Director's Report

to the

NATIONAL ADVISORY COUNCIL ON DRUG ABUSE

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TABLE OF CONTENTS

** These sections contain select information. More comprehensive information will be posted in the February 2013 Staff Report to the Director.*

RESEARCH HIGHLIGHTS

A Comparison Of Buprenorphine Taper Outcomes Between Prescription Opioid and Heroin Users. Nielsen S, Hillhouse M, Thomas C, Hasson A, Ling W. J Addict Med. Epub 2012 Dec 6.
Dependence on prescription opioids (PO) is a growing problem. Although most research with buprenorphine has focused on heroin-dependent populations, the authors hypothesize that individuals dependent on PO display characteristics that may predict different outcomes in treatment, particularly in short-term taper procedures in which comorbidities such as pain conditions may complicate taper. This secondary data analysis examined differences in outcomes between PO users (n = 90) and heroin users (n = 426) after a buprenorphine taper. Data were collected in a multisite randomized clinical trial conducted by the National Drug Abuse Treatment Clinical Trials Network at 11 study sites across the United States. After a 4-week buprenorphine induction/stabilization phase, 516 opioid-dependent individuals were randomized into 1 of 2 taper lengths (7 vs. 28 days) to assess the association between taper length and outcome. The primary outcome was measured by urine drug test for opioids at the end of the taper period. Craving, withdrawal, and buprenorphine dose were also examined. After controlling for baseline demographic and drug use differences between the opioid use groups, results indicate that a higher percentage of the PO group (49%) provided an opioid-free urine drug specimen at the end of taper compared with the heroin group (36%; $\chi 1 = 6.592$, $P < 0.010$). The authors concluded that short-term taper is not recommended as a stand-alone treatment; however, patients may taper from buprenorphine as part of a treatment plan. Despite greater comorbidity, PO users seem to have favorable taper outcomes compared with heroin users. Further studies are required to examine longer-term treatment outcomes.

A Mutation In CLOCK Leads To Altered Dopamine Receptor Function. Spencer S, Torres-Altoro MI, Falcon E, Arey R, Marvin M, Goldberg M, Bibb JA, McClung CA. J Neurochem. 2012 Oct; 123(1): 124-134. Epub 2012 Jul 27.
Mice with a mutation in the Clock gene (ClockDelta19) have a number of behavioral phenotypes that suggest alterations in dopaminergic transmission. These include hyperactivity, increased exploratory behavior, and increased reward value for drugs of abuse. However, the complex changes in dopaminergic transmission that underlie the behavioral abnormalities in these mice remain unclear. Here the authors find that a loss of CLOCK function increases dopamine release and turnover in striatum as indicated by increased levels of metabolites HVA and DOPAC, and enhances sensitivity to dopamine receptor antagonists. Interestingly, this enlarged dopaminergic tone results in downstream changes in dopamine receptor (DR) levels with a surprising augmentation of both D1- and D2-type DR protein, but a significant shift in the ratio of D1:D2 receptors in favor of D2 receptor signaling. These effects have functional consequences for both behavior and intracellular signaling, with alterations in locomotor responses to both D1-type and D2-type specific agonists and a blunted response to cAMP activation in the ClockDelta19 mutants. Taken together, these studies further elucidate the abnormalities in dopaminergic transmission that underlie mood, activity, and addictive behaviors.

Accumbens Functional Connectivity during Reward Mediates Sensation-Seeking and Alcohol Use in High-Risk Youth. Weiland BJ, Welsh RC, Yau WY, Zucker RA, Zubieta JK, Heitzeg MM. Drug Alcohol Depend. Epub 2012 Sep 4.
Differences in fronto-striatal connectivity in problem substance users have suggested reduced influence of cognitive regions on reward-salience regions. Youth with a family history of alcoholism (FH+) have disrupted ventral striatal processing compared with controls with no familial risk (FH-). As sensation-seeking represents an additional vulnerability factor, the authors hypothesized that functional connectivity during reward anticipation would differ by family history, and would mediate the relationship between sensation-seeking and drinking in high-risk subjects. Seventy 18-22 year olds (49 FH+/21 FH-) performed a monetary incentive delay task during functional magnetic resonance imaging. Group connectivity differences for incentive (reward/loss) vs. neutral conditions were evaluated with psychophysiological interaction (PPI) analysis, seeded in nucleus accumbens (NAcc). Indirect effects of sensation-seeking on drinking volume through accumbens connectivity were tested. NAcc connectivity with paracentral lobule/precuneus and sensorimotor areas was decreased for FH- vs. increased for FH+ during incentive anticipation. In FH+, task-related functional coupling between left NAcc and supplementary sensorimotor area (SSMA) and right precuneus correlated positively with sensation-seeking and drinking volume and mediated their relationship. In FH-, left NAcc-SSMA connectivity correlated negatively with sensation-seeking but was not related to drinking. These results suggest preexisting differences in accumbens reward-related functional connectivity in high-risk subjects. NAcc coupling with SSMA, involved in attention and motor networks, and precuneus, a default mode structure, appear to mediate sensation-seeking's effect on drinking in those most at-risk. Differences in accumbens connectivity with attention/motor/ default networks, rather than control systems, may influence the reward system's role in vulnerability for substance abuse.

Adolescent Morphine Exposure Affects Long-Term Microglial Function and Later-Life Relapse Liability In A Model Of Addiction. Schwarz JM, Bilbo SD. J Neurosci. 2013 Jan 16; 33(3): 961-971.
Adolescence in humans represents a unique developmental time point associated with increased risk-taking behavior and experimentation with drugs of abuse. The authors hypothesized that exposure to drugs of abuse during adolescence may increase the risk of addiction in adulthood. To test this, rats were treated with a subchronic regimen of morphine or saline in adolescence, and their preference for morphine was examined using conditioned place preference (CPP) and drug-induced reinstatement in adulthood. The initial preference for morphine did not differ between groups; however, rats treated with morphine during adolescence showed robust reinstatement of morphine CPP after drug re-exposure in adulthood. This effect was not seen in rats pretreated with a subchronic regimen of morphine as adults, suggesting that exposure to morphine specifically during adolescence increases the risk of relapse to drug-seeking behavior in adulthood. The authors have previously established a role for microglia, the immune cells of the brain, and immune molecules in the risk of drug-induced reinstatement of morphine CPP. Thus, they examined the role of microglia within the nucleus accumbens of these rats and determined that rats exposed to morphine during adolescence had a significant increase in Toll-like receptor 4 (TLR4) mRNA and protein expression specifically on microglia. Morphine binds to TLR4 directly, and this increase in TLR4 was associated with exaggerated morphine-induced TLR4 signaling and microglial activation in rats previously exposed to morphine during adolescence. These data suggest that long-term changes in microglial function, caused by adolescent morphine exposure, alter the risk of drug-induced reinstatement in adulthood.

Anti-Cocaine Antibody and Butyrylcholinesterase-Derived Cocaine Hydrolase Exert Cooperative Effects on Cocaine Pharmacokinetics and Cocaine-Induced Locomotor Activity in Mice. Brimijoin S, Orson F, Kosten TR, Kinsey B, Shen XY, White SJ, Gao Y. Chem Biol Interact. Epub 2012 Aug 31.
The authors are investigating treatments for cocaine abuse based on viral gene transfer of a cocaine hydrolase (CocH) derived from human butyrylcholinesterase, which can reduce cocaine-stimulated locomotion and cocaine-primed reinstatement of drug-seeking behavior in rats for many months. Here, in mice, they explored the possibility that anti-cocaine antibodies can complement the actions of CocH to reduce cocaine uptake in brain and block centrally-evoked locomotor stimulation. Direct injections of test proteins showed that CocH (0.3 or 1mg/kg) was effective by itself in reducing drug levels in plasma and brain of mice given cocaine (10mg/kg, s.c., or 20mg/kg, i.p). Administration of cocaine antibody per se at a low dose (8mg/kg, i.p.) exerted little effect on cocaine distribution. However, a higher dose of antibody (12mg/kg) caused peripheral trapping (increased plasma drug levels), which led to increased cocaine metabolism by CocH, as evidenced by a 6-fold rise in plasma benzoic acid. Behavioral tests with small doses of CocH and antibody (1 and 8mg/kg, respectively) showed that neither agent alone reduced mouse locomotor activity triggered by a very large cocaine dose (100mg/kg, i.p.). However, dual treatment completely suppressed the locomotor stimulation. Altogether, the authors found cooperative and possibly synergistic actions that warrant further exploration of dual therapies for treatment of cocaine abuse.

Associations between Cannabinoid Receptor-1 (*CNR1*) Variation and Hippocampus and Amygdala Volumes in Heavy Cannabis Users. Schacht JP, Hutchison KE, Filbey FM. Neuropsychopharm. Epub 2012 Jun 12.
Heavy cannabis users display smaller amygdalae and hippocampi than controls, and genetic variation accounts for a large proportion of variance in liability to cannabis dependence (CD). A single nucleotide polymorphism in the cannabis receptor-1 gene (*CNR1*), rs2023239, has been associated with CD diagnosis and intermediate phenotypes, including abstinence-induced withdrawal, cue-elicited craving, and parahippocampal activation to cannabis cues. This study compared hippocampal and amygdalar volumes (potential CD intermediate phenotypes) between heavy cannabis users and healthy controls, and analyzed interactions between group, rs2023239 variation, and the volumes of these structures. Ninety-four heavy cannabis users participated, of whom 37 (14 men, 23 women; mean age=27.8) were matched to 37 healthy controls (14 men, 23 women; mean age=27.3) for case-control analyses. Controlling for total intracranial volume and other confounding variables, matched cannabis users had smaller bilateral hippocampi (left, p=0.002; right, p=0.001) and left amygdalae (p=0.01) than controls. When genotype was considered in the case-control analyses, there was a group by genotype interaction, such that the rs2023239 G allele predicted lower volume of bilateral hippocampi among cannabis users relative to controls (both p<0.001). This interaction persisted when all 94 cannabis users were compared to controls. There were no group by genotype interactions on amygdalar volume. These data replicate previous findings of reduced hippocampal and amygdalar volume among heavy cannabis users, and suggest that *CNR1* rs2023239 variation may predispose smaller hippocampal volume after heavy cannabis use. This association should be tested in future studies of brain volume differences in CD.

Buprenorphine/Naloxone and Methadone Effects On Laboratory Indices Of Liver Health: A Randomized Trial. Saxon AJ, Ling W, Hillhouse M, Thomas C, Hasson A, Ang A, Doraimani G, Tasissa G, Lokhnygina Y, Leimberger J, Bruce RD, McCarthy J, Wiest K, McLaughlin P, Bilangi R, Cohen A, Woody G, Jacobs P. Drug Alcohol Depend. Epub 2012 Aug 22.
Buprenorphine/naloxone (BUP) and methadone (MET) are efficacious treatments for opioid dependence, although concerns about a link between BUP and drug-induced hepatitis have been raised. This study compares the effects of

BUP and MET on liver health in opioid-dependent participants. This was a randomized controlled trial of 1269 opioid-dependent participants seeking treatment at 8 federally licensed opioid treatment programs and followed for up to 32 weeks between May 2006 and August 2010; 731 participants met "evaluable" criteria defined as completing 24 weeks of medication and providing at least 4 blood samples for transaminase testing. Participants were randomly assigned to receive BUP or MET for 24 weeks. Shift table analysis determined how many evaluable participants moved between categories of low and elevated transaminase levels. Predictors of moving from low to high transaminase levels were identified. Changes in transaminase levels did not differ by medication condition. Baseline infection with hepatitis C or B was the only significant predictor of moving from low to elevated transaminase levels; 9 BUP and 15 MET participants showed extreme liver test elevations and were more likely than those without extreme elevations to have seroconverted to both hepatitis B and C during the study, or to use illicit drugs during the first 8 weeks of treatment. MET participants were retained longer in treatment than BUP participants. This study demonstrated no evidence of liver damage during the initial 6 months of treatment in either condition. Physicians can prescribe either medication without major concern for liver injury.

