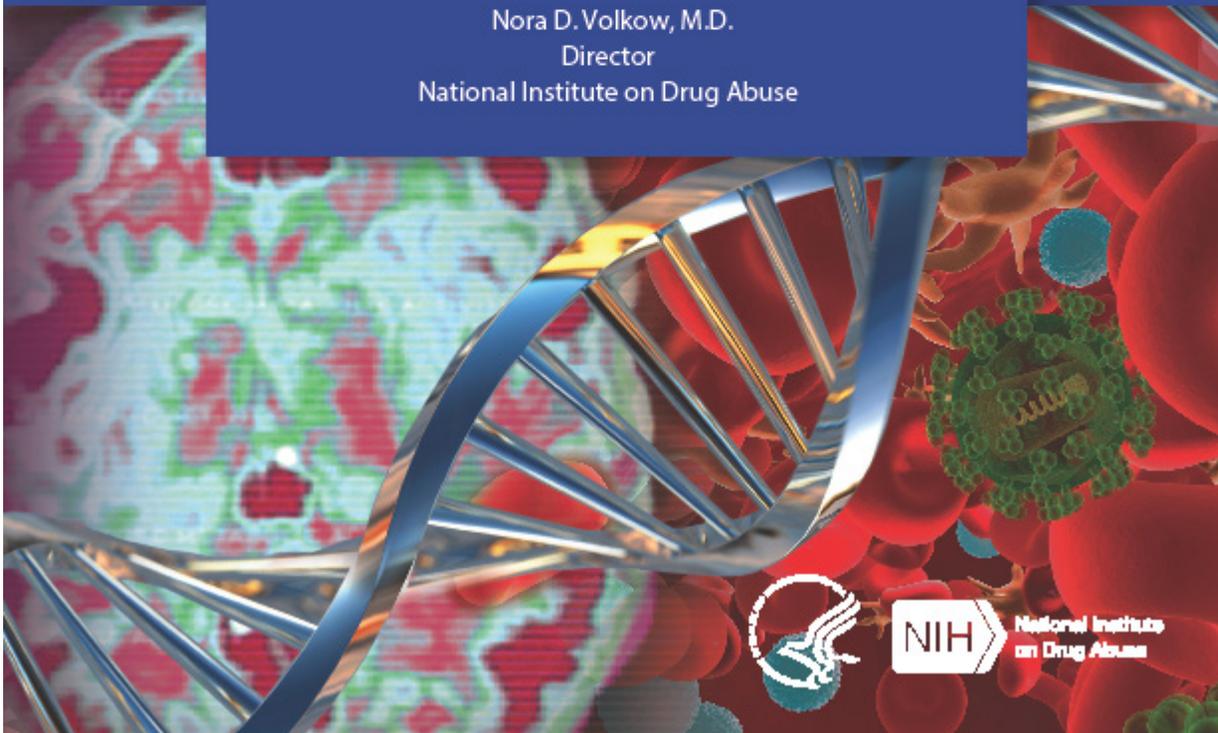




DIRECTOR'S REPORT

to the
National Advisory Council on Drug Abuse
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National Institute
on Drug Abuse

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RESEARCH HIGHLIGHTS

BASIC AND BEHAVIORAL RESEARCH

[Cell Type-Specific Transcriptional Programs In Mouse Prefrontal Cortex During Adolescence And Addiction](#) Bhattacharjee A, Djekidel MN, Chen R, Chen W, Tuesta LM, Zhang Y. Nat Commun. 2019 Sept 13; 10(1): 4169.

Coordinated activity-induced transcriptional changes across multiple neuron subtypes of the prefrontal cortex (PFC) play a pivotal role in encoding and regulating major cognitive behaviors. Yet, the specific transcriptional programs in each neuron subtype remain unknown. Using single-cell RNA sequencing (scRNA-seq), here we comprehensively classify all unique cell subtypes in the PFC. We analyze transcriptional dynamics of each cell subtype under a naturally adaptive and an induced condition. Adaptive changes during adolescence (between P21 and P60), a highly dynamic phase of postnatal neuroplasticity, profoundly impacted transcription in each neuron subtype, including cell type-specific regulation of genes implicated in major neuropsychiatric disorders. On the other hand, an induced plasticity evoked by chronic cocaine addiction resulted in progressive transcriptional changes in multiple neuron subtypes and became most pronounced upon prolonged drug withdrawal. Our findings lay a foundation for understanding cell type-specific postnatal transcriptional dynamics under normal PFC function and in neuropsychiatric disease states.

[Heroin Cue-Evoked Astrocytic Structural Plasticity At Nucleus Accumbens Synapses Inhibits Heroin Seeking](#) Kruyer A, Scofield MD, Wood D, Reissner KJ, Kalivas PW. Biol Psychiatry. 2019 Dec 1; 86(11): 811-819.

Glutamatergic synapses in the nucleus accumbens regulate the motivation to relapse to opioid use, and downregulation of glutamate transporters on astroglial processes adjacent to accumbens synapses contributes to heroin seeking induced by cues. Here the authors determined how astroglial processes respond to heroin cues. Rats were trained to self-administer heroin and were reinstated by heroin-conditioned cues. Astroglial proximity to accumbens synapses was quantified and the functional consequence of astroglial morphological plasticity on cued heroin seeking was determined. After heroin extinction, there was a reduction in astroglial synaptic proximity that was restored during 15 minutes of cued heroin seeking but returned to extinction levels by 120 minutes. Ezrin knockdown reduced astroglial association with synapses and potentiated cued heroin seeking. The results suggest that cue-induced heroin seeking transiently increases synaptic proximity of accumbens astrocytes and this is compensatory. Additionally, preventing cue-induced morphological plasticity in astrocytes potentiated heroin seeking.

[Dissociable Neural Substrates Of Opioid And Cocaine Use Identified Via Connectome-Based Modelling](#) Lichenstein SD, Scheinost D, Potenza MN, Carroll KM, Yip SW. Mol Psychiatry. 2019 Nov 12; 1-11. [Epub ahead of print].

Treatment outcomes for opioid use disorder vary widely across individuals and relapse rates remain high. Understanding neural mechanisms of treatment response may facilitate the development of personalized and/or novel treatment approaches. Methadone-maintained, polysubstance-using individuals participated in fMRI scanning before and after substance-use treatment. Connectome-based predictive modeling (CPM)—a recently developed, whole-brain

approach—was used to identify pretreatment connections associated with abstinence during the 3-month treatment. Follow-up analyses were conducted to determine the specificity of the identified opioid abstinence network across different brain states (cognitive vs. reward task vs. resting-state) and different substance use outcomes (opioid vs. cocaine abstinence). Posttreatment fMRI data were used to assess network changes over time and within-subject replication. To determine further clinical relevance, opioid abstinence network strength was compared with healthy subjects. CPM identified an opioid abstinence network ($p = 0.018$), characterized by stronger within-network motor/sensory connectivity, and reduced connectivity between the motor/sensory network and medial frontal, default mode, and frontoparietal networks. This opioid abstinence network was anatomically distinct from a previously identified cocaine abstinence network. Relationships between abstinence and opioid and cocaine abstinence networks replicated across multiple brain states but did not generalize across substances. Network connectivity measured at posttreatment related to abstinence at 6-month follow-up ($p < 0.009$). Healthy comparison subjects displayed intermediate network strengths relative to treatment responders and nonresponders. These data indicate dissociable anatomical substrates of opioid vs. cocaine abstinence. Results may inform the development of novel opioid-specific treatment approaches to combat the opioid epidemic.

Agonist Selectivity And Ion Permeation In The $\alpha 3\beta 4$ Ganglionic Nicotinic

Receptor Gharpure A, Teng J, Zhuang Y, Noviello CM, Walsh RM Jr, Cabuco R, Howard RJ, Zaveri NT, Lindahl E, Hibbs RE. *Neuron*. 2019 Nov 6; 104(3): 501-511.

Nicotinic acetylcholine receptors are pentameric ion channels that mediate fast chemical neurotransmission. The $\alpha 3\beta 4$ nicotinic receptor subtype forms the principal relay between the central and peripheral nervous systems in the autonomic ganglia. This receptor is also expressed focally in brain areas that affect reward circuits and addiction. Here, the authors used cryo-electron microscopy, electrophysiology and molecular dynamic simulations to interrogate the structure and function of the $\alpha 3\beta 4$ nicotinic receptor in complex with nicotine and the $\alpha 3\beta 4$ -selective ligand AT-1001 in a lipid environment. The structures reveal much of the architecture of the intracellular domain, where mutagenesis experiments and simulations define residues governing ion conductance.

A Discrete Presynaptic Vesicle Cycle For Neuromodulator Receptors Jullié D, Stoeber M, Sibarita J-B, Zieger HL, Bartol TM, Arttamangkul S, Sejnowski TJ, Hosy E, von Zastrow M. *Neuron*. 2020 Feb 19; 105: 1-15.

A major function of GPCRs is to inhibit presynaptic neurotransmitter release, requiring ligand-activated receptors to couple locally to effectors at terminals. The current understanding of how this is achieved is through receptor immobilization on the terminal surface. Here, we show that opioid peptide receptors, GPCRs that mediate highly sensitive presynaptic inhibition, are instead dynamic in axons. Opioid receptors diffuse rapidly throughout the axon surface and internalize after ligand-induced activation specifically at presynaptic terminals. We delineate a parallel regulated endocytic cycle for GPCRs operating at the presynapse, separately from the synaptic vesicle cycle, which clears activated receptors from the surface of terminals and locally reinserts them to maintain the diffusible surface pool. We propose an alternate strategy for achieving local control of presynaptic effectors that, opposite to using receptor immobilization and enforced proximity, is based on lateral mobility of receptors and leverages the inherent allostery of GPCR-effector coupling.

EPIDEMIOLOGY, PREVENTION, AND SERVICES RESEARCH

Adolescents' Awareness Of The Nicotine Strength And E-Cigarette Status Of JUUL E-Cigarettes Morean ME, Bold KW, Kong G, Gueorguieva R, Camenga DR, Simon P, Jackson A, Cavallo DA, Krishnan-Sarin S. *Drug Alcohol Depend.* 2019; 204: 107512.

JUUL e-cigarettes are popular among youth. However, it is unknown whether adolescents understand that 5% JUUL pods contain a high nicotine concentration or consider JUULs to be e-cigarettes. 3170 students from 4 Connecticut high schools completed a school-based survey (May-October 2018). Students reported on lifetime and past-month JUUL use and perceived JUUL nicotine strength (low/medium/high/don't know) when no information about nicotine concentration was provided and, subsequently, when informed JUULs contain 5% nicotine. Students reported whether they believe JUULs are e-cigarettes (no/yes/don't know). Students were never JUUL users (56.6%), ever users (13.2%), and past-month users (30.2%). When no information was provided, students reported that JUULs contain low (10.5%), medium (26.9%), or high nicotine levels (31.1%); 31.4% did not know. When informed JUULs contain 5% nicotine, students were more likely to believe JUUL's nicotine strength was low (29.5%) or medium (29.3%) than high (21.3%) and less likely to report not knowing (19.9%). 39% of students believed JUULs are not e-cigarettes or did not know. Most students were unaware of JUUL's high nicotine concentration, with more believing that JUULs contain low or medium nicotine concentrations when informed JUULs contain 5% nicotine. Thus, youth may misinterpret the nicotine concentration printed on JUUL pod packaging, raising concerns about inadvertent exposure to high nicotine levels and dependence risk. Further, 39% of adolescents believed JUULs are not e-cigarettes or were unsure. Regulatory efforts are needed to establish understandable nicotine concentration labels, require products to be labeled accordingly, and clarify what products constitute e-cigarettes.

