, Wang S. PLoS One. 2022; 17(7): e0270404.

Accomplishing the goals outlined in "Ending the HIV (Human Immunodeficiency Virus) Epidemic: A Plan for America Initiative" will require properly estimating and increasing access to HIV testing, treatment, and prevention services. In this research, a computational spatial method for estimating access was applied to measure distance to services from all points of a city or state while considering the size of the population in need for services as well as both driving and public transportation. Specifically, this study employed the enhanced two-step floating catchment area (E2SFCA) method to measure spatial accessibility to HIV testing, treatment (i.e., Ryan White HIV/AIDS program), and prevention (i.e., Pre-Exposure Prophylaxis [PrEP]) services. The method considered the spatial location of MSM (Men Who have Sex with Men), PLWH (People Living with HIV), and the general adult population 15-64 depending on what HIV services the U.S. Centers for Disease Control (CDC) recommends for each group. The study delineated service- and population-specific accessibility maps, demonstrating the method's utility by analyzing data corresponding to the city of Chicago and the state of Illinois. Findings indicated health disparities in the south and the northwest of Chicago and particular areas in Illinois, as well as unique health disparities for public transportation compared to driving. The methodology details and computer code are shared for use in research and public policy.

[Prescribe To Save Lives: Improving Buprenorphine Prescribing Among HIV Clinicians](#) Jawa R, Walley AY, Wilson DJ, Green TC, McKenzie M, Hoskinson R Jr, Bratberg J, Ramsey S, Rich JD, Friedmann PD. J Acquir Immune Defic Syndr. 2022; 90(5): 546-552.

Background: HIV clinicians are uniquely positioned to treat their patients with opioid use disorder using buprenorphine to prevent overdose death. The Prescribe to Save Lives (PtSL) study aimed to increase HIV clinicians' buprenorphine prescribing via an overdose prevention intervention. Methods: The quasi-experimental stepped-wedge study enrolled 22 Ryan White-funded HIV clinics and delivered a peer-to-peer training to clinicians with follow-up academic detailing that included overdose prevention education and introduced buprenorphine prescribing. Site-aggregated electronic medical record (EMR) data measured with the change in X-waivered clinicians and patients prescribed buprenorphine. Clinicians completed surveys preintervention and at 6- and 12-month postintervention that assessed buprenorphine training, prescribing, and attitudes. Analyses applied generalized estimating equation models, adjusting for time and clustering of repeated measures among individuals and sites. Results: Nineteen sites provided EMR prescribing data, and 122 clinicians returned surveys. Of the total patients with HIV across all sites, EMR data showed 0.38% were prescribed buprenorphine pre-intervention and 0.52% were prescribed buprenorphine postintervention. The intervention increased completion of a buprenorphine training course (adjusted odds ratio 2.54, 95% confidence interval: 1.38 to 4.68, $P = 0.003$) and obtaining an X-waiver (adjusted odds ratio 2.11, 95% confidence interval: 1.12 to 3.95, $P = 0.02$). There were nonsignificant increases at the clinic level, as well. Conclusions: Although the PtSL intervention resulted in increases in buprenorphine training and prescriber certification, there was no meaningful

increase in buprenorphine prescribing. Engaging and teaching HIV clinicians about overdose and naloxone rescue may facilitate training in buprenorphine prescribing but will not result in more treatment with buprenorphine without additional interventions.

Social Geonomics Of Methamphetamine Use, HIV Viral Load, And Social Adversity Li MJ, Richter EI, Okafor CN, Kalmin MM, Dalvie S, Takada S, Gorbach PM, Shoptaw SJ, Cole SW. *Ann Behav Med.* 2022; 56(9): 900-908. Social genomics has demonstrated altered inflammatory and type I interferon (IFN) gene expression among people experiencing chronic social adversity. Adverse social experiences such as discrimination and violence are linked to stimulant misuse and HIV, conditions that dysregulate inflammatory and innate antiviral responses, leading to increased HIV viral replication and risk of chronic diseases. **PURPOSE:** We aimed to determine whether methamphetamine (MA) use, unsuppressed HIV viral load (VL) (≥ 200 c/mL), and experienced intimate partner violence (IPV) (past 12 months) predicted inflammatory and type I IFN gene expression in HIV-positive Black and Latinx men who have sex with men (MSM). **METHODS:** Participants were 147 HIV-positive Black and Latinx MSM recruited from the mSTUDY, a cohort of 561 MSM aged 18-45 in Los Angeles, CA, of whom half are HIV-positive and substance-using. Transcriptomic measures of inflammatory and type I IFN activity were derived from RNA sequencing of peripheral blood mononuclear cells and matched to urine drug tests, VL, and survey data across two time points 12 months apart. Analysis used linear random intercept modeling of MA use, unsuppressed VL, and experienced IPV on inflammatory and type I IFN expression. **RESULTS:** In adjusted models, MA use predicted 27% upregulated inflammatory and 31% upregulated type I IFN expression; unsuppressed VL predicted 84% upregulated type I IFN but not inflammatory expression; and experienced IPV predicted 31% upregulated inflammatory and 26% upregulated type I IFN expression. **CONCLUSIONS:** In Black and Latinx MSM with HIV, MA use, unsuppressed VL, and experienced IPV predicted upregulated social genomic markers of immune functioning.

Daily Marijuana Use Predicts HIV Seroconversion Among Black Men Who Have Sex With Men And Transgender Women In Atlanta, GA Knox J, Hwang G, Carrico AW, Duncan DT, Watson RJ, Eaton LA. *AIDS Behav.* 2022; 26(8): 2503-2515.

We evaluated whether different types of substance use predicted HIV seroconversion among a cohort of 449 Black men who have sex with men (MSM) and transgender women (TGW). A community-based sample was recruited in Atlanta, GA between December 2012 and November 2014. Participants completed a survey and were tested for STIs (Chlamydia and gonorrhoeae using urine samples and rectal swabs) at baseline. HIV testing was conducted at 12-months post enrollment. Multivariable binary logistic regression was used to estimate adjusted odds ratios (aORs) and 95% confidence intervals (CI) for associations between substance use and HIV seroconversion. By 12-month follow-up, 5.3% (n = 24) of participants seroconverted. In multivariable analyses, daily marijuana use was positively associated with HIV seroconversion (aOR 3.07, 95% CI 1.11-8.48, P = 0.030). HIV incidence was high and daily marijuana use was associated with a more than threefold increased odds of HIV seroconversion among a community-based cohort of Black MSM and TGW.

Relative Effectiveness Of Social Media, Dating Apps, And Information Search Sites In Promoting HIV Self-testing: Observational Cohort Study Stafylis C, Vavala G, Wang Q, McLeman B, Lemley SM, Young SD, Xie H, Matthews AG, Oden N, Revoredo L, Shmueli-Blumberg D, Hichborn EG, McKelle E, Moran LM, Jacobs P, Marsch LA, Klausner JD. JMIR Form Res. 2022; 6(9): e35648.

Background: Social media sites, dating apps, and information search sites have been used to reach individuals at high risk for HIV infection. However, it is not clear which platform is the most efficient in promoting home HIV self-testing, given that the users of various platforms may have different characteristics that impact their readiness for HIV testing. **Objective:** This study aimed to compare the relative effectiveness of social media sites, dating apps, and information search sites in promoting HIV self-testing among minority men who have sex with men (MSM) at an increased risk of HIV infection. Test kit order rates were used as a proxy to evaluate promotion effectiveness. In addition, we assessed differences in characteristics between participants who ordered and did not order an HIV test kit. **Methods:** Culturally appropriate advertisements were placed on popular sites of three different platforms: social media sites (Facebook, Instagram), dating apps (Grindr, Jack'D), and information search sites (Google, Bing). Advertisements targeted young (18-30 years old) and minority (Black or Latinx) MSM at risk of HIV exposure. Recruitment occurred in 2 waves, with each wave running advertisements on 1 platform of each type over the same period. Participants completed a baseline survey assessing sexual or injection use behavior, substance use including alcohol, psychological readiness to test, attitudes toward HIV testing and treatment, and HIV-related stigma. Participants received an electronic code to order a free home-based HIV self-test kit. Follow-up assessments were conducted to assess HIV self-test kit use and uptake of pre-exposure prophylaxis (PrEP) at 14 and 60 days post enrollment. **Results:** In total, 271 participants were enrolled, and 254 were included in the final analysis. Among these 254 participants, 177 (69.7%) ordered a home HIV self-test kit. Most of the self-test kits were ordered by participants enrolled from dating apps. Due to waves with low enrollment, between wave statistical comparisons were not feasible. Within wave comparison revealed that Jack'D showed higher order rates (3.29 kits/day) compared to Instagram (0.34 kits/day) and Bing (0 kits/day). There were no associations among self-test kit ordering and HIV-related stigma, perceptions about HIV testing and treatment, and mistrust of medical organizations. **Conclusions:** Our findings show that using popular dating apps might be an efficient way to promote HIV self-testing. Stigma, perceptions about HIV testing and treatment, or mistrust of medical organizations may not affect order rates of HIV test kits promoted on the internet. **Trial registration:** ClinicalTrials.gov [NCT04155502](https://clinicaltrials.gov/ct2/show/study/NCT04155502).

