

Director's Report

to the
**NATIONAL ADVISORY COUNCIL
ON DRUG ABUSE**

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** These sections contain select information. More comprehensive information will be posted in the [May 2013 Staff Report to the Director](#).*

RESEARCH HIGHLIGHTS

[Medicinal and Recreational Marijuana Use Among HIV-infected Women in the Women's Interagency HIV Study \(WIHS\) Cohort, 1994-2010.](#)

D'souza G, Matson PA, Grady CD, Nahvi S, Merenstein D, Weber KM, Greenblatt R, Burian P, Wilson TE. *J Acquir Immune Defic Syndr*. 2012 Dec 15; 61(5): 618-626.

Despite the major benefits of effective antiretroviral therapy on HIV-related survival, there is an ongoing need to help alleviate medication side effects related to antiretroviral therapy use. Initial studies suggest that marijuana use may reduce HIV-related symptoms, but medical marijuana use among HIV-infected individuals has not been well described. The authors evaluated trends in marijuana use and reported motivations for use among 2776 HIV-infected women in the Women's Interagency HIV Study between October 1994 and March 2010. Predictors of any and daily marijuana use were explored in multivariate logistic regression models clustered by person using generalized estimating equation. In 2009, participants were asked if their marijuana use was medical, "meaning prescribed by a doctor," or recreational, or both. Over the 16 years of this study, the prevalence of current marijuana use decreased significantly from 21% to 14%. In contrast, daily marijuana use almost doubled from 3.3% to 6.1% of all women and from 18% to 51% of current marijuana users. Relaxation, appetite improvement, reduction of HIV-related symptoms, and social use were reported as common reasons for marijuana use. In 2009, most marijuana users reported either purely medicinal use (26%) or both medicinal and recreational usage (29%). Daily marijuana use was associated with higher CD4 cell count, quality of life, and older age. Demographic characteristics and risk behaviors were associated with current marijuana use overall but were not predictors of daily use. This study suggests that both recreational and medicinal marijuana use are relatively common among HIV-infected women in the United States.

[Class I HDAC Inhibition Blocks Cocaine-Induced Plasticity By Targeted Changes In Histone Methylation.](#)

Kennedy PJ, Feng J, Robison AJ, Maze I, Badimon A, Mouzon E, Chaudhury D, Damez-Werno DM, Haggarty SJ, Han MH, Bassel-Duby R, Olson EN, Nestler EJ. *Nat Neurosci*. 2013 Mar 10. [Epub ahead of print].

Induction of histone acetylation in the nucleus accumbens (NAc), a key brain reward region, promotes cocaine-induced alterations in gene expression. Histone deacetylases (HDACs) tightly regulate the acetylation of histone tails, but little is known about the functional specificity of different HDAC isoforms in the development and maintenance of cocaine-induced plasticity, and previous studies of HDAC inhibitors report conflicting effects on cocaine-elicited behavioral adaptations. Here the authors demonstrate that specific and prolonged blockade of HDAC1 in NAc of mice increased global levels of histone acetylation, but also induced repressive histone methylation and antagonized cocaine-induced changes in behavior, an effect mediated in part through a chromatin-mediated suppression of GABAA receptor subunit expression and inhibitory tone on NAc neurons. These findings suggest a new mechanism by which prolonged and selective HDAC inhibition can alter behavioral and molecular adaptations to cocaine and inform the development of therapeutics for cocaine addiction.

[Relapse Induced By Cues Predicting Cocaine Depends On Rapid, Transient Synaptic Potentiation.](#)

Gipson CD, Kupchik YM, Shen H, Reissner KJ, Thomas CA, Kalivas PW. *Neuron* 2013 Mar 6; 77(5): 867-872. Cocaine addiction is characterized by long-lasting vulnerability to relapse arising because neutral environmental stimuli become associated with drug use and then act as cues that induce relapse. It is not known how cues elicit cocaine seeking, and why cocaine seeking is more difficult to regulate than seeking a natural reward. The authors found that cocaine-associated cues initiate cocaine seeking by inducing a rapid, transient increase in dendritic spine size and synaptic strength in the nucleus accumbens. These changes required neural activity in the prefrontal cortex. This is not the case when identical cues were associated with obtaining sucrose, which did not elicit changes in spine size or synaptic strength. The marked cue-induced synaptic changes in the accumbens were correlated with the intensity of cocaine, but not sucrose seeking, and may explain the difficulty addicts experience in managing relapse to cocaine use.

[A Binding Site For Nonsteroidal Anti-Inflammatory Drugs In Fatty Acid Amide Hydrolase.](#)

Bertolacci L, Romeo E, Veronesi M, Magotti P, Albani C, Dionisi M, Lambruschini C, Scarpelli R, Cavalli A, De Vivo M, Piomelli D, Garau G. *J Am Chem Soc* 2013; 135(1): 22-25. In addition to inhibiting the cyclooxygenase (COX)-mediated biosynthesis of prostanoids, various widely used nonsteroidal anti-inflammatory drugs (NSAIDs) enhance endocannabinoid signaling by blocking the anandamide-degrading membrane enzyme fatty acid amide hydrolase (FAAH). The X-ray structure of FAAH in complex with the NSAID carprofen, along with site-directed mutagenesis, enzyme activity assays, and NMR analysis, has revealed the molecular details of this interaction, providing information that may guide the design of dual FAAH-COX inhibitors with superior analgesic efficacy.

[An fMRI-based Neurologic Signature of Physical Pain.](#) Wager TD, Atlas LY, Lindquist MA, Roy M, Woo CW, Kross E. *N Engl J Med.* 2013 Apr 11; 368(15): 1388-1397.

Persistent pain is measured by means of self-report, the sole reliance on which hampers diagnosis and treatment. Functional magnetic resonance imaging (fMRI) holds promise for identifying objective measures of pain, but brain measures that are sensitive and specific to physical pain have not yet been identified. In four studies involving a total of 114 participants, the authors developed an fMRI-based measure that predicts pain intensity at the level of the individual person. In study 1, they used machine-learning analyses to identify a pattern of fMRI activity across brain regions--a neurologic signature--that was associated with heat-induced pain. The pattern included the thalamus, the posterior and anterior insulae, the secondary somatosensory cortex, the anterior cingulate cortex, the periaqueductal gray matter, and other regions. In study 2, the authors tested the sensitivity and specificity of the signature to pain versus warmth in a new sample. In study 3, they assessed specificity relative to social pain, which activates many of the same brain regions as physical pain. In study 4, they assessed the responsiveness of the measure to the analgesic agent remifentanyl. In study 1, the neurologic signature showed sensitivity and specificity of 94% or more (95% confidence interval [CI], 89 to 98) in discriminating painful heat from nonpainful warmth, pain anticipation, and pain recall. In study 2, the signature discriminated between painful heat and nonpainful warmth with 93% sensitivity and specificity (95% CI, 84 to 100). In study 3, it discriminated between physical pain and social pain with 85% sensitivity (95% CI, 76 to 94) and 73% specificity (95% CI, 61 to 84) and with 95% sensitivity and specificity in a forced-choice test of which of two conditions was more painful. In study 4, the strength of the signature response was substantially reduced when remifentanyl was administered. The authors conclude that it is possible to use fMRI to assess pain elicited by noxious heat in healthy persons. Future studies are needed to assess whether the signature predicts clinical pain.

[Personality Trait Predictors of Placebo Analgesia and Neurobiological Correlates.](#) Peciña M, Azhar H, Love TM, Lu T, Fredrickson BL, Stohler CS, Zubieta JK. *Neuropsychopharmacology* 2013 Mar; 38(4): 639-646.

Personality traits have been shown to interact with environmental cues to modulate biological responses including treatment responses, and potentially having a role in the formation of placebo effects. Here, the authors assessed psychological traits in 50 healthy controls as to their capacity to predict placebo analgesic effects, placebo-induced activation of μ -opioid neurotransmission and changes in cortisol plasma levels during a sustained experimental pain challenge (hypertonic saline infused in the masseter muscle) with and without placebo administration. Statistical analyses showed that an aggregate of scores from Ego-Resiliency, NEO Altruism, NEO Straightforwardness (positive predictors) and NEO Angry Hostility (negative predictor) scales accounted for 25% of the variance in placebo analgesic responses. Molecular imaging showed that subjects scoring above the median in a composite of those trait measures also presented greater placebo-induced activation of μ -opioid neurotransmission in the subgenual and dorsal anterior cingulate cortex (ACC), orbitofrontal cortex, insula, nucleus accumbens, amygdala and periaqueductal gray (PAG). Endogenous opioid release in the dorsal ACC and PAG was positively correlated with placebo-induced reductions in pain ratings. Significant reductions in cortisol levels were observed during placebo administration and were positively correlated with decreases in pain ratings, μ -opioid system activation in the dorsal ACC and PAG, and as a trend, negatively with NEO Angry Hostility scores. These results show that personality traits explain a substantial proportion of the variance in placebo analgesic responses and are further associated with activations in endogenous opioid neurotransmission, and as a trend cortisol plasma levels. These initial data, if replicated in a larger sample, suggest that simple trait measures easily deployable in the field could be utilized to reduce variability in clinical trials, but may also point to measures of individual resiliency in the face of aversive stimuli such as persistent pain and potentially other stressors.

[Error Processing and Gender-Shared and -Specific Neural Predictors Of Relapse In Cocaine Dependence.](#)

Luo X, Zhang S, Hu S, Bednarski SR, Erdman E, Farr OM, Hong KI, Sinha R, Mazure CM, Li CS. *Brain.* 2013 Apr; 136(Pt 4): 1231-1244. Epub 2013 Mar 12.

Deficits in cognitive control are implicated in cocaine dependence. Previously, combining functional magnetic resonance imaging and a stop signal task, the authors demonstrated altered cognitive control in cocaine-dependent individuals. However, the clinical implications of these cross-sectional findings and, in particular, whether the changes were associated with relapse to drug use, were not clear. In a prospective study, the authors recruited 97 treatment-seeking individuals with cocaine dependence to perform the stop signal task during functional magnetic resonance imaging and participate in follow-up assessments for 3 months, during which time cocaine use was evaluated with timeline follow back and ascertained by urine toxicology tests. Functional magnetic resonance imaging data were analyzed using general linear models as implemented in Statistical Parametric Mapping 8, with the contrast 'stop error greater than stop success trials' to index error processing. Using voxelwise analysis with logistic and Cox regressions, we identified brain activations of error processing that predict relapse and time to relapse. In females, decreased error-related activations of the thalamus and dorsal anterior cingulate cortex predicted relapse and an earlier time to relapse. In males, decreased error-related activations of the dorsal anterior cingulate cortex and left insula predicted relapse and an earlier time to relapse. These regional activations were validated with data resampling and predicted relapse with an average area under the curve of 0.849 in receiver operating characteristic

analyses. These findings provide direct evidence linking deficits in cognitive control to clinical outcome in a moderate-sized cohort of cocaine-dependent individuals. These results may provide a useful basis for future studies to examine how psychosocial factors interact with cognitive control to determine drug use and to evaluate the efficacy of pharmacological or behavioural treatment in remediating deficits of cognitive control in cocaine addicts.

Individual Differences In Anterior Cingulate Activation Associated With Attentional Bias Predict Cocaine Use After Treatment. Marhe R, Luijten M, van de Wetering BJ, Smits M, Franken IH. *Neuropsychopharmacology*. 2013 May; 38(6): 1085-1093.