Cannabis Use Is Associated With Increased Risk Of Cigarette Smoking Initiation, Persistence, And Relapse Among Adults In The United States Weinberger AH, Delnevo CD, Wyka K, Gbedemah M, Lee J, Copeland J, Goodwin RD. *Nicotine Tob Res.* 2019 May 21. [Epub ahead of print].

Despite increasing use of cannabis, it is unclear how cannabis use is related to cigarette transitions. This study examined cannabis use and smoking initiation, persistence, and relapse over 1 year among a nationally representative sample of US adults. Data were from US adults (≥ 18 years) who completed two waves of longitudinal data from the Population Assessment of Tobacco and Health Study (Wave 1, 2013–2014; Wave 2, 2014–2015; $n = 26\,341$). Logistic regression models were used to calculate the risk of Wave 2 incident smoking among Wave 1 never-smokers, smoking cessation among Wave 1 smokers, and smoking relapse among Wave 1 former smokers by Wave 1 cannabis use. Analyses were adjusted for age, gender, race/ethnicity, income, and education. Among Wave 1 never-smokers, cannabis use was associated with increased odds of initiation of nondaily (adjusted odds ratio [AOR] = 5.50, 95% confidence limits [CL] = 4.02–7.55) and daily cigarette smoking (AOR = 6.70, 95% CL = 4.75–9.46) 1 year later. Among Wave 1 daily smokers, cannabis use was associated with reduced odds of smoking cessation (AOR = 0.36, 95% CL = 0.20–0.65). Among Wave 1 former smokers, cannabis use was associated with increased odds of relapse to daily and nondaily cigarette smoking (daily AOR = 1.90, 95% CL = 1.11–3.26; nondaily AOR = 2.33, 95% CL = 1.61–3.39). Cannabis use was associated with increased cigarette smoking initiation, decreased smoking cessation, and increased smoking relapse among adults in the United States. Increased public education about

the relationship between cannabis use and cigarette smoking transitions may be needed as cannabis use becomes more common among US adults. As cannabis use increases in the United States and other countries, an evaluation of the relationships of cannabis use to other health-related behaviors (e.g., cigarette smoking) is needed to understand the population-level impact of legalization. Little is known about associations between cannabis use and cigarette smoking transitions (1) using recent longitudinal data, (2) among adults, and (3) examining transitions other than smoking initiation (e.g., smoking relapse). Our results suggest that among US adults, cannabis use was associated with increased cigarette smoking initiation among never-smokers, decreased cigarette smoking cessation among current smokers, and increased cigarette smoking relapse among former smokers.

Effectiveness Of Facebook Groups To Boost Participation In A Parenting Intervention

Epstein M, Oesterle S, Haggerty KP. *Prev Sci.* 2019; 20(6): 894-903.

Although family-based prevention programs have been shown to be effective at reducing adolescent substance use, it is often difficult and costly to recruit and retain parents in programs administered in person. The current study tested whether program engagement and parenting practices could be improved by offering parents in a self-directed family program access to a private Facebook group. Parents of middle school children (N = 103) were recruited through paid Facebook ads to a 5-week self-directed teen substance use prevention program to be completed at home together by parents and their children. Two thirds of parents (N = 72) were randomly assigned to a moderated private Facebook group that provided a forum for parents in the study to interact with each other, and one third (N = 31) were randomized to use the intervention materials without additional support. Relatively few parents participated in the Facebook group and most did not find the experience useful. However, satisfaction with the program assessed 3 months after program completion was high among all parents and most parents engaged with the materials, irrespective of Facebook group assignment. Overall, parents reported significantly lower conflict and more household rules 6 months post-intervention compared to baseline. Parenting practices did not change more among those assigned to the Facebook group than among parents who used the materials on their own. The current findings suggest that providing opportunities for parents to interact online while participating in a self-directed family intervention may not help to increase engagement or improvements in parenting practices, particularly when few parents engage with each other.

Acute Care, Prescription Opioid Use, And Overdose Following Discontinuation Of Long-Term Buprenorphine Treatment For Opioid Use Disorder

Williams AR, Samples H, Crystal S, Olfson M. *Am J Psychiatry.* 2019 Dec 2. [Epub ahead of print].

OBJECTIVE: Although buprenorphine treatment reduces risk of overdose and death in opioid use disorder, most patients discontinue treatment within a few weeks or months. Adverse health outcomes following buprenorphine discontinuation were compared among patients who were successfully retained beyond 6 months of continuous treatment, a minimum treatment duration recently endorsed by the National Quality Forum.

METHODS: A retrospective longitudinal cohort analysis was performed using the MarketScan multistate Medicaid claims database (2013-2017), covering 12 million beneficiaries annually. The sample included adults (18-64 years of age) who received buprenorphine continuously for ≥ 180 days by cohorts retained for 6-9 months, 9-12 months, 12-15 months, and 15-18 months. For outcome assessment in the post-discontinuation period, patients had to be continuously

enrolled in Medicaid for 6 months after buprenorphine discontinuation. Primary adverse outcomes included all-cause emergency department visits, all-cause inpatient hospitalizations, opioid prescriptions, and drug overdose (opioid or non-opioid).

RESULTS: Adverse events were common across all cohorts, and almost half of patients (42.1%-49.9%) were seen in the emergency department at least once. Compared with patients retained on buprenorphine for 6-9 months (N=4,126), those retained for 15-18 months (N=931) had significantly lower odds of emergency department visits (odds ratio=0.75, 95% CI=0.65-0.86), inpatient hospitalizations (odds ratio=0.79, 95% CI=0.64-0.99), and filling opioid prescriptions (odds ratio=0.67, 95% CI=0.56-0.80) in the 6 months following discontinuation. Approximately 5% of patients across all cohorts experienced one or more medically treated overdoses.

CONCLUSIONS: Risk of acute care service use and overdose were high following buprenorphine discontinuation irrespective of treatment duration. Superior outcomes became significant with treatment duration beyond 15 months, although rates of the primary adverse outcomes remained high.

[Intensive Models Of Hepatitis C Care For People Who Inject Drugs Receiving Opioid Agonist Therapy: A Randomized Controlled Trial](#) Akiyama MJ, Norton BL, Arnsten JH, Agyemang L, Heo M, Litwin AH. *Ann Intern Med.* 2019; 170(9): 594-603.

Many people who inject drugs (PWID) are denied treatment for hepatitis C virus (HCV) infection, even if they are receiving opioid agonist therapy (OAT). Research suggests that HCV in PWID may be treated effectively, but optimal models of care for promoting adherence and sustained virologic response (SVR) have not been evaluated in the direct-acting antiviral (DAA) era. To determine whether directly observed therapy (DOT) and group treatment (GT) are more effective than self-administered individual treatment (SIT) in promoting adherence and achieving SVR among PWID receiving OAT. Three-group, randomized controlled trial conducted from October 2013 to April 2017. (ClinicalTrials.gov: NCT01857245). Three OAT programs in Bronx, New York. Persons aged 18 years and older with genotype 1 HCV infection who were willing to receive HCV therapy on site in the OAT program. Of 190 persons screened, 158 were randomly assigned to a study group and 150 initiated treatment: DOT (n = 51), GT (n = 48), and SIT (n = 51). 2 intensive interventions (DOT and GT) and 1 control condition (SIT). Primary: adherence, measured by using electronic blister packs. Secondary: HCV treatment completion and SVR 12 weeks after treatment completion. Mean age was 51 years; 65% of participants had positive results on urine drug testing during the 6 months before treatment, and 75% reported ever injecting drugs. Overall adherence, estimated from mixed-effects models using the daily timeframe, was 78% (95% CI, 75% to 81%) and was greater among participants randomly assigned to DOT (86% [CI, 80% to 92%]) than those assigned to SIT (75% [CI, 70% to 81%]; difference, 11% [CI, 5% to 18%]; Bonferroni-corrected P = 0.001). No significant difference in adherence was observed between participants randomly assigned to GT (80% [CI, 74% to 86%]) and those assigned to SIT (difference, 4.7% [CI, -2% to 11%]; Bonferroni-corrected P = 0.29). The HCV treatment completion rate was 97%, with no differences among groups (P = 0.53). Overall SVR was 94% (CI, 89% to 97%); the SVR rate was 98% in the DOT group, 94% in the GT group, and 90% in the SIT group (P = 0.152). These findings may not be generalizable to PWID not enrolled in OAT programs. All models of onsite HCV care delivered to PWID in OAT programs resulted in high SVR, despite ongoing drug use. Directly observed therapy was associated with greater adherence than SIT.

TREATMENT RESEARCH

Combination Lorcaserin And Nicotine Patch For Smoking Cessation Without Weight Gain

Rose JE, Davis JM. *Nicotine Tob Res.* 2019 Oct 7. [Epub ahead of print].

This study explored the efficacy of combination lorcaserin and nicotine patch for smoking cessation treatment and prevention of postsmoking cessation weight gain. We conducted a trial in which 61 adult daily smokers were asked to quit smoking using a combination of lorcaserin and nicotine patch. During the first 2 weeks of treatment prior to the quit day, participants were randomized to receive either lorcaserin (10 mg twice daily) plus nicotine patch (21 mg) or placebo plus nicotine patch (21 mg). Following this 2-week period, participants received both medications for 12 weeks. Outcomes included 4-week continuous smoking abstinence at the end of treatment (weeks 7-10 postquit attempt), weight change, ad libitum smoking, withdrawal symptoms, and ratings of cigarette reward. Biochemically confirmed continuous smoking abstinence from 7 to 10 weeks postquit attempt was 31.1% (90% confidence interval, 21.4%-40.8%). Participants who quit smoking showed no weight gain; in fact, mean weight change was minus 0.16 kg (SD = 3.27) over the study period. There was an unexpected but strong association ($p = .006$) between a decrease in sensory enjoyment of smoking and successful quit outcome on this regimen. During the prequit randomization period, lorcaserin versus placebo reduced the impact of smoking to relieve craving for cigarettes as well as the sensory enjoyment of smoking ($p = .005$). Adherence and tolerability to lorcaserin and nicotine patch was good. The combination of lorcaserin and nicotine patch was well tolerated, associated with a relatively high smoking abstinence rate, and effectively prevented weight gain associated with quitting smoking. This report provides an important contribution to the literature because it details evidence of a medication combination-lorcaserin and nicotine-that is effective for smoking cessation and for ameliorating weight gain associated with smoking cessation. For many smokers, post cessation weight gain is a major obstacle to quitting, and this medication combination provides a suitable treatment option for these smokers. NCT02906644.

Clinical Validation Of Reduction In Cocaine Frequency Level As An Endpoint In Clinical Trials For Cocaine Use Disorder

Roos CR, Nich C, Mun CJ, Babuscio TA, Mendonca J, Miguel A, DeVito EE, Yip SW, Witkiewitz K, Carroll KM, Kiluk BD. *Drug Alcohol Depend.* 2019 Dec 1; 205: 107648.