Changes In Sexual and Drug-Related Risk Behavior Following Antiretroviral Therapy Initiation Among HIV-Infected Injection Drug Users. Fu TC, Westergaard RP, Lau B, Celentano DD, Vlahov D, Mehta SH, Kirk GD. AIDS. 2012 Nov 28;26(18):2383-91.
The objective of this study was to evaluate whether HAART is associated with subsequent sexual and drug-related risk behavior compensation among injection drug users (IDUs). A community-based cohort study of 362 HIV-infected IDUs initiating HAART in Baltimore, Maryland was employed. HAART use and risk behavior was assessed at 8316 biannual study visits (median 23). Using logistic regression with generalized estimating equations (GEE), the authors examined the effect of HAART initiation on changes in risk behavior while adjusting for sociodemographics, alcohol use, CD4 cell count, year of initiation and consistency of HAART use. At HAART initiation, participants were a median of 44.4 years old, 71.3% men and 95.3% African-American. In multivariable analysis, HAART initiation was associated with a 75% reduction in the likelihood of unprotected sex [adjusted odds ratio (aOR) 0.25; 95% confidence interval (CI), 0.19-0.32] despite no change in overall sexual activity (aOR 0.95; 0.80-1.12). Odds of any injecting decreased by 38% (aOR 0.62; 0.51-0.75) after HAART initiation. Among the subset of persistent injectors, needle-sharing increased nearly two-fold (aOR 1.99; 1.57-2.52). Behavioral changes were sustained for more than 5 years after HAART initiation and did not differ by consistency of HAART use. Reporting specific high-risk behaviors in the year prior to initiation was a robust predictor of engaging in those behaviors subsequent to HAART. Overall, substantial declines in sexual risk-taking and active injecting argue against significant behavioral compensation among IDUs following HAART initiation. These data also provide evidence to support identifying persons with risky pre-HAART behavior for targeted behavioral intervention.

Combined Cocaine Hydrolase Gene Transfer and Anti-Cocaine Vaccine Synergistically Block Cocaine-Induced Locomotion. Carroll ME, Zlebnik NE, Anker JJ, Kosten TR, Orson FM, Shen X, Kinsey B, Parks RJ, Gao Y, Brimijoin S. PLoS One. 2012;7(8):e43536. Epub 2012 Aug 17.
Mice and rats were tested for reduced sensitivity to cocaine-induced hyper-locomotion after pretreatment with anti-cocaine antibody or cocaine hydrolase (CocH) derived from human butyrylcholinesterase (BChE). In Balb/c mice, direct i.p. injection of CocH protein (1 mg/kg) had no effect on spontaneous locomotion, but it suppressed responses to i.p. cocaine up to 80 mg/kg. When CocH was injected i.p. along with a murine cocaine antiserum that also did not affect spontaneous locomotion, there was no response to any cocaine dose. This suppression of locomotor activity required active enzyme, as it was lost after pretreatment with iso-OMPA, a selective BChE inhibitor. Comparable results were obtained in rats that developed high levels of CocH by gene transfer with helper-dependent adenoviral vector, and/or high levels of anti-cocaine antibody by vaccination with norcocaine hapten conjugated to keyhole limpet hemocyanin (KLH). After these treatments, rats were subjected to a locomotor sensitization paradigm involving a "training phase" with an initial i.p. saline injection on day 1 followed by 8 days of repeated cocaine injections (10 mg/kg, i.p.). A 15-day rest period then ensued, followed by a final "challenge" cocaine injection. As in mice, the individual treatment interventions reduced cocaine-stimulated hyperactivity to a modest extent, while combined treatment produced a greater reduction during all phases of testing compared to control rats (with only saline pretreatment). Overall, the present results strongly support the view that anti-cocaine vaccine and cocaine hydrolase vector treatments together provide enhanced protection against the stimulatory actions of cocaine in rodents. A similar combination therapy in human cocaine users might provide a robust therapy to help maintain abstinence.

Decisions During Negatively-Framed Messages Yield Smaller Risk-Aversion-Related Brain Activation in Substance-Dependent Individuals. Fukunaga, R, Bogg, T, Finn, PR, Brown, JW. Psychology of Addictive Behaviors: Journal of the Society of Psychologists in Addictive Behaviors, Epub 2012 Nov 12.
A sizable segment of addiction research investigates the effects of persuasive message appeals on risky and deleterious behaviors. However, to date, little research has examined how various forms of message framing and corresponding behavioral choices might by mediated by risk-related brain regions. Using event-related functional MRI, the authors investigated brain regions hypothesized to mediate the influence of message appeals on decision

making in substance-dependent (SD) compared with non-substance-dependent (non-SD) individuals. The Iowa Gambling Task (IGT) was modified to include positively-framed, negatively-framed, and control messages about long-term deck payoffs. In the positively-framed condition, the SD and non-SD groups showed improved decision-making performance that corresponded to higher risk-aversion-related brain activity in the anterior cingulate cortex (ACC) and anterior insula (AI). In contrast, in the negatively-framed condition, the SD group showed poorer performance that corresponded to lower risk-aversion-related brain activity in the AI region. In addition, only the non-SD group showed a positive association between decision quality and greater risk-related activity in the ACC, regardless of message type. The findings suggest substance-dependent individuals may have reduced neurocognitive sensitivity in the ACC and AI regions involved in risk perception and aversion during decision-making, especially in response to framed messages that emphasize reduced prospects for long-term gains.

Decline in Genetic Influence on the Co-Occurrence of Alcohol, Marijuana, and Nicotine Dependence Symptoms From Age 14 to 29. Vrieze S, Hicks B, Iacono W, McGue M. Am J Psychiatry. 2012; 1073-1081.
Cross-sectional studies have demonstrated high rates of comorbidity among substance use disorders. However, few studies have examined the developmental course of incident comorbidity and how it changes from adolescence to adulthood. The authors examine patterns of comorbidity among substance use disorders to gain insight into the effect of shared versus specific etiological influences on measures of substance abuse and dependence. They evaluated the pattern of correlations among nicotine, alcohol, and marijuana abuse and dependence symptom counts as well as their underlying genetic and environmental influences in a community-representative twin sample (N=3,762). Symptoms were assessed at ages 11, 14, 17, 20, 24, and 29 years. A single common factor was used to model the correlations among symptom counts at each age. The authors examined age-related changes in the influence of this general factor by testing for differences in the mean factor loading across time. Mean levels of abuse or dependence symptoms increased throughout adolescence, peaked around age 20, and declined from age 24 to age 29. The influence of the general factor was highest at ages 14 and 17, but decreased from age 17 to age 24. Genetic influences of the general factor declined considerably with age alongside an increase in non-shared environmental influences. The authors conclude that adolescent substance abuse or dependence is largely a function of shared etiology. As young people age, their symptoms are increasingly influenced by substance-specific etiological factors. Heritability analyses revealed that the generalized risk is primarily influenced by genetic factors in adolescence, but non-shared environmental influences increase in importance as substance dependence becomes more specialized in adulthood.

DRD4 Genotype Predicts Longevity in Mouse and Human. Grady DL, Thanos PK, Corrada MM, Barnett JC Jr, Ciobanu V, Shustarovich D, Napoli A, Moyzis AG, Grandy D, Rubinstein M, Wang GJ, Kawas CH, Chen C, Dong Q, Wang E, Volkow ND, Moyzis RK. J Neurosci. 2013 Jan 2; 33(1): 286-291.
Longevity is influenced by genetic and environmental factors. The brain's dopamine system may be particularly relevant, since it modulates traits (e.g., sensitivity to reward, incentive motivation, sustained effort) that impact behavioral responses to the environment. In particular, the dopamine D4 receptor (DRD4) has been shown to moderate the impact of environments on behavior and health. The authors tested the hypothesis that the DRD4 gene influences longevity and that its impact is mediated through environmental effects. Surviving participants of a 30-year-old population-based health survey (N = 310; age range, 90-109 years; the 90+ Study) were genotyped/resequenced at the DRD4 gene and compared with a European ancestry-matched younger population (N = 2902; age range, 7-45 years). The authors found that the oldest-old population had a 66% increase in individuals carrying the DRD4 7R allele relative to the younger sample ($p = 3.5 \times 10(-9)$), and that this genotype was strongly correlated with increased levels of physical activity. Consistent with these results, DRD4 knock-out mice, when compared with wild-type and heterozygous mice, displayed a 7-9.7% decrease in lifespan, reduced spontaneous locomotor activity, and no lifespan increase when reared in an enriched environment. These results support the hypothesis that DRD4 gene variants contribute to longevity in humans and in mice, and suggest that this effect is mediated by shaping behavioral responses to the environment.

Effects of Chronic Buspirone Treatment on Cocaine Self-Administration. Mello NK, Fivel PA, Kohut SJ, Bergman J. Neuropsychopharmacology Epub 2012 Oct 17.
Cocaine abuse and dependence is a major public health problem that continues to challenge medication-based treatment. Buspirone (Buspar) is a clinically available, non-benzodiazepine anxiolytic medication that acts on both serotonin and dopamine systems. In recent preclinical studies, acute buspirone treatment reduced cocaine self-administration at doses that did not also decrease food-reinforced behavior in rhesus monkeys (Bergman et al, 2012). The present study evaluated the effectiveness of chronic buspirone treatment on self-administration of cocaine and food. Five adult rhesus monkeys (Macaca mulatta) were trained to self-administer cocaine and food during four 1-h daily sessions under a second-order schedule of reinforcement (FR2 [VR 16:S]). Buspirone (0.32 and 0.56 mg/kg/h) was administered intravenously through one lumen of a double-lumen catheter every 20 min for 23 h each day for 7-10 consecutive days. Each buspirone treatment period was followed by saline control treatment until drug- and food-maintained responding returned to baseline levels. Buspirone significantly reduced responding maintained by

cocaine, and shifted the dose-effect curve downwards. Buspirone had minimal effects on food-maintained responding. In cocaine discrimination studies, buspirone (0.1-0.32 mg/kg, IM) did not antagonize the discriminative stimulus and rate-altering effects of cocaine in four of six monkeys. These findings indicate that buspirone selectively attenuates the reinforcing effects of cocaine in a nonhuman primate model of cocaine self-administration, and has variable effects on cocaine discrimination.

Epigenetic Inheritance Of a Cocaine-Resistance Phenotype. Vassoler FM, White, SL,Schmidt, HD, Sadri-Vakili, S, Pierce, RC. Nature Neuroscience. 2013; 16: 42–47.
The authors delineated a heritable phenotype resulting from the self-administration of cocaine in rats. They observed delayed acquisition and reduced maintenance of cocaine self-administration in male, but not female, offspring of sires that self-administered cocaine. Brain-derived neurotrophic factor (BDNF) mRNA and BDNF protein were increased in the medial prefrontal cortex (mPFC), and there was an increased association of acetylated histone H3 with BDNF promoters in only the male offspring of cocaine-experienced sires. Administration of a BDNF receptor antagonist (the TrkB receptor antagonist ANA-12) reversed the diminished cocaine self-administration in male cocaine-sired rats. In addition, the association of acetylated histone H3 with BDNF promoters was increased in the sperm of sires that self-administered cocaine. Collectively, these findings indicate that voluntary paternal ingestion of cocaine results in epigenetic reprogramming of the germline, having profound effects on mPFC gene expression and resistance to cocaine reinforcement in male offspring.

Exosome-Mediated Shuttling Of MicroRNA-29 Regulates HIV Tat and Morphine-Mediated Neuronal Dysfunction. G Hu, H Yao, A D Chaudhuri, M Duan, S V Yelamanchili, H Wen, P D Cheney, H S Fox, and S Buch. Cell Death Dis. 2012 Aug; 3(8): e381.
Neuronal damage is a hallmark feature of HIV-associated neurological disorders (HANDs). Opiate drug abuse accelerates the incidence and progression of HAND; however, the mechanisms underlying the potentiation of neuropathogenesis by these drugs remain elusive. Opiates such as morphine have been shown to enhance HIV transactivation protein Tat-mediated toxicity in both human neurons and neuroblastoma cells. In the present study, the authors demonstrate reduced expression of the tropic factor platelet-derived growth factor (PDGF)-B with a concomitant increase in miR-29b in the basal ganglia region of the brains of morphine-dependent simian immunodeficiency virus (SIV)-infected macaques compared with the SIV-infected controls. In vitro relevance of these findings was corroborated in cultures of astrocytes exposed to morphine and HIV Tat that led to increased release of miR-29b in exosomes. Subsequent treatment of neuronal SH-SY5Y cell line with exosomes from treated astrocytes resulted in decreased expression of PDGF-B, with a concomitant decrease in viability of neurons. Furthermore, it was shown that PDGF-B was a target for miR-29b as evidenced by the fact that binding of miR-29 to the 3′-untranslated region of PDGF-B mRNA resulted in its translational repression in SH-SY5Y cells. Understanding the regulation of PDGF-B expression may provide insights into the development of potential therapeutic targets for neuronal loss in HIV-1-infected opiate abusers.