CLINICAL TRIALS NETWORK RESEARCH

Machine Learning Techniques To Explore Clinical Presentations Of COVID-19 Severity And To Test The Association With Unhealthy Opioid Use: Retrospective Cross-sectional Cohort Study Thompson HM, Sharma B, Smith DL, Bhalla S, Erondy I, Hazra A, Ilyas Y, Pachwicewicz P, Sheth NK, Chhabra N, Karnik NS, Afshar M. JMIR Public Health Surveill. 2022; 8(12): e38158.

Background: The COVID-19 pandemic has exacerbated health inequities in the United States. People with unhealthy opioid use (UOU) may face disproportionate challenges with COVID-19 precautions, and the pandemic has disrupted access to opioids and UOU treatments. UOU impairs the immunological, cardiovascular, pulmonary, renal, and neurological systems and may increase severity of outcomes for COVID-19. **Objective:** We applied machine learning techniques to explore clinical presentations of hospitalized patients with UOU and COVID-19 and to test the association between UOU and COVID-19 disease severity. **Methods:** This retrospective, cross-

sectional cohort study was conducted based on data from 4110 electronic health record patient encounters at an academic health center in Chicago between January 1, 2020, and December 31, 2020. The inclusion criterion was an unplanned admission of a patient aged ≥ 18 years; encounters were counted as COVID-19-positive if there was a positive test for COVID-19 or 2 COVID-19 International Classification of Disease, Tenth Revision codes. Using a predefined cutoff with optimal sensitivity and specificity to identify UOU, we ran a machine learning UOU classifier on the data for patients with COVID-19 to estimate the subcohort of patients with UOU. Topic modeling was used to explore and compare the clinical presentations documented for 2 subgroups: encounters with UOU and COVID-19 and those with no UOU and COVID-19. Mixed effects logistic regression accounted for multiple encounters for some patients and tested the association between UOU and COVID-19 outcome severity. Severity was measured with 3 utilization metrics: low-severity unplanned admission, medium-severity unplanned admission and receiving mechanical ventilation, and high-severity unplanned admission with in-hospital death. All models controlled for age, sex, race/ethnicity, insurance status, and BMI. **Results:** Topic modeling yielded 10 topics per subgroup and highlighted unique comorbidities associated with UOU and COVID-19 (e.g., HIV) and no UOU and COVID-19 (e.g., diabetes). In the regression analysis, each incremental increase in the classifier's predicted probability of UOU was associated with 1.16 higher odds of COVID-19 outcome severity (odds ratio 1.16, 95% CI 1.04-1.29; $P=.009$). **Conclusions:** Among patients hospitalized with COVID-19, UOU is an independent risk factor associated with greater outcome severity, including in-hospital death. Social determinants of health and opioid-related overdose are unique comorbidities in the clinical presentation of the UOU patient subgroup. Additional research is needed on the role of COVID-19 therapeutics and inpatient management of acute COVID-19 pneumonia for patients with UOU. Further research is needed to test associations between expanded evidence-based harm reduction strategies for UOU and vaccination rates, hospitalizations, and risks for overdose and death among people with UOU and COVID-19. Machine learning techniques may offer more exhaustive means for cohort discovery and a novel mixed methods approach to population health.

[Centering Culture In The Treatment Of Opioid Use Disorder With American Indian And Alaska Native Communities: Contributions From A National Collaborative Board](#)

Hirchak KA, Nadeau M, Vasquez A, Hernandez-Vallant A, Smith K, Pham C, Oliver KA, Baukol P, Lizzy K, Shaffer R, Herron J, Campbell ANC, Venner KL; CTN-0096 Collaborative Board. *Am J Community Psychol.* 2022 Aug 23. Online ahead of print.

American Indian/Alaska Native (AI/AN) communities are disproportionately impacted by the opioid overdose epidemic. There remains a dearth of research evaluating methods for effectively implementing treatments for opioid use disorder (OUD) within these communities. We describe proceedings from a 2-day Collaborative Board (CB) meeting tasked with developing an implementation intervention for AI/AN clinical programs to improve the delivery of medications to treat OUD (MOUD). The CB was comprised of Elders, cultural leaders, providers, individuals with lived experience with OUD, and researchers from over 25 communities, organizations, and academic institutions. Conversations were audio-recorded, transcribed, and coded by two academic researchers with interpretation oversight provided by the CB. These proceedings provided a foundation for ongoing CB work and a frame for developing the program-level implementation intervention using a strength-based and holistic model of OUD recovery and wellbeing. Topics of discussion posed to the CB included engagement and recovery strategies, integration of extended family traditions, and addressing stigma and building trust with providers and clients. Integration of

traditional healing practices, ceremonies, and other cultural practices was recommended. The importance of centering AI/AN culture and involving family were highlighted as priorities for the intervention.

Time-Lagged Association Between Counseling And/Or 12-Step Attendance With Subsequent Opioid Use In A Secondary Analysis From A Randomized, Clinical Trial Of Medications For Opioid Use Disorder

Hefner K, Choo T, Shmueli-Blumberg D, Pavlicova M, King J, Fishman M, Shulman M, Campbell A, Greiner M, Scodes J, Meyers-Ohki S, Novo P, Nunes EV, Rotrosen J. *Drug Alcohol Depend Rep.* 2022; 5: 100100.

Introduction: Psychosocial support is recommended in conjunction with medication for opioid use disorder (MOUD), although optimal “dose,” modality, and timing of participation is not established. This study comprised a secondary analysis of counseling and 12-Step attendance and subsequent opioid use in a MOUD randomized clinical trial. **Methods:** The parent study randomly assigned 570 participants to receive buprenorphine-naloxone (BUP-NX, $n=287$) or extended-release injectable naltrexone (XR-NTX, $n=283$). Mixed-effects logistic regression models were fit with opioid use as the response variable, and a counseling/12-Step attendance predictor. Differences by treatment assignment were examined. **Results:** Any counseling or 12-Step attendance was associated with reduced odds of opioid use at the subsequent visit, whether considered individually or aggregated across type. A continuous relationship was observed for 12-Step attendance ($F(1,5083)=5.01$, $p=.025$); with each additional hour associated with 13% (95% CI: 0.83, 0.90) reduction in odds of opioid use. The strength of this association grew over time. In the BUP-NX arm, group counseling was associated with a greater reduction in odds of opioid use than for XR-NTX, (OR=0.32 (95% CI: .22, 0.48) vs. OR=0.69 (95% CI: 0.43, 1.08)). For XR-NTX, 12-Step was associated with a greater reduction in odds of opioid use (OR=0.35 (95% CI: 0.22, 0.54) vs. OR=0.65 (95% CI: 0.47, 0.89) for BUP-NX)). **Conclusions:** Psychosocial engagement has a proximal association with opioid use, the strength of that association may grow with dose and time. Alternatively, more motivated individuals may both attend more counseling/12-Step and have better treatment outcomes, or the relationship may be reciprocal.

Five-Year Incidence Of Substance Use And Mental Health Diagnoses Following Exposure To Opioids Or Opioids With Benzodiazepines During An Emergency Department Encounter For Traumatic Injury

Sprunger JG, Johnson K, Lewis D, Kaelber DC, Winhusen TJ. *Drug Alcohol Depend.* 2022; 238:109584.