Despite calls for non-abstinence endpoints in randomized clinical trials (RCTs) for cocaine use disorder, there is a lack of data validating non-abstinence endpoints. We conducted a clinical validation of reduction in cocaine frequency level as a non-abstinence endpoint in RCTs for cocaine use disorder (CUD). We utilized a pooled dataset ($n = 716$; 63.6 % male, 51.4 % non-Hispanic white) from seven RCTs for CUD. We specified three cocaine frequency levels at baseline and end of treatment (EOT): abstinence, low frequency (1-4 days/month), and high frequency (5+ days/month). Multiple regression analyses were conducted. Among the sample, 38.3 % had at least a one-level reduction from baseline to EOT, whereas 61.7 % did not change/increased frequency level. At least a one-level reduction in cocaine frequency level from baseline to EOT versus no change/increase was significantly associated with better functioning up to one year following treatment on measures of cocaine use, as well as psychological, employment, legal, and other drug use problem severity domains of the Addiction Severity Index (ASI). We also conducted analyses only among those at the high frequency level at baseline and

found those who reduced to low frequency use at EOT had similar outcomes at follow-up as those who reduced to abstinence. At least a one-level reduction in cocaine frequency level from pretreatment to EOT can be a clinically meaningful endpoint given its relation to sustained clinical benefit up to one-year following treatment. These data parallel recent findings regarding reduction in drinking risk level among individuals with alcohol use disorder.

Relationships Between Marijuana Use, Severity Of Marijuana-Related Problems, And Health-Related Quality Of Life Liao J-Y, Mooney LJ, Zhu Y, Valdez J, Yoo C, Hser Y-I. *Psychiatry Res.* 2019; 279: 237-243.

Studies on the relationships between marijuana use and quality of life have reported mixed findings. Based on a survey of 123 marijuana users conducted in Los Angeles during 2017-2018, we investigated the relationships between marijuana use frequency, severity of marijuana-related problems, and health-related quality of life (HRQoL). Results indicated that (1) marijuana use frequency was positively related to severity of marijuana-related problems; (2) severity of marijuana-related problems was negatively related to mental domain of HRQoL but was not significantly related to physical domain of HRQoL; and (3) marijuana use frequency was positively associated with mental health symptoms and physical health conditions, and both in turn were negatively linked to mental and physical domains of HRQoL, respectively. Reduction of marijuana-related problems and mitigation of mental and physical health problems may improve HRQoL among marijuana users. The study findings may contribute to developing treatment interventions for marijuana use that simultaneously address marijuana-related problems and associated mental and physical issues.

The Effects Of Mitragynine And Morphine On Schedule-Controlled Responding And Antinociception In Rats Hiranita T, Leon F, Felix JS, Restrepo LF, Reeves ME, Pennington AE, Obeng S, Avery BA, McCurdy CR, McMahan, LR, Wilkerson JL. *Psychopharmacology (Berl).* 2019; 236(9): 2725-2734.

Mitragyna speciosa (kratom) may hold promise as both an analgesic and treatment for opioid use disorder. Mitragynine, its primary alkaloid constituent, is an opioid receptor ligand. However, the extent to which the in vivo effects of mitragynine are mediated by opioid receptors, or whether mitragynine interacts with other opioid agonists, is not fully established. The effects of mitragynine and the prototypical opioid agonist morphine were compared for their capacity to decrease operant responding for food delivery, and to increase response latency to a thermal stimulus. Male and female Sprague-Dawley rats responded under a multiple cycle fixed ratio 10 schedule of food delivery and were tested on a hot plate (52 °C) immediately after each cycle. Morphine and mitragynine were administered alone, in combination with each other, and in combination with the opioid antagonist naltrexone. Morphine and mitragynine dose-dependently decreased schedule-controlled responding; the ED₅₀ values were 7.3 and 31.5 mg/kg, respectively. Both drugs increased thermal antinociception; the ED₅₀ value for morphine was 18.3. Further, doses of naltrexone that antagonized morphine did not antagonize mitragynine. Mitragynine (17.8 mg/kg) did not alter the rate-decreasing or antinociceptive effects of morphine. The antinociceptive effects of mitragynine and morphine occur at doses larger than those that disrupt learned behavior. Opioid receptors do not appear to mediate the disruptive effects of mitragynine on learned behavior. Mitragynine had lesser antinociceptive effects than morphine, and these did not appear to be mediated by opioid receptors. The pharmacology of mitragynine includes a substantial non-opioid mechanism.

Effectiveness And Selectivity Of A Heroin Conjugate Vaccine To Attenuate Heroin, 6-Acetylmorphine, And Morphine Antinociception In Rats: Comparison With Naltrexone

Schwienteck KL, Blake S, Bremer PT, Poklis JL, Townsend EA, Negus SS, Banks ML. Drug Alcohol Depend. 2019; 204: 107501.

One emerging strategy to address the opioid crisis includes opioid-targeted immunopharmacotherapies. This study compared effectiveness of a heroin-tetanus toxoid (TT) conjugate vaccine to antagonize heroin, 6-acetylmorphine (6-AM), morphine, and fentanyl antinociception in rats. Adult male and female Sprague Dawley rats received three doses of active or control vaccine at weeks 0, 2, and 4. Vaccine pharmacological selectivity was assessed by comparing opioid dose-effect curves in 50 °C warm-water tail-withdrawal procedure before and after active or control heroin-TT vaccine. Route of heroin administration [subcutaneous (SC) vs. intravenous (IV)] was also examined as a determinant of vaccine effectiveness. Continuous naltrexone treatment (0.0032-0.032 mg/kg/h) effects on heroin, 6-AM, and morphine antinociceptive potency were also determined as a benchmark for minimal vaccine effectiveness. The heroin-TT vaccine decreased potency of SC heroin (5-fold), IV heroin (3-fold), and IV 6-AM (3-fold) for several weeks without affecting IV morphine or SC and IV fentanyl potency. The control vaccine did not alter potency of any opioid. Naltrexone dose-dependently decreased antinociceptive potency of SC heroin, and treatment with 0.01 mg/kg/h naltrexone produced similar, approximate 8-fold decreases in potencies of SC and IV heroin, IV 6-AM, and IV morphine. The combination of naltrexone and active vaccine was more effective than naltrexone alone to antagonize SC heroin but not IV heroin. The heroin-TT vaccine formulation examined is less effective, but more selective, than chronic naltrexone to attenuate heroin antinociception in rats. Furthermore, these results provide an empirical framework for future preclinical opioid vaccine research to benchmark effectiveness against naltrexone.

HIV/AIDS RELATED RESEARCH

Epitranscriptomic Addition Of m⁵C To HIV-1 Transcripts Regulates Viral Gene

Expression Courtney DG, Tsai K, Bogerd HP, Kennedy EM, Law BA, Emery A, Swanstrom R, Holley CL, Cullen BR. Cell Host Microbe. 2019 Aug 14; 26: 217-227.

How the covalent modification of mRNA ribonucleotides, termed epitranscriptomic modifications, alters mRNA function remains unclear. Using purified HIV-1 genomic RNA, the authors show that this RNA bears more epitranscriptomic modifications than the average cellular mRNA, with 5-methylcytosine (m⁵C) and 2'O-methyl modifications being particularly prevalent. The methyltransferase NSUN2 serves as the primary writer for m⁵C on HIV-1 RNAs. NSUN2 inactivation inhibits not only m⁵C addition to HIV-1 transcripts but also viral replication. This inhibition results from reduced HIV-1 protein, but not mRNA, expression, which in turn correlates with reduced ribosome binding to viral mRNAs. In addition, loss of m⁵C dysregulates the alternative splicing of viral RNAs. These data identify m⁵C as a post-transcriptional regulator of both splicing and function of HIV-1 mRNA, thereby affecting directly viral gene expression.

White Matter Abnormalities Linked To Interferon, Stress Response, And Energy Metabolism Gene Expression Changes In Older HIV-Positive Patients On Antiretroviral

Therapy Solomon IH, Chettimada S, Misra V, Lorenz DR, Gorelick RJ, Gelman BB, Morgello S, Gabuzda D. Mol Neurobiol. 2019 Nov 5. [Epub ahead of print].

Neurocognitive impairment (NCI) remains a significant cause of morbidity in human immunodeficiency virus (HIV)-positive individuals despite highly active antiretroviral therapy (HAART). White matter abnormalities have emerged as a key component of age-related neurodegeneration, and accumulating evidence suggests they play a role in HIV-associated neurocognitive disorders. Viral persistence in the brain induces chronic inflammation associated with lymphocytic infiltration, microglial proliferation, myelin loss, and cerebrovascular lesions. In this study, gene expression profiling was performed on frontal white matter from 34 older HIV+ individuals on HAART (18 with NCI) and 24 HIV-negative controls. Compared to HIV-controls, HIV+ individuals exhibited increased expression of genes related to interferon, MHC-1, and stress responses, myeloid cells, and T cells and decreased expression of genes associated with oligodendrocytes and energy metabolism in white matter. These findings correlated with increased white matter inflammation and myelin pallor, suggesting interferon (IRFs, IFITM1, ISG15, MX1, OAS3) and stress response (ATF4, XBP1, CHOP, CASP1, WARS) gene expression changes are associated with decreased energy metabolism (SREBF1, SREBF2, PARK2, TXNIP) and oligodendrocyte myelin production (MAG, MOG), leading to white matter dysfunction. Machine learning identified a 15-gene signature predictive of HIV status that was validated in an independent cohort. No specific gene expression patterns were associated with NCI. These findings suggest therapies that decrease chronic inflammation while protecting mitochondrial function may help to preserve white matter integrity in older HIV+ individuals.

Alterations To The Gastrointestinal Microbiome Associated With Methamphetamine Use Among Young Men Who Have Sex With Men Cook RR, Fulcher JA, Tobin NH, Li F, Lee DJ, Woodward C, Javanbakht M, Brookmeyer R, Shoptaw S, Bolan R, Aldrovandi GM, Gorbach PM. Sci Rep. 2019; 9(1): 14840.

Methamphetamine (MA) use is a major public health problem in the United States, especially among people living with HIV (PLWH). Many MA-induced neurotoxic effects are mediated by inflammation and gut microbiota may play a role in this process, yet the effects of MA on the microbiome have not been adequately explored. Therefore, we performed 16S rRNA gene sequencing on rectal swab samples from 381 men who have sex with men, 48% of whom were PLWH and 41% of whom used MA. We compared microbiome composition between MA users and non-users while testing for potential interactions with HIV and controlling for numerous confounders using inverse probability of treatment weighting. We found that MA use explained significant variation in overall composition ($R^2 = 0.005$, $p = 0.008$) and was associated with elevated *Fingoldia*, *Parvimonas*, *Peptoniphilus*, and *Porphyromonas* and reduced *Butyrivibrio* and *Faecalibacterium*, among others. Genera including *Actinomyces* and *Streptobacillus* interacted with HIV status, such that they were increased in HIV+ MA users. *Fingoldia* and *Peptoniphilus* increased with increasing frequency of MA use, among others. In summary, MA use was associated with a microbial imbalance favoring pro-inflammatory bacteria, including some with neuroactive potential and others that have previously been associated with poor HIV outcomes.