Extended-Release Mixed Amphetamine Salts and Topiramate For Cocaine Dependence: A Randomized Controlled Trial. Mariani JJ, Pavlicova M, Bisaga A, Nunes EV, Brooks DJ, Levin FR. Biol Psychiatry. 2012 Dec 1;72(11):950-6. Epub 2012 Jul 12.
Cocaine dependence is a substantial public health problem, yet there are no clearly effective medication treatments. Amphetamine and topiramate have both shown promise for the treatment of cocaine dependence in preclinical and early-stage clinical studies. Eighty-one cocaine-dependent adults were randomized to receive a combination of extended-release mixed amphetamine salts (MAS-ER) and topiramate or placebo for 12 weeks under double-blind conditions. MAS-ER doses were titrated over 2 weeks to a maximum dose of 60 mg daily, and topiramate doses were titrated over 6 weeks to a maximum dose of 150 mg twice daily. All participants received a supportive behavioral intervention. The primary outcome was the proportion of individuals who achieved 3 consecutive weeks of abstinence as measured by urine toxicology confirmed self-report. The overall proportion of participants who achieved 3 consecutive weeks of abstinence was larger in the extended-release mixed amphetamine salts and topiramate group (33.3%) than in placebo group (16.7%). There was a significant moderating effect of baseline total number of cocaine use days (Wald $\chi(2) = 3.75$, $df = 1$, $p = .05$) on outcome, suggesting that the combination treatment was most effective for participants with a high baseline frequency of cocaine use. The results of this study supported the authors' hypothesis that the combination of MAS-ER and topiramate would be superior to placebo in achieving 3 weeks of consecutive abstinence. These findings provide evidence that the combination of MAS-ER and topiramate is efficacious in promoting abstinence in cocaine-dependent individuals.

Glycine Transporter-1 Inhibition Preceding Extinction Training Inhibits Reacquisition of Cocaine Seeking. Achat-Mendes C, Nic Dhonnchadha BA, Platt DM, Kantak KM, Spealman RD. Neuropsychopharmacology. Epub 2012 Sep 5.
Cognitive enhancers that act by increasing glycine transmission might be useful adjuncts to cocaine-cue extinction training to deter relapse. The study investigated the effects of combining treatments of the glycine transporter-1

(GlyT-1) inhibitor, Org24598, with extinction training on the subsequent reacquisition of cocaine self-administration. Squirrel monkeys and rats were trained to self-administer cocaine under a second-order schedule of intravenous drug injection in which responding was maintained by cocaine injections and a cocaine-paired visual stimulus. During three weekly extinction sessions, saline was substituted for cocaine but responding still produced the cocaine-paired stimulus. Subjects were treated with Org24598 or vehicle, either before or after each extinction session. One week later, cocaine injections were restored, and reacquisition of cocaine self-administration was evaluated over 15 sessions. Compared with vehicle, administration of Org24598 (1.0 mg/kg in monkeys; 3.0 or 7.5 mg/kg in rats) before each extinction session significantly inhibited reacquisition of cocaine self-administration in each species. In contrast, administration of Org24598 (1.0 mg/kg in monkeys) following, rather than preceding, each extinction session did not affect reacquisition compared with vehicle. When extinction training was replaced by cocaine self-administration or abstinence control conditions, treatment with the same doses of Org24598 resulted in reacquisition that was significantly more rapid than the reacquisition observed when Org24598 was administered before extinction training sessions. The results support the potential clinical utility of GlyT-1 inhibitor pretreatments combined with cocaine-cue extinction training to inhibit relapse.

Human Dorsal Anterior Cingulate Cortex Neurons Mediate Ongoing Behavioural Adaptation. Sheth SA, Mian MK, Patel SR, Asaad WF, Williams ZM, Dougherty DD, Bush G, Eskandar EN. Nature. 2012 Aug 9; 488(7410): 218-221.
The ability to optimize behavioural performance when confronted with continuously evolving environmental demands is a key element of human cognition. The dorsal anterior cingulate cortex (dACC), which lies on the medial surface of the frontal lobes, is important in regulating cognitive control. Hypotheses about its function include guiding reward-based decision making, monitoring for conflict between competing responses, and predicting task difficulty. Precise mechanisms of dACC function remain unknown, however, because of the limited number of human neurophysiological studies. Here the authors use functional imaging and human single-neuron recordings to show that the firing of individual dACC neurons encodes current and recent cognitive load. They demonstrate that the modulation of current dACC activity by previous activity produces a behavioural adaptation that accelerates reactions to cues of similar difficulty to previous ones, and retards reactions to cues of different difficulty. Furthermore, this conflict adaptation, or Gratton effect, is abolished after surgically targeted ablation of the dACC. These results demonstrate that the dACC provides a continuously updated prediction of expected cognitive demand to optimize future behavioural responses. In situations with stable cognitive demands, this signal promotes efficiency by hastening responses, but in situations with changing demands, it engenders accuracy by delaying responses.

Increased Genetic Vulnerability to Smoking at CHRNA5 in Early-Onset Smokers. Hartz SM, Short SE, Saccone NL, et al. Arch Gen Psychiatry. 2012; 69(8) 854-860.
The objective of this study was to determine whether the association between rs16969968 and smoking is modified by age at onset of regular smoking. Uniform statistical analysis scripts were run locally. Starting with 94,050 ever-smokers from 43 studies, the authors extracted the heavy smokers (CPD >20) and light smokers (CPD ≤10) with age-at-onset information, reducing the sample size to 33 348. Each study was stratified into early-onset smokers (age at onset ≤16 years) and late-onset smokers (age at onset >16 years), and a logistic regression of heavy vs. light smoking with the rs16969968 genotype was computed for each stratum. Meta-analysis was performed within each age-at-onset stratum. Individuals with 1 risk allele at rs16969968 who were early-onset smokers were significantly more likely to be heavy smokers in adulthood (odds ratio [OR] = 1.45; 95% CI, 1.36-1.55; n = 13 843) than were carriers of the risk allele who were late-onset smokers (OR = 1.27; 95% CI, 1.21-1.33, n = 19 505) (P = .01). These results highlight an increased genetic vulnerability to smoking in early-onset smokers.

Increased Vulnerability To Cocaine In Mice Lacking Dopamine D3 Receptors. Song R, Zhang HY, Li X, Bi H, Gardner EL, Xi ZX. Proc Natl Acad Sci U S A. 2012 Oct 23; 109(43): 17675-17680.
Neuroimaging studies using positron emission tomography suggest that reduced dopamine D(2) receptor availability in the neostriatum is associated with increased vulnerability to drug addiction in humans and experimental animals. The role of D(3) receptors (D(3)Rs) in the neurobiology of addiction remains unclear, however. Here the authors report that D(3)R KO (D(3)(-/-)) mice display enhanced cocaine self-administration and enhanced motivation for cocaine-taking and cocaine-seeking behavior. This increased vulnerability to cocaine is accompanied by decreased dopamine response to cocaine secondary to increased basal levels of extracellular dopamine in the nucleus accumbens, suggesting a compensatory response to decreased cocaine reward in D(3)(-/-) mice. In addition, D(3)(-/-) mice also display up-regulation of dopamine transporters in the striatum, suggesting a neuroadaptative attempt to normalize elevated basal extracellular dopamine. These findings suggest that D(3)R deletion increases vulnerability to cocaine, and that reduced D(3)R availability in the brain may constitute a risk factor for the development of cocaine addiction.

Linking Context with Reward: A Functional Circuit From Hippocampal CA3 To Ventral Tegmental Area. Luo AH, Tahsili-Fahadan P, Wise RA, Lupica CR, Aston-Jones G. Science. 2011 Jul 15;333(6040):353-7.
Reward-motivated behavior is strongly influenced by the learned significance of contextual stimuli in the environment. However, the neural pathways that mediate context-reward relations are not well understood. The authors have identified a circuit from area CA3 of dorsal hippocampus to ventral tegmental area (VTA) that uses lateral septum (LS) as a relay. Theta frequency stimulation of CA3 excited VTA dopamine (DA) neurons and inhibited non-DA neurons. DA neuron excitation was likely mediated by disinhibition because local antagonism of γ-aminobutyric acid receptors blocked responses to CA3 stimulation. Inactivating components of the CA3-LS-VTA pathway blocked evoked responses in VTA and also reinstatement of cocaine-seeking by contextual stimuli. This transsynaptic link between hippocampus and VTA appears to be an important substrate by which environmental context regulates goal-directed behavior.

Low Prefrontal PSA-NCAM Confers Risk For Alcoholism-Related Behavior. Barker JM, Torregrossa MM, Taylor JR. Nat Neurosci. 2012 Oct; 15(10): 1356-2358. Epub 2012 Aug 26.
The factors underlying vulnerability to alcoholism are largely unknown. The authors identified in rodents an innate endophenotype predicting individual risk for alcohol-related behaviors that was associated with decreased expression of the neuroplasticity-related polysialylated neural cell adhesion molecule (PSA-NCAM). Depletion of PSA-NCAM in the ventromedial prefrontal cortex was sufficient to render mice unable to extinguish alcohol seeking, indicating a causal role of naturally occurring variation. These data suggest a mechanism of aberrant prefrontal neuroplasticity that underlies enhanced propensity for inflexible addiction-related behavior.

Medical Marijuana Use among Adolescents in Substance Abuse Treatment. Salomonsen-Sautel S, Sakai JT, Thurstone C, Corley R, Hopfer C. J Am Acad Child Adolesc Psychiatry. 2012 Jul; 51(7): 694-702.
The objective of this study was to assess the prevalence and frequency of medical marijuana diversion and use among adolescents in substance abuse treatment and to identify factors related to their medical marijuana use. This study calculated the prevalence and frequency of diverted medical marijuana use among adolescents (n = 164), ages 14-18 years (mean age = 16.09, SD = 1.12), in substance abuse treatment in the Denver metropolitan area. Bivariate and multivariate analyses were completed to determine factors related to adolescents' use of medical marijuana. Approximately 74% of the adolescents had used someone else's medical marijuana, and they reported using diverted medical marijuana a median of 50 times. After adjusting for gender and race/ethnicity, adolescents who used medical marijuana had an earlier age of regular marijuana use, more marijuana abuse and dependence symptoms, and more conduct disorder symptoms compared with those who did not use medical marijuana. The authors conclude that medical marijuana use among adolescent patients in substance abuse treatment is very common, implying substantial diversion from registered users. These results support the need for policy changes that protect against diversion of medical marijuana and reduce adolescent access to diverted medical marijuana. Future studies should examine patterns of medical marijuana diversion and use in general population adolescents.

Methamphetamine Activates Nuclear Factor Kappa-Light-Chain-Enhancer Of Activated B Cells (NF-Kb) And Induces Human Immunodeficiency Virus (HIV) Transcription In Human Microglial Cells. Wires ES, Alvarez D, Dobrowolski C, Wang Y, Morales M, Karn J, Harvey BK. J Neurovirol. 2012 Oct; 18(5): 400-410. Epub 2012 May 22.
Human immunodeficiency virus (HIV) primarily infects glial cells in the central nervous system (CNS). Recent evidence suggests that HIV-infected individuals who abuse drugs such as methamphetamine (METH) have higher viral loads and experience more severe neurological complications than HIV-infected individuals who do not abuse drugs. The aim of this study was to determine the effect of METH on HIV expression from the HIV long terminal repeat (LTR) promoter and on an HIV integrated provirus in microglial cells, the primary host cells for HIV in the CNS. Primary human microglial cells immortalized with SV40 T antigen (CHME-5 cells) were cotransfected with an HIV LTR reporter and the HIV Tat gene, a key regulator of viral replication and gene expression, and exposed to METH. These results demonstrate that METH treatment induced LTR activation, an effect potentiated in the presence of Tat. The authors also found that METH increased the nuclear translocation of the nuclear factor kappa B (NF-κB), a key cellular transcriptional regulator of the LTR promoter, and the activity of an NF-κB-specific reporter plasmid in CHME-5 cells. The presence of a dominant-negative regulator of NF-κB blocked METH-related activation of the HIV LTR. Furthermore, treatment of HIV-latently infected CHME-5 (CHME-5/HIV) cells with METH induced HIV expression and nuclear translocation of the p65 subunit of NF-κB. These results suggest that METH can stimulate HIV gene expression in microglia cells through activation of the NF-κB signaling pathway. This mechanism may outline the initial biochemical events leading to the observed increased neurodegeneration in HIV-positive individuals who use METH.