Background: Benzodiazepines and opioids are used alone or in conjunction in certain care settings, but each have the potential for misuse. **Objective:** This longitudinal observational study evaluated substance use and mental health outcomes associated with providing opioids with or without benzodiazepine to treat traumatic injury in the emergency department (ED) setting. **Methods:** We analyzed a limited dataset obtained through the IBM Watson Health Explorys. Matched cohorts were defined for: 1) patients treated with opioids during the ED encounter (ED-Opioid) vs. neither opioid or benzodiazepine treatment (No medication) ($n = 5372$); 2) patients treated with opioids and benzodiazepines during the ED encounter (ED-Opioid+Benzodiazepines) vs. No Medication ($n = 2454$); and 3) ED-Opioid+Benzodiazepines vs. ED-Opioid ($n = 2454$). Patients consisted of adults with an emergency department encounter in the MetroHealth System (Cleveland, Ohio) with a chief complaint of traumatic injury and medical records for five years following the encounter. Control patients for each cohort were matched to the exposure patients on demographics, body mass index, and residential zip code median income. Outcomes were five-year incidence rates for alcohol, substance use, depression, and anxiety-related diagnoses. **Results:** Our results indicate that,

although receiving opioids during the ED visit predicted a relatively lower likelihood of subsequent substance use and mental health diagnoses, the brief co-use of benzodiazepines was strongly associated with poorer outcomes. **Conclusions:** Even brief exposure to co-prescribed opioids and benzodiazepines during emergency traumatic injury care may be associated with negative substance use and mental health consequences in the years following the event. **Keywords:** Benzodiazepines; Co-prescription; Emergency department; Opioids; Substance use disorder.

[Association Between Treatment Setting and Outcomes Among Oregon Medicaid Patients](#)

[With Opioid Use Disorder: A Retrospective Cohort Study](#) Hartung DM, Markwardt S, Johnston K, Geddes J, Baker R, Leichtling G, Hildebran C, Chan B, Cook RR, McCarty D, Ghitza U, Korthuis PT. *Addict Sci Clin Pract.* 2022; 17(1): 45.

Background: Residential treatment is a common approach for treating opioid use disorder (OUD), however, few studies have directly compared it to outpatient treatment. The objective of this study was to compare OUD outcomes among individuals receiving residential and outpatient treatment. **Methods:** A retrospective cohort study used linked data from a state Medicaid program, vital statistics, and the Substance Abuse and Mental Health Services Administration (SAMHSA) Treatment Episodes Dataset (TEDS) to compare OUD-related health outcomes among individuals treated in a residential or outpatient setting between 2014 and 2017. Multivariable Cox proportional hazards and logistic regression models examined the association between treatment setting and outcomes (i.e., opioid overdose, non-overdose opioid-related and all-cause emergency department (ED) visits, hospital admissions, and treatment retention) controlling for patient characteristics, comorbidities, and use of medications for opioid use disorders (MOUD). Interaction models evaluated how MOUD use modified associations between treatment setting and outcomes. **Results:** Of 3293 individuals treated for OUD, 957 (29%) received treatment in a residential facility. MOUD use was higher among those treated as an outpatient (43%) compared to residential (19%). The risk of opioid overdose (aHR 1.39; 95% CI 0.73-2.64) or an opioid-related emergency department encounter or admission (aHR 1.02; 95% CI 0.80-1.29) did not differ between treatment settings. Independent of setting, MOUD use was associated with a significant reduction in overdose risk (aHR 0.45; 95% CI 0.23-0.89). Residential care was associated with greater odds of retention at 6-months (aOR 1.71; 95% CI 1.32-2.21) but not 1-year. Residential treatment was only associated with improved retention for individuals not receiving MOUD (6-month aOR 2.05; 95% CI 1.56-2.71) with no benefit observed in those who received MOUD (aOR 0.75; 95% CI 0.46-1.29; interaction $p = 0.001$). **Conclusions:** Relative to outpatient treatment, residential treatment was not associated with reductions in opioid overdose or opioid-related ED encounters/hospitalizations. Regardless of setting, MOUD use was associated with a significant reduction in opioid overdose risk.

ADOLESCENT BRAIN COGNITIVE DEVELOPMENT STUDY RESEARCH

[Neuroimaging Profiling Identifies Distinct Brain Maturation Subtypes Of Youth With](#)

[Mood And Anxiety Disorders](#) Ge R, Sassi R, Yatham LN, Frangou S. *Mol Psychiatry.* 2022 Dec 28. Online ahead of print.

Mood and anxiety disorders typically begin in adolescence and have overlapping clinical features but marked inter-individual variation in clinical presentation. The use of multimodal neuroimaging data may offer novel insights into the underlying brain mechanisms. We applied Heterogeneity Through Discriminative Analysis (HYDRA) to measures of regional brain morphometry, neurite density, and intracortical myelination to identify subtypes of youth, aged 9–10 years, with mood and anxiety disorders (N = 1931) compared to typically developing youth (N = 2823). We identified three subtypes that were robust to permutation testing and sample composition. Subtype 1

evidenced a pattern of imbalanced cortical-subcortical maturation compared to the typically developing group, with subcortical regions lagging behind prefrontal cortical thinning and myelination and greater cortical surface expansion globally. Subtype 2 displayed a pattern of delayed cortical maturation indicated by higher cortical thickness and lower cortical surface area expansion and myelination compared to the typically developing group. Subtype 3 showed evidence of atypical brain maturation involving globally lower cortical thickness and surface coupled with higher myelination and neural density. Subtype 1 had superior cognitive function in contrast to the other two subtypes that underperformed compared to the typically developing group. Higher levels of parental psychopathology, family conflict, and social adversity were common to all subtypes, with subtype 3 having the highest burden of adverse exposures. These analyses comprehensively characterize pre-adolescent mood and anxiety disorders, the biopsychosocial context in which they arise, and lay the foundation for the examination of the longitudinal evolution of the subtypes identified as the study sample transitions through adolescence.

Socioeconomic Resources Are Associated With Distributed Alterations Of The Brain's Intrinsic Functional Architecture In Youth

Sripada C, Gard AM, Angstadt M, Taxali A, Greathouse T, McCurry K, Hyde LW, Weigard A, Walczyk P, Heitzeg M. *Dev Cog Neurosci.* 2022; 58: 101164.

Little is known about how exposure to limited socioeconomic resources (SER) in childhood gets “under the skin” to shape brain development, especially using rigorous whole-brain multivariate methods in large, adequately powered samples. The present study examined resting state functional connectivity patterns from 5821 youth in the Adolescent Brain Cognitive Development (ABCD) study, employing multivariate methods across three levels: whole-brain, network-wise, and connection-wise. Across all three levels, SER was associated with widespread alterations across the connectome. However, critically, we found that parental education was the primary driver of neural associations with SER. These parental education associations with the developing connectome exhibited notable concentrations in somatosensory and subcortical regions, and they were partially accounted for by home enrichment activities, child’s cognitive abilities, and child’s grades, indicating interwoven links between parental education, child stimulation, and child cognitive performance. These results add a new data-driven, multivariate perspective on links between household SER and the child’s developing functional connectome.

The Role Of Perceived Threats On Mental Health, Social, And Neurocognitive Youth Outcomes: A Multicontextual, Person-Centered Approach

Conley MI, Hernandez J, Salvati JM, Gee DG, Baskin-Sommers A. *Dev Psychopathol.* 2022 Mar 2; 1-22. Epub ahead of print.