Drug-dependent patients often relapse into drug use after treatment. Behavioral studies show that enhanced attentional bias to drug cues is a precursor of relapse. The present functional magnetic resonance imaging (fMRI) study examined whether brain regions involved in attentional bias are predictive of cocaine use after treatment. Attentional bias-related brain activity was measured with a cocaine Stroop task in cocaine-dependent patients during their first week in detoxification treatment and was used to predict cocaine use at 3-month follow-up. The predictive value of attentional bias-related brain activity in a priori defined regions of interest, in addition to other measures such as self-reports of substance severity, craving, and behavioral attentional bias were examined. The results show that craving in the week before treatment and individual variability in attentional bias-related activity in the dorsal anterior cingulate cortex (dACC) were significant predictors of days of cocaine use at 3-month follow-up and accounted for 45% in explained variance. Brain activity in the dACC uniquely contributed 22% of explained variance to the prediction model. These findings suggest that hyperactive attentional bias-related brain activity in the dACC might be a biomarker of relapse vulnerability as early as in the first week of detoxification treatment. Ultimately, this may help to develop individually tailored treatment interventions to reduce relapse risk.

Young Adults at Risk for Stimulant Dependence Show Reward Dysfunction During Reinforcement-based Decision Making. Stewart JL, Flagan TM, May AC, Reske M, Simmons AN, Paulus MP. *Biological Psychiatry*. 2013; 73(3): 235-241.

While stimulant-dependent individuals continue to make risky decisions, in spite of poor outcomes, much less is known about decision-making characteristics of occasional stimulant users (OSU) at risk for developing stimulant dependence. This study examines whether OSU exhibit inefficient learning and execution of reinforced decision-outcome contingencies. Occasional stimulant users ($n = 161$) and stimulant-naïve comparison subjects (CTL) ($n = 48$) performed a Paper Scissors Rock task during functional magnetic resonance imaging. Selecting a particular option was associated with a predetermined probability of winning, which was altered repeatedly to examine neural and behavioral characteristics of reinforced contingencies. Occasional stimulant users displayed greater anterior insula, inferior frontal gyrus, and dorsal striatum activation than CTL during late trials when contingencies were familiar (as opposed to being learned) in the presence of comparable behavioral performance in both groups. Follow-up analyses demonstrated that during late trials: 1) OSU with high cannabis use displayed greater activation in these brain regions than CTL, whereas OSU with low cannabis use did not differ from the other two groups; and 2) OSU preferring cocaine exhibited greater anterior insula, inferior frontal gyrus, and dorsal striatum activation than CTL and also displayed higher activation in the former two regions than OSU who preferred prescription stimulants. Occasional stimulant users exhibit inefficient resource allocation during the execution of reinforced contingencies that may be a result of additive effects of cocaine and cannabis use. A critical next step is to establish whether this inefficiency predicts transition to stimulant dependence.

Regional Brain Morphometry and Impulsivity in Adolescents Following Prenatal Exposure to Cocaine and Tobacco. Liu J, Lester BM, Neyzi N, Sheinkopf SJ, Gracia L, Kekatpure M, Kosofsky BE. *JAMA Pediatr*. 2013 Feb 11: 1-7.

Animal studies have suggested that prenatal cocaine exposure (PCE) deleteriously influences the developing nervous system, in part attributable to its site of action in blocking the function of monoamine reuptake transporters, increasing synaptic levels of serotonin and dopamine. The objective of this study was to examine the brain morphologic features and associated impulsive behaviors in adolescents following prenatal exposure to cocaine and/or tobacco. Magnetic resonance imaging data and behavioral measures were collected from adolescents followed up longitudinally in the Maternal Lifestyle Study. SETTING: A hospital-based research center. A total of 40 adolescent participants aged 13 to 15 years were recruited, 20 without PCE and 20 with PCE; a subset of each group additionally had tobacco exposure. Participants were selected and matched based on head circumference at birth, gestational age, maternal alcohol use, age, sex, race/ethnicity, IQ, family poverty, and socioeconomic status. Outcome measures included subcortical volumetric measures of the thalamus, caudate, putamen, pallidum, hippocampus, amygdala, and nucleus accumbens; cortical thickness measures of the dorsolateral prefrontal cortex and ventral medial prefrontal cortex; and impulsivity assessed by Conners' Continuous Performance Test and the Sensation Seeking Scale for Children. After controlling for covariates, cortical thickness of the right dorsolateral prefrontal cortex was significantly thinner in adolescents following PCE ($P = .03$), whereas the pallidum volume was smaller in adolescents following prenatal tobacco exposure ($P = .03$). Impulsivity was correlated with thalamic volume following either PCE ($P = .05$) or prenatal tobacco exposure ($P = .04$). Prenatal cocaine or tobacco exposure can

differentially affect structural brain maturation during adolescence and underlie enhanced susceptibility to impulsivity. Additional studies with larger sample sizes are warranted.

Predominance Of D2 Receptors In Mediating Dopamine's Effects In Brain Metabolism: Effects Of Alcoholism. Volkow ND, Tomasi D, Wang GJ, Telang F, Fowler JS, Logan J, Maynard LJ, Wong CT. *J Neurosci.* 2013 Mar 6; 33(10): 4527-4535.

Dopamine signals through D1-like and D2-like receptors, which can stimulate or inhibit, respectively, neuronal activity. Here the authors assessed the balance between D1 or D2 receptor signaling in the human brain and how it is affected in alcoholism. Using PET, they measured the relationship between changes in dopamine and brain glucose metabolism induced by methylphenidate in controls and alcoholics. They show that methylphenidate induced significant DA increases in striatum, amygdala, and medial orbitofrontal cortex, whereas it decreased metabolism in these brain regions. Methylphenidate-induced dopamine increases were greater in controls than in alcoholics, whereas methylphenidate-induced metabolic decreases were greater in alcoholics. For both groups, methylphenidate-induced dopamine increases were associated with decreases in regional brain metabolism, and the correlations were strongest in subthalamic nuclei, anterior cingulate, and medial orbitofrontal cortex. These correlations were more extensive and robust and the slopes steeper in alcoholics than in controls despite their attenuated dopamine responses to methylphenidate, which suggests an impaired modulation of dopamine signals in the brain of alcoholic subjects. These findings are consistent with a predominant inhibitory effect of dopamine in the human brain that is likely mediated by the prominence of dopamine D2/D3 receptors.

HIV, Age, and the Severity of Hepatitis C Virus-Related Liver Disease: A Cohort Study. Kirk G, Mehta S, Astemborski J, Galai N, Washington J, Higgins Y, Balagopal A, Thomas D. *Ann Intern Med.* 2013; 1-11.

Persons with HIV infection have been reported to develop age-related diseases at younger ages than those without HIV. Whether this finding is related to HIV infection or failure to control for other risk factors is unknown. The objective of this study was to investigate whether persons with HIV infection develop hepatitis C virus (HCV)-related liver disease at younger ages than similar persons without HIV. The study design was a comparison of the severity of liver fibrosis by age among persons who have HCV with and without HIV followed concurrently in the same protocol. The study setting was an observational cohort from Baltimore, Maryland, participating in the ALIVE (AIDS Linked to the IntraVenous Experience) study. Participants were 1,176 current and former injection drug users with antibodies to HCV. Liver fibrosis was assessed semiannually from 2006 to 2011 by elastography (FibroScan, Echosens, Paris, France) and using previously validated thresholds for clinically significant fibrosis and cirrhosis; concurrent assessment of medical history, alcohol and illicit drug use, HCV RNA levels, hepatitis B virus surface antigen level, body mass index, and (for those with HIV) CD4+ lymphocyte count and HIV RNA levels were also taken. Among 1,176 participants with antibodies to HCV, the median age was 49 years and 34% were coinfecting with HIV and HCV. Participants contributed 5,634 valid liver fibrosis measurements. The prevalence of clinically significant fibrosis without cirrhosis (12.9% vs. 9.5%) and of cirrhosis (19.5% vs. 11.0%) was greater in persons coinfecting with HIV and HCV than in those with only HCV ($P < 0.001$). Increasing age and HIV infection were independently associated with liver fibrosis, as were daily alcohol use, chronic hepatitis B virus infection, body mass index greater than 25 kg/m², and greater plasma HCV RNA levels. When these factors were kept constant, persons with HIV had liver fibrosis measurements equal to those of persons without HIV, who were, on average, 9.2 years older. A limitation of this study was that the process of liver fibrosis began before the study in most persons. The authors conclude that in this cohort, persons who have HCV with HIV have liver fibrosis stages similar to those without HIV who are nearly a decade older.

Longitudinal Effects of Universal Preventive Intervention on Prescription Drug Misuse: Three Randomized Controlled Trials With Late Adolescents and Young Adults. Spoth R, Trudeau L, Shin C, Ralston E, Redmond C, Greenberg M, Feinberg M. *Am J Public Health.* February 14, 2013; e1-e8. [Epub ahead of print]

The authors examined long-term prescription drug misuse outcomes in 3 randomized controlled trials evaluating brief universal preventive interventions conducted during middle school. The methods of these 3 studies, they tested the Iowa Strengthening Families Program (ISFP); evaluated a revised ISFP, the Strengthening Families Program: For Parents and Youth 10-14 plus the school-based Life Skills Training (SFP 10-14 + LST); and examined the SFP 10-14 plus 1 of 3 school-based interventions. Self-reported outcomes were prescription opioid misuse (POM) and lifetime prescription drug misuse overall (PDMO). The results are that in study 1, ISFP showed significant effects on POM and PDMO, relative reduction rates (RRRs; age 25 years) of 65%, and comparable benefits for higher- and lower-risk subgroups. In study 2, SFP 10-14 + LST showed significant or marginally significant effects on POM and PDMO across all ages (21, 22, and 25 years); higher-risk participants showed stronger effects (RRRs = 32%-79%). In study 3, the authors found significant results for POM and PDMO (12th grade RRRs = 20%-21%); higher-risk and lower-risk participants showed comparable outcomes. The authors conclude that brief universal interventions have potential for public health impact by reducing prescription drug misuse among adolescents and young adults.

Effect of a Paraprofessional Home-Visiting Intervention on American Indian Teen Mothers' and Infants' Behavioral Risks: a Randomized Controlled Trial.

Barlow A, Mullany B, Neault N, Compton S, Carter A, Hastings R, Billy T, Coho-Mescal V, Lorenzo S, Walkup J. *Am J Psychiatry.* 2013; 170(1): 83-93.

The authors sought to examine the effectiveness of Family Spirit, a paraprofessional-delivered, home-visiting pregnancy and early childhood intervention in improving American Indian teen mothers' parenting outcomes and mothers' and children's emotional and behavioral functioning 12 months postpartum. Pregnant American Indian teens (N=322) from four southwestern tribal reservation communities were randomly assigned in equal numbers to the Family Spirit intervention plus optimized standard care or to optimized standard care alone. Parent and child emotional and behavioral outcome data were collected at baseline and at 2, 6, and 12 months postpartum using self-reports, interviews, and observational measures. At 12 months postpartum, mothers in the intervention group had significantly greater parenting knowledge parenting self-efficacy, and home safety attitudes and fewer externalizing behaviors, and their children had fewer externalizing problems. In a subsample of mothers with any lifetime substance use at baseline (N=285; 88.5%), children in the intervention group had fewer externalizing and dysregulation problems than those in the standard care group, and fewer scored in the clinically at risk range (10th percentile) for externalizing and internalizing problems. No between-group differences were observed for outcomes measured by the Home Observation for Measurement of the Environment scale. Outcomes 12 months postpartum suggest that the Family Spirit intervention improves parenting and infant outcomes that predict lower lifetime behavioral and drug use risk for participating teen mothers and children.