Novel Cues Reinstate Cocaine-Seeking Behavior and Induce Fos Protein Expression As Effectively As Conditioned Cues. Bastle RM, Kufahl PR, Turk MN, Weber SM, Pentkowski NS, Thiel KJ, Neisewander JL. Neuropsychopharmacology. 2012 Aug; 37(9): 2109-2120. Epub 2012 Apr 25.
Cue reinstatement of extinguished cocaine-seeking behavior is a widely used model of cue-elicited craving in abstinent human addicts. This study examined Fos protein expression in response to cocaine cues or to novel cues as a control for activation produced by test novelty. Rats were trained to self-administer cocaine paired with either a light or a tone cue, or received yoked saline and cue presentations, and then underwent daily extinction training. They were then tested for reinstatement of extinguished cocaine-seeking behavior elicited by response-contingent presentations of either the cocaine-paired cue or a novel cue (that is, tone for those trained with a light or vice versa). Surprisingly, conditioned and novel cues both reinstated responding and increased Fos similarly in most brain regions. Exceptions included the anterior cingulate, which was sensitive to test cue modality in saline controls and the dorsomedial caudate-putamen, where Fos was correlated with responding in the novel, but not conditioned, cue groups. In subsequent experiments, the authors observed a similar pattern of reinstatement in rats trained and tested for sucrose-seeking behavior, whereas rats trained and tested with the cues only reinstated to a novel, and not a familiar, light or tone. The results suggest that novel cues reinstate responding to a similar extent as conditioned cues regardless of whether animals have a reinforcement history with cocaine or sucrose, and that both types of cues activate similar brain circuits. Several explanations as to why converging processes may drive drug and novel cue reinforcement and seeking behavior are discussed.

Powerful Cocaine-Like Actions Of 3,4-Methylenedioxypyrovalerone (MDPV), A Principal Constituent Of Psychoactive 'Bath Salts' Products. Baumann MH, Partilla JS, Lehner KR, Thorndike EB, Hoffman AF, Holy M, Rothman RB, Goldberg SR, Lupica CR, Sitte HH, Brandt SD, Tella SR, Cozzi NV, Schindler CW. Neuropsychopharmacology. Epub 2012 Oct 17.
The abuse of psychoactive 'bath salts' containing cathinones such as 3,4-methylenedioxypyrovalerone (MDPV) is a growing public health concern, yet little is known about their pharmacology. Here, the authors evaluated the effects of MDPV and related drugs using molecular, cellular, and whole-animal methods. In vitro transporter assays were performed in rat brain synaptosomes and in cells expressing human transporters, while clearance of endogenous dopamine was measured by fast-scan cyclic voltammetry in mouse striatal slices. Assessments of in vivo neurochemistry, locomotor activity, and cardiovascular parameters were carried out in rats. They found that MDPV blocks uptake of [^{3}H]dopamine (IC_{50}=4.1 nM) and [(3)H]norepinephrine (IC50=26 nM) with high potency but has weak effects on uptake of [^{3}H]serotonin (IC_{50}=3349 nM). In contrast to other psychoactive cathinones (eg, mephedrone), MDPV is not a transporter substrate. The clearance of endogenous dopamine is inhibited by MDPV and cocaine in a similar manner, but MDPV displays greater potency and efficacy. Consistent with in vitro findings, MDPV (0.1-0.3 mg/kg, intravenous) increases extracellular concentrations of dopamine in the nucleus accumbens. Additionally, MDPV (0.1-3.0 mg/kg, subcutaneous) is at least 10 times more potent than cocaine at producing locomotor activation, tachycardia, and hypertension in rats. These data show that MDPV is a monoamine transporter blocker with increased potency and selectivity for catecholamines when compared with cocaine. The robust stimulation of dopamine transmission by MDPV predicts serious potential for abuse and may provide a mechanism to explain the adverse effects observed in humans taking high doses of 'bath salts' preparations.

Protracted Withdrawal From Cocaine Self-Administration Flips the Switch on 5-HT(1B) Receptor Modulation of Cocaine Abuse-Related Behaviors. Pentkowski NS, Cheung TH, Toy WA, Adams MD, Neumaier JF, Neisewander JL. Biol Psychiatry. 2012 Sep 1; 72(5): 396-404.
The role of serotonin-1B receptors (5-HT(1B)Rs) in modulating cocaine abuse-related behaviors has been controversial due to discrepancies between pharmacological and gene knockout approaches and opposite influences on cocaine self-administration versus cocaine-seeking behavior. The authors hypothesized that modulation of these behaviors via 5-HT(1B)Rs in the mesolimbic pathway may vary depending on the stage of the addiction cycle. To test this hypothesis, they examined the effects of increasing 5-HT(1B)R production by microinfusing a viral vector expressing either green fluorescent protein and 5-HT(1B)R or green fluorescent protein alone into the medial nucleus accumbens shell of rats either during maintenance of cocaine self-administration (i.e., active drug use) or during protracted withdrawal. 5-HT(1B)R receptor gene transfer during maintenance shifted the dose-response curve for cocaine self-administration upward and to the left and increased breakpoints and cocaine intake on a progressive ratio schedule, consistent with enhanced reinforcing effects of cocaine. In contrast, following 21 days of forced abstinence, 5-HT(1B)R gene transfer attenuated breakpoints and cocaine intake on a progressive ratio schedule of reinforcement, as well as cue- and cocaine-primed reinstatement of cocaine-seeking behavior. This unique pattern of effects suggests that mesolimbic 5-HT(1B)Rs differentially modulate cocaine abuse-related behaviors, with a facilitative influence during periods of active drug use, in striking contrast to an inhibitory influence during protracted withdrawal. These findings suggest that targeting 5-HT(1B)Rs may lead to a novel treatment for cocaine dependence and that the therapeutic efficacy of these treatments may vary depending on the stage of the addiction cycle.

Role Of Orbitofrontal Cortex Neuronal Ensembles In The Expression Of Incubation Of Heroin Craving.
Fanous S, Goldart EM, Theberge FR, Bossert JM, Shaham Y, Hope BT. J Neurosci. 2012 Aug 22; 32(34): 11600-11609.
In humans, exposure to cues previously associated with heroin use often provokes relapse after prolonged withdrawal periods. In rats, cue-induced heroin seeking progressively increases after withdrawal (incubation of heroin craving). Here, the authors examined the role of orbitofrontal cortex (OFC) neuronal ensembles in the enhanced response to heroin cues after prolonged withdrawal or the expression of incubation of heroin craving. They trained rats to self-administer heroin (6 h/d for 10 d) and assessed cue-induced heroin seeking in extinction tests after 1 or 14 withdrawal days. Cue-induced heroin seeking increased from 1 to 14 d and was accompanied by increased Fos expression in ~12% of OFC neurons. Nonselective inactivation of OFC neurons with the GABA agonists baclofen + muscimol decreased cue-induced heroin seeking on withdrawal day 14 but not day 1. They then used the Daun02 inactivation procedure to assess a causal role of the minority of selectively activated Fos-expressing OFC neurons (that presumably form cue-encoding neuronal ensembles) in cue-induced heroin seeking after 14 withdrawal days. They trained c-fos-lacZ transgenic rats to self-administer heroin and 11 d later reexposed them to heroin-associated cues or novel cues for 15 min (induction day), followed by OFC Daun02 or vehicle injections 90 min later; they then tested the rats in extinction tests 3 d later. Daun02 selectively decreased cue-induced heroin seeking in rats previously reexposed to the heroin-associated cues on induction day but not in rats exposed previously to novel cues. Results suggest that heroin-cue-activated OFC neuronal ensembles contribute to the expression of incubation of heroin craving.

Severe Stress Switches CRF Action in the Nucleus Accumbens From Appetitive To Aversive. Lemos JC, Wanat MJ, Smith JS, Reyes BA, Hollon NG, Van Bockstaele EJ, Chavkin C, Phillips PE. Nature. 2012 Oct 18; 490(7420): 402-406. Epub 2012 Sep 19.
Stressors motivate an array of adaptive responses ranging from 'fight or flight' to an internal urgency signal facilitating long-term goals. However, traumatic or chronic uncontrollable stress promotes the onset of major depressive disorder, in which acute stressors lose their motivational properties and are perceived as insurmountable impediments. Consequently, stress-induced depression is a debilitating human condition characterized by an affective shift from engagement of the environment to withdrawal. An emerging neurobiological substrate of depression and associated pathology is the nucleus accumbens, a region with the capacity to mediate a diverse range of stress responses by interfacing limbic, cognitive and motor circuitry. Here the authors report that corticotropin-releasing factor (CRF), a neuropeptide released in response to acute stressors and other arousing environmental stimuli, acts in the nucleus accumbens of naive mice to increase dopamine release through coactivation of the receptors CRFR1 and CRFR2. Remarkably, severe-stress exposure completely abolished this effect without recovery for at least 90 days. This loss of CRF's capacity to regulate dopamine release in the nucleus accumbens is accompanied by a switch in the reaction to CRF from appetitive to aversive, indicating a diametric change in the emotional response to acute stressors. Thus, the current findings offer a biological substrate for the switch in affect which is central to stress-induced depressive disorders.

Sex differences in striatal dopamine D2/D3 receptor availability in smokers and non-smokers. Brown AK, Mandelkern MA, Farahi J, Robertson C, Ghahremani DG, Sumerel B, Moallem N, London ED. Int J Neuropsychopharm-acol. 2012 Aug; 15(7): 989-994.
In previous research, nicotine-dependent men exhibited lower putamen D2/D3 dopamine-receptor availability than non-smokers (Fehr et al. 2008), but parallel assessments were not performed in women. Women and men (19 light smokers, 18 non-smokers) were tested for differences due to sex and smoking in striatal D(2)/D(3) dopamine-receptor availability, using positron emission tomography with [(18)F]fallypride. Receptor availability was determined using a reference region method, in striatal volumes and in whole-brain, voxel-wise analysis. Significant sex × smoking interactions were observed in the caudate nuclei and putamen. Post-hoc t tests showed that male smokers had significantly lower D(2)/D(3) dopamine-receptor availability than female smokers (-17% caudate, -21% putamen) and male non-smokers (-15% caudate, -16% putamen). Female smokers did not differ from non-smokers. Whole-brain analysis demonstrated no statistically significant voxels or clusters. These results suggest that low receptor availability may confer vulnerability to nicotine dependence or that smoking selectively affects D2/D3 receptor down-regulation in men but not women.

Smoking Quit Success Genotype Score Predicts Quit Success and Distinct Patterns Of Developmental Involvement With Common Addictive Substances. Uhl GR, Walther D, Musci R, Fisher C, Anthony JC, Storr CL, Behm FM, Eaton WW, Ialongo I, Rose JE. Molecular Psychiatry Epub 2012 Nov 6.
Genotype scores that predict relevant clinical outcomes may detect other disease features and help direct prevention efforts. The authors report data that validate a previously established v1.0 smoking cessation quit success genotype score and describe striking differences in the score in individuals who display differing developmental trajectories of use of common addictive substances. In a cessation study, v1.0 genotype scores predicted ability to quit with P=0.00056 and area under receiver-operating characteristic curve 0.66. About 43% vs. 13% quit in the upper vs.

lower genotype score terciles. Latent class growth analyses of a developmentally assessed sample identified three latent classes based on substance use. Higher v1.0 scores were associated with (a) higher probabilities of participant membership in a latent class that displayed low use of common addictive substances during adolescence (P=0.0004) and (b) lower probabilities of membership in a class that reported escalating use (P=0.001). These results indicate that: (a) we have identified genetic predictors of smoking cessation success, (b) genetic influences on quit success overlap with those that influence the rate at which addictive substance use is taken up during adolescence and (c) individuals at genetic risk for both escalating use of addictive substances and poor abilities to quit may provide especially urgent focus for prevention efforts.

Synaptic and Behavioral Profile Of Multiple Glutamatergic Inputs To the Nucleus Accumbens. Britt JP, Benaliouad F, McDevitt RA, Stuber GD, Wise RA, Bonci A. Neuron 2012: 31(11): 790-803.
Excitatory afferents to the nucleus accumbens (NAc) are thought to facilitate reward seeking by encoding reward-associated cues. Selective activation of different glutamatergic inputs to the NAc can produce divergent physiological and behavioral responses, but mechanistic explanations for these pathway-specific effects are lacking. Here, the authors compared the innervation patterns and synaptic properties of ventral hippocampus, basolateral amygdala, and prefrontal cortex input to the NAc. Ventral hippocampal input was found to be uniquely localized to the medial NAc shell, where it was predominant and selectively potentiated after cocaine exposure. In vivo, bidirectional optogenetic manipulations of this pathway attenuated and enhanced cocaine-induced locomotion. Challenging the idea that any of these inputs encode motivationally neutral information, activation of each discrete pathway reinforced instrumental behaviors. Finally, direct optical activation of medium spiny neurons proved to be capable of supporting self-stimulation, demonstrating that behavioral reinforcement is an explicit consequence of strong excitatory drive to the NAc.