Perceived threat in youth's environments can elevate risk for mental health, social, and neurocognitive difficulties throughout the lifespan. However, few studies examine variability in youth's perceptions of threat across multiple contexts or evaluate outcomes across multiple domains, ultimately limiting our understanding of specific risks associated with perceived threats in different contexts. This study examined associations between perceived threat in youth's neighborhood, school, and family contexts at ages 9-10 and mental health, social, and neurocognitive outcomes at ages 11-12 within a large US cohort (N = 5525) enrolled in the Adolescent Brain Cognitive DevelopmentSM Study (ABCD Study®). Latent profile analysis revealed four distinct profiles: Low Threat in all contexts, Elevated Family Threat, Elevated Neighborhood Threat, and Elevated Threat in all contexts. Mixed-effect models and post hoc pairwise comparisons showed that youth in Elevated Threat profile had poorer mental health and social outcomes 2 years later. Youth in the Elevated Family Threat profile uniquely showed increased disruptive behavior symptoms, whereas

youth in the Elevated Neighborhood Threat profile predominantly displayed increased sleep problems and worse neurocognitive outcomes 2 years later. Together, findings highlight the importance of considering perceptions of threat across multiple contexts to achieve a more nuanced developmental picture.

[Five Recommendations For Using Large-Scale Publicly Available Data To Advance Health Among American Indian Peoples: The Adolescent Brain And Cognitive Development \(ABCD\) StudySM As An Illustrative Case](#) White EJ, Demuth MJ, Wiglesworth A, Coser AD, Garrett BA, Kominsky TK, Jernigan V, Thompson WK, Paulus M, Robin Aupperle RA. *Neuropsychopharmacology*. 2023; 48(2): 263-269.

American Indian and Alaska Native (AIAN) populations have suffered a history of exploitation and abuse within the context of mental health research and related fields. This history is rooted in assimilation policies, historical trauma, and cultural loss, and is promulgated through discrimination and disregard for traditional culture and community knowledge. In recognition of this history, it is imperative for researchers to utilize culturally sensitive approaches that consider the context of tribal communities to better address mental health issues for AIAN individuals. The public availability of data from large-scale studies creates both opportunities and challenges when studying mental health within AIAN populations. This manuscript has two goals; first, showcase an example of problematic use of Adolescent Brain Cognitive Development (ABCD) StudySM data to promulgate stereotypes about AIAN individuals and, second, in partnership with collaborators from Cherokee Nation, we provide five recommendations for utilizing data from publicly available datasets to advance health research in AIAN populations. Specifically, we argue for the consideration of (1) the heterogeneity of the communities represented, (2) the importance of focusing on AIAN health and well-being, (3) engagement of relevant communities and AIAN community leaders, (4) consideration of historical and ongoing injustices, and (5) engagement with AIAN regulatory agencies or review boards. These recommendations are founded on principles from broader indigenous research efforts emphasizing community-engaged research and principles of Indigenous Data Sovereignty and Governance.

[Morphometric Dissimilarity Between Cortical And Subcortical Areas Underlies Cognitive Function And Psychiatric Symptomatology: A Preadolescence Study From ABCD](#) Wu X, Palaniyappan L, Yu G, Zhang K, Seidlitz J, Liu Z, Kong X, Schumann G, Feng J, Sahakian BJ, Robbins TW, Bullmore E, Zhang J. *Mol Psychiatry*. 2022 December 6. Online ahead of print. Preadolescence is a critical period characterized by dramatic morphological changes and accelerated cortico-subcortical development. Moreover, the coordinated development of cortical and subcortical regions underlies the emerging cognitive functions during this period. Deviations in this maturational coordination may underlie various psychiatric disorders that begin during preadolescence, but to date these deviations remain largely uncharted. We constructed a comprehensive whole-brain morphometric similarity network (MSN) from 17 neuroimaging modalities in a large preadolescence sample (N = 8908) from Adolescent Brain Cognitive Development (ABCD) study and investigated its association with 10 cognitive subscales and 27 psychiatric subscales or diagnoses. Based on the MSNs, each brain was clustered into five modules with distinct cytoarchitecture and evolutionary relevance. While morphometric correlation was positive within modules, it was negative between modules, especially between isocortical and paralimbic/subcortical modules; this developmental dissimilarity was genetically linked to synapse and neurogenesis. The cortico-subcortical dissimilarity becomes more pronounced longitudinally in healthy children, reflecting developmental differentiation of segregated cytoarchitectonic areas.

Higher cortico-subcortical dissimilarity (between the isocortical and paralimbic/subcortical modules) were related to better cognitive performance. In comparison, children with poor modular differentiation between cortex and subcortex displayed higher burden of externalizing and internalizing symptoms. These results highlighted cortical-subcortical morphometric dissimilarity as a dynamic maturational marker of cognitive and psychiatric status during the preadolescent stage and provided insights into brain development.

INTRAMURAL RESEARCH

[Compulsive Drug-Taking Is Associated With Habenula-Frontal Cortex Connectivity](#) Duan Y, Tsai PJ, Salmeron BJ, Hu Y, Gu H, Lu H, Cadet JL, Stein EA, Yang Y. Proc Natl Acad Sci U S A. 2022; 119(50): e2208867119.

As a critical node connecting the forebrain with the midbrain, the lateral habenula (LHb) processes negative feedback in response to aversive events and plays an essential role in value-based decision-making. Compulsive drug use, a hallmark of substance use disorder, is attributed to maladaptive decision-making regarding aversive drug-use-related events and has been associated with dysregulation of various frontal-midbrain circuits. To understand the contributions of frontal-habenula-midbrain circuits in the development of drug dependence, we employed a rat model of methamphetamine self-administration (SA) in the presence of concomitant footshock, which has been proposed to model compulsive drug-taking in humans. In this longitudinal study, functional MRI data were collected at pretraining baseline, after 20 d of long-access SA phase, and after 5 d of concomitant footshock coupled with SA (punishment phase). Individual differences in response to punishment were quantified by a "compulsivity index (CI)," defined as drug infusions at the end of punishment phase, normalized by those at the end of SA phase. Functional connectivity of LHb with the frontal cortices and substantia nigra (SN) after the punishment phase was positively correlated with the CI in rats that maintained drug SA despite receiving increasing-intensity footshock. In contrast, functional connectivity of the same circuits was negatively correlated with CI in rats that significantly reduced SA. These findings suggest that individual differences in compulsive drug-taking are reflected by alterations within frontal-LHb-SN circuits after experiencing the negative consequences from SA, suggesting these circuits may serve as unique biomarkers and potential therapeutic targets for individualized treatment of addiction.

[Calcium Activity Is A Degraded Estimate Of Spikes](#) Hart EE, Gardner MPH, Panayi MC, Kahnt T, Schoenbaum G. Calcium activity is a degraded estimate of spikes. Curr Biol. 2022; 32(24): 5364-5373.

Recording action potentials extracellularly during behavior has led to fundamental discoveries regarding neural function-hippocampal neurons respond to locations in space, motor cortex neurons encode movement direction, and dopamine neurons signal reward prediction errors-observations undergirding current theories of cognition, movement, and learning. Recently it has become possible to measure calcium flux, an internal cellular signal related to spiking. The ability to image calcium flux in anatomically or genetically identified neurons can extend our knowledge of neural circuit function by allowing activity to be monitored in specific cell types or projections, or in the same neurons across many days. However, while initial studies were grounded in prior unit recording work, it has become fashionable to assume that calcium is identical to spiking, even though the spike-to-fluorescence transformation is nonlinear, noisy, and unpredictable under real-world conditions. It remains an open question whether calcium provides a high-fidelity representation of single-unit activity in awake, behaving subjects. Here, we have addressed this question by recording both signals in the lateral orbitofrontal cortex (OFC) of rats during olfactory

discrimination learning. Activity in the OFC during olfactory learning has been well-studied in humans, nonhuman primates, and rats, where it has been shown to signal information about both the sensory properties of odor cues and the rewards they predict. Our single-unit results replicated prior findings, whereas the calcium signal provided only a degraded estimate of the information available in the single-unit spiking, reflecting primarily reward value.

[Incubation Of Palatable Food Craving Is Associated With Brain-Wide Neuronal Activation In Mice](#) Madangopal R, Szelenyi ER, Nguyen J, Brenner MB, Drake OR, Pham DQ, Shekara A, Jin M, Choong JJ, Heins C, Komer LE, Weber SJ, Hope BT, Shaham Y, Golden SA. Proc. Natl. Acad. Sci. U.S.A. 2022; 119(45): e2209382119.

