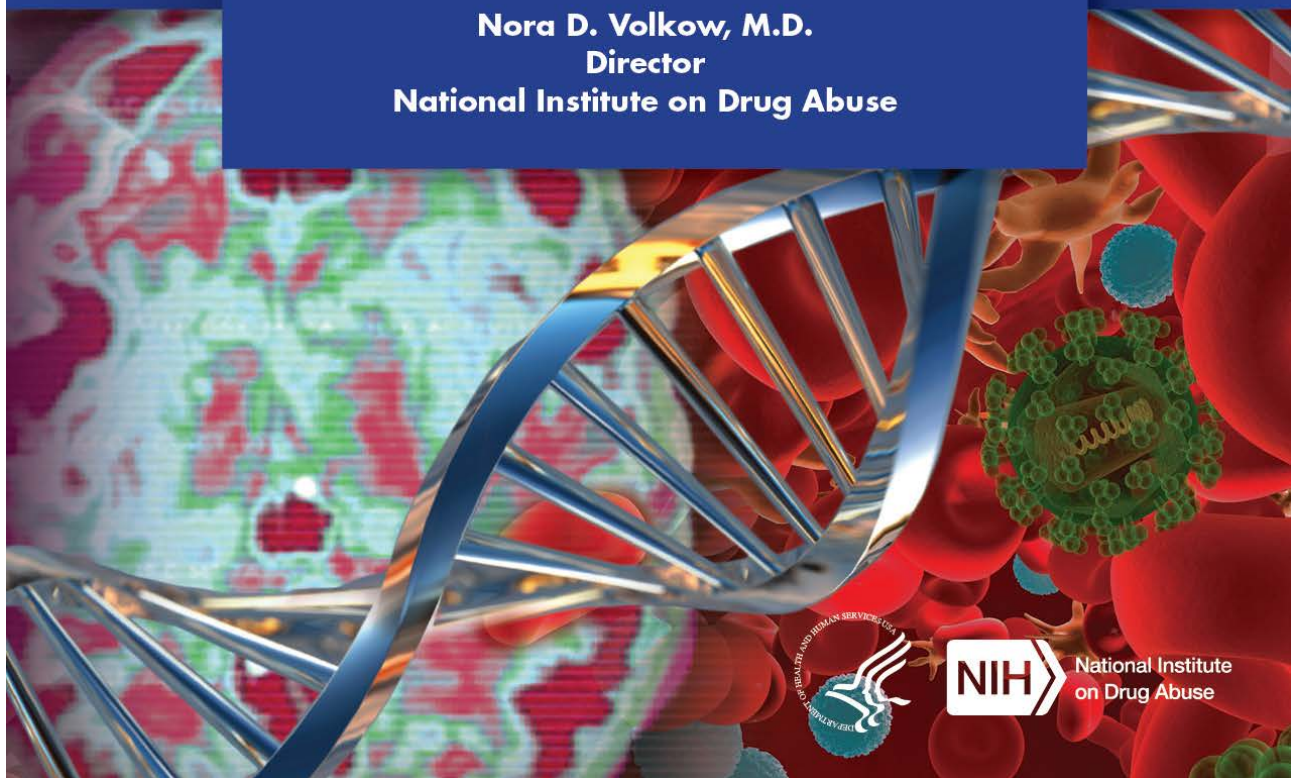




DIRECTOR'S REPORT

————— *to the* —————
National Advisory Council on Drug Abuse
————— *September 2015* —————

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National Institute
on Drug Abuse

TABLE OF CONTENTS

| | |
|--|----|
| RESEARCH HIGHLIGHTS | 1 |
| NIH/HHS POLICY UPDATES | 20 |
| CONGRESSIONAL AFFAIRS SECTION | 22 |
| PROGRAM ACTIVITIES/FOAS | 27 |
| COLLABORATIVE RESEARCH ON ADDICTION AT NIH (CRAN) ACTIVITIES | 35 |
| COMMUNICATIONS..... | 37 |
| MEETINGS/CONFERENCES | 41 |
| GRANTEE HONORS AND AWARDS | 42 |
| STAFF HONORS AND AWARDS | 45 |
| STAFF CHANGES..... | 46 |

RESEARCH HIGHLIGHTS

Division of Basic Neuroscience and Behavioral Research

Evolutionary Genomics. Evolutionary Changes in Promoter and Enhancer Activity during Human Corticogenesis Reilly SK, Yin J, Ayoub AE, Emera D, Leng J, Cotney J, Sarro R, Rakic P, Noonan JP. *Science*. 2015 Mar 6;347(6226):1155-1159.

Human higher cognition is attributed to the evolutionary expansion and elaboration of the human cerebral cortex. However, the genetic mechanisms contributing to these developmental changes are poorly understood. The authors used comparative epigenetic profiling of human, rhesus macaque, and mouse corticogenesis to identify promoters and enhancers that have gained activity in humans. These gains are significantly enriched in modules of coexpressed genes in the cortex that function in neuronal proliferation, migration, and cortical-map organization. Gain-enriched modules also showed correlated gene expression patterns and similar transcription factor binding site enrichments in promoters and enhancers, suggesting that they are connected by common regulatory mechanisms. These results reveal coordinated patterns of potential regulatory changes associated with conserved developmental processes during corticogenesis, providing insight into human cortical evolution.

A New DREADD Facilitates the Multiplexed Chemogenetic Interrogation of Behavior Vardy E, Robinson JE, Li C, Olsen RH, DiBerto JF, Giguere PM, Sassano FM, Huang XP, Zhu H, Urban DJ, White KL, Rittiner JE, Crowley NA, Pleil KE, Mazzone CM, Mosier PD, Song J, Kash TL, Malanga CJ, Krashes MJ, Roth BL. *Neuron*. 2015 May 20;86(4):936-946.

DREADDs are chemogenetic tools widely used to remotely control cellular signaling, neuronal activity, and behavior. Here the authors used a structure-based approach to develop a new Gi-coupled DREADD using the kappa-opioid receptor as a template (KORD) that is activated by the pharmacologically inert ligand salvinorin B (SALB). Activation of virally expressed KORD in several neuronal contexts robustly attenuated neuronal activity and modified behaviors. Additionally, co-expression of the KORD and the Gq-coupled M3-DREADD within the same neuronal population facilitated the sequential and bidirectional remote control of behavior. The availability of DREADDs activated by different ligands provides enhanced opportunities for investigating diverse physiological systems using multiplexed chemogenetic actuators.

Spatiotemporal Control of Opioid Signaling and Behavior Siuda ER, Copits BA, Schmidt MJ, Baird MA, Al-Hasani R, Planer WJ, Funderburk SC, McCall JG, Gereau RW 4th, Bruchas MR. *Neuron*. 2015 May 20;86(4):923-935.

Optogenetics is now a widely accepted tool for spatiotemporal manipulation of neuronal activity. However, a majority of optogenetic approaches use binary on/off control schemes. Here, the authors extend the optogenetic toolset by developing a neuromodulatory approach using a rationale-based design to generate a Gi-coupled, optically sensitive, mu-opioid-like receptor, which we term opto-MOR. They demonstrate that opto-MOR engages canonical mu-opioid signaling through inhibition of adenylyl cyclase, activation of MAPK and G protein-gated inward rectifying potassium (GIRK) channels and internalizes with kinetics similar to that of the mu-opioid receptor. To assess in vivo utility, the authors expressed a Cre-dependent viral opto-MOR in RMTg/VTA GABAergic neurons, which led to a real-time place preference. In contrast, expression of opto-MOR in GABAergic neurons of the ventral pallidum hedonic cold spot led to real-time place aversion. This tool has

generalizable application for spatiotemporal control of opioid signaling and, furthermore, can be used broadly for mimicking endogenous neuronal inhibition pathways.

Orexin-1 Receptor Signaling Increases Motivation for Cocaine-Associated Cues Bentzley BS, Aston-Jones G. *Eur J Neurosci.* 2015 May;41(9):1149-1156.

The orexin/hypocretin system is involved in multiple cocaine addiction processes that involve drug-associated environmental cues, including cue-induced reinstatement of extinguished cocaine seeking and expression of conditioned place preference. However, the orexin system does not play a role in several behaviors that are less cue-dependent, such as cocaine-primed reinstatement of extinguished cocaine seeking and low-effort cocaine self-administration. The authors hypothesized that cocaine-associated cues, but not cocaine alone, engage signaling at orexin-1 receptors (OX1Rs), and this cue-engaged OX1R signaling increases motivation for cocaine. Motivation for cocaine was measured in Sprague-Dawley rats with behavioral-economic demand curve analysis after pretreatment with the OX1R antagonist SB-334867 (SB) or vehicle with and without light + tone cues. Demand for cocaine was higher when cocaine-associated cues were present, and SB only reduced cocaine demand in the presence of these cues. The authors then investigated whether cocaine demand was linked to the cued reinstatement of cocaine seeking, as both procedures are partially driven by cocaine-associated cues in an orexin-dependent manner. SB blocked cue-induced reinstatement behavior, and baseline demand predicted SB efficacy with the largest effect in high-demand animals, i.e. animals with the greatest cue-dependent behavior. The authors conclude that OX1R signaling increases the reinforcing efficacy of cocaine-associated cues but not that of cocaine alone. This supports their view that orexin plays a prominent role in the ability of conditioned cues to activate motivational responses.

Epigenetic Basis of Opiate Suppression of BDNF Gene Expression in the Ventral Tegmental Area Koo JW, Mazei-Robison MS, LaPlant Q, Egervari G, Braunscheidel KM, Adank DN, Ferguson D, Feng J, Sun H, Scobie KN, Damez-Werno DM, Ribeiro E, Peña CJ, Walker D, Bagot RC, Cahill ME, Anderson SA, Labonté B, Hodes GE, Browne H, Chadwick B, Robison AJ, Vialou VF, Dias C, Lorsch Z, Mouzon E, Lobo MK, Dietz DM, Russo SJ, Neve RL, Hurd YL, Nestler EJ. *Nat Neurosci.* 2015 Mar;18(3):415-422.

Brain-derived neurotrophic factor (BDNF) has a crucial role in modulating neural and behavioral plasticity to drugs of abuse. The authors found a persistent downregulation of exon-specific BDNF expression in the ventral tegmental area (VTA) in response to chronic opiate exposure, which was mediated by specific epigenetic modifications at the corresponding BDNF gene promoters. Exposure to chronic morphine increased stalling of RNA polymerase II at these BDNF promoters in VTA and altered permissive and repressive histone modifications and occupancy of their regulatory proteins at the specific promoters. Furthermore, the authors found that morphine suppressed binding of phospho-CREB (cAMP response element binding protein) to BDNF promoters in VTA, which resulted from enrichment of trimethylated H3K27 at the promoters, and that decreased NURR1 (nuclear receptor related-1) expression also contributed to BDNF repression and associated behavioral plasticity to morphine. These findings suggest previously unknown epigenetic mechanisms of morphine-induced molecular and behavioral neuroadaptations.

Division of Clinical Neuroscience and Behavioral Research

Cortical Thickness in Adolescent Marijuana and Alcohol Users: A Three-year Prospective Study from Adolescence to Young Adulthood Jacobus J, Squeglia LM, Meruelo AD, Castro N, Brumback T, Giedd JN, Tapert SF. *Dev Cogn Neurosci*. 2015 Apr 27. pii: S1878-9293(15)00046-8. Studies suggest marijuana impacts gray and white matter neural tissue development, however few prospective studies have determined the relationship between cortical thickness and cannabis use spanning adolescence to young adulthood. This study aimed to understand how heavy marijuana use influences cortical thickness trajectories across adolescence. Subjects were adolescents with heavy marijuana use and concomitant alcohol use (MJ+ALC, n=30) and controls (CON, n=38) with limited substance use histories. Participants underwent magnetic resonance imaging and comprehensive substance use assessment at three independent time points. Repeated measures analysis of covariance was used to look at main effects of group, time, and Group×Time interactions on cortical thickness. MJ+ALC showed thicker cortical estimates across the brain (23 regions), particularly in frontal and parietal lobes ($p < .05$). More cumulative marijuana use was associated with increased thickness estimates by 3-year follow-up ($p < .05$). Heavy marijuana use during adolescence and into young adulthood may be associated with altered neural tissue development and interference with neuromaturation that can have neurobehavioral consequences. Continued follow-up of adolescent marijuana users will help understand ongoing neural changes that are associated with development of problematic use into adulthood, as well as potential for neural recovery with cessation of use.

Structural Connectivity of Neural Reward Networks in Youth at Risk for Substance Use Disorders Squeglia LM, Sorg SF, Jacobus J, Brumback T, Taylor CT, Tapert SF. *Psychopharmacology (Berl)*. 2015 Jul; 232(13):2217-2226. Having a positive family history of alcohol use disorders (FHP), as well as aberrant reward circuitry, has been implicated in the initiation of substance use during adolescence. This study explored the relationship between FHP status and reward circuitry in substance naïve youth to better understand future risky behaviors. Participants were 49 FHP and 45 demographically matched family history negative (FHN) substance-naïve 12-14 year-olds (54 % female). Subjects underwent structural magnetic resonance imaging, including diffusion tensor imaging. Nucleus accumbens and orbitofrontal cortex volumes were derived using FreeSurfer, and FSL probabilistic tractography probed structural connectivity and differences in white matter diffusivity estimates (e.g. fractional anisotropy, and mean, radial, and axial diffusivity) between fiber tracts connecting these regions. FHP and FHN youth did not differ on nucleus accumbens or orbitofrontal cortex volumes, white matter tract volumes, or percentages of streamlines (a proxy for fiber tract count) connecting these regions. However, within white matter tracts connecting the nucleus accumbens to the orbitofrontal cortex, FHP youth had significantly lower mean and radial diffusivity ($p < 0.03$) than FHN youth. While white matter macrostructure between salience and reward regions did not differ between FHP and FHN youth, FHP youth showed greater white matter coherence within these tracts than FHN youth. Aberrant connectivity between reward regions in FHP youth could be linked to an increased risk for substance use initiation.

Prenatal Cocaine Exposure Differentially Affects Stress Responses in Girls and Boys: Associations with Future Substance Use Chaplin TM, Visconti KJ, Molfese PJ, Susman EJ, Klein LC, Sinha R, Mayes LC. *Dev Psychopathol.* 2015 Feb; 27(1):163-180.

Prenatal cocaine exposure may affect developing stress response systems in youth, potentially creating risk for substance use in adolescence. Further, pathways from prenatal risk to future substance use may differ for girls versus boys. The present longitudinal study examined multiple biobehavioral measures, including heart rate, blood pressure, emotion, and salivary cortisol and salivary alpha amylase (sAA), in response to a stressor in 193 low-income 14- to 17-year-olds, half of whom were prenatally cocaine exposed (PCE). Youth's lifetime substance use was assessed with self-report, interview, and urine toxicology/breathalyzer at Time 1 and at Time 2 (6-12 months later). PCE \times Gender interactions were found predicting anxiety, anger, and sadness responses to the stressor, with PCE girls showing heightened responses as compared to PCE boys on these indicators. Stress Response \times Gender interactions were found predicting Time 2 substance use in youth (controlling for Time 1 use) for sAA and sadness; for girls, heightened sadness responses predicted substance use, but for boys, dampened sAA responses predicted substance use. Findings suggest distinct biobehavioral stress response risk profiles for boys and girls, with heightened arousal for girls and blunted arousal for boys associated with prenatal risk and future substance use outcomes.