The Cost-Effectiveness Of Rapid HIV Testing In Substance Abuse Treatment: Results Of A Randomized Trial. Schackman BR, Metsch LR, Colfax GN, Leff JA, Wong A, Scott CA, Feaster DJ, Gooden L, Matheson T, Haynes LF, Paltiel AD, Walensky RP. Drug Alcohol Depend. Epub 2012 Sep 6.
The President's National HIV/AIDS Strategy calls for coupling HIV screening and prevention services with substance abuse treatment programs. Fewer than half of US community-based substance abuse treatment programs make HIV testing available on-site or through referral. The authors measured the cost-effectiveness of three HIV testing strategies evaluated in a randomized trial conducted in 12 community-based substance abuse treatment programs in 2009: off-site testing referral, on-site rapid testing with information only, on-site rapid testing with risk-reduction counseling. Data from the trial included patient demographics, prior testing history, test acceptance and receipt of results, undiagnosed HIV prevalence (0.4%) and program costs. The Cost-Effectiveness of Preventing AIDS Complications (CEPAC) computer simulation model was used to project life expectancy, lifetime costs, and quality-adjusted life years (QALYs) for HIV-infected individuals. Incremental cost-effectiveness ratios (2009 US $/QALY) were calculated after adding costs of testing HIV-uninfected individuals; costs and QALYs were discounted at 3% annually. Results indicated that referral for off-site testing is less efficient (dominated) compared to offering on-site testing with information only. The cost-effectiveness ratio for on-site testing with information is $60,300/QALY in the base case, or $76,300/QALY with 0.1% undiagnosed HIV prevalence. HIV risk-reduction counseling costs $36 per person more without additional benefit. The authors conclude that a strategy of on-site rapid HIV testing offer with information only in substance abuse treatment programs increases life expectancy at a cost-effectiveness ratio <$100,000/QALY. Policymakers and substance abuse treatment leaders should seek funding to implement on-site rapid HIV testing in substance abuse treatment programs for those not recently tested.

Transient Stimulation Of Distinct Subpopulations Of Striatal Neurons Mimics Changes In Action Value. Tai LH, Lee AM, Benavidez N, Bonci A, Wilbrecht L. Nat Neurosci. 2012 Sep; 15(9): 1281-1289. Epub 2012 Aug 19.
In changing environments, animals must adaptively select actions to achieve their goals. In tasks involving goal-directed action selection, striatal neural activity has been shown to represent the value of competing actions. Striatal representations of action value could potentially bias responses toward actions of higher value. However, no study to date has demonstrated the direct effect of distinct striatal pathways in goal-directed action selection. The authors found that transient optogenetic stimulation of dorsal striatal dopamine D1 and D2 receptor-expressing neurons during decision-making in mice introduced opposing biases in the distribution of choices. The effect of stimulation on choice was dependent on recent reward history and mimicked an additive change in the action value. Although stimulation before and during movement initiation produced a robust bias in choice behavior, this bias was substantially diminished when stimulation was delayed after response initiation. Together, these data suggest that striatal activity is involved in goal-directed action selection.

Within-Family Environmental Transmission of Drug Abuse: A Swedish National Study. Kendler KS, Ohlsson H, Sundquist K, Sundquist J. Within-family environmental transmission of drug abuse: A swedish national study. Arch Gen Psychiatry. Epub 2012 Dec 10:1-8.
Drug abuse (DA) strongly runs in families. Does this result solely from genetic factors or does the family environment

contribute? The objective of this study was to determine the familial environmental contribution to the risk for DA. The study design was a follow-up in 9 public databases (1961-2009) in siblings and spouses. The study was conducted in Sweden. Participants comprised a total of 137,199 sibling pairs and 7,561 spousal pairs containing a proband with DA and matched control probands. Main outcomes measures were drug abuse recorded in medical, legal, or pharmacy registry records. In the best-fit model, which contained significant linear, quadratic, and cubic effects, among full sibling pairs containing a proband with DA, the relative risk for DA in the sibling declined from more than 6.0 for siblings born within 2 years of each other to less than 4.5 when born 10 years apart. Controlling for age differences in full sibling pairs, the hazard rate for DA in a sibling when the affected proband was older vs. younger was 1.42 (95% CI, 1.31-1.54). In the best-fit model, which contained significant linear, quadratic, and cubic effects, among spousal pairs containing a proband with DA, the relative risk for DA in the spouse declined from more than 25.0 within 1 year of proband DA registration to 6.0 after 5 years. The authors concluded that controlling for genetic effects by examining only full siblings, sibling resemblance for the risk for DA was significantly greater in pairs closer vs. more distant in age. Older siblings more strongly transmitted the risk for DA to their younger siblings than vice versa. After one spouse is registered for DA, the other spouse has a large short-lived increase in DA risk. These results support strong familial environmental influences on DA at various life stages. A complete understanding of the familial transmission of DA will require knowledge of how genetic and familial environmental risk factors act and interact over development.

ΔFosBb Differentially Modulates Nucleus Accumbens Direct and Indirect Pathway Function. Grueter BA, Robison AJ, Neve RL, Nestler EJ, Malenka RC. Proc Natl Acad Sci U S A. Epub 2013 Jan 14.
Synaptic modifications in nucleus accumbens (NAc) medium spiny neurons (MSNs) play a key role in adaptive and pathological reward-dependent learning, including maladaptive responses involved in drug addiction. NAc MSNs participate in two parallel circuits, direct and indirect pathways that subserve distinct behavioral functions. Modification of NAc MSN synapses may occur in part via changes in the transcriptional potential of certain genes in a cell type-specific manner. The transcription factor ΔFosB is one of the key proteins implicated in the gene expression changes in NAc caused by drugs of abuse, yet its effects on synaptic function in NAc MSNs are unknown. Here, the authors demonstrate that overexpression of ΔFosB decreased excitatory synaptic strength and likely increased silent synapses onto D1 dopamine receptor-expressing direct pathway MSNs in both the NAc shell and core. In contrast, ΔFosB likely decreased silent synapses onto NAc shell, but not core, D2 dopamine receptor-expressing indirect pathway MSNs. Analysis of NAc MSN dendritic spine morphology revealed that ΔFosB increased the density of immature spines in D1 direct but not D2 indirect pathway MSNs. To determine the behavioral consequences of cell type-specific actions of ΔFosB, the authors selectively overexpressed ΔFosB in D1 direct or D2 indirect MSNs in NAc in vivo and found that direct (but not indirect) pathway MSN expression enhances behavioral responses to cocaine. These results reveal that ΔFosB in NAc differentially modulates synaptic properties and reward-related behaviors in a cell type- and subregion-specific fashion.

μ-Opioid Receptor Availability in the Amygdala is Associated with Smoking for Negative Affect Relief.
Falcone M, Gold AB, Wileyto EP, Ray R, Ruparel K, Newberg A, Dubroff J, Logan J, Zubieta JK, Blendy JA, Lerman C. Psychopharmacology (Berl). 2012 Aug; 222(4): 701-708.
The perception that smoking relieves negative affect contributes to smoking persistence. Endogenous opioid neurotransmission, and the μ-opioid receptor (MOR) in particular, plays a role in affective regulation and is modulated by nicotine. The authors examined the relationship of MOR binding availability in the amygdala to the motivation to smoke for negative affect relief and to the acute effects of smoking on affective responses. Twenty-two smokers were scanned on two separate occasions after overnight abstinence using [^{11}C]carfentanil positron emission tomography imaging: after smoking a nicotine-containing cigarette and after smoking a denicotinized cigarette. Self-reports of smoking motives were collected at baseline, and measures of positive and negative affect were collected pre- and post- cigarette smoking. Higher MOR availability in the amygdala was associated with motivation to smoke to relieve negative affect. However, MOR availability was unrelated to changes in affect after smoking either cigarette. The authors conclude that increased MOR availability in amygdala may underlie the motivation to smoke for negative affective relief. These results are consistent with previous data highlighting the role of MOR neurotransmission in smoking behavior.

NIH/HHS POLICY UPDATES

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

2013

January 24	HHS issues PHS 2013-02 SBIR and STTR Omnibus Grant Solicitations Implementing Some Provisions of the SBIR/STTR Reauthorization Act of 2011
January 23	Request for Information (RFI): Input on Report from Council of Councils Working Group on Use of Chimpanzees in NIH-Supported Research
January 22	IACUC 101 Workshop and PRIM&R IACUC Conference: March 17-19, 2013 in Baltimore, MD
January 10	eRA Commons Users Can Now Generate a Publications Report for the PHS 2590 with My NCBI
January 9	Notice of Changes to Payment Management System Registration Procedures for NIH Foreign Grantees
January 9	Public Access Compliance Monitor: A New Resource for Institutions to Track Public Access Compliance
January 2	NIH Operates Under a Continuing Resolution - UPDATE

2012

December 21	Changes to the NIH Public Access Policy and the Implications to Awards: Webinar - January 15, 2013
December 4	Notice of Assistance Available to Institutions Impacted by Super Storm Sandy
November 30	Advance Notice: Revised Policy for Managing Conflict of Interest in the Initial Peer Review of NIH Grant and Cooperative Agreement Applications
November 30	Initial Electronic Submission Process for Multi-Project Applications: Webinar - December 13, 2012
November 16	Upcoming Changes to Public Access Policy Reporting Requirements and Related NIH Efforts to Enhance Compliance
November 8	Annual Reports to OLAW due January 31, 2013
October 30	Deadline Extended for Applications Due on October 29 and 30, 2012
October 26	Delays in Grant Application Submission due to Hurricane Sandy
October 18	NIH Provides Policy Clarification Concerning Disclosure Requirements for Reimbursed and Sponsored Travel - 42 CFR Part 50 Subpart F, "Responsibility of Applicants for Promoting Objectivity in Research for Which PHS Funding is Sought"
October 16	NIH Offers Commercialization Assistance Program to SBIR and STTR Phase II Awardees; Applications Due November 7, 2012
October 11	NIH Operates Under a Continuing Resolution

CONGRESSIONAL AFFAIRS

(Prepared January 23, 2013)

Appropriations/Budget

The President's Fiscal Year 2013 budget request included $1.054 billion for NIDA, essentially the same as the appropriated FY 2012 level. NIH is currently operating under a Continuing Resolution (at FY 2012 levels) that will expire on March 27. This could be affected by the current "sequestration" discussion in the Congress.

113th Congress Committees of Interest

Senate: In the Senate, primary focus is on the

- Committee on Appropriations (Subcommittee on Labor, Health and Human Services, and Education; Financial Services; and Commerce, Justice, Science;
- Committee on Health, Education, Labor, and Pensions (HELP);
- Committee on the Judiciary; and the
- Caucus on International Narcotics Control (this is an officially recognized Caucus, established by law in 1985).

House: In the House, primary focus is on the

- Committee on Appropriations (Subcommittee on Labor, Health and Human Services, Education, and Related Agencies; Financial Services; and Commerce, Justice, Science and Related Agencies);
- Committee on Energy and Commerce (Subcommittee on Health); and the
- Committee on Oversight and Government Reform (Subcommittee on Domestic Policy).

In both the House and Senate, committee and subcommittee rosters are still being finalized. To present a complete picture, details will be provided in the May Report to Council.

PROGRAM ACTIVITIES/FOAS

New NIDA RFAs

On November 16, 2012, NIDA issued an RFA entitled **U.S.-Russia Bilateral Collaborative Research Partnerships (CRP) on the Prevention and Treatment of HIV/AIDS and Co-morbidities (R21) RFA-DA-14-001**. This RFA will support both prospective and retrospective studies, which may include, but not limited to, identification and characterization of beneficial health outcomes that are associated with reduced levels of drug use. Open date: December 15, 2012. Application due date(s): January 15, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

New NIDA Program Announcements

On September 10, 2012, NIDA issued a PA entitled **AIDS-Science Track Award for Research Transition (R03) PA-12-282.** This PA seeks to facilitate the entry of both newly independent and early career investigators to the area of drug abuse research on HIV/AIDS. This FOA, AIDS--Science Track Award for Research Transition (A-START), encourages Small Research Grant (R03) applications to support research projects on drug abuse and HIV/AIDS that can be carried out in a short period of time with limited resources. Open date: August 7, 2013. Application due date(s): Not applicable. AIDS application due date(s): September 7, 2013, September 7, 2014, September 7, 2015, by 5:00 PM local time of applicant organization.