Demethylation of the Aryl Hydrocarbon Receptor Repressor as a Biomarker for Nascent Smokers. Philibert R, Beach S, Brody G. *Epigenetics.* 2012; 7(11): 1331-1338.

Epigenetic modifications to peripheral white blood cell DNA occur in response to a wide variety of exposures. In prior work, the authors and others have shown that broad changes in DNA methylation, particularly at the aryl hydrocarbon receptor repressor (AHRR) locus, occur in samples from subjects with long histories of smoking. However, given the large number of epigenetic changes that occur in response to prolonged smoking, the primacy of the response at AHRR and the sensitivity of these changes to low levels of smoking are not known. Therefore, the authors examined the association of smoking to genome lymphocyte DNA methylation status in a representative sample of 399 African American youths living in the rural South that includes 72 subjects with less than one half-pack year of exposure. Consistent with the authors' prior findings, they found a stepwise effect of smoking on DNA methylation among youth with relatively brief exposure histories at a CpG residue in AHRR (cg05575921) (FDR corrected p values; 3×10^{-7} and 0.09 in the male and female samples, respectively) that was identified in previous studies and at which the effects of smoking were significant, even in those subjects with less than one half pack year exposure. The authors conclude that AHRR demethylation at cg05575921 in peripheral cells may serve as an early, sensitive biomarker for even low levels of exposure to tobacco smoke, providing a non-self-report alternative for nascent exposure to tobacco smoke. They also suggest that the AHRR/AHR pathway may be functional in the response of peripheral white blood cells to tobacco smoke exposure.

Genome-Wide Association Study of Spontaneous Resolution of Hepatitis C Virus Infection: Data From Multiple Cohorts.

Duggal P, Thio CL, Wojcik GL, Goedert JJ, Mangia A, Latanich R, Kim AY, Lauer GM, Chung RT, Peters MG, Kirk GD, Mehta SH, Cox AL, Khakoo SI, Alric L, Cramp ME, Donfield SM, Edlin BR, Tobler LH, Busch MP, Alexander G, Rosen HR, Gao X, Abdel-Hamid M, Apps R, Carrington M, Thomas DL. *Ann Intern Med.* 2013 Feb 19; 158(4): 235-245.

Hepatitis C virus (HCV) infections occur worldwide and either spontaneously resolve or persist and markedly increase the person's lifetime risk for cirrhosis and hepatocellular carcinoma. Although HCV persistence occurs more often in persons of African ancestry and persons with genetic variants near interleukin-28B (IL-28B), the genetic basis is not well-understood. The objective of this study was to evaluate the host genetic basis for spontaneous resolution of HCV infection. The study design was a 2-stage, genome-wide association study carried out at 13 international multicenter study sites. Patients were 919 persons with serum HCV antibodies but no HCV RNA (spontaneous resolution) and 1482 persons with serum HCV antibodies and HCV RNA (persistence). Measurements were frequencies of 792,721 single nucleotide polymorphisms (SNPs). Differences in allele frequencies between persons with spontaneous resolution and persistence were identified on chromosomes 19q13.13 and 6p21.32. On chromosome 19, allele frequency differences localized near IL-28B and included rs12979860 (overall per-allele OR, 0.45; $P = 2.17 \times 10^{-30}$) and 10 additional SNPs spanning 55,000 base pairs. On chromosome 6, allele frequency differences localized near genes for HLA class II and included rs4273729 (overall per-allele OR, 0.59; $P = 1.71 \times 10^{-16}$) near DQB1*03:01 and an additional 116 SNPs spanning 1,090,000 base pairs. The associations in chromosomes 19 and 6 were independent and additive and explain an estimated 14.9% (95% CI, 8.5% to 22.6%) and 15.8% (CI, 4.4% to 31.0%) of the variation in HCV resolution in persons of European and African ancestry, respectively. Replication of the chromosome 6 SNP, rs4272729, in an additional 745 persons confirmed the findings ($P = 0.015$). A limitation of this research was that epigenetic effects were not studied. The authors conclude that IL-28B and HLA class II are independently associated with spontaneous resolution of HCV infection, and SNPs marking IL-28B and DQB1*03:01 may explain approximately 15% of spontaneous resolution of HCV infection.

Effects of Chronic Buspirone Treatment on Nicotine and Concurrent Nicotine+Cocaine Self-Administration.

Mello NK, Fivel PA, Kohut SJ. *Neuropsychopharmacology*. 2013 Jan 21. [Epub ahead of print]

Nicotine dependence and cocaine abuse are major public health problems, and most cocaine abusers also smoke cigarettes. An ideal pharmacotherapy would reduce both cigarette smoking and cocaine abuse. Buspirone (Buspar) is a clinically available, non-benzodiazepine anxiolytic medication that acts on serotonin and dopamine systems. In preclinical studies, it reduced cocaine self-administration following both acute and chronic treatment in rhesus monkeys. The present study evaluated the effectiveness of chronic buspirone treatment on self-administration of intravenous (IV) nicotine and IV nicotine+cocaine combinations. Five cocaine-experienced adult rhesus monkeys (*Macaca mulatta*) were trained to self-administer nicotine or nicotine+cocaine combinations, and food pellets (1 g) during four 1-h daily sessions under a second-order schedule of reinforcement (FR 2 (VR16:S)). Each nicotine+cocaine combination maintained significantly higher levels of drug self-administration than nicotine or cocaine alone ($P < 0.05-0.001$). Buspirone (0.032-0.56 mg/kg/h) was administered IV through one lumen of a double-lumen catheter every 20 min for 23 h each day, for 7-10 consecutive days. Each 7-10-day sequence of buspirone treatment was followed by saline-control treatment for at least 3 days until food- and drug-maintained responding returned to baseline. Buspirone dose-dependently reduced responding maintained by nicotine alone (0.001-0.1 mg/kg/inj; $P < 0.01$) and by nicotine (0.001 or 0.0032 mg/kg/inj)+cocaine combinations (0.0032 mg/kg/inj; $P < 0.05-0.001$) with no significant effects on food-maintained responding. The authors conclude that buspirone selectively attenuates the reinforcing effects of nicotine alone and nicotine+cocaine polydrug combinations in a nonhuman primate model of drug self-administration.

Nabilone Decreases Marijuana Withdrawal and a Laboratory Measure of Marijuana Relapse.

Haney M, Cooper ZD, Bedi G, Vosburg SK, Comer SD, Foltin RW. *Neuropsychopharmacology*. 2013 Feb 26 [Epub ahead of print].

Few individuals seeking treatment for marijuana use achieve sustained abstinence. The cannabinoid receptor agonist, $\Delta(9)$ -tetrahydrocannabinol (THC; dronabinol), decreases marijuana withdrawal symptoms, yet does not decrease marijuana use in the laboratory or clinic. Dronabinol has poor bioavailability, which may contribute to its poor efficacy. The FDA-approved synthetic analogue of THC, nabilone, has higher bioavailability and clearer dose-linearity than dronabinol. This study tested whether nabilone administration would decrease marijuana withdrawal symptoms and a laboratory measure of marijuana relapse relative to placebo. Daily, nontreatment-seeking marijuana smokers (8 M, 3 F), who reported smoking 8.3 ± 3.1 marijuana cigarettes/day completed this within-subject study comprising three, 8-day inpatient phases; each phase tested a different nabilone dose [0, 6, 8 mg/day, administered in counter-balanced order on days 2-8]. On the first inpatient day, participants took placebo capsules and smoked active marijuana (5.6% THC) at six timepoints. For the next 3 days, they had the opportunity to self-administer placebo marijuana (0.0% THC; Withdrawal), followed by 4 days in which active marijuana was available for self-administration (5.6% THC; Relapse). Both nabilone dose conditions decreased marijuana relapse and reversed withdrawal-related irritability and disruptions in sleep and food intake ($p < 0.05$). Nabilone (8 mg/day) modestly worsened psychomotor task performance. Neither dose condition increased ratings of capsule 'liking' or desire to take the capsules relative to placebo. Thus, nabilone maintenance produced a robust attenuation of marijuana withdrawal symptoms and a laboratory measure of relapse even with once per day dosing. These data support testing of nabilone for patients seeking marijuana treatment.

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* 2013; 76(4): 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.

Dynamic Interaction Between Sigma-1 Receptor and Kv1.2 Shapes Neuronal and Behavioral Responses To Cocaine.

Kourrich S, Hayashi T, Tsai SY, Harvey B, Su TP, Bonci A. *Cell* 2013; 152(1-2): 236-247.

The sigma-1 receptor (Sig-1R), an endoplasmic reticulum (ER) chaperone protein, is an interorganelle signaling modulator that potentially plays a role in drug-seeking behaviors. However, the brain site of action and underlying cellular mechanisms remain unidentified. The authors found that cocaine exposure triggers a Sig-1R-dependent upregulation of D-type K(+) current in the nucleus accumbens (NAc) that results in neuronal hypoactivity and thereby enhances behavioral cocaine response. Combining ex vivo and in vitro studies, they demonstrated that this

neuroadaptation is caused by a persistent protein-protein association between Sig-1Rs and Kv1.2 channels, a phenomenon that is associated to a redistribution of both proteins from intracellular compartments to the plasma membrane. In conclusion, the dynamic Sig-1R-Kv1.2 complex represents a mechanism that shapes neuronal and behavioral response to cocaine. Functional consequences of Sig-1R binding to K(+) channels may have implications for other chronic diseases where maladaptive intrinsic plasticity and Sig-1Rs are engaged.

[Risk-Responsive Orbitofrontal Neurons Track Acquired Saliency.](#) Ogawa M, van der Meer MA, Esber GR, Cerri DH, Stalnaker TA, Schoenbaum G. *Neuron*. 2013 Jan 23; 77(2): 251-258.

Decision making is impacted by uncertainty and risk (i.e., variance). Activity in the orbitofrontal cortex, an area implicated in decision making, covaries with these quantities. However, this activity could reflect the heightened salience of situations in which multiple outcomes-reward and reward omission-are expected. To resolve these accounts, rats were trained to respond to cues predicting 100%, 67%, 33%, or 0% reward. Consistent with prior reports, some orbitofrontal neurons fired differently in anticipation of uncertain (33% and 67%) versus certain (100% and 0%) reward. However, over 90% of these neurons also fired differently prior to 100% versus 0% reward (or baseline) or prior to 33% versus 67% reward. These responses are inconsistent with risk but fit well with the representation of acquired salience linked to the sum of cue-outcome and cue-no-outcome associative strengths. These results expand our understanding of how the orbitofrontal cortex might regulate learning and behavior.

[Coupling Of Functional Connectivity and Regional Cerebral Blood Flow Reveals a Physiological Basis For Network Hubs of the Human Brain.](#) Liang X, Zou Q, He Y, Yang Y. *Proc Natl Acad Sci U S A*. 2013 Jan 29; 110(5): 1929-1934.