Functional Genetic Variation in Dopamine Signaling Moderates Prefrontal Cortical Activity during Risky Decision-Making Kohno M, Nurmi EL, Laughlin CP, Morales AM, Gail EH, Helleman GS, London ED. *Neuropsychopharmacology.* 2015 Jun 29. [Epub ahead of print]. Brain imaging has revealed links between prefrontal activity during risky decision-making and striatal dopamine receptors. Specifically, striatal dopamine D2-like receptor availability is correlated with risk-taking behavior and sensitivity of prefrontal activation to risk in the Balloon Analogue Risk Task. The extent to which these associations, involving a single neurochemical measure, reflect more general effects of dopaminergic functioning on risky decision-making, however, is unknown. Here, 65 healthy participants provided genotypes and performed the Balloon Analogue Risk Task during functional magnetic resonance imaging. For each participant, dopamine function was assessed using a gene composite score combining known functional variation across five genes involved in dopaminergic signaling: DRD2, DRD3, DRD4, DAT1 and COMT. The gene composite score was negatively related to dorsolateral prefrontal cortical function during risky decision-making, and nonlinearly related to earnings on the task. Iterative permutations of all possible allelic variations (7,777 allelic combinations) was tested on brain function in an independently-defined region of the prefrontal cortex and confirmed empirical validity of the composite score, which yielded stronger association than 95% of all other possible combinations. The gene composite score also accounted for a greater proportion of variability in neural and behavioral measures than the independent effects of each gene variant, indicating that combined effects of functional dopamine pathway genes can provide a robust assessment, presumably reflecting cumulative and potentially interactive effects on brain function. Our findings support the view that the links between dopaminergic signaling, prefrontal function and decision-making vary as a function of dopamine signaling capacity.

[A Randomized Trial of Computerized vs. In-person Brief Intervention for Illicit Drug Use in Primary Care: Outcomes through 12 Months](#) Gryczynski J, Mitchell SG, Gonzales A, Moseley A, Peterson TR, Ondersma SJ, O'Grady KE, Schwartz RP. *J Subst Abuse Treat.* 2015 Mar;50:3-10. doi: 10.1016/j.jsat.2014.09.002.

This study examined outcomes through 12 months from a randomized trial comparing computerized brief intervention (CBI) vs. in-person brief intervention (IBI) delivered by behavioral health counselors for adult community health center patients with moderate-level drug misuse (N=360). Data were collected at baseline, 3-, 6-, and 12-month follow-up, and included the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST) and laboratory analysis of hair samples. Repeated measures analyses examined differential change over time. There were no significant differences in drug-positive hair tests over time or by condition. Global ASSIST scores decreased in both conditions ($p < .001$), but there were no significant differences between conditions in overall change across 12 months of follow-up ($p = .13$). CBI produced greater overall reductions in alcohol ($p = .04$) and cocaine ($p = .02$) ASSIST scores than IBI, with initial differences dissipating over time. Computerized brief interventions present a viable alternative to traditional in-person brief interventions.

Division of Pharmacotherapies and Medical Consequences of Drug Abuse

[Increased Pain Sensitivity In Chronic Pain Subjects On Opioid Therapy: A Cross-Sectional Study Using Quantitative Sensory Testing](#) Zhang Y, Ahmed S, Vo T, St Hilaire K, Houghton M, Cohen AS, Mao J, Chen L. *Pain Med.* 2015 May; 16(5):911-922.

The aim of this study was to compare the sensitivity to experimental pain of chronic pain patients on opioid therapy vs chronic pain patients on non-opioid therapy and healthy subjects by quantitative sensory testing (QST). There is a growing body of evidence demonstrating that chronic use of opioid drugs may alter pain sensitivity. Identifying the characteristic changes in thermal pain sensitivity in chronic opioid users will be helpful in diagnosing pain sensitivity alterations associated with chronic opioid use. Utilizing an office-based QST technique, the authors examined thermal pain threshold, tolerance, and temporal summation in 172 chronic pain subjects receiving opioid therapy, 121 chronic pain subjects receiving non-opioid therapy, and 129 healthy subjects. In chronic pain subjects receiving opioid therapy, there were detectable differences in QST characteristics compared with both chronic pain subjects receiving non-opioid therapy and healthy subjects. Specifically, in chronic pain subjects receiving opioid therapy, 1) sensitivity to heat pain was increased; threshold to heat pain was significantly lower; 2) tolerance to supra-threshold heat pain was significantly decreased; and 3) temporal pain summation was exacerbated, as compared with chronic pain subjects receiving non-opioid therapy. In a subgroup of chronic pain subjects receiving opioid therapy with increased heat pain sensitivity, their average opioid medication dosage was significantly higher than those who had an above-average heat pain threshold. Moreover, a subset of chronic pain subjects on opioid therapy exhibited a significant decrease in diffuse noxious inhibitory control (DNIC) compared with chronic pain subjects on non-opioid therapy. These findings suggest that a subset of QST parameters can reflect opioid-associated thermal pain sensitivity alteration, including decreased heat pain threshold, decreased cold and heat pain tolerance, diminished DNIC, and/or exacerbated temporal summation.

Efficacy, But Not Antibody Titer Or Affinity, Of A Heroin Hapten Conjugate Vaccine Correlates With Increasing Hapten Densities On Tetanus Toxoid, But Not On CRM197

Carriers Jalah R, Torres OB, Mayorov AV, Li F, Antoline JF, Jacobson AE, Rice KC, Deschamps JR, Beck Z, Alving CR, Matyas GR. *Bioconjug Chem.* 2015 Jun; 26(6):1041-1053.

Vaccines against drugs of abuse have induced antibodies in animals that blocked the biological effects of the drug by sequestering the drug in the blood and preventing it from crossing the blood-brain barrier. Drugs of abuse are too small to induce antibodies and, therefore, require conjugation of drug hapten analogs to a carrier protein. The efficacy of these conjugate vaccines depends on several factors including hapten design, coupling strategy, hapten density, carrier protein selection, and vaccine adjuvant. Previously, the authors have shown that 1 (MorHap), a heroin/morphine hapten, conjugated to tetanus toxoid (TT) and mixed with liposomes containing monophosphoryl lipid A [L(MPLA)] as adjuvant, partially blocked the antinociceptive effects of heroin in mice. Herein, we extended those findings, demonstrating greatly improved vaccine induced antinociceptive effects up to 3% mean maximal potential effect (%MPE). This was obtained by evaluating the effects of vaccine efficacy of hapten 1 vaccine conjugates with varying hapten densities using two different commonly used carrier proteins, TT and cross-reactive material 197 (CRM197). Immunization of mice with these conjugates mixed with L(MPLA) induced very high anti-1 IgG peak levels of 400-1500 $\mu\text{g/mL}$ that bound to both heroin and its metabolites, 6-acetylmorphine and morphine. Except for the lowest hapten density for each carrier, the antibody titers and affinity were independent of hapten density. The TT carrier based vaccines induced long-lived inhibition of heroin-induced antinociception that correlated with increasing hapten density. The best formulation contained TT with the highest hapten density of ≥ 30 haptens/TT molecule and induced %MPE of approximately 3% after heroin challenge. In contrast, the best formulation using CRM197 was with intermediate 1 densities (10-15 haptens/CRM197 molecule), but the %MPE was approximately 13%. In addition, the chemical synthesis of 1, the optimization of the conjugation method, and the methods for the accurate quantification of hapten density are described.

Effects Of Active Anti-Methamphetamine Vaccination On Intravenous Self-Administration In Rats

Miller ML, Aarde SM, Moreno AY, Creehan KM, Janda KD, Taffe MA. *Drug Alcohol Depend.* 2015 Aug; 153[Epub ahead of print]29-36.

d-Methamphetamine (METH) addiction is a serious public health concern for which successful treatment remains elusive. Immunopharmacotherapy has been shown to attenuate locomotor and thermoregulatory effects of METH. The current study investigated whether active vaccination against METH could alter intravenous METH self-administration in rats. Male Sprague-Dawley rats (Experiment 1: N=24; Experiment 2: N=18) were vaccinated with either a control keyhole-limpet hemocyanin conjugate vaccine (KLH) or a candidate anti-METH vaccine (MH6-KLH) or. Effects of vaccination on the acquisition of METH self-administration under two dose conditions (0.05, 0.1mg/kg/inf) and post-acquisition dose-substitution (0, 0.01, 0.05, 0.20mg/kg/inf, Experiment 1; 0.01, 0.05, 0.10, 0.15mg/kg/inf, Experiment 2) during steady-state responding were investigated. Plasma METH concentrations were determined 30min after an acute challenge dose of 3.2mg/kg METH. Active vaccination inhibited the acquisition of METH self-administration under the 0.1mg/kg/inf dose condition, with 66% of the MH6-KLH-vaccinated rats compared to 100% of the controls reaching criteria, and produced transient and dose-dependent effects on self-administration during the maintenance phase. Under the 0.05mg/kg/inf dose condition, MH6-KLH-vaccinated rats initially self-administered more METH than controls, but then self-administration decreased across the acquisition phase relative to controls; a subsequent dose-response assessment confirmed that

MH6-KLH-vaccinated rats failed to acquire METH self-administration. Finally, plasma METH concentrations were higher in MH6-KLH-vaccinated rats compared to controls after an acute METH challenge, and these were positively correlated with antibody titers. These data demonstrate that active immunopharmacotherapy for METH attenuates the acquisition of METH self-administration.

[Extended-Release Mixed Amphetamine Salts Vs Placebo For Comorbid Adult Attention-Deficit/Hyperactivity Disorder And Cocaine Use Disorder: A Randomized Clinical Trial](#) Levin FR, Mariani JJ, Specker S, Mooney M, Mahony A, Brooks DJ, Babb D, Bai Y, Eberly LE, Nunes EV, Grabowski J. JAMA Psychiatry. 2015 Jun; 72(6):593-602.

Adult attention-deficit/hyperactivity disorder (ADHD) is prevalent but often unrecognized, in part because it tends to co-occur with other disorders such as substance use disorders. Cocaine use disorder is one such disorder with high co-occurrence of ADHD. The aim of this study was to examine whether treatment of co-occurring ADHD and cocaine use disorder with extended-release mixed amphetamine salts is effective at both improving ADHD symptoms and reducing cocaine use. This was a thirteen-week, randomized, double-blind, 3-arm, placebo-controlled trial of participants meeting DSM-IV-TR criteria for both ADHD and cocaine use disorder conducted between December 1, 2007, and April 15, 2013, at 2 academic health center substance abuse treatment research sites. One hundred twenty-six adults diagnosed as having comorbid ADHD and cocaine use disorder were randomized to extended-release mixed amphetamine salts or placebo. Analysis was by intent-to-treat population. Participants received extended-release mixed amphetamine salts (60 or 80 mg) or placebo daily for 13 weeks and participated in weekly individual cognitive behavioral therapy. For ADHD, percentage of participants achieving at least a 30% reduction in ADHD symptom severity, measured by the Adult ADHD Investigator Symptom Rating Scale; for cocaine use, cocaine-negative weeks (by self-report of no cocaine use and weekly benzoylecgonine urine screens) during maintenance medication (weeks 2-13) and percentage of participants achieving abstinence for the last 3 weeks. More patients achieved at least a 30% reduction in ADHD symptom severity in the medication groups (60 mg: 30 of 40 participants [75.0%]; odds ratio [OR] = 5.23; 95% CI, 1.98-13.85; P < .001; and 80 mg: 25 of 43 participants [58.1%]; OR = 2.27; 95% CI, 0.94-5.49; P = .07) compared with placebo (17 of 43 participants [39.5%]). The odds of a cocaine-negative week were higher in the 80-mg group (OR = 5.46; 95% CI, 2.25-13.27; P < .001) and 60-mg group (OR = 2.92; 95% CI, 1.15-7.42; P = .02) compared with placebo. Rates of continuous abstinence in the last 3 weeks were greater for the medication groups than the placebo group: 30.2% for the 80-mg group (OR = 11.87; 95% CI, 2.25-62.62; P = .004) and 17.5% for the 60-mg group (OR = 5.85; 95% CI, 1.04-33.04; P = .04) vs 7.0% for placebo. Extended-release mixed amphetamine salts in robust doses along with cognitive behavioral therapy are effective for treatment of co-occurring ADHD and cocaine use disorder, both improving ADHD symptoms and reducing cocaine use. The data suggest the importance of screening and treatment of ADHD in adults presenting with cocaine use disorder. clinicaltrials.gov Identifier:NCT00553319.

[The Effects Of Ibudilast, A Glial Activation Inhibitor, On Opioid Withdrawal Symptoms In Opioid-Dependent Volunteers](#) Cooper ZD, Johnson KW, Pavlicova M, Glass A, Vosburg SK, Sullivan MA, Manubay JM, Martinez DM, Jones JD, Saccone PA, Comer SD. Addict Biol. 2015 May; [Epub ahead of print].

Glial activation is hypothesized to contribute directly to opioid withdrawal. This study investigated the dose-dependent effects of a glial cell modulator, ibudilast, on withdrawal symptoms in opioid-

dependent volunteers after abrupt discontinuation of morphine administration. Non-treatment-seeking heroin-dependent volunteers (n = 31) completed the in-patient, double-blind, placebo-controlled, within-subject and between-group study. Volunteers were maintained on morphine (30 mg, QID) for 14 days and placebo (0 mg, QID) for the last 7 days of the 3-week study. Volunteers also received placebo (0 mg, PO, BID) capsules on days 1-7. On days 8-21, volunteers were randomized to receive ibudilast (20 or 40 mg, PO, BID) or placebo capsules. Subjective and clinical ratings of withdrawal symptoms were completed daily using the Subjective Opioid Withdrawal Scale (SOWS) and Clinical Opioid Withdrawal Scale (COWS). Medication side effects were also monitored. Relative to the first 2 weeks, all groups exhibited withdrawal during the third week as assessed by the SOWS and COWS ($P \leq 0.0001$). Although overall SOWS scores did not differ between groups, exploratory analyses pooling the two ibudilast groups demonstrated that they had lower ratings of withdrawal symptoms on SOWS items ('anxious,' 'perspiring,' 'restless,' 'stomach cramps') during detoxification relative to the placebo group. Ibudilast was well tolerated; no serious adverse events occurred during the study. Pharmacological modulation of glial activity with ibudilast decreased some subjective ratings of opioid withdrawal symptoms. These exploratory findings are the first to demonstrate the potential clinical utility of glial modulators for treating opioid withdrawal in humans.

Division of Epidemiology, Services and Prevention Research

Medical Marijuana Laws and Adolescent Marijuana Use In the USA From 1991 To 2014: Results From Annual, Repeated Cross-Sectional Surveys

Hasin DS, Wall M, Keyes KM, Cerdá M, Schulenberg J, O'Malley PM, Galea S, Pacula R, Feng T. *The Lancet* 2015; 2(7): 601-608. Adolescent use of marijuana is associated with adverse later effects, so the identification of factors underlying adolescent use is of substantial public health importance. The relationship between US state laws that permit marijuana for medical purposes and adolescent marijuana use has been controversial. Such laws could convey a message about marijuana acceptability that increases its use soon after passage, even if implementation is delayed or the law narrowly restricts its use. The authors used 24 years of national data from the USA to examine the relationship between state medical marijuana laws and adolescent use of marijuana. Using a multistage, random-sampling design with replacement, the Monitoring the Future study conducts annual national surveys of 8th, 10th, and 12th-grade students (modal ages 13-14, 15-16, and 17-18 years, respectively), in around 400 schools per year. Students complete self-administered questionnaires that include questions on marijuana use. The authors analysed data from 1 098 270 adolescents surveyed between 1991 and 2014. The primary outcome of this analysis was any marijuana use in the previous 30 days. They used multilevel regression modelling with adolescents nested within states to examine two questions. The first was whether marijuana use was higher overall in states that ever passed a medical marijuana law up to 2014. The second was whether the risk of marijuana use changed after passage of medical marijuana laws. Control covariates included individual, school, and state-level characteristics. Marijuana use was more prevalent in states that passed a medical marijuana law any time up to 2014 than in other states (adjusted prevalence 15.87% vs 13.27%; adjusted odds ratio [OR] 1.27, 95% CI 1.07-1.51; $p=0.0057$). However, the risk of marijuana use in states before passing medical marijuana laws did not differ significantly from the risk after medical marijuana laws were passed (adjusted prevalence 16.25% vs 15.45%; adjusted OR 0.92, 95% CI 0.82-1.04; $p=0.185$). Results were generally robust across sensitivity analyses, including redefining

marijuana use as any use in the previous year or frequency of use, and reanalysing medical marijuana laws for delayed effects or for variation in provisions for dispensaries. The authors' consistent with previous evidence, suggest that passage of state medical marijuana laws does not increase adolescent use of marijuana. However, overall, adolescent use is higher in states that ever passed such a law than in other states. State-level risk factors other than medical marijuana laws could contribute to both marijuana use and the passage of medical marijuana laws, and such factors warrant investigation.