Internalized HIV Stigma Is Associated With Concurrent Viremia And Poor Retention In A Cohort Of US Patients In HIV Care Christopoulos KA, Neilands TB, Hartogensis W, Geng

EH, Saucedo J, Mugavero MJ, Crane HM, Fredericksen RJ, Moore RD, Mathews WC, Mayer KH, Chander G, Hurt CB, Johnson MO. *J Acquir Immune Defic Syndr.* 2019; 82(2): 116-123. The relationship of internalized HIV stigma to key care cascade metrics in the United States is not well established using large-scale, geographically diverse data. Center for AIDS Research Network of Integrated Clinical Systems (CNICS) cohort study. Beginning in February 2016, we administered a yearly, validated 4-item internalized HIV stigma scale (response scale 1 = strongly disagree to 5 = strongly agree, Cronbach's alpha 0.91) at 7 CNICS sites and obtained cohort data through November 2017. We compared mean stigma levels by sociodemographic characteristics and used multivariable logistic regression, controlling for the same sociodemographic covariates, to evaluate the association between mean stigma and (1) concurrent viremia; (2) missed visits; and (3) poor visit constancy. We used inverse probability weighting (IPW) to account for differences between patients who did and did not undergo stigma assessment. Of 13,183 CNICS patients, 6448 (49%) underwent stigma assessment. Mean stigma was 1.99 (SD 1.07), and 28.6% agreed/strongly agreed with at least 1 stigma question. Patients younger than 50 years, racial/ethnic minorities, cis-women, and heterosexuals had higher mean stigma. Mean stigma score was associated with concurrent viremia [adjusted odds ratio (AOR) 1.13, 95% confidence interval (CI): 1.02 to 1.25, P 0.02], missed visits (AOR 1.10, 95% CI: 1.02 to 1.19, P 0.01), and poor visit constancy, although the effect on visit constancy was attenuated in the IPW model (AOR 1.05, 95% CI: 0.98 to 1.13, P 0.17). Higher internalized HIV stigma had a modest but statistically significant association with concurrent viremia and poor retention in care. Further inquiry with prospective analyses is warranted.

Barriers And Facilitators To Recruitment And Enrollment Of HIV-Infected Individuals With Opioid Use Disorder In A Clinical Trial

Hoffman KA, Baker R, Kunkel LE, Waddell EN, Lum PJ, McCarty D, Korthuis PT. *BMC Health Serv Res.* 2019 Nov 21; 19(1): 862.

BACKGROUND: The CTN-0067 CHOICES trial tests implementation of extended-release naltrexone (XR-NTX) versus treatment-as-usual (TAU) for opioid use disorders (OUD) in HIV clinics to improve HIV viral suppression. The study team investigated recruitment strategies to elucidate the barriers and facilitators to recruitment and enrollment in the study.

MAIN TEXT: **Methods:** Semi-structured, in-depth, digitally recorded interviews were completed with study recruitment-related staff and medical providers (n = 26) from six participating HIV clinics in the fall of 2018. Interviews probed 1) factors that might prevent prospective participants from engaging in study recruitment and enrollment procedures and 2) strategies used by study staff that encourage eligible patient participation. Interviews were transcribed and thematically analyzed using a content analysis approach.

RESULTS: All respondents reported that barriers to recruitment and enrollment included challenging patient social and structural factors (e.g., homelessness or living environments with high substance use, criminal justice involvement), difficulty locating patients with unsuppressed HIV viral load and OUD within the HIV clinic, time-consuming study enrollment processes, and stigma around HIV and OUD which inhibited treatment seeking. Some respondents observed that distrust of research and researchers impeded recruitment activities in the community. A specific medication-related barrier was patient fear of opioid abstinence required prior to XR-NTX induction. Facilitators of recruitment included use of trusted peer outreach/recruitment workers in the community, hospitalizations that offered windows of opportunities for screening and XR-NTX induction, providing participant transportation, and partnerships with harm reduction organizations for referrals.

CONCLUSIONS: Though study personnel encountered barriers to recruitment in the CHOICES study, persons with untreated HIV and OUD can be enrolled in multisite clinical trials by using enhanced recruitment strategies that extend outside of the HIV clinic. Employing peer outreach workers and collaborating with syringe service programs may be especially helpful in facilitating recruitment and merit inclusion in similar study protocols.

Effect Of Patient Navigation On Transitions Of HIV Care After Release From Prison: A Retrospective Cohort Study Westergaard RP, Hochstatter KR, Andrews PN, Kahn D, Schumann CL, Winzenried AE, Sethi AK, Gangnon RE, Sosman JM. *AIDS Behav.* 2019; 23(9): 2549-2557.

Antiretroviral therapy is successfully administered to people living with HIV while they are incarcerated in most US prison systems, but interruptions in treatment are common after people are released. We undertook an observational cohort study designed to examine the clinical and psychosocial factors that influence linkage to HIV care and viral suppression after release from a single state prison system. In this report we describe baseline characteristics and 6-month post-incarceration HIV care outcomes for 170 individuals in Wisconsin. Overall, 114 (67%) individuals were linked to outpatient HIV care within 180 days of release from prison, and of these, 90 (79%) were observed to have HIV viral suppression when evaluated in the community. The strongest predictor of linkage to care in this study was participation in a patient navigation program: Those who received patient navigation were linked to care 84% of the time, compared to 60% of the individuals who received only standard release planning (adjusted OR 3.69, 95% CI 1.24, 10.96; $P < 0.01$). Findings from this study demonstrate that building and maintaining intensive patient navigation programs that support individuals releasing from prison is beneficial for improving transitions in HIV care.

Association Between Use Of Methadone, Other Central Nervous System Depressants, And QTc Interval-Prolonging Medications And Risk Of Mortality In A Large Cohort Of Women Living With Or At Risk For Human Immunodeficiency Virus Infection Tamraz B, Reisner L, French AL, King ST, Fischl MA, Ofotokun I, Kashuba A, Milam J, Murphy K, Augenbraun M, Liu C, Finley PR, Aouizerat B, Cocohoba J, Gange S, Bacchetti P, Greenblatt RM. *Pharmacotherapy.* 2019 Sep; 39(9): 899-911.

Associations between use of methadone, other central nervous system (CNS) depressants, and QTc interval-prolonging medications and risk of mortality was evaluated among human immunodeficiency virus (HIV)-infected and at-risk HIV-uninfected women from the multi-site, multi-observational Women's Interagency HIV Study (WIHS) cohort. A total of 4150 women enrolled in the WIHS study between 1994 and 2014 who were infected (3119 women) or not infected (1031 women) with HIV. Data on medication utilization were collected from all study participants via interviewer-administered surveys at 6-month intervals (1994-2014). Mortality was confirmed by National Death Index data. With age defining the time scale for the analysis, Cox proportional hazards models were used to estimate hazard ratios (HRs) for all-cause mortality in HIV-infected and -uninfected women and non-acquired immunodeficiency syndrome (AIDS) deaths in HIV-infected women. A total of 1046 deaths were identified, of which 429 were considered non-AIDS deaths. Use of benzodiazepines, CNS depressants (excluding methadone), and number of medications with conditional QTc interval-prolonging effects were each associated with all-cause mortality in multivariate models of HIV-infected women: hazard ratio (HR) 1.28, 95% confidence interval (CI) 1.01-1.60, $p=0.037$; HR 1.61, 95%

CI 1.35-1.92, $p < 0.0001$; and HR 1.15 per drug, 95% CI 1.00-1.33, $p = 0.047$, respectively. Other explanatory variables for all-cause mortality in this model included HIV viral load, CD4+ cell count, renal function, hemoglobin and albumin levels, HIV treatment era, employment status, existence of depressive symptoms, ever use of injection drugs, and tobacco smoking. Of interest, use of CNS depressants (excluding methadone) was also associated with non-AIDS deaths (HR 1.49, 95% CI 1.49-2.2, $p < 0.0001$). Although use of benzodiazepines and conditional QT interval-prolonging medications were associated with increased risk of non-AIDS mortality (HR 1.32 and 1.25, respectively), the effect was not statistically significant ($p > 0.05$). In this cohort of HIV-infected and at-risk HIV-uninfected women, use of benzodiazepines, CNS depressants, and conditional QTc interval-prolonging medications were associated with a higher risk of mortality independent of methadone and other well-recognized mortality risk factors.

CLINICAL TRIALS NETWORK RESEARCH

[Prevalence And Treatment Of Opioid Use Disorders Among Primary Care Patients In Six Health Systems](#) Lapham G, Boudreau DM, Johnson EA, Bobb JF, Matthews AG, McCormack J, Liu D, Samet JH, Saxon AJ, Campbell CI, Glass JE, Rossom RC, Murphy MT, Binswanger IA, Yarborough BJH, Bradley KA. Drug Alcohol Depend. 2019 Nov 15; 207: 107732. [Epub ahead of print].

BACKGROUND: The U.S. experienced nearly 48,000 opioid overdose deaths in 2017. Treatment of opioid use disorder (OUD) with buprenorphine is a recommended part of primary care, yet little is known about current U.S. practices in this setting. This observational study reports the prevalence of documented OUD and OUD treatment with buprenorphine among primary care patients in six large health systems.

METHODS: Adults with ≥ 2 primary care visits during a three-year period (10/1/2013-9/30/2016) in six health systems were included. Data were obtained from electronic health record and claims data, with measures, assessed over the three-year period, including indicators for documented OUD from ICD 9 and 10 codes and OUD treatment with buprenorphine. The prevalence of OUD treatment was adjusted for age, gender, race/ethnicity, and health system.

RESULTS: Among 1,368,604 primary care patients, 13,942 (1.0 %) had documented OUD, and among these, 21.0 % had OUD treatment with buprenorphine. For those with documented OUD, the adjusted prevalence of OUD treatment with buprenorphine varied across demographic and clinical subgroups. OUD treatment was lower among patients who were older, women, Black/African American and Hispanic (compared to white), non-commercially insured, and those with non-cancer pain, mental health disorders, greater comorbidity, and more opioid prescriptions, emergency department visits or hospitalizations.

CONCLUSIONS: Among primary care patients in six health systems, one in five with an OUD were treated with buprenorphine, with disparities across demographic and clinical characteristics. Less buprenorphine treatment among those with greater acute care utilization highlights an opportunity for systems-level changes to increase OUD treatment.

[Depressive Symptoms And Cannabis Use In A Placebo-Controlled Trial Of N-Acetylcysteine For Adult Cannabis Use Disorder](#) Tomko RL, Baker NL, Hood CO, Gilmore AK, McClure EA, Squeglia LM, McRae-Clark AL, Sonne SC, Gray KM. Psychopharmacology (Berl). 2019 Nov 11. [Epub ahead of print].

RATIONALE: Depression is common among individuals with cannabis use disorder (CUD), particularly individuals who present to CUD treatment. Treatments that consider this comorbidity are essential.

OBJECTIVES: The goal of this secondary analysis was to examine whether N-acetylcysteine (NAC) reduced depressive symptoms among adults (age 18-50) with CUD (N = 302) and whether the effect of NAC on cannabis cessation varied as a result of baseline levels of depression. Bidirectional associations between cannabis use amount and depression were also examined.