Human brain functional networks contain a few densely connected hubs that play a vital role in transferring information across regions during resting and task states. However, the relationship of these functional hubs to measures of brain physiology, such as regional cerebral blood flow (rCBF), remains incompletely understood. Here, the authors used functional MRI data of blood-oxygenation-level-dependent and arterial-spin-labeling perfusion contrasts to investigate the relationship between functional connectivity strength (FCS) and rCBF during resting and an N-back working-memory task. During resting state, functional brain hubs with higher FCS were identified, primarily in the default-mode, insula, and visual regions. The FCS showed a striking spatial correlation with rCBF, and the correlation was stronger in the default-mode network (DMN; including medial frontal-parietal cortices) and executive control network (ECN; including lateral frontal-parietal cortices) compared with visual and sensorimotor networks. Moreover, the relationship was connection-distance dependent; i.e., rCBF correlated stronger with long-range hubs than short-range ones. It is notable that several DMN and ECN regions exhibited higher rCBF per unit connectivity strength (rCBF/FCS ratio); whereas, this index was lower in posterior visual areas. During the working-memory experiment, both FCS-rCBF coupling and rCBF/FCS ratio were modulated by task load in the ECN and/or DMN regions. Finally, task-induced changes of FCS and rCBF in the lateral-parietal lobe positively correlated with behavioral performance. Together, the authors' results indicate a tight coupling between blood supply and brain functional topology during rest and its modulation in response to task demands, which may shed light on the physiological basis of human brain functional connectome.

[Rescuing Cocaine-Induced Prefrontal Cortex Hypoactivity Prevents Compulsive Cocaine Seeking.](#) Chen BT, Yau HJ, Hatch C, Kusumoto-Yoshida I, Cho SL, Hopf FW, Bonci A. *Nature* [E-pub online 2013].

Loss of control over harmful drug seeking is one of the most intractable aspects of addiction, as human substance abusers continue to pursue drugs despite incurring significant negative consequences. Human studies have suggested that deficits in prefrontal cortical function and consequential loss of inhibitory control could be crucial in promoting compulsive drug use. However, it remains unknown whether chronic drug use compromises cortical activity and, equally important, whether this deficit promotes compulsive cocaine seeking. Here the authors use a rat model of compulsive drug seeking in which cocaine seeking persists in a subgroup of rats despite delivery of noxious foot shocks. They show that prolonged cocaine self-administration decreases ex vivo intrinsic excitability of deep layer pyramidal neurons in the prelimbic cortex, which was significantly more pronounced in compulsive drug-seeking animals. Furthermore, compensating for hypoactive prelimbic cortex neurons with in vivo optogenetic prelimbic cortex stimulation significantly prevented compulsive cocaine seeking, whereas optogenetic prelimbic cortex inhibition significantly increased compulsive cocaine seeking. These results show a marked reduction in prelimbic cortex excitability in compulsive cocaine-seeking rats, and that in vivo optogenetic prelimbic cortex stimulation decreased compulsive drug-seeking behaviours. Thus, targeted stimulation of the prefrontal cortex could serve as a promising therapy for treating compulsive drug use.

[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; 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. Adolescent morphine exposure affects long-term microglial function and later-life relapse liability in a model of addiction.

[Social Deprivation Enhances VTA Synaptic Plasticity and Drug-Induced Contextual Learning.](#) Whitaker LR, Degoulet M, Morikawa H. *Neuron* 2013; 77(2): 335-345.

Drug addiction is driven, in part, by powerful drug-related memories. Deficits in social life, particularly during adolescence, increase addiction vulnerability. Social isolation in rodents has been used extensively to model the effects of deficient social experience, yet its impact on learning and memory processes underlying addiction remains elusive. Here, the authors show that social isolation of rats during a critical period of adolescence (postnatal days 21-42) enhances long-term potentiation of NMDA receptor (NMDAR)-mediated glutamatergic transmission in the ventral tegmental area (VTA). This enhancement, which is caused by an increase in metabotropic glutamate receptor-dependent Ca(2+) signaling, cannot be reversed by subsequent resocialization. Notably, memories of amphetamine- and ethanol-paired contextual stimuli are acquired faster and, once acquired, amphetamine-associated contextual memory is more resistant to extinction in socially isolated rats. The authors propose that NMDAR plasticity in the VTA may represent a neural substrate by which early life deficits in social experience increase addiction vulnerability.

[Instant Transformation Of Learned Repulsion Into Motivational 'Wanting.'](#) Robinson MJF, Berridge KC. *Curr Biol* 2013; 23(4): 282-289.

Learned cues for pleasant reward often elicit desire, which, in addicts, may become compulsive. According to the dominant view in addiction neuroscience and reinforcement modeling, such desires are the simple products of learning, coming from a past association with reward outcome. The authors demonstrate that cravings are more than merely the products of accumulated pleasure memories—even a repulsive learned cue for unpleasantness can become suddenly desired via the activation of mesocorticolimbic circuitry. Rats learned repulsion toward a Pavlovian cue (a briefly-inserted metal lever) that always predicted an unpleasant Dead Sea saltiness sensation. Yet, upon first reencounter in a novel sodium-depletion state to promote mesocorticolimbic reactivity (reflected by elevated Fos activation in ventral tegmentum, nucleus accumbens, ventral pallidum, and the orbitofrontal prefrontal cortex), the learned cue was instantly transformed into an attractive and powerful motivational magnet. Rats jumped and gnawed on the suddenly attractive Pavlovian lever cue, despite never having tasted intense saltiness as anything other than disgusting. Instant desire transformation of a learned cue contradicts views that Pavlovian desires are essentially based on previously learned values (e.g., prediction error or temporal difference models). Instead desire is recomputed at reencounter by integrating Pavlovian information with the current brain/physiological state. This powerful brain transformation reverses strong learned revulsion into avid attraction. When applied to addiction, related mesocorticolimbic transformations (e.g., drugs or neural sensitization) of cues for already-pleasant drug experiences could create even more intense cravings. This cue/state transformation helps define what it means to say that addiction hijacks brain limbic circuits of natural reward.

[The Neuron-Specific Chromatin Regulatory Subunit BAF53b Is Necessary For Synaptic Plasticity and Memory.](#) Vogel-Ciernia A, Matheos DP, Barrett RM, Kramár EA, Azzawi S, Chen Y, Magnan CN, Zeller M, Sylvain A, Haettig J, Jia Y, Tran A, Dang R, Post RJ, Chabrier M, Babayan AH, Wu JI, Crabtree GR, Baldi P, Baram TZ, Lynch G, Wood MA. *Nat Neurosci.* 2013 Mar 24. [Epub ahead of print].

Recent exome sequencing studies have implicated polymorphic Brg1-Associated Factor (BAF) complexes (mammalian SWI/SNF chromatin remodeling complexes) in several human intellectual disabilities and cognitive disorders. However, it is currently unknown how mutations in BAF complexes result in impaired cognitive function. Postmitotic neurons express a neuron-specific assembly, nBAF, characterized by the neuron-specific subunit BAF53b. Mice harboring selective genetic manipulations of BAF53b have severe defects in long-term memory and long-lasting forms of hippocampal synaptic plasticity. The authors rescued memory impairments in BAF53b mutant mice by reintroducing BAF53b in the adult hippocampus, which suggests a role for BAF53b beyond neuronal development. The defects in BAF53b mutant mice appeared to derive from alterations in gene expression that produce abnormal postsynaptic components, such as spine structure and function, and ultimately lead to deficits in

synaptic plasticity. These results provide new insight into the role of dominant mutations in subunits of BAF complexes in human intellectual and cognitive disorders.

Hierarchical Recruitment Of Phasic Dopamine Signaling In the Striatum During the Progression Of Cocaine Use. Willuhn I, Burgeno LM, Everitt BJ, Phillips PEM. Proc Natl Acad Sci U S A 2012; 109(50): 20703-20708.

Drug addiction is a neuropsychiatric disorder that marks the end stage of a progression beginning with recreational drug taking but culminating in habitual and compulsive drug use. This progression is considered to reflect transitions among multiple neural loci. Dopamine neurotransmission in the ventromedial striatum (VMS) is pivotal in the control of initial drug use, but emerging evidence indicates that once drug use is well established, its control is dominated by the dorsolateral striatum (DLS). In the current work, the authors conducted longitudinal neurochemical recordings to ascertain the spatiotemporal profile of striatal dopamine release and to investigate how it changes during the period from initial to established drug use. Dopamine release was detected using fast-scan cyclic voltammetry simultaneously in the VMS and DLS of rats bearing indwelling i.v. catheters over the course of 3 wk of cocaine self-administration. The authors found that phasic dopamine release in DLS emerged progressively during drug taking over the course of weeks, a period during which VMS dopamine signaling declined. This emergent dopamine signaling in the DLS mediated discriminated behavior to obtain drug but did not promote escalated or compulsive drug use. The authors also demonstrate that this recruitment of dopamine signaling in the DLS is dependent on antecedent activity in VMS circuitry. Thus, the current findings identify a striatal hierarchy that is instantiated during the expression of established responses to obtain cocaine.

Adolescents Are More Vulnerable To Cocaine Addiction: Behavioral and Electrophysiological Evidence.

Wong WC, Ford KA, Pagels NE, McCutcheon JE, Marinelli M. J Neurosci. 2013 Mar 13; 33(11): 4913-4922. In humans, adolescence is a period of heightened propensity to develop cocaine addiction. It is unknown whether this is attributable to greater access and exposure to cocaine at this age, or whether the adolescent brain is particularly vulnerable to the addictive properties of cocaine. Here, the authors subjected male adolescent (P42) and adult (~P88) rats to a wide range of cocaine self-administration procedures. In addition, to determine whether behavioral differences are associated with developmental differences in dopaminergic activity, they examined and manipulated the activity of dopamine neurons. Relative to adults, adolescent rats took cocaine more readily, were more sensitive to lower doses, showed greater escalation of cocaine intake, and were less susceptible to increases in price (i.e., were more "inelastic"). In parallel, adolescents also showed elevated activity of ventral tegmental area dopamine neurons, a feature known to be associated with increased self-administration behavior. Pharmacological manipulation of dopamine D2 receptor function with quinpirole (agonist) or eticlopride (antagonist), to alter dopamine neuron activity, eliminated age differences in cocaine self-administration. These data suggest a causal relationship between behavioral and electrophysiological determinants of cocaine addiction liability. In conclusion, adolescents show behavioral and electrophysiological traits of heightened addiction liability.

MicroRNA-182 Regulates Amygdala-Dependent Memory Formation. Griggs EM, Young EJ, Rumbaugh G, Miller CA. J Neurosci. 2013 Jan 23; 33(4): 1734-1740.

De novo protein synthesis supports long-lasting functional and structural plasticity and is a molecular requirement for new memory formation. Recent evidence has suggested that microRNAs may be involved in regulating the molecular mechanisms underlying neural plasticity. MicroRNAs are endogenous, noncoding RNAs capable of post-transcriptional repression of their mRNA targets. To explore the potential for microRNA-mediated regulation of amygdala-dependent memory formation, the authors performed expression profiling of microRNAs in the lateral amygdala of rats 1 h after auditory fear conditioning. Microarray analysis revealed that over half of all known microRNAs are endogenously expressed in the lateral amygdala, with 7 microRNAs upregulated and 32 downregulated by auditory fear training. Bioinformatic analysis identified several of the downregulated microRNAs as potential repressors of actin-regulating proteins known to be involved in plasticity and memory. Downregulation of one of these microRNAs by auditory fear conditioning, miR-182, was confirmed by quantitative real-time PCR. Overexpression of miR-182 within the lateral amygdala resulted in decreased expression of the protein but not mRNA of two synapse-enriched regulators of actin known to modulate structural plasticity, cortactin and Rac1. The overexpression of miR-182 also disrupted long-term but not short-term auditory fear memory. These data indicate that learning-induced suppression of miR-182, a microRNA previously uncharacterized in the brain, supports long-term memory formation in the amygdala and suggests it does so, at least in part, through the derepression of key actin-regulating proteins. These findings further indicate that microRNAs may represent a previously underappreciated mechanism for regulating protein synthesis during memory consolidation.