Studies using rodent models have shown that relapse to drug or food seeking increases progressively during abstinence, a behavioral phenomenon termed “incubation of craving”. Mechanistic studies of incubation of craving have focused on specific neurobiological targets within preselected brain areas. Recent methodological advances in whole-brain immunohistochemistry, clearing, and imaging now allow unbiased brainwide cellular resolution mapping of regions and circuits engaged during learned behaviors. However, these whole-brain imaging approaches were developed for mouse brains, while incubation of drug craving has primarily been studied in rats, and incubation of food craving has not been demonstrated in mice. Here, we established a mouse model of incubation of palatable food craving and examined food reward seeking after 1, 15, and 60 abstinence days. We then used the neuronal activity marker Fos with intact brain mapping procedures to identify corresponding patterns of brain-wide activation. Relapse to food seeking was significantly higher after 60 abstinence days than after 1 or 15 days. Using unbiased ClearMap analysis, we identified increased activation of multiple brain regions, particularly corticostriatal structures, following 60 but not 1 or 15 abstinence days. We used orthogonal SMART2 analysis to confirm these findings within corticostriatal and thalamocortical subvolumes and applied expert-guided registration to investigate subdivision and layer-specific activation patterns. Overall, we 1) identified brain-wide activity patterns during incubation of food seeking using complementary analytical approaches and 2) provide a single-cell resolution whole-brain atlas that can be used to identify functional networks and global architecture underlying the incubation of food craving.

[A Red Nucleus-VTA Glutamate Pathway Underlies Exercise Reward And The Therapeutic Effect Of Exercise On Cocaine Use](#) He Y, Madeo G, Liang Y, Zhang C, Hempel B, Liu X, Mu L, Liu S, Bi GH, Galaj E, Zhang HY, Shen H, McDevitt RA, Gardner EL, Liu QS, Xi ZX. Sci Adv. 2022; 8(35): eabo1440.

Physical exercise is rewarding and protective against drug abuse and addiction. However, the neural mechanisms underlying these actions remain unclear. Here, we report that long-term wheel-running produced a more robust increase in c-fos expression in the red nucleus (RN) than in other brain regions. Anatomic and functional assays demonstrated that most RN magnocellular portion (RNm) neurons are glutamatergic. Wheel-running activates a subset of RNm glutamate neurons that project to ventral tegmental area (VTA) dopamine neurons. Optogenetic stimulation of this pathway was rewarding, as assessed by intracranial self-stimulation and conditioned place preference, whereas optical inhibition blocked wheel-running behavior. Running wheel access decreased cocaine self-administration and cocaine seeking during extinction. Last, optogenetic stimulation of the RNm-to-VTA glutamate pathway inhibited responding to cocaine. Together, these findings indicate that physical exercise activates a specific RNm-to-VTA glutamatergic pathway, producing exercise reward and reducing cocaine intake.

Spironolactone As A Potential New Pharmacotherapy For Alcohol Use Disorder: Convergent Evidence From Rodent And Human Studies

Farokhnia M, Rentsch CT, Chuong V, McGinn MA, Elvig SK, Douglass EA, Gonzalez LA, Sanfilippo JE, Marchette RCN, Tunstall BJ, Fiellin DA, Koob GF, Justice AC, Leggio L, Vendruscolo LF. *Mol Psychiatry*. 2022; 27(11): 4642-4652.

Evidence suggests that spironolactone, a nonselective mineralocorticoid receptor (MR) antagonist, modulates alcohol seeking and consumption. Therefore, spironolactone may represent a novel pharmacotherapy for alcohol use disorder (AUD). In this study, we tested the effects of spironolactone in a mouse model of alcohol drinking (drinking-in-the-dark) and in a rat model of alcohol dependence (vapor exposure). We also investigated the association between spironolactone receipt for at least 60 continuous days and change in self-reported alcohol consumption, using the Alcohol Use Disorders Identification Test-Consumption (AUDIT-C), in a pharmacoepidemiologic cohort study in the largest integrated healthcare system in the US. Spironolactone dose-dependently reduced the intake of sweetened or unsweetened alcohol solutions in male and female mice. No effects of spironolactone were observed on drinking of a sweet solution without alcohol, food or water intake, motor coordination, alcohol-induced ataxia, or blood alcohol levels. Spironolactone dose-dependently reduced operant alcohol self-administration in dependent and nondependent male and female rats. In humans, a greater reduction in alcohol consumption was observed among those who received spironolactone, compared to propensity score-matched individuals who did not receive spironolactone. The largest effects were among those who reported hazardous/heavy episodic alcohol consumption at baseline (AUDIT-C ≥ 8) and those exposed to ≥ 50 mg/day of spironolactone. These convergent findings across rodent and human studies demonstrate that spironolactone reduces alcohol use and support the hypothesis that this medication may be further studied as a novel pharmacotherapy for AUD.

GRANTEE HONORS AND AWARDS

Tallie Z. Baram, M.D., Ph.D., Professor at the University of California (UC), Irvine was awarded the Public Impact Award from the UC Irvine Center for the Neurobiology of Learning and Memory and elected to the Scientific Review Board of the Brain and Behavior Research Foundation.

Michael Bruchas, Ph.D., Professor at the University of Washington, was awarded the Daniel H. Efron Award from the American College of Neuropsychopharmacology (ACNP) for outstanding basic research contributions to neuropsychopharmacology.

Gail D’Onofrio, M.D., M.S., of the CTN New England Consortium Node, was awarded the 2022 American College of Emergency Physicians’ Innovation and Excellence in Behavioral Health and Addiction Medicine Award.

Linda Dwoskin, Ph.D., Professor at the University of Kentucky, was awarded the 2022 Innovator Award by the College on Drug Dependence. This award is given to individuals who have developed innovative approaches in basic science, clinical research, or treatment and prevention science that reflect ground-breaking strides with potential for significant impact in the field of drug dependence.

Damien Fair, Ph.D., Professor at the University of Minnesota, was awarded the Eva King Killam Award from the ACNP for outstanding translational research contributions to neuropsychopharmacology.

David Fiellin, M.D., of the CTN New England Consortium Node, was named the new Editor in Chief of the *Journal of Addiction Medicine*.

Terry Jernigan, Ph.D., Distinguished Professor of Cognitive Science, Psychiatry and Radiology at UC San Diego, received a recognition as one of the 1,000 best female researchers in the world from Research.com (<https://research.com/scientists-rankings/best-female-scientists>).

Asaf Keller Ph.D., Professor at the University of Maryland, was awarded the Donald E. Wilson Distinguished Professorship and Chair of Anatomy and Neurobiology.

Justus Klebschull, Ph.D., Assistant Professor Johns Hopkins University and Avenir Award winner in Genetics and Epigenetics, was awarded a Packard Foundation Fellowship in Science and Engineering.

Lee-Yuan Liu-Chen, Ph.D., Professor at Temple University, was elected Treasurer of the International Narcotics Research Conference.

Chris McCurdy, Ph.D., Professor at the University of Florida, was appointed to the Frank A. Duckworth Eminent Scholar Chair of the College of Pharmacy, in support of his work in drug discovery. Chris’s research has been focused on the design, synthesis, and development of drugs to treat pain, and mental and substance use disorders. He is internationally recognized for his research on the chemistry and pharmacology of kratom and kratom alkaloids.

José Szapocznik, Ph.D., a Principal Investigator of CTN’s Florida Node Alliance and Professor and Chair Emeritus at the Department of Public Health Sciences at the University of Miami Miller School of Medicine, was elected to the Academy of Science, Engineering and Medicine of Florida (ASEMFL). In recognition of José’s four and a half decades of work developing and testing interventions in the areas of mental health and drug abuse, ASEMFL elected him for exemplary contributions to prevention science and globally impactful substance use prevention for youth and families.

Kamilla Venner, Ph.D., of the CTN Southwest Node, was awarded the Duane Mackey Award at the 2022 Great Plains Behavioral Health Conference for her presentation titled “Creating Bridges and Culturally Adapting Western Science.” The purpose of the Dr. Duane Mackey ‘Waktaya Naji’ Award is to acknowledge individuals who, in their addiction research careers, have made significant contributions in education, science, mentoring, and service among Native American peoples. and have untiringly promoted and espoused the ideals of equality and justice for all peoples.