METHODS: Data for this secondary analysis were from a National Drug Abuse Treatment Clinical Trials Network (NIDA CTN) multi-site clinical trial for CUD. Adults with CUD (N = 302) were randomized to receive 2400 mg of NAC daily or matched placebo for 12 weeks. All participants received abstinence-based contingency management. Cannabis quantity was measured by self-report, and weekly urinary cannabinoid levels (11-nor-9-carboxy- Δ 9-tetrahydrocannabinol) confirmed abstinence. Depressive symptoms were measured by the Hospital Anxiety and Depression Scale.

RESULTS: Depressive symptoms did not differ between the NAC and placebo groups during treatment. There was no significant interaction between treatment and baseline depression predicting cannabis abstinence during treatment. Higher baseline depression was associated with decreased abstinence throughout treatment and a significant gender interaction suggested that this may be particularly true for females. Cross-lagged panel models suggested that depressive symptoms preceded increased cannabis use amounts (in grams) during the subsequent month. The reverse pathway was not significant (i.e., greater cannabis use preceding depressive symptoms).

CONCLUSIONS: Results from this study suggest that depression may be a risk factor for poor CUD treatment outcome and therefore should be addressed in the context of treatment. However, results do not support the use of NAC to concurrently treat co-occurring depressive symptoms and CUD in adults. **TRIAL REGISTRATION:** Clinicaltrials.gov: [NCT01675661](https://clinicaltrials.gov/ct2/show/study/NCT01675661).

Trajectory Classes Of Opioid Use Among Individuals In A Randomized Controlled Trial Comparing Extended-Release Naltrexone And Buprenorphine-Naloxone

Ruglass LM, Scodes J, Pavlicova M, Campbell ANC, Fitzpatrick S, Barbosa-Leiker C, Burlew K, Greenfield SF, Rotrosen J, Nunes EV Jr. Drug Alcohol Depend. 2019 Dec 1; 205: 107649.

OBJECTIVES: To advance our understanding of medication treatments for opioid use disorders (OUDs), identification of distinct subgroups and factors associated with differential treatment response is critical. We examined trajectories of opioid use for patients with OUD who were randomized to (but not in all cases inducted onto) buprenorphine-naloxone (BUP-NX) or extended-release naltrexone (XR-NTX), and identified characteristics associated with each trajectory.

METHODS: Growth mixture models (GMMs) were run to identify distinct trajectories of days of opioid use among a subsample of 535 individuals with OUD who participated in a 24-week randomized controlled trial (RCT; 2014-2016) of BUP-NX (n = 281) or XR-NTX (n = 254).

RESULTS: Four distinct opioid use trajectory classes were identified for BUP-NX (near abstinent/no use (59%); low use (13.2%); low use, increasing over time (15%); and moderate use, increasing over time (12.8%)). Three distinct opioid use trajectory classes were found for XR-NTX (near abstinent/no use (59.1%); low use (14.6%); and moderate use, increasing over time (26.4%)). Across both BUP-NX and XR-NTX, the near abstinent/no use class had the

highest number of medical management visits. Within BUP-NX, the low use class had a greater proportion of individuals with a previous successful treatment history compared with other classes. Within XR-NTX, the moderate use, increasing over time class had the highest proportion of Hispanic participants compared with other classes.

CONCLUSIONS: Findings highlight the significant heterogeneity of opioid use during a RCT of BUP-NX and XR-NTX and factors associated with opioid use patterns including medical management visits and history of treatment success.

Electronic Self-Administered Screening For Substance Use In Adult Primary Care Patients: Feasibility And Acceptability Of The Tobacco, Alcohol, Prescription Medication, And Other Substance Use (myTAPS) Screening Tool

Adam A, Schwartz RP, Wu LT, Subramaniam G, Laska E, Sharma G, Mili S, McNeely J. *Addict Sci Clin Pract.* 2019 Oct 15; 14(1): 39.

BACKGROUND: The TAPS Tool is a substance use screening and brief assessment instrument that was developed for use in primary care medical settings. It is one of the first screening instruments to provide rapid assessment of all commonly used substance classes, including illicit and prescription opioids, and is one of the only available screeners designed and validated in an electronic self-administered format (myTAPS). This secondary analysis of data from the TAPS Tool validation study describes the feasibility and acceptability of the myTAPS among primary care patients.

METHODS: Adult patients (N = 2000) from five primary care clinics completed the TAPS Tool on a tablet computer (myTAPS), and in an interviewer-administered format. Requests for assistance and time required were tracked, and participants completed a survey on ease of use, utilization of audio guidance, and format preference. Logistic regression was used to examine outcomes in defined subpopulations, including groups that may have greater difficulty completing an electronic screener, and those that may prefer an electronic self-administered approach.

RESULTS: Almost all participants (98.3%) reported that the myTAPS was easy to use. The median time to complete myTAPS screening was 4.0 min (mean 4.48, standard deviation 2.57). More time was required by participants who were older, Hispanic, Black, or reported non-medical prescription drug use, while less time was required by women. Assistance was requested by 25% of participants and was more frequently requested by those who with lower education (OR = 2.08, 95% CI 1.62-2.67) or age > 65 years (OR = 2.79, 95% CI 1.98-3.93). Audio guidance was utilized by 18.3% and was more frequently utilized by participants with lower education (OR = 2.01, 95% CI 1.54-2.63), age > 65 years (OR = 1.79, 95% CI 1.22-2.61), or Black race (OR = 1.30, 95% 1.01-1.68). The myTAPS format was preferred by women (OR = 1.29, 95% CI 1.00-1.66) and individuals with drug use (OR = 1.43, 95% CI 1.09-1.88), while participants with lower education preferred the interviewer-administered format (OR = 2.75, 95% CI 2.00-3.78).

CONCLUSIONS: Overall, myTAPS screening was feasible and well accepted by adult primary care patients. Clinics adopting electronic screening should be prepared to offer assistance to some patients, particularly those who are older or less educated, and should have the capacity to use an interviewer-administered approach when required.

Screening For Substance Use In Rural Primary Care: A Qualitative Study Of Providers And Patients

Saunders EC, Moore SK, Gardner T, Farkas S, Marsch LA, McLeman B, Meier A, Nesin N, Rotrosen J, Walsh O, McNeely J. J Gen Intern Med. 2019 Dec; 34(12): 2824-2832.

BACKGROUND: Substance use frequently goes undetected in primary care. Though barriers to implementing systematic screening for alcohol and drug use have been examined in urban settings, less is known about screening in rural primary care.

OBJECTIVE: To identify current screening practices, barriers, facilitators, and recommendations for the implementation of substance use screening in rural federally qualified health centers (FQHCs).

DESIGN: As part of a multi-phase study implementing electronic health record-integrated screening, focus groups (n = 60: all stakeholder groups) and individual interviews (n = 10 primary care providers (PCPs)) were conducted.

PARTICIPANTS: Three stakeholder groups (PCPs, medical assistants (MAs), and patients) at three rural FQHCs in Maine.

APPROACH: Focus groups and interviews were recorded, transcribed, and content analyzed. Themes surrounding current substance use screening practices, barriers to screening, and recommendations for implementation were identified and organized by the Knowledge to Action (KTA) Framework.

KEY RESULTS: Identifying the problem: Stakeholders unanimously agreed that screening is important, and that universal screening is preferred to targeted approaches. Adapting to the local context: PCPs and MAs agreed that screening should be done annually. Views were mixed regarding the delivery of screening; patients preferred self-administered, tablet-based screening, while MAs and PCPs were divided between self-administered and face-to-face approaches. Assessing barriers: For patients, barriers to screening centered around a perceived lack of rapport with providers, which contributed to concerns about trust, judgment, and privacy. For PCPs and MAs, barriers included lack of comfort, training, and preparedness to address screening results and offer treatment.

CONCLUSIONS: Though stakeholders agree on the importance of implementing universal screening, concerns about the patient-provider relationship, the consequences of disclosure, and privacy appear heightened by the rural context. Findings highlight that strong relationships with providers are critical for patients, while in-clinic resources and training are needed to increase provider comfort and preparedness to address substance use.

ADOLESCENT BRAIN COGNITIVE DEVELOPMENT STUDY RESEARCH

Associations Among Body Mass Index, Cortical Thickness, And Executive Function In Children

Laurent JS, Watts R, Adise S, Allgaier N, Chaarani B, Garavan H, Potter A, Mackey S. JAMA Pediatr. 2019 Dec 9. [Epub ahead of print].

IMPORTANCE: A total of 25.7 million children in the United States are classified as overweight or obese. Obesity is associated with deficits in executive function, which may contribute to poor dietary decision-making. Less is known about the associations between being overweight or obese and brain development.

OBJECTIVE: To examine whether body mass index (BMI) is associated with thickness of the cerebral cortex and whether cortical thickness mediates the association between BMI and executive function in children.

DESIGN, SETTING, AND PARTICIPANTS: In this cross-sectional study, cortical thickness maps were derived from T1-weighted structural magnetic resonance images of a large, diverse sample of 9 and 10-year-old children from 21 US sites. List sorting, flanker, matrix reasoning, and Wisconsin card sorting tasks were used to assess executive function.

MAIN OUTCOMES AND MEASURES: A 10-fold nested cross-validation general linear model was used to assess mean cortical thickness from BMI across cortical brain regions. Associations between BMI and executive function were explored with Pearson partial correlations. Mediation analysis examined whether mean prefrontal cortex thickness mediated the association between BMI and executive function.

RESULTS: Among 3190 individuals (mean [SD] age, 10.0 [0.61] years; 1627 [51.0%] male), those with higher BMI exhibited lower cortical thickness. Eighteen cortical regions were significantly inversely associated with BMI. The greatest correlations were observed in the prefrontal cortex. The BMI was inversely correlated with dimensional card sorting ($r = -0.088$, $P < .001$), list sorting ($r = -0.061$, $P < .003$), and matrix reasoning ($r = -0.095$, $P < .001$) but not the flanker task. Mean prefrontal cortex thickness mediated the association between BMI and list sorting (mean [SE] indirect effect, 0.014 [0.008]; 95% CI, 0.001-0.031) but not the matrix reasoning or card sorting task.

CONCLUSIONS AND RELEVANCE: These results suggest that BMI is associated with prefrontal cortex development and diminished executive functions, such as working memory.

[Prediction Of Neurocognition In Youth From Resting State fMRI](#) Sripada C, Rutherford S, Angstadt M, Thompson WK, Luciana M, Weigard A, Hyde LH, Heitzeg M. Mol Psychiatry. 2019 Aug 19. [Epub ahead of print].

Difficulties with higher-order cognitive functions in youth are a potentially important vulnerability factor for the emergence of problematic behaviors and a range of psychopathologies. This study examined 2013 9-10 year olds in the first data release from the Adolescent Brain Cognitive Development 21-site consortium study in order to identify resting state functional connectivity patterns that predict individual-differences in three domains of higher-order cognitive functions: General Ability, Speed/Flexibility, and Learning/Memory. For General Ability scores in particular, we observed consistent cross-site generalizability, with statistically significant predictions in 14 out of 15 held-out sites. These results survived several tests for robustness including replication in split-half analysis and in a low head motion subsample. We additionally found that connectivity patterns involving task control networks and default mode network were prominently implicated in predicting differences in General Ability across participants. These findings demonstrate that resting state connectivity can be leveraged to produce generalizable markers of neurocognitive functioning. Additionally, they highlight the importance of task control-default mode network interconnections as a major locus of individual differences in cognitive functioning in early adolescence.