Should Pathological Gambling and Obesity Be Considered Addictive Disorders? A Factor Analytic Study In A Nationally Representative Sample

Blanco C, Garcia-Anaya M, Wall M, de Los Cobos JCP, Swierad E, Wang S, Petry NM. *Drug Alcohol Depend.* 2015; 150: 129-134. Pathological gambling (PG) is now aligned with substance use disorders in the DSM-5 as the first officially recognized behavioral addiction. There is growing interest in examining obesity as an addictive disorder as well. The goal of this study was to investigate whether epidemiological data provide support for the consideration of PG and obesity as addictive disorders. Factor analysis of data from a large, nationally representative sample of US adults (N=43,093), using nicotine dependence, alcohol dependence, drug dependence, PG and obesity as indicators. It was hypothesized that nicotine dependence, alcohol dependence and drug use dependence would load on a single factor. It was further hypothesized that if PG and obesity were addictive disorders, they would load on the same factor as substance use disorders, whereas failure to load on the addictive factor would not support their conceptualization as addictive disorders. A model with one factor including nicotine dependence, alcohol dependence, drug dependence and PG, but not obesity, provided a very good fit to the data, as indicated by CFI=0.99, TLI=0.99 and RMSEA=0.01 and loadings of all indicators >0.4. Data from this study support the inclusion of PG in a latent factor with substance use disorders but do not lend support to the consideration of obesity, as defined by BMI, as an addictive disorder. Future research should investigate whether certain subtypes of obesity are best conceptualized as addictive disorders and the shared biological and environmental factors that account for the common and specific features of addictive disorders.

Discrimination, Racial Identity, and Cytokine Levels Among African-American Adolescents

Brody GH, Yu T, Miller GE, Chen E. *J Adolesc Health.* 2015;56(5):496-501.

Low-grade inflammation, measured by circulating levels of cytokines, is a pathogenic mechanism for several chronic diseases of aging. Identifying factors related to inflammation among African-American youths may yield insights into mechanisms underlying racial disparities in health. The purpose of the study was to determine whether (1) reported racial discrimination from ages 17-19 years forecasts heightened cytokine levels at the age of 22 years and (2) this association is lower for youths with positive racial identities. A longitudinal research design was used with a community sample of 160 African-Americans who were aged 17 years at the beginning of the study.

Discrimination and racial identity were measured with questionnaires, and blood was drawn to measure basal cytokine levels. Ordinary least squares regression analyses were used to examine the hypotheses. After controlling for socioeconomic risk, life stress, depressive symptoms, and body mass index, racial discrimination (*307; $p < .01$), racial identity (*-.179; $p < .05$), and their interaction (*-.180; $p < .05$) forecast cytokine levels. Youths exposed to high levels of racial discrimination evinced elevated cytokine levels 3½ years later. This association was not significant for young adults with positive racial identities. High levels of interpersonal racial discrimination and the development of a positive racial identity operate jointly to determine low-grade

inflammation levels that have been found to forecast chronic diseases of aging, such as coronary disease and stroke.

Increasing Progesterone Levels are Associated with Smoking Abstinence among Free-cycling Women Smokers Who Receive Brief Pharmacotherapy Saladin ME, McClure EA, Baker NL, Carpenter MJ, Ramakrishnan V, Hartwell KJ, Gray KM. *Nicotine Tob Res.* 2015;17(4):398-406. Preclinical and human laboratory research suggests that (a) progesterone may decrease drug reward, craving, and smoking behavior, and (b) estradiol may enhance drug reward and smoking behavior. A modest majority of treatment research examining the relationship between menstrual cycle phase and outcomes suggests that the luteal menstrual phase, with its uniquely higher progesterone levels, is associated with better cessation outcomes. However, no studies to date have examined the effects of naturally occurring variation in progesterone and estradiol levels on medication-assisted smoking cessation. The present study sought to fill this notable gap in the treatment literature. Weekly plasma progesterone and estradiol levels were obtained from nicotine-dependent female smokers enrolled in a 4-week cessation trial. Participants (N = 108) were randomized to receive a 4-week course of either varenicline (VAR) tablets and placebo patches or placebo tablets and nicotine patches. Plasma samples were obtained 1 week before their cessation attempt and weekly during medication administration. Abstinence was assessed weekly. Weekly hormone data replicated commonly observed menstrual cycle patterns of progesterone and estradiol levels. Importantly, increases in progesterone level were associated with a 23% increase in the odds for being abstinent within each week of treatment. This effect was driven primarily by nicotine patch-treated versus VAR-treated females. This study was the first to identify an association between progesterone level (increasing) and abstinence outcomes in free-cycling women smokers who participated in a medication-based treatment. Furthermore, the potential benefits of progesterone may vary across different pharmacotherapies. Implications of these findings for smoking cessation intervention are discussed.

Childhood Maltreatment and Its Effect On Neurocognitive Functioning: Timing and Chronicity Matter Cowell RA, Cicchetti D, Rogosch FA, Toth SL. *Dev Psychopathol.* 2015; 27(2): 521-533.

Childhood maltreatment represents a complex stressor, with the developmental timing, duration, frequency, and type of maltreatment varying with each child (Barnett, Manly, & Cicchetti, 1993; Cicchetti & Manly, 2001). Multiple brain regions and neural circuits are disrupted by the experience of child maltreatment (Cicchetti & Toth, in press; DeBellis et al., 2002; McCrory & Viding, 2010; Teicher, Anderson, & Polcari, 2012). These neurobiological compromises indicate the impairment of a number of important cognitive functions, including working memory and inhibitory control. The present study extends prior research by examining the effect of childhood maltreatment on neurocognitive functioning based on developmental timing of maltreatment, including onset, chronicity, and regency, in a sample of 3- to 9-year-old nonmaltreated (n = 136) and maltreated children (n = 223). Maltreated children performed more poorly on inhibitory control and working-memory tasks than did nonmaltreated children. Group differences between maltreated children based on the timing of maltreatment and the chronicity of maltreatment also were evident. Specifically, children who were maltreated during infancy, and children with a chronic history of maltreatment, exhibited significantly poorer inhibitory control and working-memory performance than did children without a history of maltreatment. The results suggest that maltreatment occurring during infancy, a period of major brain organization, disrupts normative structure and function, and

these deficits are further instantiated by the prolonged stress of chronic maltreatment during the early years of life.

[Long-term Nicotine Replacement Therapy: A Randomized Clinical Trial](#) Schnoll RA, Goelz PM, Veluz-Wilkins A, Blazekovic S, Powers L, Leone FT, Gariti P, Wileyto EP, Hitsman B. *JAMA Intern Med.* 2015; 175(4): 504-511.

The US Food and Drug Administration adopted labeling for nicotine patches to allow use beyond the standard 8 weeks. This decision was based in part on data showing increased efficacy for 24 weeks of treatment. Few studies have examined whether the use of nicotine patches beyond 24 weeks provides additional therapeutic benefit. To compare 8 (standard), 24 (extended), and 52 (maintenance) weeks of nicotine patch treatment for promoting tobacco abstinence, the authors recruited 525 treatment-seeking smokers for a randomized clinical trial conducted from June 22, 2009, through April 15, 2014, through 2 universities. Smokers received 12 smoking cessation behavioral counseling sessions and were randomized to 8, 24, or 52 weeks of nicotine patch treatment. The primary outcome was 7-day point prevalence abstinence, confirmed with breath levels of carbon monoxide at 6 and 12 months (intention to treat). At 24 weeks, 21.7% of participants in the standard treatment arm were abstinent, compared with 27.2% of participants in the extended and maintenance treatment arms ($\chi^2_1 = 1.98$; $P = .17$). In a multivariate model controlled for covariates, participants in the extended and maintenance treatment arms reported significantly greater abstinence rates at 24 weeks compared with participants in the standard treatment arm (odds ratio [OR], 1.70 [95% CI, 1.03-2.81]; $P = .04$), had a longer duration of abstinence until relapse ($\beta = 21.30$ [95% CI, 10.30-32.25]; $P < .001$), reported smoking fewer cigarettes per day if not abstinent (mean [SD], 5.8 [5.3] vs 6.4 [5.1] cigarettes per day; $\beta = .43$ [95% CI, 0.06-0.82]; $P = .02$), and reported more abstinent days (mean [SD], 80.5 [38.1] vs 68.2 [43.7] days; OR, 1.55 [95% CI, 1.06-2.26]; $P = .02$). At 52 weeks, participants in the maintenance treatment arm did not report significantly greater abstinence rates compared with participants in the standard and extended treatment arms (20.3% vs 23.8%; OR, 1.17 [95% CI, 0.69-1.98]; $P = .57$). Similarly, we found no difference in week 52 abstinence rates between participants in the extended and standard treatment arms (26.0% vs 21.7%; OR, 1.33 [95% CI, 0.72-2.45]; $P = .36$). Treatment duration was not associated with any adverse effects or adherence to the counseling regimen, but participants in the maintenance treatment arm reported lower adherence to the nicotine patch regimen compared with those in the standard and extended treatment arms (mean [SD], 3.94 [2.5], 4.61 [2.0], and 4.7 [2.4] patches/wk, respectively; $F_{2,522} = 6.03$; $P = .003$). The findings support the safety of long-term use of nicotine patch treatment, although they do not support efficacy beyond 24 weeks of treatment in a broad group of smokers.

AIDS Research Program

[Phosphorylation of HEXIM1 at Tyr271 and Tyr274 Promotes Release of P-TEFb from the 7SK snRNP Complex and Enhances Proviral HIV Gene Expression](#) Mbonye UR, Wang B, Gokulrangan G, Chance MR, Karn J. *Proteomics.* 2015 Jun;15(12):2078-2086.

Efficient HIV transcription requires P-TEFb, an essential co-factor for Tat. In actively replicating cells, P-TEFb is incorporated into the 7SK snRNP complex together with the repressor protein HEXIM1. Using an affinity purification-tandem mass spectrometry approach to identify modification sites on HEXIM1 that regulate the sequestration of P-TEFb by 7SK snRNP, the

authors found that HEXIM1 can be phosphorylated on adjacent residues in a region immediately upstream of the coiled-coil dimerization domain (Ser268, Thr270, Tyr271, and Tyr274). Phosphomimetic mutations of Tyr271 and Tyr274 disrupted the assembly of P-TEFb and HEXIM1 into the 7SK snRNP complex. Although Y271E/Y274E did not adversely affect the nuclear localization pattern of HEXIM1, it induced the redistribution of the CDK9 subunit of P-TEFb into the cytoplasm. By contrast, the Y271F/Y274F HEXIM1 mutant assembled normally with P-TEFb within the 7SK snRNP complex but severely reduced proviral gene expression in T cells in response to activation signals and caused a severe growth defect of Jurkat T cells. Thus, Y271F/Y274F, which cannot be phosphorylated on these residues, appears to block the exchange of active P-TEFb from the 7SK complex, thereby limiting the level of P-TEFb below the threshold required to support transcription elongation of the HIV provirus and cellular genes.

Targeting Prevention based on Molecular Epidemiology among Deeply Sampled Sub-Networks of Men Have who Sex with Men Wang X, Wu Y, Mao L, Xia W, Zhang W, Dai L, Mehta SR, Wertheim JO, Dong X, Zhang T, Wu H, Smith DM. Clin Infect Dis. 2015 Jun 30. pii: civ526.

Molecular epidemiology can be useful in identifying high-risk clusters of transmission that can be targeted for prevention interventions. Regular screening of 2,000 MSM in Beijing China for HIV infection every two months identified 176 primary infections (2007- 2010). HIV-1 pol sequences were obtained and used to infer the transmission network and identify transmitted drug resistance (TDR) among these individuals. The authors evaluated the use of clinical and network information to target prevention efforts. Prevention efficiency was calculated as number of infections saved per number of interventions. This cohort was infected with HIV-1 subtype B (28%), CRF_01 AE (53%), and CRF_07 BC (16%). The overall rate of TDR was low (5%) but the rate of clustering was very high (63%), suggesting deep sampling of the local sub-network. Provision of a theoretically high efficacy intervention, like antiretroviral therapy, to all participants had a prevention efficiency of 23%. The efficiency of targeting prevention based on lower CD4 counts (<200 cells/ml, <350 cells/ml or <500 cells/ml) and higher HIV viral loads (>100,000 copies/ml and >50,000 copies/ml) were between 10 and 18%. The efficiency of targeting prevention based on number of network connections was much higher (30-42%). For example, treating the 33 participants with ≥ 5 connections in 2009 would have theoretically prevented 14 infections in 2010 (42% prevention efficacy). Regular HIV testing of MSM in Beijing can deeply sample the local transmission sub-network, and targeting prevention efforts based on network connectivity may be an efficient way to deliver prevention interventions.

Cocaine Promotes both Initiation and Elongation Phase of HIV-1 Transcription by Activating NF- κ B and MSK1 and Inducing Selective Epigenetic Modifications at HIV-1LTR Sahu G, Farley K, El-Hage N, Aiamkitsumrit B, Fassnacht R, Kashanchi F, Ochem A, Simon GL, Karn J, Hauser KF, Tyagi M. Virology 2015; 483:185-202.

Cocaine accelerates human immunodeficiency virus (HIV-1) replication by altering specific cell-signaling and epigenetic pathways. The authors have elucidated the underlying molecular mechanisms through which cocaine exerts its effect in myeloid cells, a major target of HIV-1 in central nervous system (CNS). They demonstrate that cocaine treatment promotes HIV-1 gene expression by activating both nuclear factor-kappa B (NF- κ B) and mitogen- and stress-activated kinase 1 (MSK1). MSK1 subsequently catalyzes the phosphorylation of histone H3 at serine 10, and p65 subunit of NF- κ B at 276th serine residue. These modifications enhance the interaction of NF-

κ B with P300 and promote the recruitment of the positive transcription elongation factor b (P-TEFb) to the HIV-1 LTR, supporting the development of an open/relaxed chromatin configuration, and facilitating the initiation and elongation phases of HIV-1 transcription. Results are also confirmed in primary monocyte derived macrophages (MDM). Overall, this study provides detailed insights into cocaine-driven HIV-1 transcription and replication.

The Causal Effect of Opioid Substitution Treatment on HAART Medication Refill Adherence

Nosyk B, Min JE, Colley G, Lima VD, Yip B, Milloy M-JS, Wood E, Montaner JSG. AIDS 2015; 29(8):965-973.

People who inject drugs (PWID) account for roughly 13% of the prevalent HIV/AIDS population outside of sub-Saharan Africa, and access to opioid substitution treatment (OST) is limited in many settings globally. OST likely facilitates access to HAART, yet sparse evidence is available to support this hypothesis. Our objective was to determine the causal impact of OST exposure on HAART adherence among HIV-positive PWID in a Canadian setting. The authors executed a retrospective cohort study using linked population-level data for British Columbia, Canada (January 1996-March 2010). They considered HIV-positive PWID after meeting HAART initiation criteria. A marginal structural model was estimated on a monthly timescale using inverse probability of treatment weights. The primary outcome was 95% HAART adherence, according to pharmacy refill compliance. Exposure to OST was defined as 95% of OST receipt, and we controlled for a range of fixed and time-varying covariates. This study included 1852 (63.3%) HIV-positive PWID with a median follow-up of 5.5 years; 34% were female and 39% had previously accessed OST. The baseline covariate-adjusted odds of HAART adherence following OST exposure was 1.96 (95% confidence interval: 1.72-2.24), although the adjusted odds estimated within the marginal structural model was 1.68 (1.48-1.92). Findings were robust to sensitivity analyses on model specification. The authors conclude that in a setting characterized by universal healthcare and widespread access to both office-based OST and HAART, OST substantially increased the odds of HAART adherence. This underlines the need to address barriers to OST globally to reduce the disease burden of both opioid dependence and HIV/AIDS.