The Primate Amygdala Combines Information About Space and Value. Peck CJ, Lau B, Salzman CD. Nat Neurosci 2013; 16(3): 340-348.

A stimulus predicting reinforcement can trigger emotional responses, such as arousal, and cognitive ones, such as increased attention toward the stimulus. Neuroscientists have long appreciated that the amygdala mediates spatially nonspecific emotional responses, but it remains unclear whether the amygdala links motivational and spatial

representations. To test whether amygdala neurons encode spatial and motivational information, the authors presented reward-predictive cues in different spatial configurations to monkeys and assessed how these cues influenced spatial attention. Cue configuration and predicted reward magnitude modulated amygdala neural activity in a coordinated fashion. Moreover, fluctuations in activity were correlated with trial-to-trial variability in spatial attention. Thus, the amygdala integrates spatial and motivational information, which may influence the spatial allocation of cognitive resources. These results suggest that amygdala dysfunction may contribute to deficits in cognitive processes normally coordinated with emotional responses, such as the directing of attention toward the location of emotionally relevant stimuli.

[Phasic Mesolimbic Dopamine Release Tracks Reward Seeking During Expression of Pavlovian-to-Instrumental Transfer.](#) Wassum KM, Ostlund SB, Loewinger GC, Maidment NT. *Biol Psychiatry* 2013. [Epub ahead of print.]

Recent theories addressing mesolimbic dopamine's role in reward processing emphasize two apparently distinct functions, one in reinforcement learning (i.e., prediction error) and another in incentive motivation (i.e., the invigoration of reward seeking elicited by reward-paired cues). Here, the authors evaluate the latter. Using fast-scan cyclic voltammetry, they monitored, in real time, dopamine release in the nucleus accumbens core of rats ($n = 9$) during a Pavlovian-to-instrumental transfer task in which the effects of a reward-predictive cue on an independently trained instrumental action were assessed. Voltammetric data were parsed into slow and phasic components to determine whether these forms of dopamine signaling were differentially related to task performance. They found that a reward-paired cue, which increased reward-seeking actions, induced an increase in phasic mesolimbic dopamine release and produced slower elevations in extracellular dopamine. Interestingly, phasic dopamine release was temporally related to and positively correlated with lever-press activity generally, while slow dopamine changes were not significantly related to such activity. Importantly, the propensity of the reward-paired cue to increase lever pressing was predicted by the amplitude of phasic dopamine release events, indicating a possible mechanism through which cues initiate reward-seeking actions. These data suggest that those phasic mesolimbic dopamine release events thought to signal reward prediction error may also be related to the incentive motivational impact of reward-paired cues on reward-seeking actions.

[Active Avoidance Learning Requires Prefrontal Suppression Of Amygdala-Mediated Defensive Reactions.](#) Moscarello JM, Ledoux JE. *J Neurosci* 2013; 33(9): 3815-3823.

Signaled active avoidance (AA) paradigms train subjects to prevent an aversive outcome by performing a learned behavior during the presentation of a conditioned cue. This complex form of conditioning involves pavlovian and instrumental components, which produce competing behavioral responses that must be reconciled for the subject to successfully avoid an aversive stimulus. In signaled AA paradigm for rat, the authors tested the hypothesis that the instrumental component of AA training recruits infralimbic prefrontal cortex (ilPFC) to inhibit central amygdala (CeA)-mediated Pavlovian reactions. Pretraining lesions of ilPFC increased conditioned freezing while causing a corresponding decrease in avoidance; lesions of CeA produced opposite effects, reducing freezing and facilitating avoidance behavior. Pharmacological inactivation experiments demonstrated that ilPFC is relevant to both acquisition and expression phases of AA learning. Inactivation experiments also revealed that AA produces an ilPFC-mediated diminution of pavlovian reactions that extends beyond the training context, even when the conditioned stimulus is presented in an environment that does not allow the avoidance response. Finally, injection of a protein synthesis inhibitor into either ilPFC or CeA impaired or facilitated AA, respectively, showing that avoidance training produces two opposing memory traces in these regions. These data support a model in which AA learning recruits ilPFC to inhibit CeA-mediated defense behaviors, leading to a robust suppression of freezing that generalizes across environments. Thus, ilPFC functions as an inhibitory interface, allowing instrumental control over an aversive outcome to attenuate the expression of freezing and other reactions to conditioned threat.

[Stress Produces Aversion and Potentiates Cocaine Reward By Releasing Endogenous Dynorphins In The Ventral Striatum To Locally Stimulate Serotonin Reuptake.](#) Schindler AG, Messinger DI, Smith JS, Shankar H, Gustin RM, Schattauer SS, Lemos JC, Chavkin NW, Hagan CE, Neumaier JF, Chavkin C. *J Neurosci* 2012; 32(49): 17582-17596.

Activation of the dynorphin/ κ -opioid receptor (KOR) system by repeated stress exposure or agonist treatment produces place aversion, social avoidance, and reinstatement of extinguished cocaine place preference behaviors by stimulation of p38 α MAPK, which subsequently causes the translocation of the serotonin transporter (SERT, SLC6A4) to the synaptic terminals of serotonergic neurons. In the present study the authors extend those findings by showing that stress-induced potentiation of cocaine conditioned place preference occurred by a similar mechanism. In addition, SERT knock-out mice did not show KOR-mediated aversion, and selective reexpression of SERT by lentiviral injection into the dorsal raphe restored the prodepressive effects of KOR activation. Kinetic analysis of several neurotransmitters demonstrated that repeated swim stress exposure selectively increased the V_{max} but not K_m of SERT without affecting dopamine transport or the high-capacity, low-affinity transporters. Although the serotonergic neurons in the dorsal raphe project throughout the forebrain, a significant stress-induced increase in

cell-surface SERT expression was only evident in the ventral striatum, and not in the dorsal striatum, hippocampus, prefrontal cortex, amygdala, or dorsal raphe. Stereotaxic microinjections of the long-lasting KOR antagonist norbinaltorphimine demonstrated that local KOR activation in the nucleus accumbens, but not dorsal raphe, mediated this stress-induced increase in ventral striatal surface SERT expression. Together, these results support the hypothesis that stress-induced activation of the dynorphin/KOR system produces a transient increase in serotonin transport locally in the ventral striatum that may underlie some of the adverse consequences of stress exposure, including the potentiation of the rewarding effects of cocaine.

[The Context of Desire to use Marijuana: Momentary Assessment of Young People Who Frequently Use Marijuana.](#) Shrier LA, Walls CE, Kendall AD, Blood EA. *Psychol Addict Behav.* 2012 Dec; 26(4): 821-829.

Drawing on factors identified in the literature, this study explored in-the-moment associations of social, emotional, and temporal contexts and perceived marijuana availability with desire to use the drug, using momentary sampling methodology with young people who frequently use marijuana. Forty-one adolescent/young adult medical outpatients aged 15 to 24 years who reported using marijuana at least twice a week completed 2,912 brief questionnaires on a handheld computer in response to signals emitted at random four to six times a day for 2 weeks. The questionnaires assessed, for the moment when signaled, desire to use marijuana, location, companionship, perceived ease of getting marijuana (availability), positive affect, and negative affect. Participants reported any desire to use marijuana on 1,528 reports (55%). Companionship, perceived availability, and positive affect were independently associated with having any desire to use marijuana. Once desire to use marijuana was present, time of day, positive affect, and negative affect were independently associated with strength of desire. By collecting data in real time, in real life, this study highlights the importance of examining and intervening on emotional, environmental, and temporal contexts for youth who frequently use marijuana in order to reduce their desire to use the drug.

[Long-Term Influence of Normal Variation in Neonatal Characteristics on Human Brain Development.](#) Walhovd KB, Fjell AM, Brown TT, Kuperman JM, Chung Y, Hagler DJ Jr, Roddey JC, Erhart M, McCabe C, Akshoomoff N, Amaral DG, Bloss CS, Libiger O, Schork NJ, Darst BF, Casey BJ, Chang L, Ernst TM, Frazier J, Gruen JR, Kaufmann WE, Murray SS, van Zijl P, Mostofsky S, Dale AM. *Proc Natl Acad Sci U S A.* 2012 Dec 4; 109(49): 20089-20094.

It is now recognized that a number of cognitive, behavioral, and mental health outcomes across the lifespan can be traced to fetal development. Although the direct mediation is unknown, the substantial variance in fetal growth, most commonly indexed by birth weight, may affect lifespan brain development. The authors investigated effects of normal variance in birth weight on MRI-derived measures of brain development in 628 healthy children, adolescents, and young adults in the large-scale multicenter Pediatric Imaging, Neurocognition, and Genetics study. This heterogeneous sample was recruited through geographically dispersed sites in the United States. The influence of birth weight on cortical thickness, surface area, and striatal and total brain volumes was investigated, controlling for variance in age, sex, household income, and genetic ancestry factors. Birth weight was found to exert robust positive effects on regional cortical surface area in multiple regions as well as total brain and caudate volumes. These effects were continuous across birth weight ranges and ages and were not confined to subsets of the sample. The findings show that (i) aspects of later child and adolescent brain development are influenced at birth and (ii) relatively small differences in birth weight across groups and conditions typically compared in neuropsychiatric research (e.g., Attention Deficit Hyperactivity Disorder, schizophrenia, and personality disorders) may influence group differences observed in brain parameters of interest at a later stage in life. These findings should serve to increase our attention to early influences.

[Imaging Dopamine Transmission in the Frontal Cortex: a Simultaneous Microdialysis and \[\(11\)C\]FLB 457 PET Study.](#) Narendran R, Jedema HP, Lopresti BJ, Mason NS, Gurnsey K, Ruskiewicz J, Chen C-M, Deutch L, Frankle WG, Bradberry CW. *Molecular Psychiatry.* 2013. [Epub ahead of print].

In a recent human positron emission tomography (PET) study the authors demonstrated the ability to detect amphetamine-induced dopamine (DA) release in the prefrontal cortex as a reduction in the binding of the DA D(2/3) radioligand [(11)C]FLB 457. A key requirement for validating this paradigm for use in clinical studies is demonstrating that the changes in [(11)C]FLB 457 binding observed with PET following amphetamine are related to changes in dialysate DA concentration as measured with microdialysis. Microdialysis and PET experiments were performed to compare, in five rhesus monkeys, amphetamine-induced DA release and [(11)C]FLB 457 displacement in the frontal cortex after three doses of amphetamine (0.3 mg/kg, 0.5 mg/kg and 1.0 mg/kg). Amphetamine led to a significant dose-dependent increase in dialysate (0.3 mg/kg): $999 \pm 287\%$; 0.5 mg/kg): $1320 \pm 432\%$; 1.0 mg/kg): $2355 \pm 1026\%$ as measured with microdialysis and decrease in [(11)C]FLB 457 binding potential (BP(ND)) 0.3 mg/kg: $-6 \pm 6\%$; 0.5 mg/kg): $-16 \pm 4\%$; 1.0 mg/kg): $-24 \pm 2\%$ as measured with PET. The relationship between amphetamine-induced peak Δ DA and Δ [(11)C]FLB 457 BP(ND) in the frontal cortex was linear. The results of this study clearly demonstrate that the magnitude of dialysate DA release is correlated with the magnitude of the reduction in [(11)C]FLB 457 BP(ND) in the frontal cortex. The use of the [(11)C]FLB 457-amphetamine imaging paradigm in humans should allow for characterization of prefrontal cortical DA release in neuropsychiatric disorders such as schizophrenia and addiction.