Kelly Young-Wolff, PhD, MPH, a clinical psychologist, Kaiser Permanente Division of Research and Health Systems Node investigator who studies substance use among vulnerable populations, including pregnant women, was awarded the 2022 Young Professional Award by the American Public Health Association (APHA) Maternal and Child Health (MCH) Section. The Young Professional Award recognizes an MCH section member aged 40 or younger who has made a significant contribution to maternal and child health, and who has potential for making a sustained and meaningful impact on the field. Young-Wolff was recognized for her “outstanding program of research, teaching, and mentoring.”

STAFF HONORS AND AWARDS

2022 NIH DIRECTOR'S AWARDS to NIDA Staff

Scientific/Medical – For exemplary leadership of NIDA's Services Research Branch, the Justice Community Opioid Innovation Network, and the HEAL TRPTOA team.

Tisha Wiley

Mentoring – For exemplary performance while demonstrating significant leadership, skill, and ability in serving as a mentor.

Yavin Shaham

Recognition Across NIH – The following NIDA staff are recognized as part of groups hosted by another Institute or Center.

National Heart, Lung, and Blood Institute

Amy Newman

National Institute of Allergy and Infectious Diseases

Minnjuan Flournoy Floyd

Vasundhara Varthakavi

Richard Jenkins

National Institute of General Medical Sciences

Kathleen Etz

National Institute of Mental Health

Christine Frate

Jeffrey Moore

Christopher Halstead

Brian O'Laughlin

Kyle Miller

National Institute of Neurological Disorders and Stroke

Albert Avila

National Institute of Nursing Research

Minnjuan Flournoy Floyd

Julia Zur

Jonathan Pollock

Office of the Director

Osama Abulseoud

Karran Phillips

Albert Avila

Daniel Stimson

Kathleen Etz

Stacy Yung

2022 NIDA DIRECTOR'S AWARDS

Individual Award: In recognition of your leadership in planning and establishing a CTN-wide Community Representative Council (CIRCL) to improve the way that NIDA CTN Research is planned, carried out, and used.

Carmen Rosa

Individual Award: In recognition of your exemplary contributions to developing the next generation of addiction science researchers and recruiting highly diverse NIDA review panels members in support of the NIDA mission.

Rebekah Feng

Group Award: In recognition of your exemplary contributions over and above your significant workloads to leverage the lessons learned and accomplishments of ABCD to ensure the successful launch of HBCD.

Auxiliary HBCD Launch Team:

Elizabeth Hoffman

Kim LeBlanc

Katia Howlett

Traci Murray

Group Award: In recognition of your exemplary leadership and teamwork in completing highly expedited review meetings in response to multiple NIH Helping to End Addictions Long-term (HEAL) initiatives.

Scientific Review Branch HEAL Team:

Jenny Browning

Jason Hill

Sindhu Madathil

Sheila Pirooznia

Dharm Rathore

Nicole Slade-Acty

Trinh Tran

Soyoun Cho

Angelina Jordan

Preethy Nayar

Ipolia Ramadan

Michael Renwick

Marisa Srivareerat

Brian Wolff

Individual Award: In recognition of your outstanding contributions to innovate and advance health services research in support of the NIDA mission.

Sarah Duffy

Individual Award: In recognition of your outstanding prevention research leadership in support of NIDA's mission.

Amy Goldstein

Individual Award: In recognition of your advancing the NIDA HIV basic research program by opening new approaches and avenues for HIV research.

Da-Yu Wu

Group Award: In recognition of your bringing to light the importance of research on neurocognitive mechanisms of structural racism.

Organizing Committee for the Workshop on Neurocognitive Mechanisms of Structural Racism:

Crystal Barksdale

Gaya Dowling

Aria Crump

Mark Egli

*Kathy Etz
Nic Johnston
Jessica McKlveen
Vani Pariyadath
Mauricio Rangel Gomez*

*Elizabeth Hoffman
Collene Lawhorn
Holly Moore
Janani Prabhakar
Alexa Romberg*

Individual Award: In recognition of your outstanding scientific leadership of the Medications Discovery and Toxicology Program in DTMC.

Nathan Appel

Individual Award: In recognition of your work to develop clinical outcome assessments and alternative endpoints for substance use disorder treatment.

Tanya Ramey

Group Award: In recognition of your leadership and collaboration to develop an NIH workshop which assessed the potential of psychedelic agents as therapeutics for neuropsychiatric indications.

Psychedelics as Therapeutics Workshop Team:

Aidan Hampson

Kevin Walton

Carlos Zarate

Jenica Patterson

Steven Zalcman

Group Award: In recognition of the major and collaborative contribution of the "NIDA IRP Spironolactone Team" towards the understanding of the biological mechanisms of alcohol use disorder.

NIDA IRP Spironolactone Team:

Vicky Chuong

Sophie Elvig

Luis Gonzales

Lorenzo Leggio

Adrienne McGinn

Brendan Tunstall

Eliza Douglass

Mehdi Farokhnia

George Koob

Renata Marchette

Jenna Sanfilippo

Leandro Vendruscolo

Group Award: In recognition of the outstanding collaborative effort of IRP NIDA researchers to characterize the first CRISPR-based Oprm1-Cre knock-in transgenic rat to be used globally by other researchers.

TEAM MOR Cre:

Lindsay Altidor

Jennifer Bossert

Jonathan Chow

Ida Fredriksson

Brandon Harvey

Michael Michaelides

Christopher Richie

Francois Vautier

Ashley Batista

Kiera Caldwell

Sarah Claypool

Juan Gomez

Carlos Mejias-Aponte

David Reiner

Yavin Shaham

Individual Award: In recognition of your harmonizing over 100 variables from 12 different federal, state, and private administrative data sources across the 4 HCS sites.

Jennifer Villani

Group Award: In recognition of the of developing and leading the implementation of the first ever trans-NIH Diversity Supplement Professional Development and Networking Workshop, August 30-31, 2022.

NIH Diversity Supplement and Professional Development Workshop:
Albert Avila *Angela Holmes*
Isabela Lopes

Group Award: In recognition of the special contribution to develop a coordinated suite of funding opportunity announcements to promote racial equity in NIDA’s research portfolio.

Racial Equity Initiative (REI), Research Gaps and Opportunities FOA Development Subgroup:

Keva Collier Kidemu *Aria Crump*
Nathaniel Davis *Bethany Deeds*
Sheba Dunston *Kathy Etz*
John Fedota *Evan Herrmann*
Keisher Highsmith *Angela Holmes*
Mary Kautz *Heather Kimmel*
Flair Lindsey *Holly Moore*
Vani Pariyadath *Alexa Romberg*
Carmen Rosa *Vasundhrara Varthakavi*

Group Award: In recognition of your leadership of NIDA's relinquishment of one-third of HQ space in a compressed timetable.

HQ 3WFN Space Consolidation Leadership Team:
Dave Daubert *Amy Doster*
Gregg Friedman *Berhane Yitbarek*

Group Award: In recognition of the Tiger Team's development and launch of the NIDA Workplace Flexibility Policy.

NIDA Workplace Flexibility Policy Tiger Team:
Allison Adams *Molly Cluster*
Gloria Dabbondanza *Amy Doster*
Deon Harvey *Keisha Miller*
Leslie Premo

Individual Award: In recognition of your outstanding execution of bringing the NIDA Strategic Plan to publication.

Julie Frost-Bellgowan

Group Award: In recognition of role in marshaling evidence to support the work of the HHS Behavioral Health Coordinating Council.

Behavioral Health Coordination Council Support Team:
Elizabeth Barfield *Emily Einstein*
Daniel Stimson

NIDA’s Director’s Award for Collaboration (Group): In recognition of your leadership in establishing a new partnership with the FDA Center for Devices and Radiological Health.

Joint NIDA/FDA Public Workshops on Medical Devices for Opioid Use Workforce:
Leonardo Angelone *Stacie Gutowski*
Jonathan Pollock

NIDA’s Director’s Award for Collaboration (Group): In recognition of the DTMC and IRMB’s successful modernization and Implementation of NIDA's Drug Inventory Supply & Control System (DISCS).