INTRAMURAL RESEARCH

[Altered Corticolimbic Control Of The Nucleus Accumbens By Long-Term Δ9-Tetrahydrocannabinol Exposure](#) Hwang E-K, Lupica CR. Biol Psychiatry 2019 Aug 6; S0006-3223(19)31559-8. [Epub ahead of print].

The decriminalization and legalization of cannabis and the expansion of availability of medical cannabis in North America have led to an increase in cannabis use and the availability of high-

potency strains. Cannabis potency is determined by the concentration of Δ^9 -tetrahydrocannabinol (Δ^9 -THC), a psychoactive constituent that activates cannabinoid CB1 and CB2 receptors. The use of high-potency cannabis is associated with cannabis use disorder and increased susceptibility to psychiatric illness. The nucleus accumbens (NAc) is part of a brain reward circuit affected by Δ^9 -THC through modulation of glutamate afferents arising from corticolimbic brain areas implicated in drug addiction and psychiatric disorders. Moreover, brain imaging studies show alterations in corticolimbic and NAc properties in human cannabis users. METHODS: Using in vitro electrophysiology and optogenetics, we examined how Δ^9 -THC alters corticolimbic input to the NAc in rats.

RESULTS: We found that long-term exposure to Δ^9 -THC weakens prefrontal cortex glutamate input to the NAc shell and strengthens input from basolateral amygdala and ventral hippocampus. Further, whereas long-term exposure to Δ^9 -THC had no effect on net strength of glutamatergic input to NAc shell arising from midbrain dopamine neurons, it alters fundamental properties of these synapses.

CONCLUSIONS: Long-term exposure to Δ^9 -THC shifts control of the NAc shell from cortical to limbic input, likely contributing to cognitive and psychiatric dysfunction that is associated with cannabis use.

[Habenular And Striatal Activity During Performance Feedback Are Differentially Linked With State-Like And Trait-Like Aspects Of Tobacco Use Disorder](#) Flannery JS, Riedel MC, Poudel R, Laird AR, Ross TJ, Salmeron BJ, Stein EA, Sutherland MT. Sci Adv. 2019; 5(10): eaax2084.

The habenula, an epithalamic nucleus involved in reward and aversive processing, may contribute to negative reinforcement mechanisms maintaining nicotine use. We used a performance feedback task that differentially activates the striatum and habenula and administered nicotine and varenicline (versus placebos) to overnight-abstinent smokers and nonsmokers to delineate feedback-related functional brain alterations both as a function of smoking trait (smokers versus nonsmokers) and drug administration state (drug versus placebo). Smokers showed less striatal responsivity to positive feedback, an alteration not mitigated by drug administration, but rather correlated with trait-level addiction severity. Conversely, nicotine administration reduced habenula activity following both positive and negative feedback among abstinent smokers, but not nonsmokers, and increased habenula activity among smokers correlated with elevated state-level tobacco cravings. These outcomes highlight a dissociation between neurobiological processes linked with the dependence severity trait and the nicotine withdrawal state. Interventions simultaneously targeting both aspects may improve currently poor cessation outcomes.

[Operant Social Reward Decreases Incubation Of Heroin Craving In Male And Female Rats](#) Venniro M, Russell TI, Zhang M, Shaham Y. Biol Psychiatry. 2019; 86: 848–856.

BACKGROUND: We recently reported that operant social choice-induced voluntary abstinence prevents incubation of methamphetamine craving. Here, we determined whether social choice-induced voluntary abstinence would prevent incubation of heroin craving. We also introduce a fully automatic social reward self-administration model that eliminates the intense workload and rat-human interaction of the original semiautomatic model.

METHODS: In experiment 1, we trained male and female rats for social self-administration (6 days) and then for heroin self-administration (12 days). Next, we assessed relapse to heroin

seeking after 1 and 15 abstinence days. Between tests, the rats underwent either forced or social choice-induced abstinence. In experiment 2, we developed a fully automatic social self-administration procedure by introducing a screen between the self-administration chamber and the social-peer chamber; the screen allows physical contact but prevents rats from crossing chambers. Next, we compared incubation of craving in rats with a history of standard (no-screen) or automatic (screen) social self-administration and social choice-induced abstinence.

RESULTS: The time-dependent increase in heroin seeking after cessation of drug self-administration (incubation of craving) was lower after social choice-induced abstinence than after forced abstinence. There were no differences in social self-administration, social choice-induced abstinence, and incubation of craving in rats trained in the standard semiautomatic procedure versus the novel fully automatic procedure.

CONCLUSIONS: Our study demonstrates the protective effect of rewarding social interaction on heroin self-administration and incubation of heroin craving and introduces a fully automatic social self-administration and choice procedure to investigate the role of volitional social interaction in drug addiction and other psychiatric disorders.

High-Potency Ligands For DREADD Imaging And Activation In Rodents And Monkeys

Bonaventura J, Eldridge MAG, Hu F, Gomez JL, Sanchez-Soto M, Abramyan AM, Lam S, Boehm MA, Ruiz C, Farrell MR, Moreno A, Galal Faress IM, Andersen N, Lin JY, Moaddel R, Morris PJ, Shi L, Sibley DR, Mahler SV, Nabavi S, Pomper MG, Bonci A, Horti AG, Richmond BJ, Michaelides M. *Nat Commun.* 2019; 10(1): 4627.

Designer Receptors Exclusively Activated by Designer Drugs (DREADDs) are a popular chemogenetic technology for manipulation of neuronal activity in uninstrumented awake animals with potential for human applications as well. The prototypical DREADD agonist clozapine N-oxide (CNO) lacks brain entry and converts to clozapine, making it difficult to apply in basic and translational applications. Here we report the development of two novel DREADD agonists, JHU37152 and JHU37160, and the first dedicated 18F positron emission tomography (PET) DREADD radiotracer, [18F]JHU37107. We show that JHU37152 and JHU37160 exhibit high in vivo DREADD potency. [18F]JHU37107 combined with PET allows for DREADD detection in locally-targeted neurons, and at their long-range projections, enabling noninvasive and longitudinal neuronal projection mapping.

Dopamine Neuron Ensembles Signal The Content Of Sensory Prediction Errors

Stalnaker TA, Howard JD, Takahashi YK, Gershman SJ, Kahnt T, Schoenbaum G. *Elife* 2019; 8: e49315. Dopamine neurons respond to errors in predicting value-neutral sensory information. These data, combined with causal evidence that dopamine transients support sensory-based associative learning, suggest that the dopamine system signals a multidimensional prediction error. Yet such complexity is not evident in the activity of individual neurons or population averages. How then do downstream areas know what to learn in response to these signals? One possibility is that information about content is contained in the pattern of firing across many dopamine neurons. Consistent with this, here we show that the pattern of firing across a small group of dopamine neurons recorded in rats signals the identity of a mis-predicted sensory event. Further, this same information is reflected in the BOLD response elicited by sensory prediction errors in human midbrain. These data provide evidence that ensembles of dopamine neurons provide highly specific teaching signals, opening new possibilities for how this system might contribute to learning.

Orbitofrontal Cortex Is Selectively Activated In A Primate Model Of Attentional Bias To Cocaine Cues Baeg E, Jedema HP, Bradberry CW. *Neuropsychopharmacology* 2019 Aug 28; 1-8 [Epub ahead of print].

Attentional bias to drug-associated cues correlates with extent of current use, and risk of relapse among those attempting abstinence. Electroencephalogram (EEG) and functional imaging measures in clinical studies have previously investigated the neural basis of attentional bias, but the lack of animal models precluded investigation at the single-unit level. To complement results obtained from clinical studies, we have employed a non-human primate model of attentional bias to cocaine cues while simultaneously recording single-unit activity in cortical and striatal regions implicated in reward processing. Rhesus macaques conditioned to associate particular colors with cocaine or water reward performed an attentional bias task, in which those colors served as irrelevant distractors. Concurrently, multiple electrode arrays for recording single-unit activity were acutely implanted into the orbitofrontal cortex, anterior cingulate cortex, dorsal anterior striatum, and ventral striatum. As in clinical studies, attentional bias was indicated by elongated response times on trials with cocaine-associated distractors compared with trials with water-associated, or control unconditioned distractors. In both animals studied, across an unbiased sample of neurons, the orbitofrontal cortex differentiated distractor condition by the proportion of single-units activated, as well as by population response. In one of the two, the anterior cingulate cortex did as well, but neither striatal region did in either animal. These direct measures of single-unit activity in a primate model complement clinical imaging observations suggesting that cortical mechanisms, especially in orbitofrontal cortex, are likely involved in attentional bias to cocaine-associated environmental cues.

GRANTEE HONORS AND AWARDS

Grantee Honors

Huda Akil, Ph.D., the Gardner C. Quarton Distinguished Professor of Neuroscience and Psychiatry at the University of Michigan, was the recipient of the 2019 Julius Axelrod Prize for distinguished achievements in neuropharmacology.

Nancy Ator, Ph.D., Professor of Psychiatry and Behavioral Sciences at Johns Hopkins University, was awarded the Paul Hoch Distinguished Service Award from the American College of Neuropsychopharmacology.

In June 2019, CTN Northeast Node Core Investigators **Steven H. Chapman, M.D.**, and **Daisy Goodman, CNM, DNP, M.P.H.**, alongside colleagues at Dartmouth-Hitchcock Medical Center (DHMC) **Bonny Whalen, M.D.**, **Alison Holmes, M.D., M.S., M.P.H.**, and **Julia Frew, M.D.**, received the Academic Pediatric Association's Health Care Delivery award on behalf of the DHMC Center for Addiction Recovery in Pregnancy & Parenting (CARPP) for their tireless efforts to improve care and outcomes for opioid-exposed newborns and their moms. CARPP is a multidisciplinary network of experienced clinicians and researchers that engages in research, patient education, and advocacy in the treatment of pregnant and parenting moms and children affected by substance use disorders.

Ziva Cooper, Ph.D., Associate Professor at the University of California, Los Angeles, was awarded the Neator Award, from *Neuropsychopharmacology*, the journal of the American College of Neuropsychopharmacology, for the best transformative original report.

Gail D'Onofrio, M.D., M.S., received the American College of Emergency Physicians (ACEP) "Outstanding Contributions in Research Award." Gail is a Lead Investigator for a Helping to End Addiction Long-term (HEAL) Initiative NIDA CTN study that will implement Emergency Department (ED)-initiated buprenorphine in a large number of EDs and will conduct a randomized trial to compare daily buprenorphine and weekly injectable buprenorphine.

Deborah Hasin, Ph.D., Professor in Psychiatry at Columbia University, was awarded the Neuropsychopharmacology Editors Award for Reviews (NEAR) award from *Neuropsychopharmacology*, the journal of the American College of Neuropsychopharmacology for the best transformative review.

Katherine Hawk, M.D., M.H.S., received the American College of Emergency Physicians (ACEP) "Young Investigator Award." Katherine is a NIDA investigator co-leading CTN studies, and it is a significant recognition of her research accomplishments to receive this award.