[Brief Intervention for Drug-Abusing Adolescents in a School Setting: Outcomes and Mediating Factors.](#)

Winters KC, Fahnhorst T, Botzet A, Lee S, Lalone B. J Subst Abuse Treat. 2012 Apr; 42(3): 279-288.

This randomized controlled trial evaluated the use of two brief intervention conditions for adolescents (aged 12-18 years) who have been identified in a school setting as abusing alcohol and other drugs. Adolescents and their parents (N = 315) were randomly assigned to receive either a two-session adolescent-only (BI-A), two-session adolescent and additional parent session (BI-AP), or assessment-only control condition (CON). Interventions were manually guided and delivered in a school setting by trained counselors. Adolescents and parents were assessed at intake and at 6 months following the completion of the intervention. Analyses of relative (change from intake to 6 months) and absolute (status at 6 months) outcome variables indicated that for the most part, adolescents in the BI-A and BI-AP conditions showed significantly more reductions in drug use behaviors compared with the CON group. In addition, youth receiving the BI-AP condition showed significantly better outcomes compared with the BI-A group on several variables. Problem-solving skills and use of additional counseling services mediated outcome. The value of a school-based brief intervention for students is discussed.

NIH/HHS POLICY UPDATES

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

- April 19** [NIH Reminds Grantee Institutions of the Requirement to Use the Research Performance Progress Report \(RPPR\) for All SNAP and Fellowship Progress Reports for Awards with Start Dates On or After July 1, 2013](#)
- April 17** [Notice of Clarification of the Funded Extension Option in RFA-OD-13-199 "NIH Administrative Supplements to Recover Losses Due to Hurricane Sandy Under the Disaster Relief Appropriations Act Non-Construction \(Admin Supp\)"](#)
- April 16** [Discontinuation of Form Using the 1977 Office of Management and Budget \(OMB\) Racial Standards](#)
- April 9** [Reminder of NIH's Policy for Handling Electronic System Issues that Threaten On-Time Grant Application Submission](#)
- April 8** [FAQs for Costing of NIH-Funded Core Facilities](#)
- March 1** [Implementation of the Updated AVMA Guidelines for the Euthanasia of Animals: 2013 Edition](#)
- March 1** [Registration Now Open for the 2013 NIH Regional Seminar on Program Funding and Grants Administration in Baltimore, MD](#)
- February 28** [Notice of Correction to NOT-OD-13-010 "Advance Notice: Revised Policy for Managing Conflict of Interest in the Initial Peer Review of NIH Grant and Cooperative Agreement Applications"](#)
- February 21** [NIH Operation Plan in the Event of a Sequestration](#)
- February 21** [Notice of Change to Electronic Submission of Final Noncompliance Reports to the Office of Laboratory Animal Welfare](#)
- February 21** [Request for Information \(RFI\): Inviting Comments and Suggestions on the Implementation of the Recommendations of the Advisory Committee to the NIH Director Working Group on the Biomedical Research Workforce](#)
- February 14** [NIH Requires Use of RPPR for All SNAP and Fellowship Progress Reports, and Expands RPPR Functionality](#)

CONGRESSIONAL AFFAIRS

(Prepared April 24, 2013)

Appropriations

Last month, the President released the FY 2014 President's Budget. The sequester is not taken into account for purposes of this budget. For NIH, the FY 2014 request is \$31.3 billion, an increase of \$471 million, or 1.5 percent, over the enacted FY 2012 level. For NIDA, the FY 2014 request is \$1.072 billion, an increase of \$20.2 million, or approximately 2 percent over the enacted FY 2012 level.

113th Congress

The most relevant committee-related information for NIDA is listed below.

Senate The 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 (Crime and Terrorism Subcommittee); and the
- Caucus on International Narcotics Control (this is an officially recognized Caucus, established by law in 1985).

House The primary focus is on the:

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

Congressional Meetings/ Briefings

March 4, 2013, Congressman Joseph Kennedy – On March 4, Dr. Volkow met with newly-elected Representative Joseph Kennedy (D-MA) to discuss drug abuse and addiction issues in general, with a particular focus on prescription drug abuse and marijuana.

March 11, 2013, Capitol Hill Briefing – Military Personnel, Veterans, and Their Families: How Substance Abuse Research is Effecting Positive Change. This briefing was organized and sponsored by the Friends of NIDA and highlighted recent research relevant to military personnel, veterans and their families and efforts to address substance abuse issues in the military community. The briefing was the 18th in the coalition's [Charles R. Schuster Educational Briefing Series](#) on Capitol Hill, designed to educate policy makers about current initiatives and advancements in science funded by NIDA. Cosponsored by the Congressional Addiction, Treatment and Recovery Caucus, the Congressional Caucus on Prescription Drug Abuse and 23 member organizations of the Friends of NIDA, the briefing was attended by over 100 congressional staff, federal agency staff, and members of the science advocacy community. Presenters included Dr. Wilson Compton (Director, NIDA Division of Epidemiology, Services and Prevention Research), Dr. Michael Kilpatrick (Deputy Director for Force Health Protection and Readiness Programs at the Department of Defense), Dr. Abigail Gewirtz (University of Minnesota) and Dr. Kathleen Carroll (Yale University).

April 3, 2013, Congressman (and Appropriations Chairman) Hal Rogers (R-KY) – While at the second annual Rx Drug Summit, Dr. Volkow met with Representative Rogers to continue their discussions around prescription drug issues. They also met with several teens who had experienced a death in their family as the result of prescription drug addiction.

Bills of Interest

HR 486 – On February 4, 2013, Representative William Keating (D-MA) introduced the Stop Tampering of Prescription Pills act of 2013, to amend the Food, Drug and Cosmetic Act to incentivize the development of abuse-deterrent drugs. The bill was referred to the Committee on Energy and Commerce.

HR 498 – On February 5, 2013, Representative Lucille Roybal-Allard (D-CA) introduced a bill to reauthorize the Sober Truth on Preventing Underage Drinking (STOP) Act. Representatives Rosa DeLauro (D-CT), and Frank Wolf (R-VA) were the only two original co-sponsors of the legislation. The bill was referred to the House Committee on Energy and Commerce.

HR 499 – On February 5, Representative Jared Polis (D-CO) introduced the Ending Federal Marijuana Prohibition Act of 2013, to generally decriminalize and change the way the Controlled Substances Act is applied to marijuana. The bill was referred to the Committee on the Judiciary, the Committee on Ways and Means, the Committee on Energy and Commerce, the Committee on Natural Resources, and the Committee on Agriculture.

HR 672 -- On February 13, Representative Nick Rahall (D-WV) introduced the Prescription Drug Abuse Prevention and Treatment Act of 2013, to provide for increased federal oversight of prescription opioid treatment and assistance to states in reducing opioid abuse, diversion, and deaths. The bill was referred to the Committee on Energy and Commerce and the Committee on the Judiciary. See also S 348.

HR 1285 – On March 20, 2013, Representative Vern Buchanan (R-FL) introduced Safe Prescribing Act of 2013, to amend the Controlled Substances Act to make any substance containing hydrocodone a schedule II drug. The bill was referred to the Committee on the Judiciary. See also S 621.

HR 1523 – On April 12, 2013, Representative Dana Rohrbacher (R-CA) introduced the Respect State Marijuana Laws Act of 2013, to amend the Controlled Substances Act to provide for a new rule regarding the application of the Act to marijuana, and for other purposes. The bill was referred to the Committee on the Judiciary and the Committee on Energy and Commerce.

S 237 – On February 7, 2013, Senator Lisa Murkowski (R-AK) introduced the Advancing FASD (fetal alcohol spectrum disorders) Research, Prevention and Services Act, to amend the Public Health Service Act to reauthorize and extend the FAS prevention and services program, and for other purposes. The bill was referred to the Committee on Health, Education, Labor and Pensions.

S. 348 – On February 14, Senator John Rockefeller (D-WV) introduced the Prescription Drug Abuse Prevention and Treatment Act of 2013, to provide for increased federal oversight of prescription opioid treatment and assistance to states in reducing opioid abuse, diversion, and deaths. The bill was referred to the Committee on Health, Education, Labor and Pensions. See also HR 672.

S. 621 – On March 20, 2013, Senator Joe Manchin (D-WV) introduced the Safe Prescribing Act of 2013, to amend the Controlled Substances Act to make any substance containing hydrocodone a schedule II drug. The bill was referred to the Committee on the Judiciary. See also HR 1285.

S. 644 – On March 21, 2013, Senator Robert Casey (D-PA) introduced the Preventing Abuse of Cough Treatments Act of 2013, to amend the Food, Drug, and Cosmetic Act to prevent the abuse of dextromethorphan, and for other purposes. The bill was referred to the Committee on Health, Education, Labor, and Pensions.

FUNCTIONAL INTEGRATION

Functional Integration (FI): Although the planned structural reorganization of the NIH institutes supporting addiction-related research did not go forward, the call for a “functional integration” is being realized with the creation of a strong collaborative framework to enhance and expand activities related to substance use, abuse, and addiction research. Functional integration will enable ICs [especially NIDA, the National Institute on Alcohol Abuse and Alcoholism (NIAAA), and the National Cancer Institute (NCI)] to pool resources and expertise and better capitalize on synergies in addiction science, address research opportunities, and meet public health needs.

New FOAs Issued that Support the FI

On January 30, 2013, NIDA issued an RFA entitled **Prevention and Health Promotion Interventions to Prevent Alcohol and Other Drug Abuse and Associated Physical and Psychological Health Problems in U.S. Military Personnel, Veterans and their Families (R01)** [RFA-DA-13-012](#) (R34) [RFA-DA-13-013](#). The purpose of this RFA is to accelerate research on health promotion and prevention interventions with foci on reducing the onset and progression of alcohol, tobacco, and other drug use and abuse (including illicit and prescription drugs) and associated mental and physical health problems and on the promotion of health-enhancing behaviors among active-duty or recently separated (e.g., Iraq and Afghanistan) military troops, Veterans, and their families. Open date: April 1, 2013. Application due date(s): May 1, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

On March 27, 2013, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Research on Comparative Effectiveness and Implementation of HIV/AIDS and Alcohol Interventions (R01)** [RFA-AA-13-003](#) (R21) [RFA-AA-13-004](#). This new initiative seeks to advance knowledge of the effective implementation and comparative effectiveness of alcohol-focused interventions among HIV+ individuals. Multiple factors need to be investigated, including potentially important patient and provider characteristics, and the organizational, financial, and structural factors that facilitate or inhibit the delivery of evidence-based services for HIV+ individuals with a range of alcohol use disorders. Open date: April 29, 2013. Letter of Intent due date(s): April 29, 2013. Application due date(s): May 29, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): May 29, 2013, by 5:00 PM local time of applicant organization.

On April 12, 2013, NIAAA issued a PA entitled **Mechanisms of Alcohol and Nicotine Co-Addiction (R21)** [PA-13-193](#) (R01) [PA-13-194](#), which NIDA subsequently signed on to: ([NOT-DA-13-024](#)); ([NOT-DA-13-025](#)). This FOA encourages R21 or R01 applications from institutions/organizations that propose to study neurobiological and behavioral mechanisms contributing to concurrent alcohol and nicotine co-addiction. Open date: September 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.

FI Highlight: Upcoming Meeting

NIDA (DCNBR) and NIAAA are co-sponsoring a workshop: **Building the Next Generation of Integrative Approaches for Understanding Comorbid Alcohol, Drug Abuse, and Attention Disorders** in Rockville, MD – May 13-14, 2013.