NIDA Drug Inventory Supply & Control System (DISCS) Modernization Team:

Stuart Berlin

Enoch Chuang

Gregg Friedman

Rik Kline

Wayne Mascarella

Judy Noble

Andy Pruchniewski

Idriss Tchakounte

Marcus Chin

Rumeet Dutta

Teresa Jester

Anil Koninty

Kelly Mathews

Amy Plank

Ken Rehder

Robert Walsh

NIDA’s Director’s Award for Diversity (Individual): In recognition of your championing the promotion of diversity, equity and inclusion (DEI) for the NIDA workplace and the extramural community.

Mary Kautz

NIDA’s Director’s Award for Diversity (Individual): In recognition for being a true champion for diversity and inclusion at NIDA.

Yeka Aponte

NIDA’s Director’s Rising Star Award (Individual): In recognition of your accomplishments, creativity, energy, and ability to inspire others at NIDA.

Katherine Cole

Sunila Nair

Morgen Slager

Rachel Evans

Jorge Vizcaino-Riveros

Janette Lebron

Vicky Perez

NIDA’s Director’s Innovator Award (Individual): In recognition of his work in the development of novel transcranial magnetic stimulation technology for treatment of substance use disorders.

Hanbing Lu

NIDA’s Director’s Innovator Award (Individual): In recognition of the devoted work to envision new ways to bridge the gap between NIDA academic discoveries and products that benefit citizens.

Elena Koustova

NIDA’s Director’s PHS NIH Commissioned Corps Award Commendation Medal

(Individual): In recognition of your outstanding leadership, sustained performance, and continued outreach to local underserved communities in support of NIH/NIDA during COVID crisis.

John Hubbard

NIDA’s Director’s PHS NIH Commissioned Corps Award Unit Commendation (Group): In recognition of their teamwork and superior performance exhibited in planning coordinating, and successful execution of a workplace BLS program.

OCD BLS Clinical Staff:

John Hubbard

Lois Blue

Stacy Yung

Kathy Lightfoot

Length of Service Award – 30 years

Sarah Duffy
Julie Huffman

Charles Marschke

Length of Service Award – 50 years

Paul Hillery

OTHER NIDA STAFF AWARDS

Carlos Blanco, M.D., Ph.D., Director of NIDA’s Division of Epidemiology, Prevention and Services Research (DESPR), was selected for membership in the National Academy of Medicine.

Kauê Machado Costa, Ph.D., Postdoctoral Visiting Fellow in the laboratory of Geoffrey Schoenbaum, M.D., Ph.D., at the NIDA Intramural Research Program (IRP), was named an Allen Institute Next Generation Leader (NGL). The Allen Institute has announced six new NGLs to be members of a unique neuroscience advisory panel comprising early-career investigators. The panel will help advise research efforts at the Allen Institute for Brain Science, the MindScope Program, and the Allen Institute for Neural Dynamics.

Gisela Andrea Camacho Hernandez, Ph.D., Postdoctoral Visiting Fellow at the NIDA IRP, was the Selected Highlighted Trainee Author for the month of November 2022 for her article in the *Journal of Pharmacology and Experimental Therapeutics*. She received a Travel Award for the 7th Chemistry & Pharmacology of Drug Abuse meeting held in Boston, MA in August 2022.

John Hubbard, PA-C, of the NIDA IRP Office of the Clinical Director, has been awarded the 2022 Humanitarian and Service Physician Assistant of the Year Award from the Maryland Academy of Physician Assistants. This award recognizes a physician assistant who has shown incredible service to the community, providing care to the most vulnerable and underserved populations, and/or those in crisis.

Iván Montoya, M.D., M.P.H., Acting Director of the Division of Therapeutics and Medical Consequences (DTMC), received the International Society of Addiction Medicine Lifetime Achievement Award in recognition of his outstanding contributions in the field of addiction psychiatry. Iván was also named Honorary Professor of the University of Valencia (Spain).

Emily Wang, M.D., of DESPR’s Services Research Branch was selected as a 2022 MacArthur Fellow.

STAFF CHANGES

New Appointments

Shkeda Johnson, M.P.A., NIDA Deputy Executive Officer, will be serving as the NIDA Acting Executive Officer starting January 3, 2023. The search for the next NIDA Executive Officer is underway; application receipt closed on December 30, 2022. The announcement of a selection will be made after clearance by NIH, The Department of Health and Human Services, and the Office of Personnel Management, as required for this position. During this interim period, **Patrick Shirdon, M.S.**, National Institute on Aging Executive Officer, has agreed to serve as the NIDA Deputy Ethics Counselor.

Aria Crump, Sc.D., has been selected as Director of NIDA's Office of Diversity and Health Disparities (ODHD) and Deputy Director of the Office of Research Training, Diversity, and Disparities (ORTDD). She received her doctoral degree from the Johns Hopkins University Bloomberg School of Public Health and completed postdoctoral studies in prevention research at the Eunice Kennedy Shriver National Institute of Child Health and Human Development. After teaching and conducting research at the University of Maryland in the Department of Public and Community Health, Aria embarked on a more than 20-year career at NIH as a Health Scientist Administrator in the Prevention Research Branch of DESPR.

New Staff

Robert Bailey, J.D., joined the Office of Acquisitions (OA) Team in October 2022 as a member of the NIDA section. Before joining the OA team, Robert spent more than 7 years working for the Department of Defense's (DoD) Defense Logistics Agency (DLA). He began his career with DLA as an Attorney in the Office of Counsel. He then transitioned to contracting where he leveraged his experience as an attorney to continue to support DoD. Prior to his time with the federal government, Robert spent 5 years in private practice, specializing in civil litigation and transactional work.

Karinne Chevalier-Davis, M.S., M.B.A., joined NIDA in December 2022 as a Senior Grants Management Specialist. Prior to joining NIDA, Karinne was a Grants Management Specialist at the National Institute of Allergy and Infectious Diseases (NIAID) for 2 years during which she managed a diverse grant portfolio. Before coming to NIH, Karinne was a Senior Grants and Contracts Analyst at Johns Hopkins University, where she was responsible for managing pre-award activities.

Katherine Cole, Ph.D. is a Scientific Program Manager for the HEALthy Brain and Child Development (HBCD) Study within the Division of Extramural Research (DER) at NIDA. Prior to joining NIDA, she was a research fellow and postdoctoral fellow at the National Institute of Mental Health (NIMH) Division of Intramural Research Programs for 8 years. She worked on a longitudinal study of pubertal neurodevelopment in typically developing children. Katherine is experienced in both human and non-human primate neuroimaging, with a focus on the impact of sex steroid hormones and stress on brain structure and function.

Morris Flood, D.H.Sc., joined NIDA's Office of Translational Initiatives and Program Innovations on October 24, 2022. Morris serves as a Health Scientist Administrator (Program Officer) in the SBIR/STTR Program assisting in the commercialization of Non-FDA regulated devices and tools. Morris comes to us from SAMHSA/CSAP (Center for Substance Abuse Prevention), where he was a Public Health Advisor (Project Officer) in the Division of Primary Prevention.

Tiffany Jackson joined NIDA in January 2023 as a Senior Grants Management Specialist. Prior to joining NIDA, Tiffany was a Grants Management Specialist at NIAID where she managed a diverse grant portfolio. Before coming to NIH, Tiffany was a Senior Grants and Contracts Analyst at Johns Hopkins University where she was responsible for compiling sponsored project proposals.

Krista Lyles joined NIDA's Grants Management Branch on September 12, 2022. Krista comes to us from the Agency for Healthcare Research and Quality where she served as a management analyst for 9 years. Her most recent work was largely in grants closeout, but she is familiar with several routine aspects of grants management. In her spare time, Krista has enjoyed learning how to code.

Sean Lynch, Ph.D., LCSW, has joined DESPR's Services Research Branch as a Program Officer and will administer a portfolio of research grants on various topics (e.g., behavioral health workforce, telehealth, and rural settings). He has more than 15 years of experience in behavioral health services research and the evaluation of physical and behavioral health programs.

Jeanette Marketon, Ph.D., has joined the DER as NIDA's Receipt and Referral Officer. She comes from the National Cancer Institute (NCI) where she served primarily as a Referral Officer, but also acted as a Scientific Review Officer (SRO), as needed. Prior to joining the NCI, Jeanette worked in grants administration and scientific review for a number of agencies, including the Cancer Prevention and Research Institute of Texas, the Congressionally Directed Medical Research Programs, and the U.K. Medical Research Council.