HIV Latency Is Established Directly and Early in Both Resting and Activated Primary CD4 T Cells

Chavez L, Calvanese V, Verdin E. PLoS Pathogens Published: June 11, 2015

Highly active antiretroviral therapy (HAART) suppresses human immunodeficiency virus (HIV) replication to undetectable levels but cannot fully eradicate the virus because a small reservoir of CD4⁺ T cells remains latently infected. Since HIV efficiently infects only activated CD4⁺ T cells and since latent HIV primarily resides in resting CD4⁺ T cells, it is generally assumed that latency is established when a productively infected cell recycles to a resting state, trapping the virus in a latent state. In this study, the authors use a dual reporter virus—HIV Duo-Fluo I, which identifies latently infected cells immediately after infection—to investigate how T cell activation affects the establishment of HIV latency. They show that HIV latency can arise from the direct infection of both resting *and* activated CD4⁺ T cells. Importantly, returning productively infected cells to a resting state is not associated with a significant silencing of the integrated HIV. The authors further show that resting CD4⁺ T cells from human lymphoid tissue (tonsil, spleen) show increased latency after infection when compared to peripheral blood. These findings raise significant questions regarding the most commonly accepted model for the establishment of latent HIV and suggest that infection of both resting and activated primary CD4⁺ T cells produce latency.

The Effects of Opioid Substitution Treatment and Highly Active Antiretroviral Therapy on the Cause-Specific Risk of Mortality Among HIV-Positive People Who Inject Drugs Nosyk B, Min JE, Evans E, Li L, Liu L, Lima VD, Wood E, Montaner JSG. *Clinical Infectious Diseases* 2015; civ476v2-civ476.

Prior studies indicated opioid substitution treatment (OST) reduces mortality risk and improves the odds of accessing highly active antiretroviral therapy (HAART); however, the relative effects of these treatments for human immunodeficiency virus (HIV)-positive people who inject drugs (PWID) are unclear. The authors determine the independent and joint effects of OST and HAART on mortality, by cause, within a population of HIV-positive PWID initiating HAART. Using a linked population-level database for British Columbia, Canada, the authors used time-to-event analytic methods, including competing risks models, proportional hazards models with time-varying covariates, and marginal structural models, to identify the independent and joint effects of OST and HAART on all-cause as well as drug- and HIV-related mortality, controlling for covariates. Among 1727 HIV-positive PWID, 493 (28.5%) died during a median 5.1 years (interquartile range, 2.1–9.1) of follow-up: 18.7% due to drug-related causes, 55.8% due to HIV-related causes, and 25.6% due to other causes. Standardized mortality ratios were 12.2 (95% confidence interval [CI], 9.8, 15.0) during OST and 30.0 (27.1, 33.1) during periods out of OST. Both OST (adjusted hazard, 0.34; 95% CI, .23, .49) and HAART (0.39 [0.31, 0.48]) decreased the hazard of all-cause mortality; however, individuals were at lowest risk of death when these medications were used jointly (0.16 [0.10, 0.26]). Both OST and HAART independently protected against HIV-related death, drug-related death and death due to other causes. While both OST and HAART are life-saving treatments, joint administration is urgently needed to protect against both drug- and HIV-related mortality.

Center for Clinical Trials Network

Health-Related Quality Of Life Among Prescription Opioid-Dependent Patients: Results From A Multi-Site Study Griffin ML, Bennett HE, Fitzmaurice GM, Hill KP, Provost SE, Weiss RD. *Am J Addict.* 2015 Jun;24(4):308-314. Epub 2015 Mar 24.

Although prescription opioid use disorder has recently increased sharply in the United States, relatively little is known about the general well-being of this population. Assessment of quality of life in patients with substance use disorders has been recommended to improve clinical care. Health-related quality of life was examined in prescription opioid-dependent patients at entry to a national multi-site clinical trial, to compare quality of life scores in the study sample to other populations; further, background variables associated with quality of life in the literature were examined. Prescription opioid-dependent patients (N = 653) were compared to general populations on the Medical Outcome Study Short Form-36 (SF-36) quality of life measure; and the association between patient background variables and quality of life was examined. Compared to a general population, the current sample of prescription opioid-dependent patients had worse physical (-1.7 points, $p < .001$) and mental quality of life (-12.3 points, $p < .001$) as measured by the SF-36, similar to other opioid-use disorder populations. Within the present sample, women showed more impairment than men in mental quality of life (-4.3 points, $p < .001$); older patients scored worse on physical (-5.2 points, $p < .001$), but not mental, quality of life. Chronic pain was associated with poorer physical quality of life (-9.0 points, $p < .001$). The growing focus on wellness underscores the importance of measuring quality of life in addition to substance use outcomes. Routine assessment

of health-related quality of life can add an important dimension to overall evaluation of patients' treatment response.

Anxiety and Depressed Mood Decline Following Smoking Abstinence In Adult Smokers With Attention Deficit Hyperactivity Disorder Covey LS, Hu M-C, Winhusen T, Lima J, Berlin I, Nunes E. *J Subst Abuse Treat* (2015), available online 17 July 2015.

A preponderance of relevant research has indicated reduction in anxiety and depressive symptoms following smoking abstinence. This secondary analysis investigated whether the phenomenon extends to smokers with attention deficit hyperactivity disorder (ADHD). The study setting was an 11-Week double-blind placebo-controlled randomized trial of osmotic release oral system methylphenidate (OROS-MPH) as a cessation aid when added to nicotine patch and counseling. Participants were 255 adult smokers with ADHD. The study outcomes are: anxiety (Beck Anxiety Inventory (BAI)) and depressed mood (Beck Depression Inventory II (BDI)) measured one Week and six Weeks after a target quit day (TQD). The main predictor is point -prevalence abstinence measured at Weeks 1 and 6 after TQD. Covariates are treatment (OROS-MPH vs placebo), past major depression, past anxiety disorder, number of cigarettes smoked daily, demographics (age, gender, education, marital status) and baseline scores on the BAI, BDI, and the DSM-IV ADHD Rating Scale. Abstinence was significantly associated with lower anxiety ratings throughout the post-quit period ($p < 0.001$). Depressed mood was lower for abstainers than non-abstainers at Week 1 ($p < 0.05$), but no longer at Week 6 ($p = 0.83$). Treatment with OROS-MPH relative to placebo showed significant reductions at Week 6 after TQD for both anxiety ($p < 0.05$) and depressed mood ($p < 0.001$), but not at Week 1. Differential abstinence effects of gender were observed. Anxiety and depression ratings at baseline predicted increased ratings of corresponding measures during the post-quit period. Stopping smoking yielded reductions in anxiety and depressed mood in smokers with ADHD treated with nicotine patch and counseling. Treatment with OROS-MPH yielded mood reductions in delayed manner.

The Effects Of Brief Strategic Family Therapy (BSFT) On Parent Substance Use and the Association Between Parent and Adolescent Substance Use Horigian VE, Feaster DJ, Brincks A, Robbins MS, Perez MA, Szapocznik J. *Addict Behav.* 2015 Mar;42:44-50. Epub 2014 Nov 4.

The effects of family therapy for adolescent substance use on parent substance use have not been explored. The objectives of this study were to determine the effects of Brief Strategic Family Therapy® (BSFT®) on parent substance use, and the relationship between parent substance use and adolescent substance use. 480 adolescents and parents were randomized to BSFT or Treatment as Usual (TAU) across eight outpatient treatment programs. Parent substance use was assessed at baseline and at 12months post-randomization. Adolescent substance use was assessed at baseline and monthly for 12months post-randomization. Family functioning was assessed at baseline, 4, 8, and 12months post-randomization. Parents in BSFT significantly decreased their alcohol use as measured by the ASI composite score from baseline to 12months ($\chi^2(1)=4.46, p=.04$). Change in family functioning mediated the relationship between Treatment Condition and change in parent alcohol use. Children of parents who reported drug use at baseline had three times as many days of reported substance use at baseline compared with children of parents who did not use or only used alcohol ($\chi^2(2)=7.58, p=.02$). Adolescents in BSFT had a significantly lower trajectory of substance use than those in TAU ($\beta=-7.82, p<.001$) if their parents used drugs at baseline.

BSFT is effective in reducing alcohol use in parents, and in reducing adolescents' substance use in families where parents were using drugs at baseline. BSFT may also decrease alcohol use among parents by improving family functioning.

[A Systematic Approach To Subgroup Analyses In A Smoking Cessation Trial](#) Westover AN, Kashner TM, Winhusen TM, Golden RM, Nakonezny PA, Adinoff B, Henley SS. Am J Drug Alcohol Abuse. 2015 Jun 11:1-10. [Epub ahead of print].

Traditional approaches to subgroup analyses that test each moderating factor as a separate hypothesis can lead to erroneous conclusions due to the problems of multiple comparisons, model misspecification, and multicollinearity.

The objective of this study was to demonstrate a novel, systematic approach to subgroup analyses that avoids these pitfalls. A Best Approximating Model (BAM) approach that identifies multiple moderators and estimates their simultaneous impact on treatment effect sizes was applied to a randomized, controlled, 11-week, double-blind efficacy trial on smoking cessation of adult smokers with attention-deficit/hyperactivity disorder (ADHD), randomized to either OROS-methylphenidate (n = 127) or placebo (n = 128), and treated with nicotine patch. Binary outcomes measures were prolonged smoking abstinence and point prevalence smoking abstinence. Although the original clinical trial data analysis showed no treatment effect on smoking cessation, the BAM analysis showed significant subgroup effects for the primary outcome of prolonged smoking abstinence: (1) lifetime history of substance use disorders (adjusted odds ratio [AOR] 0.27; 95% confidence interval [CI] 0.10-0.74), and (2) more severe ADHD symptoms (baseline score >36; AOR 2.64; 95% CI 1.17-5.96). A significant subgroup effect was also shown for the secondary outcome of point prevalence smoking abstinence - age 18 to 29 years (AOR 0.23; 95% CI 0.07-0.76).

The BAM analysis resulted in different conclusions about subgroup effects compared to a hypothesis-driven approach. By examining moderator independence and avoiding multiple testing, BAMs have the potential to better identify and explain how treatment effects vary across subgroups in heterogeneous patient populations, thus providing better guidance to more effectively match individual patients with specific treatments.

Women and Sex/Gender Differences Research Program

[Sex Differences in Behavioral Impulsivity in At-Risk and Non-Risk Drinkers](#) Weafer J, De Arcangelis J, de Wit H. Front Psychiatry. 2015 May 13;6:72.

Mounting evidence from both animal and human studies suggests that females are more vulnerable to drug and alcohol abuse than males. Some of this increased risk may be related to behavioral traits, such as impulsivity. Here, the authors examined sex differences in two forms of behavioral impulsivity (inhibitory control and impulsive choice) in young men and women, in relation to their level of alcohol consumption and alcohol-related problems (at-risk or non-risk). Participants performed a go/no-go task to assess inhibitory control and a measure of delay discounting to assess impulsive choice. On the measure of inhibitory control, at-risk women committed significantly more inhibitory errors than at-risk men, indicating poorer behavioral control among the women. By contrast, no sex differences were observed between at-risk men and women in delay discounting, or between the male and female non-risk drinkers on any measure. Heavy drinking women displayed poorer inhibitory control than heavy drinking men. It remains to be determined whether the sex

differences in inhibitory control are the result of drinking, or whether they pre-dated the problematic drinking in these individuals.

Intramural Research Program

Allosteric Interactions Between Agonists and Antagonists Within the Adenosine A2A Receptor-Dopamine D2 Receptor Heterotetramer Bonaventura J, Navarro G, Casadó-Anguera V, Azdad K, Rea W, Moreno E, Brugarolas M, Mallol J, Canela EI, Lluís C, Cortés A, Volkow ND, Schiffmann SN, Ferré S, Casadó V. Proceedings of the National Academy of Sciences USA 2015; 112: E3609-E3618.

Adenosine A2A receptor (A2AR)-dopamine D2 receptor (D2R) heteromers are key modulators of striatal neuronal function. It has been suggested that the psychostimulant effects of caffeine depend on its ability to block an allosteric modulation within the A2AR-D2R heteromer, by which adenosine decreases the affinity and intrinsic efficacy of dopamine at the D2R. The authors describe novel unsuspected allosteric mechanisms within the heteromer by which not only A2AR agonists, but also A2AR antagonists, decrease the affinity and intrinsic efficacy of D2R agonists and the affinity of D2R antagonists. Strikingly, these allosteric modulations disappear on agonist and antagonist coadministration. This can be explained by a model that considers A2AR-D2R heteromers as heterotetramers, constituted by A2AR and D2R homodimers, as demonstrated by experiments with bioluminescence resonance energy transfer and bimolecular fluorescence and bioluminescence complementation. As predicted by the model, high concentrations of A2AR antagonists behaved as A2AR agonists and decreased D2R function in the brain.

Sigma-1 Receptor Regulates Tau Phosphorylation and Axon Extension By Shaping P35 Turnover Via Myristic Acid Tsai SY, Pokrass MJ, Klauer NR, Nohara H, Su TP. Proc. Natl. Acad. Sci. USA 2015; 112: 6742-6747.

Dysregulation of cyclin-dependent kinase 5 (cdk5) per relative concentrations of its activators p35 and p25 is implicated in neurodegenerative diseases. P35 has a short half-life and undergoes rapid proteasomal degradation in its membrane-bound myristoylated form. P35 is converted by calpain to p25 which, along with an extended half-life, promotes aberrant activation of cdk5 and causes abnormal hyperphosphorylation of tau, thus leading to the formation of neurofibrillary tangles. The sigma-1 receptor (Sig-1R) is an endoplasmic reticulum chaperone that is implicated in neuronal survival. However, the specific role of the Sig-1R in neurodegeneration is unclear. Here the authors found that Sig-1Rs regulate proper tau phosphorylation and axon extension by promoting p35 turnover through the receptor's interaction with myristic acid. In Sig-1R knockout neurons, a greater accumulation of p35 is seen, which is neither due to elevated transcription of p35 nor to disrupted calpain activity, but rather to the slower degradation of p35. In contrast, Sig-1R overexpression causes a decrease of p35. Sig-1R knockout neurons exhibit shorter axons with lower densities. Myristic acid is found here to bind Sig-1R as an agonist that causes the dissociation of Sig-1R from its cognate partner BiP. Remarkably, treatment of Sig-1R knockout neurons with exogenous myristic acid mitigates p35 accumulation, diminishes tau phosphorylation, and restores axon elongation. These results define the involvement of Sig-1Rs in neurodegeneration and provide a mechanistic explanation that Sig-1Rs help maintain proper tau phosphorylation by potentially carrying and providing myristic acid to p35 for enhanced p35 degradation to circumvent the formation of over-reactive cdk5/p25.

[Incubation Of Methamphetamine Craving Is Associated With Selective Increases In Expression Of BDNF and Trkb, Glutamate Receptors, and Epigenetic Enzymes In Cue-Activated Fos-Expressing Dorsal Striatal Neurons](#) Li X, Rubio FJ, Zeric T, Bossert JM, Cates H, Kennedy P, Liu QR, Cimbroti R, Nestler EJ, Hope BT, Shaham Y. *The Journal of Neuroscience* 2015; 35: 8232-8244.

Cue-induced methamphetamine seeking progressively increases after withdrawal (incubation of methamphetamine craving) but the underlying mechanisms are largely unknown. The authors determined whether this incubation is associated with alterations in candidate genes in dorsal striatum (DS), a brain area implicated in cue- and context-induced drug relapse. They first measured mRNA expression of 24 candidate genes in whole DS extracts after short (2 d) or prolonged (1 month) withdrawal in rats following extended access methamphetamine or saline (control) self-administration (9-h/day; 10-days). They found minimal changes. Next, using FACS, they compared gene expression in Fos-positive dorsal striatal neurons, which were activated during 'incubated' cue-induced drug-seeking tests after prolonged withdrawal, with non-activated Fos-negative neurons. They found significant increases in mRNA expression of immediate early genes (IEGs: Arc, Egr1), Bdnf and its receptor (Trkb), glutamate receptor subunits (Gria1, Gria3, Grm1), and epigenetic enzymes (Hdac3, Hdac4, Hdac5, GLP, Dnmt3a, Kdm1a) in the Fos-positive neurons only. Using RNAscope® to determine striatal sub-region and cell-type specificity of the activated neurons, the authors measured co-labeling of Fos with Drd1 and Drd2 in three DS sub-regions. Fos expression was neither sub-region nor cell-type specific (52.5% and 39.2% of Fos expression co-labeled with Drd1 and Drd2, respectively). Finally, they found that DS injections of SCH23390, a D1-family receptor antagonist known to block cue-induced Fos induction, decreased 'incubated' cue-induced methamphetamine seeking after prolonged withdrawal. Results demonstrate a critical role of DS in incubation of methamphetamine craving and that this incubation is associated with selective gene-expression alterations in cue-activated D1- and D2-expressing DS neurons.