On September 10, 2012, NIDA issued a PA entitled **HIV/AIDS, Drug Use, and Vulnerable Populations in the US (R21) PA-12-280 (R01) PA-12-281.** This PA encourages research to identify the role(s) that drug abuse plays in fueling the epidemic in vulnerable groups (racial/ethnic minorities, men who have sex with men (MSM), youth) in the United States and to develop effective interventions to prevent new infections and to improve the health and well-being of those living with HIV/AIDS. Open date: December 7, 2012. Application due date(s): Not applicable. AIDS application due date(s): Standard dates apply, by 5:00 PM local time of applicant organization.

On September 25, 2012, NIDA issued a PA entitled **Drug Abuse Aspects of HIV/AIDS (R01) PA-12-293 (R03) PA-12-294 (R21) PA-12-295.** This PA encourages Exploratory/Developmental Research Grant (R21) applications to examine the drug abuse aspects of HIV/AIDS, including research on drug-related risk behaviors, addiction and HIV disease, and drug use/HIV-related co-morbidities and consequences. Open date: April 7, 2013. Application due date(s): Not applicable. AIDS application due date(s): Standard dates apply, by 5:00 PM local time of applicant organization.

On September 26, 2012, NIDA issued a PAR entitled **Mechanism for Time-Sensitive Drug Abuse Research (R21) PAR-12-297.** This PAR is intended to support pilot, feasibility or exploratory research for up to 2 years in 4 priority areas, including: 1) responses to unexpected and time-sensitive medical system issues (e.g. opportunities to understand addiction services in the evolving health care system); 2) responses to emerging drug abuse-related HIV trends and topics (e.g. rapidly evolving drug abuse-related epidemics, time-sensitive policy or environmental changes); 3) responses to unexpected and time-sensitive criminal justice opportunities (e.g. new system and/or structural level changes) that relate to drug abuse and access and provision of health care service; and 4) responses to unexpected and time-sensitive prescription drug abuse opportunities (e.g., new state or local efforts). Open date: February 6, 2013. Application due date(s): March 6, 2013, June 4, 2013, September 9, 2013, December 9, 2013; March 6, 2014, June 4, 2014, September 9, 2014, December 9, 2014; March 6, 2015, June 4, 2015, September 9, 2015, December 9, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

On November 2, 2012, NIDA issued a PA entitled **Prescription Drug Abuse (R01) PA-13-015 (R21) PA-13-016**. This PA is intended to encourage development of innovative research applications on prescription drug abuse, including research to examine the factors contributing to prescription drug abuse; to characterize the adverse medical, mental health and social consequences associated with prescription drug abuse; and to develop effective prevention and service delivery approaches and behavioral and pharmacological treatments. Open date: January 5, 2013 (R01) or January 16, 2013 (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 January 9, 2013, NIDA issued a PAR entitled **Accelerating the Pace of Drug Abuse Research Using Existing Data (R01) PAR-13-080.** The purpose of this PAR is to invite applications proposing the innovative analysis of existing social science, behavioral, administrative, and neuroimaging data to study the etiology and epidemiology of drug using behaviors (defined as alcohol, tobacco, prescription and other drug) and related disorders, associated HIV risk behaviors, prevention of drug use and HIV, and health service utilization. Open date: January 9, 2013. 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 January 9, 2013, NIDA issued a PA entitled **Behavioral & Integrative Treatment Development Program (R01) PA-13-077.** The purpose of this PA is to encourage behavioral intervention development research to test efficacy, conduct clinical trials, examine mechanisms of behavior change, determine dose-response, optimize combinations, and/or ascertain best sequencing of behavioral, combined, sequential, or integrated behavioral and pharmacological (1) drug abuse treatment interventions, including interventions for patients with comorbidities, in diverse settings; (2) drug abuse treatment and adherence interventions for use in primary care; (3) drug abuse treatment and adherence interventions that utilize technologies to boost effects and increase implementability; (4) interventions to prevent the acquisition or transmission of HIV infection among individuals in drug abuse treatment; (5) interventions to promote adherence to drug abuse treatment, HIV and addiction medications; and (6) interventions to treat chronic pain. Open date: January 9, 2013. 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 January 9, 2013, NIDA issued a PA entitled **Behavioral & Integrative Treatment Development Program (R34) PA-13-078 (R03) PA-13-079.** The purpose of this PA is to encourage investigators to propose discrete well-defined projects that can be completed within three years for R34s and two years for R03s. Projects of interest fall within the research domain of behavioral or integrated (e.g., behavioral and pharmacological) interventions targeting: (a)

substance abuse (including comorbidities); (b) prevention of acquisition or transmission of HIV infection among individuals in substance abuse treatment; (c) promotion of adherence to substance abuse treatment, HIV and addiction medications; and (d) chronic pain. Open date: January 16, 2013. 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 January 10, 2013, NIDA issued a PAR entitled **NIDA Research Education Program for Clinical Researchers and Clinicians (R25) PAR-13-084.** The purpose of this PAR is to support research education for those in clinically focused careers, in a topic area related to substance use/abuse/addiction. Participants (those receiving the research education) should be training for careers as clinical researchers, clinicians/service providers, or optimally, a combination of the two. Open date: April 22, 2013. Application due date(s): May 22, 2013, May 22, 2014, May 22, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): September 9, 2013, September 8, 2014, September 7, 2015, by 5:00 PM local time of applicant organization.

New FOAs Issued by the NIH Roadmap

On November 16, 2012, the NIH Common Fund issued a Roadmap RFA entitled **Enhancing GTEx with molecular analyses of stored biospecimens (U01) RFA-RM-12-009.** The purpose of this RFA is to support molecular analyses of stored biospecimens from the Genotype-Tissue Expression (GTEx) project. Open date: February 28, 2013. Application due date(s): March 28, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

On November 21, 2012, the NIH Common Fund issued a Roadmap RFA entitled **Determinants and Consequences of Personalized Health Care and Prevention (U01) RFA-RM-12-024**. The purpose of this FOA is to expand generalizable understanding of the determinants and consequences of personalization in health care and prevention; it is not primarily intended to support evaluation of specific interventions or strategies for addressing particular health conditions. Open date: January 28, 2013. Application due date(s): February 28, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

New Administrative Supplement Program Announcements Issued by NIH

On June 13, 2012, NIDA, in collaboration with numerous other NIH components, issued an administrative supplement entitled **Administrative Supplements for Research on Sex/Gender Differences (Admin Supp) PA-13-018**. The NIH announces the availability of administrative supplements to support research highlighting the impact of sex/gender differences (or similarities) in human health, including behavioral, clinical or preclinical studies. Included are studies relevant to the pathophysiology, clinical presentation, prevention, or treatment of disease. The proposed research should address the objectives of the NIH Strategic Plan for Women's Health and Sex Differences Research (http://orwh.od.nih.gov/research/strategicplan/index.asp). Open date(s): December 12, 2012. Application due date(s): January 11, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): January 11, 2013, by 5 PM local time of applicant organization.

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

On September 11, 2012, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Basic social and behavioral research on culture, health, and wellbeing (R24) RFA-LM-12-002**. This RFA, issued on behalf of the NIH Basic Behavioral and Social Sciences Opportunity Network (OppNet), will provide grants for infrastructure support to develop, strengthen, and evaluate transdisciplinary approaches and methods for basic behavioral and/or social research on the relationships among cultural practices/beliefs, health, and wellbeing. Letter of Intent due date(s): November 16, 2012. Application due date(s): December 17, 2012. AIDS application due date(s): February 13, 2013.

On December 7, 2012, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Exceptional Unconventional Research Enabling Knowledge Acceleration (EUREKA) for Neuroscience and Disorders of the Nervous System (R01) RFA-NS-13-007.** This RFA solicits Research Project Grant (R01) applications addressing exceptionally novel hypotheses and/or remarkably difficult problems in neuroscience and disorders of the nervous system. This announcement is for support of new rather than ongoing projects, and is not intended for pilot research. Open date: February 21, 2013. Application due date(s): March 21, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): March 21, 2013.

On December 18, 2012, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **NIH Revision Applications for Research Relevant to the Family Smoking Prevention and Tobacco Control Act (P30) RFA-OD-12-007.** This RFA invites revision applications from investigators and institutions/organizations with active National Institutes of Health (NIH)-supported P30 project awards to support an expansion of the scope of approved and funded scientific research programs involving smoking and tobacco-related products and/or their constituents. Letter of Intent due date(s): February 26, 2013. Application due date(s): March 26, 2013. AIDS application due date(s): Not applicable.

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

On September 11, 2012, NIDA, in collaboration with numerous other NIH components, issued a PA entitled **Exploratory/Developmental Bioengineering Research Grants (EBRG) [R21] PA-12-284.** The purpose of this PA is to encourage Exploratory/Developmental Bioengineering Research Grants (EBRG) applications which establish the feasibility of technologies, techniques or methods that: 1) explore a unique multidisciplinary approach to a biomedical challenge; 2) are high-risk but have a considerable pay-off; and 3) develop data which can lead to significant future research. Open date(s): January 16, 2013. Application due date(s): Standard dates apply, by 5:00 PM local time of applicant organization. AIDS application due date(s): Standard dates apply.

On November 28, 2012, NIDA, in collaboration with numerous other NIH components, issued a PAR entitled **Opportunities for Collaborative Research at the NIH Clinical Center (U01) PAR-13-029**. The purpose of this PAR is to support collaborative translational research projects aligned with NIH efforts to enhance the translation of basic biological discoveries into clinical applications that improve health. Open date(s): February 20, 2013. Application due date(s): March 20, 2013, March 20, 2014, March 20, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): March 20, 2013, March 20, 2014, March 20, 2015, by 5:00 PM local time of applicant organization.

On December 18, 2012, NIDA, in collaboration with numerous other NIH components, issued a PAR entitled **Drug Discovery for Nervous System Disorders (R01) PAR-13-048 (R21) PAR-13-049.** This PAR encourages research grant applications directed toward the discovery and preclinical testing of novel compounds for the prevention and treatment of nervous system disorders. Open date(s): January 5, 2013. 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 December 20, 2012, NIDA, in collaboration with numerous other NIH components, issued a PA entitled **Pain in Aging (R01) PA-13-058.** This PA encourages Research Project Grant (R01) applications from institutions/organizations that propose to study pain from an aging perspective, including studies of older populations, studies of age differences and age-related changes in pain processes and experiences, and studies of pain treatment and management in older adults. Open date(s): January 5, 2013. 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 January 9, 2013, NIDA, in collaboration with numerous other NIH components, issued a PAR entitled **Dissemination and Implementation Research in Health (R21) PAR-13-054 (R01) PAR-13-055 (R03) PAR-13-056.** This PAR encourages investigators to submit research grant applications that will identify, develop, evaluate and refine effective and efficient methods, systems, infrastructures, and strategies to disseminate and implement research-tested health behavior change interventions, evidence-based prevention, early detection, diagnostic, treatment and management, and quality of life improvement services, and data monitoring and surveillance reporting tools into public health and clinical practice settings that focus on patient outcomes. Open date(s): January 16, 2013 (R21) and (R03) or January 9, 2013 (R01). 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 January 11, 2013, NIDA, in collaboration with numerous other NIH components, issued a PAR entitled **National Cooperative Drug Discovery/Development Groups (NCDDG) for the Treatment of Mental Disorders, Drug or Alcohol Addiction (U19) PAR-13-086 (UM1) PAR-13-087.** The purpose of the National Cooperative Drug Discovery/Development Group (NCDDG) Program is to create multidisciplinary research groups or partnerships for the discovery of pharmacological agents to treat and to study mental illness, drug or alcohol addiction. This PAR encourages applications to advance the discovery, preclinical development, and proof of concept testing of new, rationally based candidate agents to treat mental disorders or drug or alcohol addiction, and to develop novel ligands as tools to further characterize existing or to validate new drug targets. Open date(s): January 22, 2013. Application

due date(s): February 22, 2013; June 24, 2013; October 24, 2013; February 24, 2014; June 22, 2014; October 22, 2014; February 22, 2015; June 22, 2015; October 22, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

On January 24, 2012, NIDA, in collaboration with numerous other NIH components, issued a PA entitled **PHS 2013-02 Omnibus Solicitation of the NIH for Small Business Technology Transfer Grant Applications (Parent STTR [R41/R42]) PA-13-089**. This PA invites eligible United States small business concerns (SBCs) to submit Small Business Technology Transfer (STTR) grant applications. United States SBCs that have the research capabilities and technological expertise to contribute to the R&D mission(s) of the NIH awarding components identified in this FOA are encouraged to submit STTR grant applications in response to identified topics (see PHS 2013-2 SBIR/STTR Program Descriptions and Research Topics for NIH.). Open date(s): March 5, 2013. 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 January 24, 2012, NIDA, in collaboration with numerous other NIH components, issued a PA entitled **PHS 2013-02 Omnibus Solicitation of the NIH, CDC, FDA and ACF for Small Business Innovation Research Grant Applications (Parent SBIR [R43/R44]) PA-13-088**. This PA invites eligible United States small business concerns (SBCs) to submit Small Business Innovation Research (SBIR) grant applications. United States SBCs that have the research capabilities and technological expertise to contribute to the R&D mission(s) of the NIH, CDC, FDA or ACF awarding components identified in this FOA are encouraged to submit SBIR grant applications in response to identified topics (see PHS 2013-2 SBIR/STTR Program Descriptions and Research Topics for NIH, CDC, FDA and ACF). Open date(s): March 5, 2013. 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.