Nikkilette 'Nikki' McKay joined the NIDA Grants Management Branch in December 2022. Prior to joining NIDA, Nikki was a Contracting Officer for NCI and the DoD, holding a FAC-C Level III Certification and an unlimited warrant. She also worked in NIH's Office of the Director as an Other Transaction Agreement Specialist. Before joining the Federal Government, Nikki worked as a Contractor for the Department of Energy and in the private sector.

Rosemary Moody, M.P.P., joined NIDA in September 2022 as a Program Specialist in the DER's Office of Extramural Policy (OEP). Rosemary was previously employed at the National Institute of Environmental Health Sciences (NIEHS) as a Program Specialist for the Division of Extramural Research and Training. Rosemary will work closely with the Council Coordinator, OEP Team, and OEP Director in support of NIDA's Operations Planning Processes (OPS) and National Advisory Council on Drug Abuse activities, working in close collaboration with other DER staff.

Caitlin Moyer, Ph.D., joined NIDA's DER as an SRO in September 2022. Caitlin received her Ph.D. in Neuroscience from the Center for Neuroscience at University of Pittsburgh in 2013. Her postdoctoral work at University of California Santa Cruz focused on investigating the synaptic basis of motor dysfunction in an animal model of childhood heavy metal exposure. She subsequently joined *PLoS Medicine* as an Associate Editor, a journal focused on advancing clinical care, novel medical science breakthroughs, and informing health policy.

Michele Pastorek joined NIDA's Office of Management as a Contract Specialist on October 9, 2022. Prior to coming to NIDA, Michele was a Contract Specialist with the Department of Veterans Affairs Great Lakes Acquisition Center. In that role, she was involved in the acquisition of many different types of products and services. Prior to that, she held positions in the private sector as a Senior Buyer with Generac Power Systems, Buyer II with DRS Power and Control Technologies, and a Purchasing Agent with Konecranes.

Rachel Tillage, Ph.D., joined NIDA in November 2022 as a Scientific Program Specialist in the Office of Science Policy and Communications (OSPC). Rachel originally worked at NIDA in August 2021 as an American Association for the Advancement of Science, Science and Technology Policy Fellow. Rachel received her Ph.D. in neuroscience from Emory University, focusing on the role of the noradrenergic system in stress-related disorders to identify potential new therapeutic targets. In her new role, Rachel will be supporting trans-NIH initiatives, such as the Helping to End Addiction Long-term (HEAL) Initiative, developing tools for data-driven program administration and contributing broadly to science policy efforts within the office.

Kelley Villers rejoined NIDA as a Program Specialist in the ORTDD in October 2022. Before her return to NIDA, she spent three years as an Army Civilian program manager supporting the U.S. Army Garrison Fort Detrick and the Medical Research and Development Command. Prior to her time as an Army Civilian, Kelley served as Executive Assistant to Deputy Director of NIDA. She began her Federal Civilian service with NIAID.

Marian Wachtel, Ph.D., joined DER as the Director of the OEP. She comes to NIDA from NIAID, where she served as a Scientific Initiatives Officer in the Office of Initiative Development, NIAID Challenge Manager, and Program Officer in the Division of Microbiology and Infectious Diseases. In addition, Marian completed an extended detail at the NIH Office of Extramural Research Guide Office, performing policy review and quality control of Funding Opportunity Announcements and Notices published by the NIH. Prior to this, she was an SRO at the Center for Scientific Review, Infectious Diseases and Microbiology Integrated Review Group, managing study sections to review both basic and applied research, as well as small business applications.

Staff Departures

Albert Avila, Ph.D., departed NIDA in October 2022, after 14 years of service, for a new position at NIBIB. For the past 9 years, Albert has been the Director of NIDA's ODHD, including the last 2 years with additional responsibilities as Deputy Director of ORTDD. Albert joined NIDA following 5 years at the NIDCR where he worked after completing his Ph.D. in neuro-psychopharmacology at Georgetown University. He will be joining NIBIB to foster the national biomedical engineering workforce through collaborations across the research, academic, and government domains.

Rebecca Mao, Ph.D., a Social and Behavioral Health Scientist Administrator in DESPR's Services Research Branch, left NIDA on November 20, 2022, for a position with the Centers for Medicare & Medicaid Services.

Retirements

Ann Anderson, M.D., Medical Officer at DTMC's Clinical Medical Branch, retired on January 28th, 2022, after 23 years of Federal Service at NIDA. Ann began her career in NIDA in 1999, serving as a Medical Safety Officer or Lead Investigator for several large multicenter clinical trials, including ones that studied selegiline, lofexidine, bupropion, and modafinil. Ann managed the Division's Data and Safety Monitoring Board and served on the NIDA IRP Institutional Review Board in Baltimore. She oversaw the research portfolio on therapeutics development for women and children affected by substance use disorders, including medication to treat neonatal opioid withdrawal.

Nathan (Nate) Appel, Ph.D., Toxicologist in the Medications Discovery, and Toxicology Branch (MDTB) of DTMC, retired on January 28th, 2022, after 35 years of Federal service. Nate was a Staff Fellow at NIDA's Addiction Research Center in Baltimore (now the IRP) from 1988 to 1992, then worked at the Food and Drug Administration. He subsequently joined the NIDA Extramural Program in 1999 as a Toxicologist in DTMC. Nate was responsible for coordinating the Division's contract- and grant-based medications discovery and preclinical safety assessment efforts. Nate also coordinated grant-related issues in medications discovery and activities of the Addiction Treatment Discovery Program and directed the Division's Toxicology Program. Most recently, Nate served as Acting Chief of the MDTB.

Joellen M. Austin, M.P.Aff., M.S.M., retired effective December 31, 2022, following 7 years with NIDA and more than 33 years working at NIH. Joellen joined NIDA in October 2015 as the NIDA Deputy Director for Management (DDM). Prior to that, she served as the Executive Officer at NIEHS and the National Institute of Neurological Disorders and Stroke. As NIDA DDM, Joellen led NIDA's management operations and strategy. She brought a renewed emphasis on accountability, fairness, excellence, communication, and transparency. Joellen also helped to create a culture of inclusiveness and appreciation. Among her myriad achievements, Joellen expanded transparency within NIDA during the COVID-19 pandemic by holding monthly town hall meetings alongside NIDA Director Dr. Nora Volkow. Her goal was to ensure staff knew that leadership cares as much about the NIDA mission as the health and safety of all the people at the Institute.

Dave Daubert retired effective December 31, 2022, after working at NIDA for more than 20 years, most recently as the NIDA Deputy Executive Officer. Dave first joined the federal government in 1982 under a student program while attending college and later became a full-time employee with NIMH, one of the three Institutes that were part of the Alcohol, Drug Abuse, and Mental Health Administration before they were incorporated into NIH. Dave joined NIDA in March 2002 as Deputy Chief of the Headquarters (HQ) Management Analysis and Services Branch. Since that time, he has served other critical roles, including HQ Administrative Branch Chief, Deputy Executive Officer, Acting Executive Officer, and directing NIDA's Ethics Program. One of Dave's major accomplishments was his management of NIDA's move from the Neuroscience Center to Three White Flint North during the unprecedented and challenging COVID-19 era.

Jurij Mojsiak, M.S., Pharmacologist at DTMC's Clinical Medical Branch, retired on December 31, 2022, after 31 years of Federal service at NIDA. Jurij began his career in 1992, where he served as Clinical Trials Specialist directing and managing Phase 1 clinical trials. Jurij is one of the founding members of NIDA's Medications Development Division (MDD) and made major contributions to the management of the Data Safety Monitoring Board, clinical trial contracts, and interagency agreements.

Suzie Stinson, M.B.A., retired at the end of January 2023 from the NIDA Office of Acquisitions after a successful career in federal service. Suzie joined the Health Resources and Services Administration in 1990 as a secretary in an acquisition office. She became a Procurement Assistant after about a year and a Contract Specialist afterward. In December 2002, Suzie moved to NIMH and received a Contracting Officer warrant. Suzie came to NIDA in 2006 where she served as Branch Chief and later as a Policy Analyst.



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