[Impaired Functional Connectivity Within and Between Frontostriatal Circuits Is Associated With Compulsive Drug Use and Trait Impulsivity In Cocaine Addiction](#) Hu, Y, Salmeron, BJ, Gu, H, Stein, EA, Yang, Y. *JAMA Psychiatry* 2015; 72, 584-592.

Converging evidence has long identified both impulsivity and compulsivity as key psychological constructs in drug addiction. Although dysregulated striatal-cortical network interactions have been identified in cocaine addiction, the association between these brain networks and addiction is poorly understood. The aims of this study were to test the hypothesis that cocaine addiction is associated with disturbances in striatal-cortical communication as captured by resting-state functional connectivity (rsFC), measured from coherent spontaneous fluctuations in the blood oxygenation level-dependent functional magnetic resonance imaging signal, and to explore the relationships between striatal rsFC, trait impulsivity, and uncontrolled drug use in cocaine addiction. A case-control, cross-sectional study was conducted at the National Institute on Drug Abuse Intramural Research Program outpatient magnetic resonance imaging facility. Data used in the present study were collected between December 8, 2005, and September 30, 2011. Participants included 56 non-treatment-seeking cocaine users (CUs) (52 with cocaine dependence and 3 with cocaine abuse) and 56 healthy individuals serving as controls (HCs) matched on age, sex, years of education, race, estimated intelligence, and smoking status. Voxelwise statistical parametric analysis testing the rsFC strength differences between CUs and HCs in brain regions functionally connected to 6 striatal subregions defined a priori. Increased rsFC strength was observed predominantly in striatal-frontal circuits; decreased rsFC was found between the striatum and cingulate, striatal, temporal,

hippocampal/amygdalar, and insular regions in the CU group compared with the HCs. Increased striatal-dorsal lateral prefrontal cortex connectivity strength was positively correlated with the amount of recent cocaine use (uncorrected $P < .046$) and elevated trait impulsivity in the CUs (uncorrected $P < .012$), and an index reflecting the balance between striatal-dorsal anterior cingulate cortex and striatal-anterior prefrontal/orbitofrontal cortex circuits was significantly associated with loss of control over cocaine use (corrected $P < .012$). Cocaine addiction is associated with disturbed rsFC in several specific striatal-cortical circuits. Specifically, compulsive cocaine use, a defining characteristic of dependence, was associated with a balance of increased striatal-anterior prefrontal/orbitofrontal and decreased striatal-dorsal anterior cingulate connectivity; trait impulsivity, both a risk factor for and a consequence of cocaine use, was associated with increased dorsal striatal-dorsal lateral prefrontal cortex connectivity uniquely in CUs. These findings provide new insights toward the neurobiological mechanisms of addiction and suggest potential novel therapeutic targets for treatment.

Structure-Activity Relationships Of (+)-Naltrexone-Inspired Toll-Like Receptor 4 (TLR4)

Antagonists Selfridge BR, Wang X, Zhang Y, Yin H, Grace PM, Watkins LR, Jacobson AE, Rice KC. *J Med Chem.* 2015; 58(12): 5038-5052.

Activation of Toll-like receptors has been linked to neuropathic pain and opioid dependence. (+)-Naltrexone acts as a Toll-like receptor 4 (TLR4) antagonist and has been shown to reverse neuropathic pain in rat studies. The authors designed and synthesized compounds based on (+)-naltrexone and (+)-noroxymorphone and evaluated their TLR4 antagonist activities by their effects on inhibiting lipopolysaccharide (LPS) induced TLR4 downstream nitric oxide (NO) production in microglia BV-2 cells. Alteration of the N-substituent in (+)-noroxymorphone gave us a potent TLR4 antagonist. The most promising analog, (+)-N-phenethylnoroxymorphone ((4S,4aR,7aS,12bR)-4a,9-dihydroxy-3-phenethyl-2,3,4,4a,5,6-hexahydro-1H-4,12-methanobenzofuro[3,2-e]isoquinolin-7(7aH)-one, 1j) showed ~75 times better TLR-4 antagonist activity than (+)-naltrexone, and the ratio of its cell viability IC₅₀, a measure of its toxicity, to TLR-4 antagonist activity (140 μ M/1.4 μ M) was among the best of the new analogs. This compound (1j) was active in vivo; it significantly increased and prolonged morphine analgesia.

NIH/HHS POLICY UPDATES

For a complete list see <http://grants.nih.gov/grants/policy/policy.htm>

April 29, 2015

Chimpanzee Research Use (CRU) Reporting System

Applicants who propose to use chimpanzees (Pan troglodytes) in research can use the Chimpanzee Research Use (CRU) Reporting System to submit CRU Form information to NIH. ([NOT-OD-15-097](#))

April 30, 2015

ASSIST an Option for R01, U01 and Career Dev Apps

ASSIST is a submission option for NIH's Research Grant (R01), Cooperative Agreement (U01) and Individual Career Development Award (K, excluding KM1 and K12) programs. ([Rock Talk Blog post](#)) ([NOT-OD-15-098](#))

May 25, 2015

NIH and AHRQ Require New Biosketch Format

NIH and AHRQ require use of a new biosketch format in applications for research grants submitted for due dates on or after May 25, 2015. ([Rock Talk Blog post](#)) ([NOT-OD-15-032](#))

May 25, 2015

Publications in Training and Career Dev Progress Reports & Renewals

Clarification regarding publications in progress reports and renewal applications for institutional training, career development, and related awards. ([NOT-OD-15-091](#))

May 28, 2015

Reminder of Transition to PMS Subaccounts

Reminder of implementation timeline for the NIH transition to new U.S. DHHS payment policies for domestic, non-competing continuation awards and use of Payment Management System (PMS) subaccounts. ([NOT-OD-15-105](#))

June 9, 2015

Enhancing Reproducibility through Rigor and Transparency

NIH announces plans to clarify application instructions and review criteria to enhance reproducibility of research findings through increased scientific rigor and transparency. Effective for for grant applications due January 25, 2016 and beyond. ([Rock Talk Blog post](#)) ([NOT-OD-15-103](#))

June 9, 2015

Consideration of Sex as Biological Variable in Research

NIH clarifies expectations for how scientists will account for the possible role of sex as a biological variable in vertebrate animal and human studies in applications due January 25, 2016 and beyond. ([NOT-OD-15-102](#))

June 9, 2015

Clarifying Publication Reporting for RPPR and Renewals

NIH clarifies which papers arising from institutional training, career development, and related awards should be compliant with the public access policy and reported in the publication list of an RPPR or a renewal application. ([NOT-OD-15-091](#))

June 17, 2015

Deadline for Final Closeout Reports

NIH reminds applicants of deadlines for the submission of final reports required for grant closeout. ([NOT-OD-15-111](#))

June 29, 2015

Future Changes to Research Training Data Tables

NIH plans to adopt new training table formats in FY16 for institutional training grant applications and progress reports. The max number of tables will be reduced from 12 to 8, reporting of individual-level information will be minimized, and the tracking of trainee outcomes will be extended from 10 to 15 years. ([NOT-OD-15-112](#))

CONGRESSIONAL AFFAIRS SECTION
(Prepared August 24, 2015)

APPROPRIATIONS

Committees in the House and Senate have approved bills, and the process is currently stalled. There is general expectation that a Continuing Resolution will be needed to fund agency operations as of October 1.

CONGRESSIONAL HEARINGS/BRIEFINGS, etc.

Capitol Hill Activity continued briskly in this time period. Events included:

- May 12 – Marijuana briefing sponsored by the American Association for the Advancement of Science. Dr. Volkow provided remarks on the health effects associated with cannabis use. See <http://www.aaas.org/news/legal-use-marijuana-spreads-researchers-seek-better-assess-risks-and-benefits>.
- May 12 – At the request of Representative Hal Rogers (R-KY), Dr. Volkow participated in a Capitol Hill briefing sponsored by the Congressional Prescription Drug Caucus. She presented on the research and science around opioid addiction and treatment.
- May 12 – At the request of Representative John Fleming (R-LA), Dr. Volkow met with him and staff to discuss marijuana research and health issues.
- May 19 – Dr. Volkow accompanied NIH Director Dr. Francis Collins to the inaugural meeting of the Senate NIH Caucus. See <http://www.durbin.senate.gov/newsroom/press-releases/durbin-graham-launch-senate-nih-caucus>.
- May 27 – Several staff from the Senate Committee on Health, Education, Labor and Pensions visited NIH. Dr. Volkow provided them with a short briefing on NIDA issues and priorities.
- June 1 – The Friends of NIDA sponsored another outstanding Capitol Hill Briefing, this one focused on heroin and opioid addiction and overdose. Dr. Volkow provided remarks, and the event was very heavily attended. See <http://www.apa.org/science/about/psa/2015/07/heroin-opioid-addiction.aspx>
- 6/19 – At the request of the House Energy and Commerce Committee staff, Dr. Volkow provided a briefing on marijuana research and health issues.
- 6/24 – The Senate Caucus on International Narcotics Control held a hearing focused on barriers to cannabidiol research. Dr. Volkow and others testified – see <http://www.drugcaucus.senate.gov/content/drug-caucus-hearing-barriers-cannabidiol->

[research](#) for more information, and <http://www.drugcaucus.senate.gov/hearings> for video of the hearing.

- 7/29 -- The Addiction Policy Forum held another in its series of Capitol Hill briefings focused on opioids issues. This installment focused particularly on military personnel and veterans, and NIDA staff worked with the Forum to help frame issues. See <http://addictionpolicy.org/vets-forum/>.

LEGISLATION OF INTEREST

Marijuana Focus

H.R. 262 – On January 9, Representative Barbara Lee (D-CA) introduced the States’ Medical Marijuana Property Rights Protection Act, to amend the Controlled Substances Act so as to exempt real property from civil forfeiture due to medical marijuana-related conduct that is authorized by State law. The bill was referred to the Committees on Judiciary and Energy and Commerce.

H.R. 525 -- On January 26, Representative Massie Thomas (R-KY) introduced the Industrial Hemp Farming Act of 2015, to amend the Controlled Substances Act to exclude industrial hemp from the definition of marijuana, and for other purposes. The bill was referred to the Judiciary Committee and Energy and Commerce Committee. See S.134.

H.R. 667 – On February 3, Representative Earl Blumenauer (D-OR) introduced the Veterans Equal Access act, to authorize the Department of Veterans Affairs health care providers to provide recommendations and opinions to veterans regarding participation in state medical marijuana programs. The bill was referred to the Committee on Energy and Commerce.

H.R. 1013 – On February 20, Representative Jared Polis (D-CO) introduced the Regulate Marijuana like Alcohol Act, to decriminalize marijuana at the federal level, to leave to the states the power to regulate marijuana in a similar way to the way they regulate alcohol, and for other purposes. The bill was referred to several committees: Judiciary, Ways and Means, Energy and Commerce, Natural Resources.

H.R. 1014 – On February 20, Representative Earl Blumenauer introduced the Marijuana Tax Revenue act of 2015, to amend the IRS code of 1986 to provide for the taxation of marijuana. The bill was referred to the Committee on Ways and Means.

H.R. 1538 – On March 23, Representative Steve Cohen (D-TN) introduced the CARERS Act, to extend the principle of federalism to State drug policy, provide access to medical marijuana, and enable research into the medicinal properties of marijuana. The bill was referred to the committees on Energy and Commerce, Judiciary, Veterans, and Financial Services. See S.683.

H.R. 1635 – On March 25, Representative Scott Perry (R-PA) introduced the Charlotte’s Web Medical Access Act of 2015, to amend the controlled substances act to exclude cannabidiol-rich

plants from the definition of marijuana. The bill was referred to the committees on Energy and Commerce and Judiciary. See S. 1333

H.R. 1774 – On April 14, Representative Morgan Griffith (R-VA) introduced the Compassionate Access Act, to provide for the rescheduling of marijuana, the medical use of marijuana in accordance with state law, and the exclusion of cannabidiol from the definition of marijuana. The bill was referred to the committees on Energy and Commerce and Judiciary.

H.R. 1855 – On April 16, Representative Earl Blumenauer (D-OR) introduced the Small Business Tax Equity act, a bill to amend the Internal Revenue Code of 1986 to allow deductions and credits relating to expenditures in connection with marijuana sales conducted in compliance with State law. The bill was referred to the Committee on Ways and Means. See S. 987.

H.R. 1940 – On April 22, Representative Dana Rohrbacher (R-CA) introduced the Respect State Marijuana Laws Act of 2015, to amend the Controlled Substances Act to provide for a new rule regarding the application of the Act to marihuana, and for other purposes. The bill was referred to the Committees on Energy and Commerce, Judiciary.

H.R. 2076 – On April 28, Representative Ed Perlmutter (D-CO) introduced the Marijuana Businesses Access to Banking Act of 2015, to create protections for depository institutions that provide financial services to marijuana-related businesses, and for other purposes. The bill was referred to the Committees on Financial Services and Judiciary. See S. 1726

H.R. 2331 – On May 14, Representative Paul Gosar (R-AZ) introduced the No Welfare for Weed Act of 2015, to amend the Food and Nutrition Act of 2008 to prohibit the use of benefits to purchase marijuana products, to amend Part A of Title IV of the Social Security Act to prohibit assistance provided under the program of block grants to states for temporary assistance for needy families from being accessed through the use of an electronic benefit transfer card at any store that offers marijuana for sale, and for other purposes. The bill was referred to the Committees on Ways and Means and Agriculture.

H.R. 2373 – On May 15, Representative Morgan Griffith (R-VA) introduced the Legitimate Use of Medicinal Marijuana Act, to provide for the legitimate use of medicinal marijuana in accordance with the laws of the various states. The bill was referred to the Committee on Energy and Commerce.

H.R. 2598 – On June 1, Representative Jared Polis (D-CO) introduced the Lucid Act of 2015, to amend title 23 of the U.S. Code to establish requirements relating to marijuana-impaired driving, to direct the Administrator of the National Highway Traffic Safety Administration to issue comprehensive guidance on the best practices to prevent marijuana-impaired driving, and for other purposes. The bill was referred to the Committee on Transportation and Infrastructure.

H.R. 3010 – On July 9, Representative David Reichert (R-WA) introduced the Preserving Welfare for Needs for Weed Act, to prohibit assistance provided under the program of block grants to states for temporary assistance for needy families from being accessed through the use of an electronic

benefit card at any store that offers marijuana for sale. The bill was referred to the Committee on Ways and Means.

H.R. 3124 – July 21, Representative Earl Blumenauer (D-OR) introduced the Clean Slate for Marijuana Offenses Act of 2015, to permit the expungement of records of certain marijuana-related offenses. The bill was referred to the Committee on the Judiciary.

S. 134 – On January 8, Senator Ron Wyden (D-OR) introduced the Industrial Hemp Farming Act of 2015, to amend the Controlled Substances Act to exclude industrial hemp from the definition of marijuana, and for other purposes. The bill was referred to the Judiciary Committee. See H.R. 525.

S.683 – On March 10, Senator Cory Booker (D-NJ) introduced the CARERS Act, to extend the principle of federalism to State drug policy, provide access to medical marijuana, and enable research into the medicinal properties of marijuana. The bill was referred to the Judiciary Committee. See H.R. 1538

S. 987 – On April 16, Senator Ron Wyden (D-OR) introduced the Small Business Tax Equity Act, to amend the Internal Revenue Code of 1986 to allow deductions and credits relating to expenditures in connection with marijuana sales conducted in compliance with State law. The bill was referred to the Committee on Finance. See H.R. 1855.

S. 1333 – On May 13, Senator Cory Gardner (R-CO) introduced the Therapeutic Hemp Medical Access Act of 2015 to amend the Controlled Substances Act to exclude cannabidiol and cannabidiol-rich plants from the definition of marijuana, and for other purposes. The bill was referred to the Committee on the Judiciary. See H.R. 1635

S. 1726 – On July 9, Senator Jeff Merkley (D-OR) introduced the Marijuana Businesses Access to Banking Act of 2015, to create protections for depository institutions that provide financial services to marijuana-related businesses, and for other purposes. The bill was referred to the Committee on Banking, Housing and Urban Affairs. See H.R. 2076

S. 1984 – On August 5, Senator James Lankford (R-OK) introduced the Keeping Out Illegal Drugs Act of 2015, to prevent Indian tribes and tribal organizations that cultivate, manufacture, or distribute marijuana on Indian land from receiving federal funds. The bill was referred to the Committee on Indian Affairs.