Christina Hoven, Ph.D., Columbia University, has been appointed as a member of the Global Task Force in Psychiatry of citiesRISE, a global platform addressing needs of children and adolescents and a member of the Scientific Planning Committee, World Psychiatric Association,

for the 2020 Meeting in Bangkok, and appointed as Commissioner, Lancet, Depression Commission.

Thomas Kash, Ph.D., the John R. Andrews Distinguished Professor in the Department of Pharmacology at the University of North Carolina, was awarded the Jacob P. Waletzky Award for research leading to contributions to the understanding of drug addiction.

Stephen Patrick, M.D., M.P.H., M.S., Director of the Vanderbilt Center for Child Health Policy, received the Society for Pediatrics Research's Young Investigator Award, May 2019.

Marina Picciotto, Ph.D., Professor of Psychiatry, Pharmacology and Neuroscience at Yale, is the 2019 honoree of the Bernice Grafstein Award for Outstanding Accomplishments in Mentoring.

Lauren Mackenzie Reynolds, Ph.D., Sorbonne Universite and McGill University, was awarded the Nemko Prize in Cellular or Molecular Neuroscience.

Tracy Smith, Ph.D., of the Medical University of South Carolina Department of Psychiatry & Behavioral Sciences, is the recipient of the Society for Research in Nicotine and Tobacco's 2020 Jarvik-Russel Early Career Award, honoring members early in their careers who have made extraordinary contributions to the field of nicotine and tobacco research.

Brian Sweis, Ph.D., University of Minnesota, was awarded the Donald B. Lindsley Prize, which recognizes an outstanding Ph.D. thesis in the area of Behavioral Neuroscience.

Anna Taylor, Ph.D., Postdoctoral Fellow at the University of California, Los Angeles, was awarded the Neuropsychopharmacology Editors' Early Career Award (NEECA) Award from *Neuropsychopharmacology*, the journal of the American College of Neuropsychopharmacology, for the best original report from an Early Career Investigator.

STAFF HONORS AND AWARDS

NIDA DIRECTOR'S AWARDS (2019)

OFFICE OF THE DIRECTOR

The Helping to End Addiction Long-termSM Leadership Team

Redonna Chandler, Office of the Director

Ronald Dobbins, Center for Clinical Trials Network

Michelle Freund, Division of Extramural Research

Donna Jones, Office of Management

Elena Koustova, Office of the Director

Jacqueline Lloyd, Division of Epidemiology, Services and Prevention Research

Ivan Montoya, Division of Therapeutics and Medical Consequences

Jack Stein, Office of Science Policy and Communications

Tracy Waldeck, Division of Extramural Research

Tisha Wiley, Division of Epidemiology, Services and Prevention Research

In recognition of tireless devotion and exemplary leadership in developing and implementing NIDA's HEAL initiatives.

Vasundhara Varthakavi

In recognition of your leadership on the development of high-priority research areas at the intersection of substance abuse and the human immunodeficiency virus for NIDA.

DIVISION OF EXTRAMURAL RESEARCH

Grants Management Team

Azeezat (Yinka) Abu

Carol Alderson

Amy Bucheimer

Jennifer Cho

Amy Connolly

Edith Davis

Nadia Felix

Pamela Fleming

Penny Greene

Lennin Greenwood

Garlin Hallas

Cheryl Nathaniel

Jennifer Schermerhorn

Aida Vasquez

Ericka Wells

In recognition of effective stewardship of NIDA's extramural funds during high demands, challenging parameters, truncated deadlines, complex mechanisms, and burdens beyond normal grants management process.

DIVISION OF EPIDEMIOLOGY, SERVICES AND PREVENTION RESEARCH

Kathleen Etz

In recognition of your programmatic support of American Indian and Alaska Native communities and researchers, facilitating reciprocal trust and collaboration across the NIH.

INTRAMURAL RESEARCH PROGRAM

Da-Ting Lin

In recognition of the development of novel in vivo deep brain optical imaging techniques in freely behaving rodent that will significantly impact our understanding of the brain mechanisms controlling drug reward and relapse.

OFFICE OF MANAGEMENT

Office of Acquisitions National Institute of Mental Health Section

Michelle Cecilia
Sally Ibrahim
Kristina Jenkins
Robin Knightly
Thien Nguyen
Kimberlee Stapleton
Valerie Whipple

In recognition of your willingness to take on additional workload from other sections to ensure that NIDA and our customer Institutes and Centers obligated its fiscal year 2019 funds in support of the mission.

NIDA, Office of Acquisitions Paperless Initiative Team

Charlotte Annan
April Hill
Tonya Mansfield
Gail Pointer

In recognition of your outstanding efforts to prepare NIDA Office of Acquisitions for its move by preparing 804 boxes of contract files for shipment to the Federal Records Center.

NIDA, Office of Acquisitions Policy Liaison Team

Evanthia Bouzis
Tracy Cain
Danny Cohn

Christine Frate
Jon Gottschalk
Mark McNally
Rieka Plugge
Suzanne Stinson

In recognition of strengthening partnerships with our customer Institutes, improving communication, and increasing collaboration to achieve success in awarding contracted projects and programs.

Jill Beklik, NIH Office of Human Resources

In recognition of sustained, exemplary employee relations services to NIDA managers and staff.

OFFICE OF SCIENCE POLICY AND COMMUNICATIONS

Jennifer Hobin

In recognition of outstanding leadership in advising NIDA leadership on complex policy matters.

NIDA Press Team

Kimberly DiFonzo
Shirley Simson

In recognition of your outstanding and tireless work in disseminating and promoting cutting-edge NIDA science to the media

NIDA Director's Award for Diversity

Michelle Jobes

In recognition of your contributions in providing resources and opportunities for trainees from underrepresented and disadvantaged backgrounds to grow and thrive in the scientific community.

NIDA Director's Award for Quality of Worklife

NIDA, Office of Acquisitions Morale Group

Kimberly Espinosa
Christine Frate
Robin Knightly
Tonya Mansfield
Rieka Plugge
Sneha Singh

In recognition of your outstanding efforts to sponsor events and outreach to improve the morale of the Office of Acquisitions, thus increasing employee engagement and enhancing the overall quality of worklife at NIDA.

NIDA Director's Rising Star Award

Olivier Berton

In recognition of your accomplishments, creativity, energy, and ability to inspire others at NIDA.

Yeka Aponte

In recognition of your accomplishments, creativity, energy, and ability to inspire others at NIDA.

NIDA Director's Innovator Award

NIDA Transgenic Rat Team

Brandon Harvey

Janette Lebron

Christopher Richie

In recognition of your innovative work on developing transgenic rat lines and making them publicly available to the scientific community as important research tools.

PHS NIH Commissioned Corps Achievement Medal Award

CDR Keisher Highsmith

For leadership in establishing the HEALing Communities Study Data and Safety Monitoring Board to improve the quality of research and ensure performance and scientific integrity.

CDR John Hubbard

For sustained leadership and performance, commitment to promoting public health, and his community outreach efforts to Baltimore City Youth.

PHS NIH Commissioned Corps, Unit Commendation Award

NIDA Federal Prescription Drug Take Back Day Committee

CAPT Jinhee Lee

CAPT Paul Na

LCDR James Pitt

David Anderson

Josie Anderson

Michelle Corbin

Kimberly Difonzo

Mark Fleming

Tara Garwood

Janet Linton

Brian Marquis

Shirley Simson

In recognition of exceptional team effort resulting in successful prescription and over-the-counter drug take back interventions at NIDA and NIH.

Length of Service Award

30 Years of Government Service Recognition

Quandra Blackeney
Jean Cadet
Pamela Fleming
Amy Newman Greig
Theresa Kopajtic
Michael Mccoy
Carmen Rosa
Donna Walther

The Donna M. Jones Award for Dedicated Service to NIDA

Donna Jones

In recognition of sustained superior performance leading NIDA financial management and 46 years of unmatched dedication to the NIDA mission.

OTHER STAFF HONORS AND AWARDS

Miguel Arenivar, Intramural Research Program, received both the Scientific Director's Fellowship for Diversity in Research Award and the Best Oral Presentation Award from The Society for the Advancement of Chicanos/Hispanics and Native Americans in Science-NIH Chapter.

Kris Bough, Ph.D., Division of Neuroscience and Behavior, co-authored National Institutes of Health Executive Meeting Summary: Developing Medical Countermeasures to Rescue Opioid-Induced Respiratory Depression (a Trans-Agency Scientific Meeting)-August 6/7, 2019. David T. Yeung, Kristopher J. Bough, Jill R. Harper, Gennady E. Platoff Jr. *J Med Toxicol.* 2020; 16(1): 87-105.

Mehdi Farokhnia, Ph.D., and **Chloe Jordan, Ph.D.**, Intramural Research Program, were two of 58 travel awardees (out of 314 applications) to the American College of Neuropsychopharmacology meeting, December 2019.

Marisela Morales, Ph.D., Intramural Research Program, received the National Award of Excellence in Research from the National Hispanic Science Network.

Lorenzo Leggio, M.D., Intramural Research Program, was selected as one of the speakers at the NIH Director's Seminar Series.

Kenzie Preston, Ph.D., Intramural Research Program, was elected as a Fellow in the American College of Neuropsychopharmacology.

John Satterlee, Ph.D., Division of Neuroscience and Behavior, published The NIH Common Fund/Roadmap Epigenomics Program: Successes of a comprehensive consortium. John S. Satterlee, Lisa H. Chadwick, Frederick L. Tyson, Kim McAllister, Jill Beaver, Linda Birnbaum, Nora D Volkow, Elizabeth L. Wilder, James M. Anderson and Ananda L Roy. *Sci. Adv.* 2019; 5: eaaw6507.

Rita Valentino, Ph.D., Division of Neuroscience and Behavior, Walter Koroshetz, M.D., Director, National Institute of Neurological Disorders and Stroke, and Nora Volkow, M.D., Director, NIDA, co-edited the January 1, 2020, Special Issue of *Biological Psychiatry* on the Neurobiology of the Opioid Epidemic.

STAFF CHANGES

New Appointments

Emily Einstein, Ph.D., has been selected as the new Chief of the Science Policy Branch within the Office of Science Policy and Communications. Emily was serving as the Acting Branch Chief since September 2019 and Deputy Branch Chief, Science Policy Branch, since 2017. Emily joined NIDA in 2015 following her American Association for the Advancement of Science fellowship in the Office of Autism Research Coordination at the National Institute of Mental Health. Her B.S. is in English and Biology from The College of William and Mary, and her Ph.D. is in Neuroscience from Yale University, where she trained faculty on evidence-based pedagogical practices and conducted research focused on mechanisms of opioid drug reward.

New Staff

Julie Frost Bellgowan joined the Science Policy Branch, Office of Science Policy and Communications, in September 2019 as our newest Health Science Policy Analyst. Prior to joining the Science Policy Branch, she worked in the National Institute of Mental Health's Office of Science Policy, Planning, and Communications, where she planned, developed, and disseminated key communications for senior leadership, staff, Congress, and the public regarding Institute priorities, policies, scientific contributions, and strategic planning. Before entering the field of science policy, Julie conducted neuroimaging and neuropsychiatric research at the Medical College of Wisconsin, the Intramural Research Program at the National Institute of Mental Health, the Laureate Institute for Brain Research, and the National Intrepid Center of Excellence at Walter Reed National Military Medical Center. Over the course of her neuroimaging research career, she investigated neurological, environmental, and psychosocial factors associated with typically-developed brain language systems, developmental dyslexia, childhood depression and anxiety, and traumatic brain injury. She earned her bachelor's and master's degrees in Psychology with a focus on Neuroscience from the University of Wisconsin-Milwaukee.