New NIH FOAs Issued in Collaboration with the FDA Center for Tobacco Products

On December 18, 2012, NIDA, in collaboration with numerous other NIH components and with the FDA Center for Tobacco Products, issued a Request for Application entitled **NIH Revision Applications for Research Relevant to the Family Smoking Prevention and Tobacco Control Act (P30) RFA-OD-12-007.** This Funding Opportunity Announcement (FOA) invites revision applications from investigators and institutions/organizations with active National Institutes of Health (NIH)-supported P30 project awards to support an expansion of the scope of approved and funded scientific research programs involving smoking and tobacco-related products and/or their constituents. Application due date(s): March 26, 2012. Start date: December 1, 2013.

NIDA PUBLICATIONS

Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition)
NIH Pub Number: 12-4180
Presents research-based principles of addiction treatment for a variety of drugs, including nicotine, alcohol, and illicit and prescription drugs, that can inform drug treatment programs and services. En Español

Spanish Language Videos
NIDA produced three Spanish language videos that have been posted on the NIDA website. The videos cover 1) Addiction & Adolescents; 2) Dopamine & Pleasure Sensors; and 3) Multiple Factors Affecting Addiction. The videos are part of an online “speakers kit” package created to equip Spanish-speaking community educators to give a talk about drugs and teens. In addition to the videos, the kit includes:

- A glossary of terms specific to the presentation
- Tips for giving a presentation
- Questions and answers

PRESS RELEASES

September 27, 2012 – NIDA/ONDCP to launch online physician training tools

October 1, 2012 – White House Drug Policy Office and National Institute on Drug Abuse Unveil New Training Materials to Combat National Prescription Drug Abuse Epidemic

October 9, 2012 – NIDA accepting proposals to create mobile app that helps patients take medications as prescribed

October 10, 2012 – NIDA launches new tool for parents: Family Checkup: Positive Parenting Prevents Drug Abuse

October 11, 2012 – Special journal edition focuses on substance abuse issues impacting American Indians/Alaska Natives

October 16, 2012 – Actors Elizabeth Marvel and Reed Birney to raise the curtain in NIDA's Addiction Performance Project

October 31, 2012 – New online resources for opioid prescribers now available on NIDA's website

November 1, 2012 – NIDA announces 2012 SCOR Awards for research on gender differences

December 5, 2012 – New Bath Salts Resource Available from NIDA

December 18, 2012 – National Institute on Drug Abuse to Announce Results of 2012 Monitoring the Future Survey

December 19, 2012 – Regular marijuana use by teens continues to be a concern

MEETINGS/CONFERENCES

Select Meetings and Conferences in which NIDA played a significant role

On September 20-21, 2012, NIDA's DCNBR hosted the **Translational Research on Child Neglect Consortium: Final Meeting** at the NIH Neuroscience Center in Rockville, MD. An evening poster session highlighting early investigators and travel awardees was held on September 20, 2012. A special community videocast co-chaired by Dr. Jacqueline Lloyd (DESPR) and Dr. Cheryl Anne Boyce on "Home Visitation and Child Neglect" on September 21, 2012 highlighted recent research on home visitation to reduce child neglect and featured introductory remarks by Agnes Leshner, Director, Child Welfare Services, Montgomery County. Presenters included Dr. David Olds, Ph.D., University of Colorado, Dr. Anne Duggan, Johns Hopkins University, and Dr. Brenda Jones Harden, University of Maryland, College Park.

On October 4-5, 2012, the Special Populations Office and convened a two-day **"Diversity Supplements Workshop"** at the National Institute on Drug Abuse (NIDA) headquarters in Bethesda, Maryland. Twenty-two current recipients of postdoctoral and early investigator-level diversity supplements from NIDA and NIAAA met and interacted with program staff and with funded NIDA investigators, many of whom were past recipients of diversity supplement awards through NIDA. In addition, they were presented overviews of NIDA's research program priorities, the NIH research grant application and peer review processes, and shared posters of their own NIDA and NIAAA-supported research. This workshop was coordinated by Pamela Goodlow.

On October 12, 2012, the **2012 Frontiers in Addiction Research NIDA Mini-convention** was held at the annual Society for Neuroscience (SfN) meeting in New Orleans. This year's mini-convention featured four symposia, the SfN Jacob P. Waletzky Memorial Lecture, and a poster session for early career investigators. The 2012 Jacob P. Waletzky winner and speaker was Dr. Andrew Holmes from the NIAAA Intramural Research Program. The mini-convention symposia included: Ghrelin, Leptin, and Insulin Modulates Reward; Role of Phagocytes in Sympatic Placticity and remodeling of Tissues in the Nervous System; Brain Energetics and Neurotransmission: Fueling Neurons and Glia; and Central Nervous System Immune Signaling and Addiction.

On October 12, 2012, in honor of the life and scientific achievements of **Dr. Toni S. Shippenberg**, a former Branch Chief in the NIDA Intramural Research Program and a long-time scientific leader and mentor, NIDA held a symposium following the Frontiers in Addiction Research Mini-convention at the SfN meeting. Dr. Howard Fields gave the keynote address, Research on Pain and Addiction, followed by brief comments from numerous colleagues.

October 13-17, 2012, NIDA staff participated in the **43rd Annual Society for Neuroscience Meeting**, including attending numerous scientific sessions and staffing NIDA's exhibit booth. As in past years, the exhibit booth provided information on NIDA's programs and various publications and it also served as a central point at which grantees and prospective grantees could speak with NIDA program staff about funding possibilities. The NIDA booth also served as the location for meeting attendees to interact with the NIDA and NICHD co-funded Pediatric Imaging Neurocognition and Genetics (PING) project, a large interactive MRI and genetics data resource that will soon be shared openly with the scientific community.

On October 14, 2012, NIDA, NINDS and NIMH co-organized the **Sixth Annual Julius Axelrod Symposium** at the annual Society for Neuroscience Meeting in New Orleans to celebrate the career of Dr. Julius Axelrod, one of the founders of modern neuropharmacology. This year's prize winner and speaker was Dr. Richard W. Tsien of New York University Langone Medical Center. Three Rapid-Fire Presentations were given by Drs. Amanda K. Fakira, Hsien-Sung Huang, and Sila K. Ultanir. A networking and young investigator poster session was held following the talks.

On October 15, 2012, **NIDA and the Institut National de la Santé et de la Recherche Médicale (INSERM)** cosponsored a satellite event at the annual Society for Neuroscience Meeting to help foster collaborations between French and U.S. scientists. The event included talks by Dr. Nora Volkow and Dr. Etienne Hirsch, followed by a keynote address by Dr. Pier Vincenzo Piazza. Following the presentations, an invited poster session that included posters by both French and U.S. scientists was held.

On October 16, 2012, NIDA held a **NIDA/NIH Grant Workshop for Early Career Investigators** at the annual Society for Neuroscience meeting in New Orleans. As in previous years, this event was very well attended by young investigators seeking information on how to choose the grant mechanism most appropriate to their career stage. Following presentations on various aspects of the NIH grant process, the attendees had the opportunity to meet directly with NIDA staff to get their specific questions answered.

On December 3-4, 2012, the Special Populations Office and Kathy Etz, Ph.D., Prevention Research Branch, DESPR, convened a 2-day meeting of the **American Indian/Alaska Native (AI/AN) Researchers and Scholars Workgroup** at the NIDA headquarters in Bethesda, Maryland. In attendance were 20 scholars and select NIDA staff members. This workgroup was brought together to discuss and identify critical issues in the research and research development needs of the AI/AN community and to provide guidance to the NIDA Director and staff.

On December 14-15, 2012, NIDA's **African American Researchers and Scholars Workgroup (AARSWG)** held a two-day "Booster Session" grant writing workshop intended for underrepresented early career investigators applying for research grant funding through the NIH. The workshop is a follow-up to the annual week-long Addiction Research Training Institute (ARTI) sponsored by the AARSWG workgroup, and limited in attendance. One-on-one interaction between invited early career scholars and assigned faculty mentors resulted in fine tuning research grant proposals. Six scholars and six faculty mentors participated in this workshop, held in Baltimore, Maryland.

Upcoming Conferences/Exhibits

Community Anti-Drug Coalitions of America's 2013 National Leadership Forum – Gaylord National Hotel & Convention Center, National Harbor, MD – February 4-7, 2013.

National Rx Drug Abuse Summit – Orlando, FL – April 2-4, 2013.

American Academy of Pain and Medicine's Annual Meeting – Fort Lauderdale, FL – April 11-14, 2013.

American Society of Addiction Medicine Annual Medical-Scientific Conference – Chicago, IL – April 25-28, 2013.

American Psychiatric Association Annual Meeting – San Francisco, CA – May 18-22, 2013.

COMMUNITY AND PRESS EVENTS

Summer Research with NIDA Program
June 1, 2012. The Special Populations Office held the 16th Annual Summer Research with NIDA program. Sixty seven high school and undergraduate students engaged in drug abuse research at various NIDA-supported institutions for 8-10 weeks during the summer. Participants received certificates of participation signed by Dr. Nora Volkow and the site principal investigator. This program was coordinated by Flair Lindsey, Program Analyst, Special Populations Office.

The Medicine Abuse Project (MAP)
NIDA partnered with The Partnership at DrugFree.org to help promote the launch of Medicine Abuse Project (MAP) in September via Facebook and Twitter posts, which encouraged parents to talk to their children about the dangers of prescription drug abuse.

Addiction Performance Project (APP)
October 20, 2012. Performances were held in Philadelphia at the American Academy of Family Physicians.

Monitoring the Future (MTF) Press Conference
December 19, 2012. The National Institute on Drug Abuse (NIDA) held a press conference on Wednesday, December 19, to announce the results of its 2012 Monitoring the Future survey. The survey, funded by NIDA -- part of the National Institutes of Health -- tracks annual drug abuse trends and attitudes of 8th, 10th, and 12th-grade students. The 2012 MTF survey will include use of "bath salts" among students for the first time.

National Drug Facts Week (NDFW)
January 28 to February 3, 2013. National Drug Facts Week is a week-long health observance for teens that aims to shatter the myths about drugs and addiction. In community and school events all over America, teens, scientists and other experts will come together for an honest conversation about how drugs affect the brain, body and behavior. 2013 is the first year that all 50 states registered for events. This year, NIDA's Drug Facts Chat day was held on Thursday, January 31, 2013.

STAFF HONORS AND AWARDS

Staff Honors and Awards

Dr. David Schwope, IRP, also a recent doctoral student in CDM, received the Society of Forensic Toxicology (SOFT) EDIT award for the best manuscript in the Journal of Analytical Toxicology. Dr. Schwope's paper was entitled "Psychomotor Performance, Subjective and Physiological Effects and Whole Blood D9-Tetrahydrocannabinol Concentrations in Heavy, Chronic Cannabis Smokers Following Acute Smoked Cannabis." The research was performed as part of CDM's clinical research program and also fulfilled his doctoral degree requirements.

Dr. Harold Perl, DESPR, was honored with the "Best Workshop of 2011 Award" for the workshop entitled, "Unlock the Mysteries of NIH Research Funding: Improve Your Grant Application and Improve Your Chance at Success", at the 36th Annual National Conference of the Association for Medical Education and Research in Substance Abuse on November 3, 2012 in Bethesda, MD.