Opioids Focus

H.R. 953 -- On February 12 Representative James Sensenbrenner (R-WI) introduced the Comprehensive Addiction Recovery Act, to authorize the Attorney General to award grants to address the national epidemics of prescription drug and heroin abuse. The bill was referred to the committees on the Judiciary and Energy and Commerce. See S. 524

H.R. 1462 – On March 19, Representative Katherine Clark (D-MA) introduced the Protecting Our Infants Act, to combat the rise of prenatal opioid abuse and neonatal abstinence syndrome. The bill was referred to the Committee on Energy and Commerce. See S.799

S. 524 – On February 12 Senator Sheldon Whitehouse (D-RI) introduced the Comprehensive Addiction Recovery Act, to authorize the Attorney General to award grants to address the twin epidemics of prescription drug and heroin abuse. The bill was referred to the Judiciary Committee. See H.R. 953

S. 799 – On March 19, Senator Mitch McConnell (R-KY) introduced the Protecting Our Infants Act, to combat the rise of prenatal opioid abuse and neonatal abstinence syndrome. The bill was referred to the Committee on Health, Education, Labor and Pensions. See H.R. 1462.

Other Topics

H.R. 6 – On May 19, Representative Fred Upton (R-MI) introduced the 21st Century Cures Act – it passed the House on July 10. See appendix for a full summary from the NIH Office of Legislative Policy and Analysis.

H.R. 1988 -- On April 23, Representative Marcia Fudge (D-OH) introduced the Breaking Addiction Act of 2015, to provide for the waiver of the Medicaid IMD limitation in order to permit Medicaid coverage for substance use disorder treatment services furnished to certain individuals in a community-based institution for mental diseases. The bill was referred to the committee on Energy and Commerce.

S. 728 - On March 12, Senator Charles Schumer (D-NY) introduced the Sober Truth on Preventing Underage Drinking Reauthorization Act, or the STOP Act. This bill would direct the Secretary to continue to conduct research and collect data on the short and long-range impact of alcohol use and abuse upon adolescent brain development and other organ systems as well as work in collaboration with the Directors of NIAAA and NIDA, among other federal officials, on the Interagency Coordinating Committee Annual Report on underage drinking and prevention. This legislation would prohibit making, selling, distributing, or possessing powdered alcohol. The bill was referred to the Senate Committee on Health, Education, Labor, and Pensions.

PROGRAM ACTIVITIES/FOAS

New NIDA RFAs

On August 12, 2015, NIDA issued an RFA entitled **Avenir Award Program for Genetics or Epigenetics of Substance Abuse (DP1)** [RFA-DA-16-007](#). This FOA replaces the Avenir Award Program for Genetics or Epigenetics of Substance Abuse (DP2) (RFA-DA-15-006) with a DP1 mechanism. The award will support those in an early stage of their career who may lack the preliminary data required for an R01 grant, but who propose high impact research and who show promise of being tomorrow's leaders in the field. NIDA has developed two Avenir Award Programs, one for HIV/AIDS research and the other for genetics or epigenetics studies. The Genetics or Epigenetics of Substance Abuse Avenir Award program supports early stage investigators proposing highly innovative studies that open new areas of research for the genetics or epigenetics of addiction. These may be novel methods or approaches that can potentially be applied to the analysis of the genetics or epigenetics of addiction. Investigators outside the field of addiction interested in applying their novel approaches to the genetics or epigenetics of addiction are encouraged to apply. Open date: September 20, 2015. Application due date(s): October 20, 2015 and October 20, 2016, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

On July 21, 2015, NIDA issued RFAs entitled **Tools for Monitoring and Manipulating Modified RNAs in the Nervous System (R43/R44)** [RFA-DA-16-005](#) and **(R41/R42)** [RFA-DA-16-006](#). The purpose of this initiative is to incentivize small businesses to generate tools, technologies, and products for monitoring and manipulating covalently modified eukaryotic RNA. Open date: October 18, 2015. Application due date(s): November 18, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

On May 27, 2015, NIDA issued an RFA entitled **Harnessing Genome Editing Technologies to Functionally Validate Genetic Variants in Substance Use Disorders (R21/R33)** [RFA-DA-16-004](#). The purpose of this initiative is to harness genome or epigenome editing technologies to functionally validate and characterize genetic or epigenetic variants involved in substance use disorders. The purpose is also that the genetic resources generated will be made broadly available to the scientific community to probe more deeply into the neurobiological mechanisms involved in the function of a variant, gene, or pathway and provide critical foundational knowledge for the development of future prevention, diagnostic, and therapeutic strategies. Open date: July 25, 2015. Application due date(s): August 25, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): August 25, 2015, by 5:00 PM local time of applicant organization.

New NIDA Program Announcements

On August 7, 2015, NIDA issued a PAR entitled **Imaging - Science Track Award for Research Transition (I/START) (R03)** [PAR-15-326](#). This funding opportunity announcement (FOA) encourages Small Research Grant (R03) applications to facilitate the entry of investigators to the area of neuroimaging, including both new investigators and established investigators seeking to

adopt neuroimaging methodologies in their research programs, to enable the conduct of small "proof of concept" studies. The R03 is intended to support research projects that can be carried out in a short period of time with limited resources. Open date: September 16, 2015. Application due date(s): [Standard dates](#) apply, by 5:00 PM local time of applicant organization. AIDS application due date(s): [Standard AIDS dates](#) apply, by 5:00 PM local time of applicant organization.

On June 19, 2015, NIDA issued PARs entitled **Extracellular Vesicles and Substance Abuse (R21) [PAR-15-284](#)** and **(R01) [PAR-15-283](#)**. The purpose of this FOA is to encourage research projects that investigate the interplay between extracellular vesicles (EVs) and addictive processes. In particular NIDA is interested in the potential utility of EVs with respect to understanding neuroplastic mechanisms relevant to substance abuse or as biomarkers or therapeutics. Open date: October 3, 2015. Application due date(s): November 3, 2015 and November 3, 2016, by 5:00 PM local time of applicant organization. AIDS application due date(s): November 3, 2015 and November 3, 2016, by 5:00 PM local time of applicant organization.

On May 28, 2015, NIDA issued a PA entitled **Development and Testing of Novel Interventions to Improve HIV Prevention, Care, and Program Implementation (R34) [PA-15-268](#)**. This FOA provides resources to support (a) pilot or feasibility studies of new or adapted interventions to prevent HIV infection among populations where substance use may be a contributing factor; (b) pilot or feasibility studies of new or adapted interventions to improve the care of HIV infection among populations where substance use is prevalent, including interventions that integrate treatment for substance use disorders and HIV infection; or (c) pilot or feasibility studies to increase the scale, uptake, delivery, and/or quality of HIV prevention or care interventions with established evidence of efficacy. Both primary and secondary prevention will be supported. The full range of substance use will be considered including problematic episodic use and substance use disorders, as well as a full range of substances and modes of administration. The most important consideration is that substance use may affect transmission directly as in the case of injection or may affect transmission risk behavior. Domestic and overseas populations will be considered, with particular attention to populations with disproportionate burden of HIV infection and those where HIV infection and/or drug use are emergent. Open date: August 7, 2015. Application due date(s): [Standard AIDS dates](#) apply, by 5:00 PM local time of applicant organization. AIDS application due date(s): [Standard AIDS dates](#) apply, by 5:00 PM local time of applicant organization

On May 26, 2015, NIDA issued a PAR entitled **Fast-Track Development of Medications to Treat Cannabis Use Disorders (UG3/UH3) [PAR-15-267](#)**. The purpose of this Funding Opportunity Announcement (FOA) is to accelerate the discovery and development of medications to treat Cannabis Use Disorders (CUDs). The objective is to advance medications toward the ultimate goal of obtaining FDA approval. Advances in understanding the cannabinoid systems and the effects of marijuana on the brain, coupled with the availability of both novel and marketed medications that may be efficacious to treat these disorders, offer unprecedented opportunities to develop safe and effective pharmacotherapies for CUDs. Open date: June 28, 2015. Application due date(s): July 28, 2015; March 28, 2016; July 28, 2016; March 28, 2017; July 28, 2017; March 28, 2018, by 5:00 PM local time of applicant organization AIDS application due date(s): September 7, 2015; May 7, 2016; September 7, 2016; May 7, 2017; September 7, 2017; May 7, 2018, by 5:00 PM local time of applicant organization.

On May 8, 2015, NIDA issued PAs entitled **Health Services and Economic Research on the Prevention and Treatment of Drug, Alcohol, and Tobacco Abuse (R03) [PA-15-252](#), (R01) [PA-15-251](#), (Pilot - R34) [PA-15-250](#), and (R21) [PA-15-253](#)**. This Funding Opportunity Announcement (FOA) encourages grant applications (R01 and R21), small grant applications (R03), and pilot and preliminary research in preparation for larger-scale services research (R34) to conduct rigorous health services and economic research to maximize the delivery of efficient, high-quality drug, tobacco, and alcohol prevention, treatment, and recovery support services. Examples of such research include: (1) clinical quality improvement; (2) quality improvement in services organization and management; (3) implementation research; (4) economic and cost studies; and (5) development or improvement of research methodology, analytic approaches, and measurement instrumentation used in the study of drug, alcohol, and tobacco prevention, treatment, and recovery services. Open date: May 8 (R01), May 16, 2015 (R03, R34, R21). Application due date(s): [Standard dates](#) apply, by 5:00 PM local time of applicant organization. AIDS application due date(s): [Standard AIDS dates](#) apply, by 5:00 PM local time of applicant organization.

On April 28, 2015, NIDA issued a PA entitled **Developing the Therapeutic Potential of the Endocannabinoid System for Pain Treatment (R01) [PA-15-188](#)**. The purpose of this Funding Opportunity Announcement (FOA) is to support projects that will elucidate the therapeutic potential of the cannabinoids and endocannabinoid system in the development of mechanism-based therapies for pain. Open date: September 5, 2015. Application due date(s): [Standard AIDS dates](#) apply, by 5:00 PM local time of applicant organization. AIDS application due date(s): [Standard AIDS dates](#) apply, by 5:00 PM local time of applicant organization

New FOAs Issued by the NIH Roadmap

On July 14, 2015, the NIH Common Fund issued Roadmap RFAs entitled **Novel and Innovative Tools to Facilitate Identification, Tracking, Manipulation, and Analysis of Glycans and their Functions (R21) [RFA-RM-15-008](#), (U01) [RFA-RM-15-009](#)**. This FOA solicits development of new, more easily accessible tools, reagents, and technologies to facilitate identification, tracking, manipulation, and analysis of glycans with their biological binding partners and determine their functions. This initiative may build on efforts that interface with existing technologies and procedures to make them easier to access and use. As applicable, efforts must consider: factors for scale-up; efforts to make instrumentation broadly accessible and cost-effective for the end-user; and compatibility of data generated with integration into existing databases. Open date: September 15, 2015. Application due date(s): October 15, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

On July 14, 2015, the NIH Common Fund issued a Roadmap RFA entitled **Facile Methods and Technologies for Synthesis of Biomedically Relevant Carbohydrates (U01) [RFA-RM-15-007](#)**. This FOA is intended to develop new approaches (catalytic methods, chemical/chemo-enzymatic methods, and technologies) to facilitate the rapid, robust, and affordable synthesis, and/or functionalization of bio-medically relevant glycans and glyco-conjugates representing 1) mammalian glycomes and 2) microbial glycans. Open date: September 15, 2015. Application due date(s): October 15, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

On June 1, 2015, the NIH Common Fund issued a Roadmap RFA entitled **NIH Transformative Research Awards (R01) [RFA-RM-15-005](#)**. The NIH Transformative Research Awards complement NIH's traditional, investigator-initiated grant programs by supporting individual scientists or groups of scientists proposing groundbreaking, exceptionally innovative, original and/or unconventional research with the potential to create new scientific paradigms, establish entirely new and improved clinical approaches, or develop transformative technologies. Little or no preliminary data are expected. Projects must clearly demonstrate the potential to produce a major impact in a broad area of biomedical or behavioral research. Open date: September 9, 2015. Application due date(s): October 9, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): October 9, 2015, by 5:00 PM local time of applicant organization.

New FOAs Issued by the NIH Blueprint for Neuroscience Research

On May 6, 2015, the NIH Blueprint for Neuroscience Research issued an RFA entitled **Neuroimaging Informatics Tools and Resources Clearinghouse (U24) [RFA-EB-15-005](#)**. The Neuroimaging Informatics Tools and Resources Clearinghouse (NITRC) (<http://www.nitrc.org>), originally funded by the NIH Blueprint for Neuroscience Research in 2006, is a dynamic inventory of web-based neuroimaging informatics resources: software, data, and tools accessible via any computer connected to the internet. The purpose of the NITRC project is to promote the enhancement, sharing, adoption, and evolution of neuroimaging informatics tools and resources by providing access, information, and forums for interaction for the user community and the associated developers. Open date: June 14, 2015; Application due date(s): July 14, 2015.

New FOAs Issued by the BRAIN INITIATIVE

On July 31, 2015, the NIH Brain Initiative issued an RFA entitled **BRAIN: Theories, Models and Methods for Analysis of Complex Data from the Brain (R01) [RFA-EB-15-006](#)**. This FOA is designed to solicit new theories, ideas and conceptual frameworks; computational models; and mathematical and statistical methods for driving experimental data collection, and analyzing complex data from the nervous system. It is expected that this next generation of analytical tools will be developed such that the wider neuroscience research community can easily share and use them. Open date: September 21, 2015; Letter of Intent Due Date: September 21, 2015; Application due date(s): October 21, 2015.

New Administrative Supplement Program Announcements Issued by NIH

Administrative Supplements for Research on Sexual and Gender Minority (SGM) Populations (Admin Supp) [PA-15-329](#)

Research Supplements to Promote Diversity in Health-Related Research (Admin Supp) [PA-15-322](#)

Research Supplements to Promote Re-Entry into Biomedical and Behavioral Research Careers (Admin Supp) [PA-15-321](#)

New RFAs Issued by Other NIH/HHS Components in which NIDA is a participant

**Big Data to Knowledge (BD2K) Development of Software Tools and Methods for Biomedical Big Data in Targeted Areas of High Need (U01) [RFA-CA-15-017](#)
Martin Delaney Collaboratories for HIV Cure Research (UM1) [RFA-AI-15-029](#)**

New PAs Issued by Other NIH/HHS Components in which NIDA is a participant

Direct Phase II SBIR Grants to Support Extended Development, Hardening, and Dissemination of Technologies in Biomedical Computing, Informatics, and Big Data Science (R44) [PAR-15-288](#)

Opportunities for Collaborative Research at the NIH Clinical Center (U01) [PAR-15-287](#)

Pre-application: Opportunities for Collaborative Research at the NIH Clinical Center (X02) [PAR-15-286](#)

Multidisciplinary Studies of HIV/AIDS and Aging (R03) [PAR-15-281](#), (R01) [PAR-15-280](#), (R21) [PAR-15-282](#)

Harnessing Big Data to Halt HIV (R01) [PA-15-273](#)

PHS 2015-02 Omnibus Solicitation of the NIH for Small Business Technology Transfer Grant Applications (Parent STTR [R41/R42]) [PA-15-270](#)

PHS 2015-02 Omnibus Solicitation of the NIH, CDC, FDA and ACF for Small Business Innovation Research Grant Applications (Parent SBIR [R43/R44]) [PA-15-269](#)

The Health of Sexual and Gender Minority (SGM) Populations (R01) [PA-15-261](#), (R03) [PA-15-262](#), (R15) [PA-15-260](#), (R21) [PA-15-263](#)

Lasker Clinical Research Scholars Program (Si2/R00) [PAR-15-189](#)

Other Program Activities

CTN Update

Thirteen applications in response to the RFA DA-15-008, entitled “The National Drug Abuse Treatment Clinical Trials Network (UG1),” were selected for award.