PROGRAM ACTIVITIES/FOAS

New NIDA RFAs

On March 1, 2013, NIDA issued an RFA entitled **Short-term Mentored Career Enhancement Awards in the Basic Behavioral and Social Sciences (b-BSSR): Cross-Training at the Intersection of Animal Models and Human Investigation (K18)** [RFA-DA-14-002](#). This funding mechanism will support development of research capability in b-BSSR, with specific emphasis on cross-training and establishing collaborations between researchers with expertise in animal models of basic behavioral and social processes and those studying similar or related processes in human subjects. Open date: November 11, 2013. Application due date(s): December 11, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

On March 20, 2013, NIDA issued an RFA entitled **Advancing Exceptional Research on HIV/AIDS (R01)** [RFA-DA-14-003](#). This RFA will support highly innovative R01 applications on HIV/AIDS and drug abuse and will complement the Avant-Garde Award Program for HIV/AIDS research. The RFA focuses on innovative research projects that have the potential to open new areas of HIV/AIDS research and/or lead to new avenues for prevention and treatment of HIV/AIDS among substance abusers. Open date: July 1, 2013. Application due date(s): August 1, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): August 1, 2013, by 5:00 PM local time of applicant organization

On April 26, 2013, NIDA issued an RFA entitled **Medications Development Centers of Excellence Cooperative Program (U54)** [RFA-DA-14-004](#). This RFA solicits Specialized Center Cooperative Agreement (U54) applications to provide support for Medications Development Centers of Excellence (MDCE) with emphasis on clinical research directed towards the identification, evaluation, and development of safe and effective medications and biologics for treatment of substance use disorders (SUDs). Letter of Intent due date(s): July 15, 2013. Application due date(s): August 15, 2013. AIDS application due date(s): August 15, 2013.

New NIDA PAs

On March 28, 2013, NIDA issued a PAR entitled **NIDA Mentored Clinical Scientists Development Program Award in Drug Abuse and Addiction (K12)** [PAR-13-163](#). This PAR encourages applications for institutional research career development (K12) programs that propose to support intensive supervised research training and career development experiences for clinician scientists (scholars) leading to research independence in the area of drug abuse and addiction. Open date: May 12, 2013. Application due date(s): June 12, 2013; June 12, 2014; June 12, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): September 7, 2013; September 7, 2014; September 7, 2015, by 5:00 PM local time of applicant organization.

On April 5, 2013, NIDA issued a PAR entitled **Drug Abuse Dissertation Research (R36)** [PAR-13-182](#). The purpose of this PAR is to invite applications for support of drug abuse doctoral dissertation research. Open date: May 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.

New FOAs Issued by the NIH Roadmap

On March 4, 2013, the NIH Common Fund issued a Roadmap RFA entitled **NIH Director's Biomedical Research Workforce Innovation Award: Broadening Experiences in Scientific Training (BEST) (DP7)** [RFA-RM-12-022](#). The purpose of this is to seek, identify and support bold and innovative approaches to broaden graduate and postdoctoral training, such that training programs reflect the range of career options that trainees (regardless of funding source) ultimately may pursue and that are required for a robust biomedical, behavioral, social and clinical research enterprise. Open date: April 10, 2013. Letter of Intent due date(s): April 10, 2013. Application due date(s): May 10, 2013 by 5:00 PM local time of applicant organization.. AIDS application due date(s): Not applicable.

On March 7, 2013, the NIH Common Fund issued a Roadmap RFA entitled **Planning Grants for the NIH Building Infrastructure Leading to Diversity (BUILD) Initiative (P20)** [RFA-RM-13-001](#). The purpose of this FOA is to encourage organizations with experience in the mentorship of individuals underrepresented in the biomedical research workforce to submit planning grant applications for the NIH National Research Mentoring Network (NRMN). The NRMN will establish a nationwide consortium to provide networking and mentorship experiences for individuals from backgrounds underrepresented in biomedical research from the undergraduate to junior faculty level. Letter of Intent due date(s): April 10, 2013. Application due date(s): May 10, 2013. AIDS application due date(s): Not applicable.

On March 7, 2013, the NIH Common Fund issued a Roadmap RFA entitled **Planning Grants for the NIH National Research Mentoring Network (NRMN) (P20)** [RFA-RM-13-002](#). The purpose of this FOA is to encourage institutions with expertise and innovative strategies for developing research and mentoring opportunities for undergraduate students from backgrounds underrepresented in biomedical research to submit applications for 6 month planning grants for the NIH Building Infrastructure Leading to Diversity (BUILD) initiative. The BUILD initiative aims to increase the diversity of the NIH-funded workforce by supporting collaborative programs that include novel approaches for enhancing undergraduate education, training, and mentorship, as well as infrastructure support and faculty development to facilitate those approaches. Letter of Intent due date(s): April 10, 2013. Application due date(s): May 10, 2013. AIDS application due date(s): Not applicable.

On April 2, 2013, the NIH Common Fund issued a Roadmap RFA entitled **Undiagnosed Diseases Gene Function Research (R21) [RFA-RM-13-003](#)**. The purpose of this FOA is to support gene function studies in collaboration with the Undiagnosed Diseases Network (UDN) building upon the NIH Intramural Research Program's Undiagnosed Diseases Program (NIH-UDP). Open date: May 14, 2013. Application due date(s): June 14, 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 issued an administrative supplement entitled **Research on Marijuana Legalization in the US (Admin Supp) [PA-13-138](#)**. The NIDA announces the availability of administrative supplements to inform social, behavioral, and public health impacts of recent US marijuana legalization laws/policies. Open date(s): April 30, 2013. Application due date(s): May 31, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

On April 15, 2012, NIDA, in collaboration with numerous other NIH components, issued an administrative supplement entitled **NIH Administrative Supplements to Recover Losses Due to Hurricane Sandy Under the Disaster Relief Appropriations Act Non-Construction (Admin Supp) [RFA-OD-13-199](#)**. The purpose of this funding opportunity is for investigators and institutions impacted by Hurricane Sandy and with active NIH grants to request: 1) a 24-month extension of the current budget period, with 12-months of funding at the same funding level as the current year of the grant; and/or, 2a) one-time administrative supplements of up to \$50,000 in direct costs (excluding consortium F&A costs) to replace lost and/or damaged research resources; and/or 2b) up to \$100,000 to replace a single item of equipment so long as that request is accompanied by well-documented support for the need to replace that item of equipment. Open date(s): May 12, 2013. Application due date(s): June 12, 2013; January 14, 2014. AIDS application due date(s): June 12, 2013; January 14, 2014.

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

On March 8, 2013, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Lasker Clinical Research Scholars Program (Si2) [RFA-OD-13-004](#)**. This RFA solicits applications for the Lasker Clinical Research Scholars Program for the purpose of supporting the research activities during the early stage careers of independent clinical researchers. Letter of Intent due date(s): May 24, 2013. Application due date(s): June 24, 2013. AIDS application due date(s): Not applicable.

On March 8, 2013, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Limited Competition - Multicenter AIDS Cohort Study: Center for the Coordination, Analysis, and Management of the MACS (CAMACS) (UM1) [RFA-AI-13-010](#)**. The purpose of this RFA is to renew the Center for the Coordination, Analysis, and Management of the Multicenter AIDS Cohort Study (CAMACS), and continue support for clinical, epidemiologic and basic research on a cohort of men who report sex with men (MSM). The MACS will continue to characterize the long-term, natural and treated history of HIV infection in MSM, provide insight into the clinical epidemiology of HIV, and further our understanding of predictors of disease among HIV positive MSM. Letter of Intent due date(s): June 11, 2013. Application due date(s): July 11, 2013. AIDS application due date(s): July 11, 2013.

On March 8, 2013, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Limited Competition Multicenter AIDS Cohort Study (MACS) Clinical Research Sites (U01) [RFA-AI-13-011](#)**. The purpose of this RFA is to renew the clinical research sites (CRSs) of the Multicenter AIDS Cohort Study (MACS) and continue support for clinical, epidemiologic and basic research on a cohort of men who report sex with men (MSM). The MACS will continue to characterize the long-term, natural and treated history of HIV infection in MSM, provide insight into the clinical epidemiology of HIV, and further our understanding of predictors of disease among HIV positive MSM. Open date: June 11, 2013. Letter of Intent due date(s): June 11, 2013. Application due date(s): July 11, 2013. AIDS application due date(s): July 11, 2013, by 5:00 PM local time of applicant organization.

On March 12, 2013, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Pilot Projects on Sports-Related Brain and Spinal Cord Injury (R21) [RFA-NS-13-014](#) (R03) [RFA-NS-13-015](#)**. This initiative will support pilot projects on sports-related traumatic brain injury and spinal cord injury. Open date: April 14, 2013. Letter of Intent due date(s): April 14, 2013. Application due date(s): May 14, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

On March 13, 2013, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Collaborative Research on Chronic Traumatic Encephalopathy and Delayed Effects of Traumatic Brain Injury:**

Neuropathology and Neuroimaging Correlation (U01) [RFA-NS-13-013](#). The initiative will support a multicenter, systematic and comprehensive investigation of the neuropathology of Chronic Traumatic Encephalopathy and the delayed effects of traumatic brain injury using postmortem biospecimens, and histological and neuroimaging tools as a foundation for future studies to develop in vivo diagnostics. Open date: April 14, 2013. Letter of Intent due date(s): April 14, 2013. Application due date(s): May 14, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

On March 20, 2013, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Limited Competition: Revision Applications for Basic Social and Behavioral Research on the Social, Cultural, Biological, and Psychological Mechanisms of Stigma (R01) [RFA-MD-13-005](#).** This RFA encourages revision applications to incorporate basic research on behavioral and social mechanisms underlying stigma into active R01 research projects. Open date: July 2, 2013. Letter of Intent due date(s): July 2, 2013. Application due date(s): August 2, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): August 2, 2013.

On March 27, 2013, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Eradication of HIV-1 from CNS Reservoirs: Implications for Therapeutics (R01) [RFA-MH-14-170](#) (R21) [RFA-MH-14-171](#).** This RFA invites research grant applications to address the problem of HIV-1 persistence focused solely on the central nervous system (CNS) of HIV-infected persons treated with Highly Active Anti-Retroviral Therapy (HAART). Open date: August 17, 2013. Letter of Intent due date(s): August 17, 2013. Application due date(s): September 17, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): September 17, 2013, by 5:00 PM local time of applicant organization.

On April 15, 2013, NIDA, in collaboration with numerous other NIH components, issued an RFA entitled **Limited Competition: Restoration of New Investigator Pilot Projects Adversely Affected by Hurricane Sandy (R21) [RFA-OD-13-005](#).** This RFA solicits applications from research institutions damaged as a result of Hurricane Sandy for the purpose of supporting recovery and restoration of new and early stage investigator pilot research and data destroyed or damaged as a result of the hurricane. Open date: May 19, 2013. Letter of Intent due date(s): May 19, 2013. Application due date(s): June 19, 2013, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

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

On February 1, 2013, NIDA, in collaboration with numerous other NIH components, issued a PAR entitled **NIH Summer Research Experience Programs (R25) [PAR-13-104](#).** The purpose of the NIH Summer Research Experience Program (referred to as the “Summer Research Program”) is to provide a high quality research experience for high school and college students and for science teachers during the summer academic break. The NIH expects that such programs will: help attract young students to careers in science; provide opportunities for college students to gain valuable research experience to help prepare them for graduate school; and enhance the skills of science teachers and enable them to more effectively communicate the nature of the scientific process to their students. The programs would also contribute to enhancing overall science literacy. Open date(s): March 2, 2013. Application due date(s): April 2, 2013; April 2, 2014; April 2, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): May 21, 2013, May 21, 2014 and May 21, 2015 by 5:00 PM local time of applicant organization.