Dr. Karl Scheidweiler, IRP, received the Patsalos Prize for the best manuscript published in Therapeutic Drug Monitoring during the previous 2 years at the meeting of the International Association of Therapeutic Drug Monitoring – Clinical Toxicology in Stuttgart, Germany for his manuscript entitled "Pharmacokinetics of Cocaine and Metabolites in Human Oral Fluid and Correlation with Plasma Concentrations following Controlled Administration."

Drs. Kevin Conway and **Augusto Diana**, DESPR, were granted the Contracting Officer's Representative of the Year Award on October 23, 2012, in recognition of outstanding service overseeing NIDA contracts.

Dr. Marilyn Huestis, IRP, received the University of Mississippi's 2012 Coy W. Waller Distinguished Lecture award in Oxford, MS and presented a public lecture on "Chronic Daily Cannabis Use, Neuroadaptation and Psychomotor Impairment."

Dr. Rao Rapaka, DBNBR, has been elected as the AAAS Fellow for outstanding service as an innovative and creative research administrator at the NIH and for distinguished scholarship in drug abuse research. Dr. Rapaka will be presented the honor in February 2013.

Dr. Roger Sorensen, DBNBR, received a 2012 NIH Director's Award for his participation in developing the new annual NIH grant progress report form, Research Performance Progress Report (RPPR), which will replace current Form PHS 2590.

Steven W. Gust, Ph.D., NIDA IP Director, was a member of the team of NIH program officers who received the 2012 NIH Director's Award for their work on the Fogarty International Center (FIC) program Brain Disorders in the Developing World: Research Across the Lifespan. The Brain Disorders Program Director Kathleen Michels, Ph.D., and her colleagues from eight NIH Institutes and Centers were honored in recognition of an "exceedingly successful, decade-long, multi-Institute/Center partnership to address the major global impact of brain disorders across the lifespan." The Brain Disorders Program develops innovative, collaborative research and sustainable research capacity building projects in developing countries on a broad range of brain and nervous system disorders.

Dr. Teresa Gray, IRP, received the prestigious Irving Sunshine Award from the American Academy of Forensic Sciences in February, 2012 for her research on in utero drug exposure conducted at CDM that recently completed her doctoral degree requirements.

Grantee Honors and Awards

The American Institutes for Research (AIR) was awarded the 2012 Mentor International Best Practice Award, September 20, 2012. This Award bestowed by the Mentor Foundation recognizes AIR's *Good Behavior Game* program and model of training and support, as an example of evaluated best practice for preventing substance abuse. **Drs. Jeanne Poduska**, AIR, and **Sheppard Kellam**, Johns Hopkins University, accepted the award. The Mentor Foundation was founded in 1994 by Her Majesty Queen Silvia of Sweden in collaboration with the World Health Organization (WHO) as an independent, non-governmental, not for profit, working in the field of drug abuse prevention at a global level.

CTN -- New England Consortium

Dr. Roger Weiss, Principal Investigator of the New England Consortium, is the recipient of the 2012 Jack H. Mendelson Memorial Research Award from McLean Hospital. The late Dr. Mendelson was the Co-Director of the Alcohol and Drug Abuse Research Center at McLean Hospital and the first Chief of the National Center for Prevention and Control of Alcoholism at the National Institutes of Health. McLean Hospital established the annual research award for excellence in behavioral and biological research on substance abuse.

CTN-- Southern Consortium Node

Bob Hiott, Executive Director of Behavioral Health Services of Pickens County, was recently awarded the *Addiction Professional of the Year* by the South Carolina Association of Alcohol and Drug Abuse Counselors for his contribution to addiction services in the state. The Southern Consortium is incredibly grateful for the opportunity to work with their dedicated and talented community providers like Bob Hiott, who has been an integral part of their Node since they first joined the CTN. Beginning January 1, 2013, Bob will assume the role of Community Treatment Representative for the Southern Consortium Node and will work with Louise Haynes to promote collaboration with our community providers.

STAFF CHANGES

New Employees

Drs. Brandon Selfridge and **Joshua Antoline** have joined the IRP's Chemical Biology Research Branch, Section on Drug Design and Synthesis as IRTA Postdoctoral Fellows.

Ellie Johnson joined the NIDA Office of the Director as a Supervisory Staff Assistant and provides executive support to Glenda Conroy, Susan Weiss (Associate Director for Scientific Affairs) and Helio Chaves (Deputy Executive Officer) as well as oversight to OD office operations. Ellie was previously the Executive Assistant to the Director, National Institute of Nursing Research at NIH and has a wealth of experience in administrative and executive support in the public and private settings.

Josie Anderson, B.A. joined NIDA in November as an Audio Visual Production Specialist in the Public Information Liaison Branch, OSPC. Josie served in the United States Air Force (USAF) for more than ten years, as part of their broadcast journalist team. She pioneered the first USAF media outreach team in Iraq, and served as the on-location correspondent during combat, training and humanitarian missions in over 15 countries. She was the lead videographer for the USAF premier air demonstration team for the Air Combat Command and was an aerial videographer for the USAF Thunderbirds. In addition, Josie has provided media training to over one hundred military and civilian leaders to ensure accuracy and consistency of communications themes and messages.

Maggie Stevenson joined the NIDA Office of the Director as a Staff Assistant and provides support to the NIDA OD and NIDA Executive Secretariat. Maggie was previously a Program Coordinator in the NIMH Office of Science Policy, Planning and Communications and has a wealth of experience in administrative and executive support in public and private settings. She has a Bachelor of Arts degree from the University of Maryland and Certifications from George Washington University and HHS University.

Dr. Mariela Shirley (NIAAA) has renewed her part time detail assignment for 2013 to serve as a science officer to BBDB, DCNBR and NIDA's Child and Adolescent Workgroup.

Dr. Masaki Suzuki has joined the IRP's Chemical Biology Research Branch, Section on Drug Design and Synthesis as a Special Volunteer, on a two year sabbatical from Otsuka Pharmaceutical Co., Ltd., Japan.

Zoe Shieh joined the Information and Resource Management Branch (IRMB) in the NIDA Office of Management as an Information Technology Specialist (Information Security.) He will be supporting NIDA's IT systems and enhancing security programs, policies, procedures, and tools. Zoe was previously a Computer Analyst/Team Leader with Terrapin Systems and provided technical IT support to NIDA. Zoe has a Bachelor of Arts degree from the University of Maryland and Certifications in IT Security, Network Administration, and an A+ Certification in network hardware, installation, and troubleshooting.

New Appointments

Gaya Dowling, Ph.D. has been named Chief, Science Policy Branch, OSPC.

Glenda Conroy will be assuming the role of Acting NIDA Chief Information Officer (CIO) and was appointed as the NIDA Deputy Ethics Counselor.

Helio Chaves will serve as the Acting Chief, Information and Resource Management Branch (IRMB.)

Dr. Jag Khalsa, DPMCDA, was on a detail to the Office of Assistant Secretary for Health (OASH), DHHS, to work on issues of viral hepatitis in IDUs. Currently, he is leading an effort to plan and present, in collaboration with other Federal partners (NIH [NIAID, NIDA, NIDDK], HRSA, SAMHSA, and CDC), an HHS-sponsored Technical Consultation on HCV infection in young IDUs.

Jennifer Cooke Katt, M.A. (formerly Jennifer Elcano) has been promoted to the role of Deputy Branch Chief, Science Policy Branch, OSPC.

Departures

Dr. Cecelia Spitznas of the Behavioral & Integrative Treatment Branch left NIDA December 15, 2013 and has accepted a new a position in the Office of Research & Data at the Office of National Drug Control Policy.

Garlin Hallas left her position of Management Analyst within the Management Analysis Branch, Office of Management at NIDA to start a new role at the FDA Center on Tobacco Products. She will be responsible for setting up the Risk Management program as well as writing policies and procedures for the Center.

Jennifer Bidle is leaving her position as the Branch Chief of the Management Analysis Branch, Office of Management, NIDA to start her new role as the Chief of the Management Analysis Section (MAS) within the Office of Administrative Management at the National Heart, Lung, and Blood Institute. As the Section Chief, Jennifer will be responsible for managing the formal management analysis functions for the IC.

Susan Cook has accepted a position as the Director, Division of Amenities and Transportation Services, Office of Research Services (ORS), NIH. Over the last seven years, Susan has been involved in several initiatives touching various programs at NIDA. She was instrumental in establishing the GMB Telework Program which included the NIDA hoteling suites. Also, she developed the NIDA Onboarding Program. While serving as the Acting CIO and Branch Chief for IRMB, as well as the Acting Branch Chief of MAB, she implemented NIH IT directives and the NIDA Risk Management program. She continued to serve as the NIDA Emergency Coordinator, A-76 Coordinator and Mandatory Training Coordinator. In 2010, Susan was appointed the NIDA Deputy Ethics Counselor by Dr. Raynard Kington and has strived to strengthen the NIDA ethics program.

Susan Nsangou, previously Chief of the Station Support/Simplified Acquisitions Branch in the NIDA COAC has accepted the position of Acquisition Director of the Clinical Center where she oversees all of the purchasing and contracts for NIH's clinical research hospital. Susan has worked at NIDA in the Branch Chief role since the COAC's inception in 2005 and has done an exceptional job supporting COAC customers and member Institutes. Under her leadership, the branch consistently achieved high customer satisfaction ratings for acquisitions support. Susan has also succeeded in training and mentoring junior staff members, assisting them in achieving individual goals. Susan joined the Clinical Center on December 30th.

Retirements

Ana Anders, previously Special Advisor in NIDA's Special Populations Office, retired in January after 51 years of federal service. Ana came to NIDA to help promote Hispanic researchers in drug abuse and helped establish National Hispanic Science Network, whose core mission is to improve the health equity of Hispanics through increasing research and fostering the development and advancement of Hispanic scientists. One of the NHSN's founding members, Dr. Hortensia Amaro, said of Ana, "Ana's contribution to the formation, development and success of the NHSN can't be overstated."

Jan Lipkin retired on December 31, 2012 after 15 years as the Deputy Branch Chief of the Public Information and Liaison Branch, OSPC. While at NIDA, Jan played a key role in coordinating all aspects of NIDA publications development, press activities, health campaigns, and development and growth of NIDA's Web site. She created and managed the NIDA Teen Web site, which has seen more than ten million visitors since 2005. She led the teams that built the HIV/AIDS "Learn the Link" campaign and most recently was the manager and creative force behind NIDA's Rx campaign for teens, "PEERx." She was also the PILB lead behind the HBO Addiction Special. Jan plans to spend her retirement years working at her beloved National Zoo, where she has been a volunteer for 20 years, working mostly with the reptiles and Great Apes.

Joan Nolan retired on January 3, 2013 from her role as NIDA's Publications, Graphics, and Exhibits Manager, a position she has held since 1980. As Publications Manager, she developed and executed NIDA's comprehensive long-range publications plan. She was responsible for all phases of publication development and execution, including maintaining standards, integrity, and continuity throughout NIDA's publication and graphic programs. As Exhibits Manager, she developed and implemented strategies for reaching NIDA's principal target audiences. Joan had been with NIDA since 1972, starting her career as an editorial assistant.

Dr. Mark Green, the Deputy Director of OEA, retired January 3, 2013 after a long and distinguished career in the Public Health Service and at the National Institutes of Health. Dr. Green was responsible for a variety of activities, including managing the processing of applications for Certificates of Confidentiality, serving as the Privacy Act Coordinator and managing clinicaltrials.com activities for the Institute as well as being the point of contact for R13 conference grant applications. Furthermore, he developed and administered a number of tracking procedures and data bases used not only by OEA but also by other parts of NIDA. Mark was recognized throughout the Institute as a resource on matters of extramural policies, procedures and practices and he served on many NIDA and NIH committees.

Sharan Jayne, Special Assistant to the Director for Media, retired on September 30, 2012. Sharan had a long and illustrious 33 year federal career in media management for high profile government directors. She joined the FDA in 1979 where she was a broadcast media advisor to six FDA Commissioners. She handled media appearances for Commissioner David Kessler during FDA's emerging years addressing tobacco. Sharan was also responsible for all aspects of the FDA's media strategy for 17 years until she moved to the Office of the Director at NIH. For the last seven years, Sharan was responsible for coordinating a number of articles highlighting NIDA science in publications including Time, Newsweek, AP, CNN, Bloomberg, and The New York Times.