A total of 60 protocols have been initiated since 2001, including multi-site clinical trials (43), multi-site surveys (3), studies in special populations (8), and secondary analyses of data across various trials (6). In addition, 28 ancillary studies have been supported by CTN and non-CTN funds. Over 19,000 participants have been enrolled in CTN studies. Information on protocols can be found at: <http://www.drugabuse.gov/about-nida/organization/cctn/ctn/research-studies>

NIDA's Blending Initiative

Accelerating the dissemination of research-based substance use disorder treatment into clinical practice is a priority for the National Institute on Drug Abuse (NIDA) and represents the core mission of the Blending Initiative (<http://www.drugabuse.gov/blending-initiative>).

The broad reaching, web-based educational effort, *Talking to Patients about Health Risk Behaviors*, continues to reach many groups of healthcare providers including physicians, nurses, physician assistants, pharmacists and others. As of July 13, 2015, 60,478 persons have accessed the program, and 30,449 certificates have been issued since its October 2014 launch. The two programs comprising this novel educational opportunity provide a unique forum where the Online Course and the Patient Simulation jointly provide practical guidance for physicians and other clinicians in effective Motivational Interviewing techniques that will facilitate conversations with adult patients to address Health Risk Behaviors. The Online Course guides physicians and other clinicians through practical skills building and technique development using videos to model effective communication, while the Patient Simulation allows for real time testing and reinforcement of these skills in the clinical setting. Both programs now provide an opportunity for professionals to obtain CME or CE credit. Links to the education are found at <http://www.drugabuse.gov/blending-initiative/cme-ce-simulation>.

Through the Blending Initiative, NIDA partners with professional organizations and other institutions dedicated to the training and education of fellows and residents to support the development of expertise in substance use disorders (SUDs) within medical and clinical settings. These training awards aim: 1) to promote knowledge of evidence-based SUD treatment within medical specialties, 2) to advance medical care for patients with substance use disorders, and 3) to facilitate the academic growth, advanced education, and development of future researchers and clinicians in SUDs and medicine and thereby invest in the future of the field. The Blending Initiative continues its partnerships with four organizations to support this effort. These organizations are:

- Society of Teachers of Family Medicine
- American Academy of Child and Adolescent Psychiatry
- Society for Adolescent Health and Medicine
- American College of Emergency Physicians/Emergency Medicine Foundation

During this period the Blending Initiative supported seminars and exhibits at the following national meetings:

- National Rx Drug Abuse Summit, Atlanta GA, April 6-9, 2015
- Society of General Internal Medicine (SGIM), Toronto, CAN, April 22-25, 2015
- Society of Teachers of Family Medicine (STFM), Orlando FL, April 25-29, 2015

Women & Gender Junior Investigator Travel Awards

NIDA's Women & Sex/Gender Differences Research Program awarded 20 Women & Gender Junior Investigator Travel Awards for the annual meeting of the College on Problems of Drug Dependence (CPDD), June 13-18, 2015 in Phoenix, AZ. These \$1000 awards provide travel support to first author junior investigators who make presentations on the topic of women or sex/gender differences. These travel awards have been made annually beginning in 1999 and are designed to promote entry of junior investigators into drug abuse research on women and sex/gender differences. To further promote research in this field, NIDA published an electronic mini-program book, *Focus on Women & Sex/Gender Differences*, for the CPDD meeting. Excerpted from the CPPD program book, it contains only those program listings related to women and sex/gender differences as well as the abstracts. The mini-program also contains a listing of all awardees since 1999, information about the Women & Gender Junior Investigator Travel Awardees presentations, announcement of the travel award program for CPDD 2016, and information on current NIDA funding opportunity announcements in this area. These efforts were led by Dr. Samia Noursi and were supported by Drs. Cora Lee Wetherington, Lynda Erinoff and Joe Frascella. The mini-program is posted on the program site, <http://www.drugabuse.gov/about-nida/organization/offices/office-nida-director-od/women-sexgender-differences-research-program>, as well as the CPDD website, <http://www.cpdd.org>.

NIDA Diversity Scholars Network (NDSN)

In April 2015, NIDA's Office of Diversity and Health Disparities (ODHD) launched the NIDA Diversity Scholars Network (NDSN). The NDSN is a rigorous and comprehensive mentorship program aimed at improving the funding of outstanding underrepresented early stage minority investigators in substance abuse research. This program will support a cohort of underrepresented scholars in transitioning to independent research positions; and to gain research project grant (RPG) or equivalent funding in order to build a sustainable career in biomedical research, namely in the areas of substance abuse and addiction research. This year NIDA accepted 19 underrepresented scholars into the program which consists of two in-person research development meetings as well as distant mentoring with their mentor in order to further refine their grant proposal. The NDSN Part I meeting took place prior to the CPDD annual conference in Phoenix, Arizona on Friday, June 12, 2015 and was co-chaired by Drs. Albert Avila and Debbie Furr-Holden. This meeting provided scholars with information on NIDA's research funding priorities, grant development and review, research grant mechanisms, funding opportunity announcements, grant application/submission process, review and research/career tips. Additional presentations included common pitfalls in grant applications, how to respond to reviewers' critiques, using appropriate statistical measures in data analysis, and NIDA data sets available for secondary analysis. In addition, scholars met with their matched mentor to discuss their research proposal and development strategies to move forward with a future NIH grant application. Participants will submit their mock grant applications for the Part II workshop, a mock review of completed grant applications.

Research Supplements to Promote Diversity in Health-Related Research

In fiscal year 2015, The NIDA Office of Diversity and Health Disparities received 36 applications for the "Research Supplements to Promote Diversity in Health-Related Research" program and funded 27 supplements. All applications received a review at the Division level as well as a secondary level of review by the NIDA Consortium on Diversity Affairs Workgroup. The 27 funded recipients consisted of 12 pre-doctoral students, 11 postdoctoral fellows, and 4 early

investigators; 14 of the recipients were female and 13 male. African American, Hispanic, and Native American ethnicities were represented among this year's funded recipients. The program is coordinated by Pamela Goodlow within the ODHD.

Minority Early Stage Investigator Awards

The NIDA Office of Diversity and Health Disparities supported seven minority early stage investigators to present at the NIDA/NIAAA poster session at the APA Division 28/50 social hour on August 7, 2015. Each awardee won a travel award to support their travel and registration costs for the meeting.

Primm-Singleton Travel Awards

The NIDA Office of Diversity and Health Disparities supported five Primm-Singleton travel awardees to attend the 2015 Annual Scientific Meeting of CPDD in June 2015. The Underrepresented Populations Primm-Singleton awards are made possible with joint funding from the CPDD and the National Institute on Drug Abuse (NIDA) Office of Diversity and Health Disparities (ODHD).

Director's Travel Awards

NIDA awarded 20 Director's Travel Awards for the annual meeting of the College on Problems of Drug Dependence (CPDD), June 13-18, 2015, in Phoenix, Arizona. Awardees, who are National Research Service Award (NRSA) trainees and fellows and Diversity Supplement recipients, present at the CPDD meeting and attend the NIDA Grant-Writing and Career Workshop.

IRP Office of Education and Career Development Poster Day and Mentoring Awards

On May 13, 2015, the IRP Office of Education and Career Development hosted the NIDA Poster Day and Mentoring Awards Ceremony. IRP postdocs, grad students, and postbacs presented 45 posters. Mentoring Awards were presented to Drs. Daniele Caprioli, Alex Hoffman, Elliot Stein, and Charles Schindler. The day also featured a celebration of the career of Dr. Roy Wise with a symposium entitled, "40 Years of Dopamine and Reward."

IRP Workshops and Seminars

From April to June 2015, the IRP Office of Education and Career Development, together with the NIH Office of Intramural Training and Education, offered the following workshops or seminars: Scientists Teaching Science (9-week course); Workplace Dynamics; Mentoring a Summer Student; Introduction to R for Non-programmers; Postbac Poster Day (Bethesda); NIDA Poster Day and Mentoring Awards; NIH Career Symposium; Postbac Graduation Luncheon; and Graduate School Planning and Applying.

COLLABORATIVE RESEARCH ON ADDICTION AT NIH (CRAN) ACTIVITIES

Collaborative Research on Addiction at NIH (CRAN) is a consortium of Institutes supporting research on drug use, abuse and addiction. Included are the: National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Drug Abuse (NIDA), and National Cancer Institute (NCI). For more information about CRAN, see: www.addictionresearch.nih.gov

- A CRAN grantee workshop was held on May 12 – 13, 2015 at the National Cancer Institute (NCI) Shady Grove Campus in Rockville, Maryland, for recipients of administrative or competitive supplements. The workshop included poster sessions, oral presentations, discussion panels, and a plenary talk by Dr. George Koob.
 - Feedback from participants was very positive. They especially appreciated the opportunity to interact and initiate collaborations with scientists working outside of participants' usual network—i.e., on other substances, or at other levels of analysis.
 - Among the concerns expressed at the meeting was the lack of appreciation by scientific review committees for the value of CRAN, i.e., multi-substance, research to the ICs. The CRAN coordinating committee is developing language to share with the various CSR committees that review NIDA, NIAAA, and NCI applications to help address this issue.
 - Another suggestion was to embed CRAN research workshops at the main scientific meetings of each of the Institutes, in order to “brand” CRAN and emphasize its importance.
- The CRAN coordinating committee is developing a strategic plan to highlight areas of research that are priorities or gap areas for the CRAN ICs, and is considering strategies to better coordinate addictions training programs across ICs.

Adolescent Brain Cognitive Development (ABCD) Study: FOAs released on February 4th 2015; Application Due Date: April 14, 2015; CSR Review: July 16, 17, 2015; Funding expected by Sept 30, 2015.

- This is a multi-Institute project led by CRAN, in partnership with the Eunice Kennedy Shriver Institute of Child Health and Human Development (NICHD), National Institute of Mental Health (NIMH), National Institute on Minority Health and Health Disparities (NIMHD), Office of Behavioral and Social Sciences Research (OBSSR), National Institute on Neurological Disorders and Stroke (NINDS), and the Office of Research on Women's Health (ORWH).
- The goal is to establish a national, multisite, longitudinal cohort study to prospectively examine the neurodevelopmental and behavioral effects of substance use from early adolescence (approximately age 9-10) through the period of risk for substance use and substance use disorders.
- A collaborative research mechanism is being used for this project (U01, and U54s) and its structure shall consist of three highly integrated components: (1) a set of Research Project Sites; (2) a central Data Analysis and Informatics Center, and (3) a Coordinating Center.
- A robust response was received to these FOAs; funding is expected to be allocated by the end of this fiscal year.

- Discussions are ongoing with potential International collaborators to harmonize procedures, data collection, and data access for other similar cohorts.

COMMUNICATIONS

PUBLICATIONS & ONLINE RESOURCES

Nationwide Trends (Drug Facts) – Revised June 2015

Khat (DrugFacts) – Revised June 2015

Marijuana Research Report – Updated June 2015

Marijuana: Facts Parents Need to Know – Updated June 2015

Marijuana (Drug Facts) – Updated June 2015

ABCD Study Fact Sheet (2-pager) – Created June 2015

Therapeutic Community Research Report – Revised August 2015

Substance Use in Women (new online resource) – Published August 2015

Spanish-language publications:

- **Revised *Marijuana DrugFacts* – Revised June 2015**
- **Revised *Marijuana Medicine DrugFacts* – Revised June 2015**
- **Translated *Marijuana: Facts for Teens* – Revised June 2015**

NIDA NOTES (now online only)

Highlights:

Can Magnets Treat Cocaine Addiction? This new entry in our Narratives of Discovery articles introduces Dr. Marco Diana and Dr. Diana Martinez in the first in a series of pieces that will follow them as they attempt to adapt transcranial magnetic stimulation to treat cocaine addiction.

Video Interview with Dr. Thomas Kosten: The interview focuses on how a leading vaccine researcher conceives that antidrug vaccines may be used, emphasizing that they are intended primarily for treatment, and may backfire if used for prevention.

NIDA Notes-IRETA CEU Module: Social workers and clinicians are earning professional educational credits by watching a mixed-media presentation based on *NIDA Notes* articles and taking a quiz on the contents.

Additional selected articles cover research describing the biological pathway whereby stress increases the risk of relapse to cocaine use; a low-resource, a text-messaging substance use aftercare intervention for teens; a high-impact intervention to improve the health of American Indian teen mothers and their children; and two brief screeners for teen substance use.

NIDA Notes receives 35,000-55,000 visits monthly and is further shared via, and promoted on, Twitter, Linked-In, and Facebook, and YouTube.

VIDEOS

SBIR/STTR Video Series, 6 Unlisted videos

- SF424 (R&R) SBIR/STTR Application Tutorial Registration: <https://youtu.be/Jim8WbSij5g>
- SF424 (R&R) SBIR/STTR Application Tutorial Pages 1-3: <https://youtu.be/I4vHpEQEduU>
- SF424 (R&R) SBIR/STTR Application Tutorial Pages 4-6: https://youtu.be/Cc_WEm89vU0
- SF424 (R&R) SBIR/STTR Application Tutorial Pages 7-8: <https://youtu.be/NU3ryVi7fM>
- SF424 (R&R) SBIR/STTR Application Tutorial Pages 9-12: <https://youtu.be/eJkqjRc6Ces>
- SF424 (R&R) SBIR/STTR Application Tutorial Pages 13-15: <https://youtu.be/K-idlqdEs30>

Public Videos

- 2015 Lifetime Science Award: Dr. Charles P. O'Brien: <https://youtu.be/7jPBE3fEi58>
- How Will Anti-Drug Vaccines Be Used? An Interview With Dr. Thomas Kosten: <https://youtu.be/soYFdU67TCA>
- NIDA Science Spotlight- Cannabis Effects on Driving Performance: https://youtu.be/VrLSr_O7e0Y
- NIDA's 2015 Avenir Awards Announced (plus corrected update): <https://youtu.be/MLIEpZ3oixw>

Vines

- <https://vine.co/u/1146557546770108416>
 - **Drugged Driving BROLL for media outlets**
 - **Dr. Volkow Video for Baja, Mexico Conference**

CTN-Related Publications

Four editions of the CTN Bulletin Board were distributed. The Bulletin Board is an electronic report on the progress of the protocols, committees, and Node activity in the CTN. The Bulletin has wide readership within and outside the CTN and NIDA.

Data from 36 CTN studies and 5 DPMC studies are now available on the NIDA Data Share website <http://datashare.nida.nih.gov/>. Nearly 4,000 data sets have been downloaded by researchers from 78 countries. These data sets are in compliance with HIPAA and CDISC (Clinical Data Interchange Standards Consortium) standards in support of the interoperability required by the NIH Roadmap. The NIDA Data Share is also part of the Neuroscience Information Framework (NIF), which is a dynamic inventory of Web-based neuroscience resources: data, materials, and tools accessible via any computer connected to the Internet.

The NIDA Common Data Elements (CDE) web portal (<http://cde.drugabuse.gov/>) provides a single source for CTN recommended CDEs for Substance Use Disorders. All the CDEs displayed on this

website are created and housed in the National Cancer Institute (NCI) cancer Data Standards Repository (caDSR) (<https://cdebrowser.nci.nih.gov/CDEBrowser/>). Currently, 17 instruments have been added to this web site with plans to add more.

Other Publications

A Commentary on “A New Initiative on Precision Medicine”. Ghitza UE. Front Psychiatry. 2015 Jun 8;6:88. eCollection 2015.

MEDIA SUPPORT OF EVENTS AND MEETINGS

Media Outreach Surrounding APA Annual Meeting

On May 18, 2015, at the annual meeting of the **American Psychiatric Association**, in Toronto, Canada, Dr. Nora Volkow delivered the **William C. Menninger Memorial Convocation lecture** about the neurobiology of addiction. Dr. Volkow’s lecture was transcribed and posted on the NIDA website. At the meeting, Dr. Volkow also conducted an interactive session titled “Let’s Talk About Marijuana” with NIAAA Director Dr. George Koob. She also participated in a live interview with *Sirius XM-Doctor Radio* to discuss her substance abuse research and was featured in an article in the *APA Daily Bulletin*. The NIDA press team coordinated social media outreach surrounding this event.