Steven Brito joined NIDA's Office of Management, Management Analysis Branch as a Management Analyst on October 27, 2019. Steven comes to NIDA from a position with the U.S. Air Force.

MeLisa Creamer, Ph.D., joined the Division of Epidemiology, Services and Prevention Research on December 10, 2019, as a Health Scientist Administrator. MeLisa received her Ph.D. in Epidemiology from the University of Texas School of Public Health in Austin. Upon completion of her degree, MeLisa stayed on in a research faculty position in the department of Health Promotion and Behavioral Sciences and was then promoted to Assistant Professor. While at the University of Texas, MeLisa was the Primary Research Coordinator and Co-Investigator of the Texas Tobacco Center of Regulatory Science on Youth and Young Adults. In 2018, she left Texas to move to Atlanta where she was an Oak Ridge Institute for Science and Education Fellow in the Centers for Disease Control and Prevention's (CDC's) Office on Smoking and

Health. At CDC, MeLisa was on the Surveillance Team and worked extensively on the National Youth Tobacco Survey, National Health Interview Survey, and Behavioral Risk Factor Surveillance System. MeLisa holds a bachelor's degree in Sociology from the American University and a master's in Public Health from the University of Texas School of Public Health in Austin.

Rashiid Cummins joined NIDA's Office of Management, Office of Acquisitions as a Contract Specialist on October 27, 2019. Rashiid comes to NIDA from a position with the U.S. Postal Service.

Brandin Michael DeChabert rejoined Division of Epidemiology, Services and Prevention Research on December 9, 2019, in a program/management team leader position. He earned his bachelor's degree in Sociology in 2000 from Trinity University in San Antonio, Texas. Brandin was previously at the National Center for Advancing Translational Sciences in the Division of Clinical Innovation as a Staff Assistant.

Scott Duernberger joined NIDA's Office of Management, Office of Acquisitions as a Contract Specialist on August 18, 2019. Scott comes to NIDA from a position in the private sector.

Cheryl Embree joined NIDA's Office of Management as an Ethics Specialist on September 29, 2019. Cheryl comes to NIDA from the private sector.

Chloe Jordan, Ph.D., joined NIDA as the Scientific Program Manager to the Division of Extramural Research HEALTHy Brain and Child Development Team. Chloe received her B.A. in Psychology and Biology with a specialization in Neuroscience in 2010 and her Ph.D. in Psychological and Brain Sciences in 2015 from Boston University. Her dissertation focused on understanding the long-term consequences of adolescent Attention-Deficit Hyperactivity Disorder medications on cocaine abuse risk, using a preclinical model. She then worked for 2 years in the Department of Psychiatry at McLean Hospital/Harvard Medical School with Susan L. Andersen, Ph.D., studying sex differences in neurodevelopmental risk factors and exercise interventions for cocaine use. In August 2017, she joined the NIDA-Intramural Research Program as an Intramural Research Training Award Postdoctoral Fellow in the Addiction Biology Unit, Medicinal Chemistry Section in the Molecular Targets and Medications Discovery Branch. Her research at the Intramural Research Program focused on cell type-specific neural circuits underlying drug reward and neurochemical mechanism-driven medication development for the treatment of substance use disorders. While in Baltimore, Chloe also worked with the Center for Addiction and Pregnancy at Johns Hopkins.

Elizabeth Hoffman, Ph.D., joined the Division of Extramural Research's Office of the Director as a Health Scientist Administrator (Program Officer) on September 1, 2019. Elizabeth comes to NIDA from the private sector.

Ty Lawson joined NIDA's Office of Management, Office of Acquisitions as a Contract Specialist on September 1, 2019. Ty comes to NIDA from the National Institute of Environmental Health Sciences.

Isabela Lopes joined NIDA's Office of the Director on December 22, 2019. Isabela comes to NIDA from the NIH Office of Diversity and Health Disparities.

Christine Mack has joined the Financial Management Branch of NIDA's Office of Management as a Budget Analyst. Christine previously worked in the budget offices at the National Institute of Diabetes and Digestive and Kidney Diseases, Office of the Director, and served on a detail at NIDA.

Dharmendar Rathore, Ph.D., joined NIDA's Scientific Review Branch in the Division of Extramural Research as a Supervisory "Health Scientist Administrator (Scientific Review Officer) on August 4, 2019. Dharmendar comes to NIDA from a position with the National Institute of Allergy and Infectious Diseases.

Michael Renwick joined NIDA in December 2019 as an Extramural Staff Assistant in the Office of Extramural Policy and Review where he will support many peer review meetings conducted by the Scientific Review Branch. Michael joins us from the National Institute of Allergy and Infectious Diseases where he held a similar role.

Neshia Hamiel Schaub joined NIDA's Office of Management, Management Analysis Branch as a Program Analyst on November 11, 2019. Neshia comes to NIDA from a position with the U.S. Navy.

Jason Sousa, Ph.D., joined the Chemistry and Therapeutics Branch of NIDA Division of Therapeutics and Medical Consequences last September. Jason received his B.S. in Chemistry at the University of Massachusetts-Dartmouth (North Dartmouth) and his Ph.D. in Analytical Chemistry at the University of North Carolina at Chapel Hill. Working under the direction of James Jorgenson, Ph.D., Jason's graduate research focused on the synthesis, modification, and characterization of sub-micron chromatographic packing materials and the investigation of strong-cation exchange chromatography at ultra-high pressures (>50K psi). Prior to joining NIDA, he spent 13 years as a contractor and civilian with the Department of the Army as part of its small molecule drug development efforts for the prevention and treatment of malaria and other militarily relevant infectious diseases. Jason served as Chief of the Drug Metabolism and Disposition Laboratory within the Experimental Therapeutics Branch at the Walter Reed Army Institute of Research, overseeing all preclinical metabolism and pharmacokinetics studies. A frequent collaborator with intramural and external partners, Jason has coauthored 30 publications in peer-reviewed journals and has presented his research at a variety of scientific meetings. As a member of the Defense Acquisition Workforce, Jason is Level III certified in Science & Technology Management and Level I certified in Program Management and has extensive experience as a Contracting Officer's Representative.

Trinh Tran, Ph.D., joined us from the Congressionally Directed Medical Research Programs (CDMRP) where she was a Biomedical Life Scientist under a Leidos contract. At CDMRP, Trinh was responsible for organizing programmatic review of grant submissions in several areas of biomedical and behavioral research including Psychological Health, Traumatic Brain Injury, and Multiple Sclerosis research program. Trinh earned a Ph.D. in Pharmacology from the University of Houston and conducted her postdoctoral studies at the Mind/Brain Institute of the

Johns Hopkins University. Her postdoctoral research focused on examining synaptic plasticity in hippocampus, particularly with respect to Alzheimer's and aging.

Staff Departures

Emily Jones, Ph.D., left NIDA in September 2019 for a position at the Centers for Medicare and Medicaid Services Innovation Center to lead the Division of Population Health Incentives and Infrastructure, where she will oversee pilot programs to improve care for patients who are experiencing substance use disorders, mental health issues, and/or adverse social determinants of health.

On August 17, 2019, **Sussana Morales**, a Management Analyst in NIDA's Management Analysis Branch, left NIDA for a position with the National Cancer Institute.

On December 7, 2019, **Sally Ibrahim**, a Contract Specialist in the Office of Acquisitions, Office of Management, left NIDA for a position with the Internal Revenue Service.

On December 12, 2019, **Eva Bouzis**, a Contract Specialist in the Office of Acquisitions, Office of Management, left NIDA for a position with the Office of the Assistant Secretary for Preparedness and Response within the U.S. Department of Health and Human Services.

Retirements

David Anderson, Public Health Advisor and editor of *NIDA Notes*, retired in September 2019.

Evelyn Anderson, a Program Specialist in the Office of Management's Management Analysis Branch, retired from federal service on December 1, 2019.

Hirsch Davis, a Psychologist in the Division of Therapeutics and Medical Consequences' Medications Discovery and Toxicology Branch, retired from federal service after 35 years on January 31, 2020.

Lyle Furr, a Contract Review Specialist retired on December 31, 2019, after 35-plus years with NIDA's review team in the Division of Extramural Research/Office of Extramural Policy and Review/Scientific Review Branch. Having deep expertise in the contracts process and nuances of review, Lyle has been an invaluable resource to the contract management and review teams.

Hal Gordon, Ph.D., retired on January 29, 2020, after 28 ½ years at NIDA. Hal's first career was in neuropsychology/neuroscience research: 25 years at Caltech, Technion Medical School (Behavioral Biology) (Haifa, Israel), and University of Pittsburgh Medical School (Psychiatry). Hal was originally recruited to NIDA in 1991 to add a neuroscience dimension to the Epidemiology Branch of the Division of Epidemiology and Prevention Research (which predates the Division of Epidemiology, Services and Prevention Research [DESPR]) and then joined the Clinical Division when it was created, where he oversaw research in hemispheric laterality,

sleep, dyslexia, among other areas. Hal rejoined the Epidemiology Branch of DESPR when NIDA was reorganized.

Donna M. Jones, NIDA Budget Officer and Chief, Financial Management Branch, retired on January 2, 2019, after 46 years of federal service. Donna has been an integral part of NIDA's leadership team with a unique skill set and broad knowledge that has substantially advanced the accomplishment of NIDA's mission. Donna began her federal career, with NIDA, in October of 1973, and served in a number of important roles during her tenure in the Institute, leading to the permanent role of Budget Officer in 1995. Donna has served seven NIDA Directors and seven Executive Officers. Her contributions to NIDA and NIH are too numerous to count, and the critical role that she has played at NIDA is evidenced by the creation of a major NIDA award in her name.

Philip Krieter, Ph.D., retired last September from NIDA's Division of Therapeutics and Medical Consequences, where he served as the key pharmaceuticals and pharmacodynamics expert. He was involved in many critical projects, including leading the pivotal studies for the approval of intranasal naloxone to treat opioid overdose.

Rao Rapaka, Ph.D., Chief of the Chemistry, Pharmacology and Physiology Branch of the Division of Neuroscience and Behavior, has retired from federal service. While at NIDA, Rao shaped the field of chemistry and pharmacology of drugs of abuse by discovering and promoting talent and innovative ideas, fostering collaborations, and promoting the dissemination of knowledge. He has been recognized by several scientific organizations for his contributions, including multiple lifetime achievement awards. Kris Bough, Ph.D., will serve as Acting Branch Chief while a search for the next Branch Chief takes place.

Karen Sirocco, Ph.D., a Health Scientist Administrator in NIDA's Prevention Research Branch, Division of Epidemiology, Services and Prevention Research, retired from federal service on August 31, 2019.

Cora Lee Wetherington, Ph.D., a Health Scientist Administrator in the Division of Neuroscience and Behavior's Behavioral and Cognitive Neuroscience Branch, retired from federal service on September 28, 2019.



National Institute
on Drug Abuse