PRESS RELEASES

- | | |
|-------------------------|--|
| May 15, 2015 | Pain reliever investigation wins top NIH Addiction Science Award |
| June 1, 2015 | Carlos Blanco, M.D. to join NIDA as division director |
| June 26, 2015 | NIDA announces new awards for early stage investigators |
| August, 18, 2015 | Teens using e-cigarettes may be more likely to start smoking tobacco |

SCIENCE SPOTLIGHTS AND ANNOUNCEMENTS

- | | |
|---------------------|--|
| May 18, 2015 | NIDA highlights drug use trends among college-age and young adults in new online resource |
| May 29, 2015 | Methadone maintenance in prison results in treatment retention, lower drug usage following release |
| June 9, 2015 | Prescribing lifesaving naloxone: Addressing attitudes of primary care clinicians |

- June 12, 2015** [Nasal spray naloxone one step closer to public availability](#)
- June 23, 2015** [Effects of marijuana – with and without alcohol – on driving performance](#)
- July 28, 2015** [NIDA announces two online resources](#)
- July 29, 2015** [NIDA and NIAAA commentary strongly supports brain disease model of addiction](#)

MEETINGS/CONFERENCES

Select Meetings and Conferences in which NIDA played a significant role

On Monday, June 15, 2015, NIDA and CPDD held their **Pre- and Postdoctoral Trainees' Networking Event**. Coordinated by Dr. Mimi Ghim and Flair Lindsey of DER's Office of Research Training, along with Usha Charya of OSPC, the networking event provided a forum for training directors, trainees and NIDA staff to learn about the many institutional training (T32) programs that NIDA supports and for trainees to identify future training and employment opportunities.

On Wednesday, June 17, 2015, Dr. Mimi Ghim and Flair Lindsey of DER's Office of Research Training, along with Usha Charya of OSPC, coordinated the **NIDA Grant-Writing and Career Workshop** at the CPDD Annual Meeting. The workshop provided information to more than 80 junior investigators on NIDA research priorities, program interests and funding opportunities, review procedures, and training on grantsmanship and other career-building skills. NIDA staff members Drs. Marsha Lopez and Gerald McLaughlin presented some of the workshop's core content, along with guest speakers Drs. Scott E. Lukas (McLean Hospital-Harvard University), Marc I. Rosen (Yale University) and Linda B. Cottler (University of Florida). The workshop was moderated by Dr. Ericka Boone (NIDA).

The NIDA National Drug Abuse Treatment Clinical Trials Network (CTN) Steering Committee Meetings were held April 14-16, 2015 in Gaithersburg, Maryland. During the meeting, the CTN Design and Analysis Workgroup provided a workshop titled "Topics in Subgroup Analysis." During the main Steering Committee Meeting, attendees were provided an update on the activities of the Committees (Executive, Research Development, Research Utilization and Publications), and two symposia — "Efficacy of Interventions Linking Patients in General Medical Care Settings to SUD Treatment Programs," and "Gender Differences in SUD Treatment: Recent Findings from the CTN."

GRANTEE HONORS AND AWARDS

Dr. Kathleen Brady, Medical University of South Carolina and CTN Southern Consortium Node PI, recently received three honors/appointments: She was recipient of the *2015 Marian W. Fischman Lectureship Award* from the College on Problems of Drug Dependence (CPDD). Given in memory of Dr. Fischman, a respected leader in drug abuse research and an outstanding scientist, this award was established in 2001 to recognize the contributions of an outstanding woman scientist in drug abuse research. The award was presented to Dr. Brady during the *77th Annual CPDD* meeting in Phoenix in June, 2015.

Dr. Brady was named President-Elect of the *International Society of Addiction Medicine (ISAM)*, the largest international organization of physicians focused on the advancement of knowledge about addiction as a treatable disease and recognition that physicians worldwide have a major role to play in educational activities, and understanding, treating and prevention of addictions.

Lastly, Dr. Brady was named Chairperson of the Scientific Advisory Board for the intramural programs at the National Institute of Alcohol Abuse and Alcoholism.

Dr. Marilyn Carroll, University of Minnesota, was elected to the Board of Directors of College on Problems of Drug Dependence (CPDD).

Dr. Linda Collins, Pennsylvania State University; **Dr. Thomas Dishion**, Arizona State University; and **Dr. Mark Greenberg**, Pennsylvania State University were selected for the 3rd cohort of Fellows of the Society for Prevention Research (SPR), during the 22nd annual meeting, on May 29, 2015. The SPR Fellows Program is an honor SPR bestows upon a small and select group of members who have a particularly distinguished record of contributions in the field of prevention science.

Dr. Diana Fishbein, University of Maryland, was a co-recipient of the 2015 Public Service Award, from the Society for Prevention Research. This award is given in recognition of extensive and effective advocacy for prevention science and research-based programs. Dr. Fishbein co-led the development of the National Prevention Science coalition to Improve Lives. NPSC made significant progress on a number of important initiatives to advance the use of prevention science in policy.

Dr. Nancy Gonzales, Arizona State University, received the 2015 Advances in Culture and Diversity in Prevention Science Award, from the Society for Prevention Research. This award is given for contributions to the field of prevention science in the area of culture. Dr. Gonzales was recognized for research that enhances understanding of culture in prevention science and the development of and adaptation of effective prevention strategies for traditionally underserved and/or underrepresented populations.

Dr. Deborah Gorman-Smith, University of Chicago, received the 2015 Prevention Science Award, from the Society for Prevention Research, for her more than 20 years of research developing and testing prevention strategies. Dr. Gorman-Smith's research has focused on

individual and environmental influences on academic performance and aggression predominantly among economically-disadvantaged urban youth.

Dr. Roland Griffiths, The Johns Hopkins University School of Medicine, was awarded the Nathan B. Eddy Award at the 2015 College on Problems of Drug Dependence meeting in Phoenix, AZ. This award acknowledges outstanding research efforts that have advanced our knowledge of drug dependence.

Dr. Kevin Haggerty, University of Washington, received the 2015 Translational Science Award from the Society for Prevention Research, which is given to an individual in recognition for contributions to the field of prevention science in the area of Type 1 or Type 2 translational research.

Dr. Karl Hill, University of Washington, received the 2015 Friend of ECPN (Early Career Preventionist Network), award. This award is presented to a mid or senior career preventionists who has supported and encouraged early career prevention scientists.

Dr. Viviana E. Horigian, Executive Director of the CTN Florida Node Alliance, was presented with the 2015 NIDA International Program Award of Excellence in International Leadership at the 2015 NIDA International Forum, “Building International Collaborative Research of Drug Abuse,” held in Phoenix, Arizona June 12-15, 2015. The NIDA International Program Awards of Excellence recognize individuals for outstanding contributions to international cooperation in drug abuse research and training. The Excellence in International Leadership Award presented to Dr. Horigian recognizes U.S. or non-U.S. drug abuse researchers who have made significant contributions to international collaborative research and/or capacity building outside the United States. Dr. Horigian was recognized for her commitment to help improve scientific understanding of drug abuse and addiction and to develop and implement science-based prevention and treatment programs in Latin America. Her outstanding efforts in mentoring colleagues at the National Institute of Psychiatry (NIP) in Mexico enabled them to transfer necessary technology and to conduct randomized clinical trials with the same rigor used in the CTN. This resulted in Mexico’s first substance abuse clinical trials network. Supported by the U.S. Department of State and under Dr. Horigian’s mentorship, the Clinical Trials Unit at the NIP successfully designed, led, and implemented its first clinical trial, trained community treatment providers and monitored study progress using quality standards set by the NIH. Dr. Horigian continues her work in Latin America, more recently in Ecuador and Chile, using this technology transfer model.

Dr. Terry Horton, CTN Delaware Valley Node, has received the *ASAM Annual Conference Program Planning Committee Award* for his abstract titled: “Hospital-based Peer Counseling Reduces 30-Day Readmission of Alcohol Abusing Medical Inpatients.” The award is given to the author of the submitted abstract receiving the highest rating for its scientific merit. The award is made on the basis of new ideas or findings of importance to the field of addiction medicine, their methodology and clarity of presentation, as judged by the Committee. The award was presented during the Awards Luncheon on Saturday, April 25, 2015, from 12:30 PM to 2:30 PM.

Dr. Adam Leventhal, an Associate Professor at the University of Southern California Keck School of Medicine, was awarded the Joseph Cochin Young Investigator Award at the 2015 College on Problems of Drug Dependence meeting in Phoenix, AZ. This award recognizes research contributions in any facet of the field of drug abuse. It is given annually to an investigator who has not attained his/her 40th birthday by July 1st in the year of the award.

Dr. R. Kathryn McHugh, CTN New England Consortium Node, was awarded The Alfred Pope Award for Young Investigators at McLean Hospital, on June 4, 2015. This award recognizes the publication of an exceptional peer-reviewed, first-authored article on basic or clinical research performed at McLean Hospital. Dr. McHugh received the award for her study of “Craving as a Predictor of Prescription Opioid Use,” which was a secondary data analysis from the Prescription Opioid Addiction Treatment Study (CTN 0030, POATS) which was recently published in *Drug and Alcohol Dependence*. The article is titled “Assessing craving and its relationship to subsequent prescription opioid use among treatment-seeking prescription opioid dependent patients.” This article can be found at the link below or at *Drug and Alcohol Dependence*, Volume 145, 1 December 2014, Pages 121-126. <http://www.ncbi.nlm.nih.gov/pubmed/25454409>

Dr. Brenda Miller, Pacific Institute for Research and Evaluation received the 2015 Service to SPR Award, from the Society for Prevention Research. The Service to SPR Award is given in recognition of outstanding service to organizations.

Dr. Leslie Miller and her team at Rice University have developed several web based educational games for students with grants from NIDA’s SEDAPA program, a grant from the Blueprint for Neuroscience Research K-12 program and an NSF grant. In recognition of the quality of these educational web based games, they have recently received **the American Library Association’s Great Websites for Kids Award** and will be included on their web listing of great websites. These educational games, which have a broad audience of teachers and students, have been successful in providing engaging activities that teachers can use to teach science and drug abuse topics. The usage varies depending on the particular game, but the most popular, CSI: THE EXPERIENCE, receives over 59,000 visits/month. There is considerably more usage of the sites during the school year, in correlation with their use by teachers. The games can be accessed at <http://webadventures.rice.edu>.

Dr. Gavril Pasternak, was chosen to deliver the Founder’s Lecture, entitled “40 Years on drugs: It’s all in the telling of the tail“ at the International Narcotic Conference (INRC) Meeting, 2015, Phoenix, AZ.

Dr. Richard Spoth, Iowa State University, received the 2015 Presidential Award from the Society for Prevention Research. This award is given to those who have made a major lifetime contribution to prevention science research. Dr. Spoth was recognized for his national and international leadership in the field of prevention science. He has made a significant contribution to the body of knowledge in the prevention field, most notably concerning community-based universal preventive intervention, including intervention efficacy and effectiveness, and the research on sustained high quality community-based delivery of evidence-based interventions.

STAFF HONORS AND AWARDS

Dr. Comfort Boateng, IRP, received a travel award to attend the 2015 Gordon Research Conference on Medicinal Chemistry.

Drs. Comfort Boateng and **Rachel Slack**, IRP, received 2015 NIH FARE Travel Awards.

Rebecca Hartman and **Marisol Castaneto**, MS, IRP, successfully defended their dissertation research in April 2015 and received their doctoral degrees from the University of Maryland Baltimore Medical School.

Dr. Marilyn Huestis, IRP, received the Norman P. Kubasik award and presented the plenary lecture at the American Association for Clinical Chemistry, Upstate New York Section's meeting from May 6-8, 2015 in Albany, New York.

Dr. William Kowalczyk, IRP, was awarded a competitive renewal of the NIH Intramural AIDS Research Fellowship for his project "A Pilot Mobile Intervention Utilizing the Strength Model of Self-Control to Decrease HIV Risk Behaviors."

Dr. Karran Phillips, IRP, was named Special Symposia Chair for the Society of General Internal Medicine (SGIM) Program Committee, 2014-2015, and was Session Coordinator and Presenter of the Addiction Update for the Internist at the SGIM Annual Meeting in April 2015. She was also named to the CPDD Awards Committee, 2015-2018.

Dr. Rao Rapaka, DBNBR, was awarded "Special Recognition Award" at the INRC 2015 Phoenix Conference for his Leadership and Service in providing long-standing and continued support for opioid research and support of young researchers. This is a special award as INRC usually does not give awards routinely except when a special recognition or honor is warranted.

Dr. Nadine Rogers, DER, is a recent graduate of Cohort 14 of the NIH Mid-Level Leadership Program. The group received certificates on June 12, 2015.

Dr. Jose Ruiz, DER, graduated from the NIH Mid-Level Leadership Program on July 17, 2015.

Dr. Charles Schindler, IRP, received the NIDA Intramural Research Program Diversity Mentoring Award for 2015.

Dr. Cora Lee Wetherington, DCNBR, was presented the Martin and Toby Adler Distinguished Service Award by the **College on Problems of Drug Dependence** at its annual meeting, June 13-18, 2015 in Phoenix, AZ. This was described in the July 17, 2015 issue of the *NIH Record*.

STAFF CHANGES

New Employees

Carlos Blanco, M.D., Ph.D. accepted offer to join NIDA as the Director of the Division of Epidemiology, Services and Prevention Research (DESPR), with a starting date of June 15. Carlos is currently Professor of Clinical Psychiatry at Columbia University in New York City and is well known for his research at the interface between epidemiology and the treatment of addictive disorders. Carlos' accomplishments include a detailed examination of the course and stages of substance use disorders, the development of methodologies to improve clinical trials in mental health, and the development and testing of interventions that combine key elements of current evidence-based techniques. His research has recently shown that, contrary to popular belief, people in recovery from a substance use disorder may not be at increased risk for a new addiction.

Jesus Bonet joined NIDA's Office of Management as an IT Specialist in the Information & Resource Management Branch on May 31, 2015. Jesus comes to NIDA from a position in the private sector.

Departures

Dr. Ericka Boone of OSPC's Science Policy Branch will begin a new chapter in her career as the Director of the Division of Loan Repayment under the Office of Extramural Programs and the Office of Extramural Research (NIH OD). For the past seven years, Ericka has served as a Health Scientist Administrator in OSPC. Here she helped to advance NIDA's scientific mission by developing and targeting science-based publications, outreach initiatives and other activities that educate a variety of audiences – including members of Congress, other Federal agencies, the scientific community and the general public – about the science of drug use, abuse and addiction. For her role in these efforts, Ericka earned several NIDA Director's Awards of Merit and a NIH Director's Award. At NIDA, Ericka also was a valued member of our research training team, served in key roles on numerous NIH and Trans-NIH committees and served as Liaison for the NIH Loan Repayment Program. Prior to coming to NIH, Ericka conducted research at the University of Illinois at Chicago focusing on the neurobiology and development of socially monogamous traits, including parenting and pair-bonding behaviors, in prairie voles. She also taught numerous undergraduate courses, including neuroanatomy and physiological psychology, and served volunteer for several organizations that aimed to increase scientific curiosity and exploration among elementary school-aged children. Ericka's academic background includes a B.A. in Biology from Talladega College and a Ph.D. in Biobehavioral Health from The Pennsylvania State University.

Will Etti, a Management Analyst in the Office of Management, Administrative Management and Analysis Branch left NIDA on June 27, 2015 for a position with the FDA.

David Marzilli, a Contract Specialist in the Office of Management, Office of Acquisitions, NIDA R&D left NIDA on July 11, 2015 for a position with the Social Security Administration.

Dr. Eve Reider, DESPR, Prevention Research Branch, started at the National Center for Complementary and Integrative Health (NCCIH) on March 23, 2015 leading their military/veteran initiative and expanding their prevention/health promotion portfolio. She worked in the Prevention Research Branch at NIDA for 15 years.

Dr. Paul Wakim departed the CCTN to join the NIH Clinical Center in July 2015 as Chief Biostatistician in the Biostatistics and Clinical Epidemiology Service.

Retirements

Dr. Harold Perl, DESPR, Prevention Research Branch Chief, retired from the federal government on May 30th, after nearly 10 years here at NIDA and 16 years at NIAAA.



National Institute
on Drug Abuse