On February 15, 2013, NIDA, in collaboration with numerous other NIH components, issued a PA entitled **Mechanisms, Models, Measurement, & Management in Pain Research (R03) [PA-13-117](#) (R01) [PA-13-118](#) (R21) [PA-13-119](#).** The purpose of this PA is to inform the scientific community of the pain research interests of the various Institutes and Centers (ICs) at the National Institutes of Health (NIH) and to stimulate and foster a wide range of basic, clinical, and translational studies on pain as they relate to the missions of these ICs. Open date(s): May 16, 2013. Application due date(s): [Standard dates](#), 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 March 6, 2013, NIDA, in collaboration with numerous other NIH components, issued a PAR entitled **High Throughput Screening (HTS) to Discover Chemical Probes (X01) [PAR-13-134](#) (R03) [PAR-13-135](#).** This Resource Access Opportunity is to promote and support discovery and development of new chemical probes as research tools for use by the research community to advance the understanding of biological functions and disease mechanisms. The announcement encourages partnership between assay submitters and a funded High Throughput Screening (HTS)/chemical probe discovery facility to conduct the joint research. Open date(s): March 4, 2013. Application due date(s): August 6, 2013; December 4, 2013; April 4, 2014; August 6, 2014; December 4, 2014; April

3, 2015; August 6, 2015; December 4, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not applicable.

On March 8, 2013, NIDA, in collaboration with numerous other NIH components, issued a PAR entitled **Bioengineering Research Grants (BRG) (R01) [PAR-13-137](#)**. The purpose of this PAR is to encourage collaborations between the life and physical sciences that: 1) apply a multidisciplinary bioengineering approach to the solution of a biomedical problem; and 2) integrate, optimize, validate, translate or otherwise accelerate the adoption of promising tools, methods and techniques for a specific research or clinical problem in basic, translational, or clinical science and practice. Open date(s): May 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.

On March 13, 2013, NIDA, in collaboration with numerous other NIH components, issued a PA entitled **Development of Highly Innovative Tools and Technology for Analysis of Single Cells (SBIR) (R43/R44) [PA-13-140](#)**. This PA encourages Small Business Innovation Research (SBIR) research grant applications to develop next-generation tools that distinguish heterogeneous states among cells and have commercial potential. Open date(s): July 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.

On March 25, 2013, NIDA, in collaboration with numerous other NIH components, issued a PA/PAR entitled **Development and Application of PET and SPECT Imaging Ligands as Biomarkers for Drug Discovery and for Pathophysiological Studies of CNS Disorders (R21) [PA-13-157](#) (R21/R33) [PAR-13-158](#)**. This PA/PAR invites research grant applications from organizations/institutions that propose the development of novel radioligands for positron emission tomography (PET) or single photon emission computed tomography (SPECT) imaging in human brain, and that incorporate pilot or clinical feasibility evaluation in pre-clinical studies, model development, or clinical studies. Open date(s): May 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.

On April 25, 2013, NIDA, in collaboration with numerous other NIH components, issued a PAR entitled **Limited Competition: Fogarty HIV Research Training Program for Low-and Middle-Income Country Institutions (D43) [PAR-13-126](#)**. The purpose of this PAR is to encourage applications for research training programs to develop and strengthen the scientific leadership and expertise needed for HIV-related research at eligible Low-and Middle-Income Country (LMIC) institutions. Open date(s): June 24, 2013. Application due date(s): July 24, 2013, July 24, 2014, July 30, 2015, by 5:00 PM local time of applicant organization. AIDS application due date(s): July 24, 2013, July 24, 2014, July 30, 2015 by 5:00 PM local time of applicant organization.

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

No new FOAs issued in Collaboration with the FDA Center for Tobacco Products.

NIDA COMMUNICATIONS

Publications and Online Resources

[Substance Abuse in the Military \(DrugFacts\)](#)

Published March 2013.

Offers an overview of trends of drug use in the military and the special risks faced by this population. [En Español](#)

NIDA's Teen website (www.teens.drugabuse.gov) launched a new design.

Select Meetings and Conferences in which NIDA played a significant role

On February 4-7, 2013, NIDA participated in a number of sessions at the [Community Anti-Drug Coalitions of America \(CADCA\) National Leadership Forum](#). Dr. Ruben Baler presented two workshops; one to CADCA's youth

leadership group titled, ***Giving Youth a Scientific Voice*** designed to empower young leaders with essential information about the connections between our brains and our behaviors, and the second to the general audience titled, ***Where Do Addictions Come From?*** Dr. Jack Stein, Dr. Gaya Dowling and Carol Krause participated in a “Power Session” on ***Using Science to Prevent Drug Abuse: What’s New From NIDA?*** This session highlighted some of the latest findings from NIDA-supported research of relevance to community coalitions. New educational resources developed by NIDA, such as the “Family Check-Up” and outcomes of the most recent National Drug Facts Week were presented. Lastly, Dr. Harold Perl and NIDA researcher Dr. Richard Spoth presented, ***The PROSPER Model: Implementing Effective Prevention Interventions in Local Communities -- A National Institute on Drug Abuse (NIDA) Research-to-Practice Workshop***. NIDA also held an Invitational Forum to discuss and receive feedback on a draft of the proposed publication titled ***Early Childhood Interventions for the Prevention of Drug Abuse: A Research Guide***.

On February 26-27, 2013, Dr. Jag Khalsa, DPMCD, and Dr. Wilson M. Compton, DESPR, participated in a **Technical Consultation on HCV Infection in Young IDUs** in Washington, DC. They worked with Dr. Ron Valdiserri, Deputy Asst. Sec Health, Ms. Corinna Dan and other members of OASH, non-federal academic researchers, federal scientists from NIAID, NIDDK, NIDA, CDC, and SAMHSA, and various public health officials from the Appalachian region states – an area hard hit by HCV infections in young IDUs. The meeting was co-funded by NIAID, NIDA, and SAMHSA, and discussions led to numerous recommendations for additional research. A manuscript co-authored by the participating federal staff is in preparation.

On March 9, 2013, Dr. Gayathri Dowling, Chief, Science Policy Branch, OSPC, participated on a panel **[“Raising Meth Addiction Awareness through Film”](#)** at the DC Independent Film Festival. The discussion followed the world premiere of METH HEAD, the first feature film to offer an honest and compelling portrayal of a methamphetamine addict. Other panelists included representatives from SAMHSA, Faces and Voices of Recovery, the Entertainment Industries Council, Jane Clark, the filmmaker, and John W. McLaughlin, one of the film’s producers and the inspiration for the METH HEAD story.

On March 12, 2013, NIDA participated in the **[14th annual Brain Awareness Week](#)** activities at the National Museum of Health and Medicine. NIDA sponsored **“NIDA Brain Derby,”** an interactive fast-moving game designed to teach children about drugs of abuse and neuroscience. Drs. Cathrine Sasek, Dave Thomas, Roger Sorensen, Mary Kautz, Rik Kline, and Dave White took part in the events.

On March 16, 2013, Dr. Joni Rutter, Acting Director, DBNBR, organized two symposia at the **[Society for Research on Nicotine and Tobacco \(SRNT\)](#)** to promote recent findings in basic science. **Symposium 1** – Bench to bedside: translation of basic, pre-clinical and -omics-based discovery to prevention and treatment of smoking and smoking related disease, with Drs. Thorgeir Thorgeirsson, Laura Bierut, Chris Amos, and Andrew Bergen. **Symposium 2** – Mice to men: basic science and preclinical research informing drug discovery and development through novel molecular targets, with Drs. Marina Piccioto, Paul Kenny, Elliot Hong, and Ron Hart.

In April 2013, Operation Unite hosted the **[Second Annual Prescription Drug Abuse Summit](#)** to facilitate meaningful dialogue and cooperation in addressing the prescription drug abuse epidemic. Multiple stakeholders and representatives from Federal government, advocacy, and constituent organizations attended, drawing more than 800 participants. Sessions were organized into six educational tracks tailored to provide stakeholders timely and relevant information for their particular field. Keynote speakers included Congressmen Hal Rogers, Michael Grimm, Daniel Webster, Nick Rahall, and Bill Keating; ONDCP Director Gil Kerlikowske; CDC Director Thomas Frieden; FDA Administrator Margaret Hamburg; Mayor Michael Bloomberg; CSAP Director Fran Harding, DEA Deputy Assistant Administrator Joe Rannazzisi, Florida Attorney General Pam Bondi; and NIDA Director Nora Volkow.

On April 3 & 4, 2013, Drs. Lisa Onken, DCNBR, Wilson Compton, DESPR, and Varda Shoham, NIMH, co-chaired a meeting, **[“Improving Smoking Cessation Treatment for People with Schizophrenia,”](#)** in Bethesda, MD. The meeting was co-sponsored by NIMH and NCI, and the planning committee included Drs. Bill Riley and Yvonne Hunt (NCI); Debra Grossman, Petra Jacobs, Ivan Montoya, Jeff Schulden, and Kay Wanke (NIDA); Susan Azrin, Amy Goldstein, Denise Juliano-Bult, & Sarah Morris (NIMH). The state of the science of smoking cessation treatment for individuals with schizophrenia was discussed, as well as gaps and opportunities in the field.

On April 25, 2013, NIDA sponsored a series of activities at the NSC and on the NIH main campus in recognition of **[Take Your Child to Work Day](#)**. In addition, this year NIMH partnered with NIDA to include two activities, **The Brain Collector**, which featured Archie Fobbs from the National Museum of Health and Medicine and **See Your BRAIN in Action**. NIDA and NIMH staff who developed and led the activities included Drs. Cathrine Sasek, Mary Kautz, Sheri

Grabus, and Dave Thomas, as well as Stephanie Older, Quandra Scudder, Hirsch Davis and Phyllis Quartey-Ampofo.

On April 25 – 26, 2013, Flair Lindsey from NIDA's Special Populations Office (SPO) coordinated the **Research Development Seminar Series Workshop "Mock Review"** for early career scholars to learn about the NIH grant review process.

On May 14, 2013, Dr. Cathrine Sasek, Science Policy Branch, OSPC, gave a presentation titled "Update: Science Education Drug Abuse Partnership Award (SEDAPA)" at the annual NIH science education conference, "[NIH SciEd 2013: Annual Conference for NIH Science Education Projects Implementing the Framework for K-12 Education and the Next Generation Science Standards.](#)" In addition, she participated with the NIH Office of Science Education in a National Science Teachers Association webinar titled "**Hands-on Life Science for Your [Next Generation Science Standards \(NGSS\) Classroom](#)**" on May 7, 2013.

Upcoming Conferences/Exhibits

[American Psychiatric Association Annual Meeting](#) – San Francisco, CA – May 18-22, 2013.

[College on Problems of Drug Dependence \(CPDD\) Annual Scientific Meeting](#) – San Diego, California – June 15–20, 2013.

Community and Press Events

January 28, 2013 - [National Drug Facts Week events now in all 50 states](#)

February 14, 2013 - [Prevention efforts focused on youth reduce prescription abuse into adulthood](#)

February 28, 2013 - [Dr. Nora Volkow appeared with Katie Couric on her show *Katie* to answer questions about teen drug abuse.](#)

March 14, 2013 - [Prior marijuana use could increase addictive power of nicotine](#)

March 26, 2013 - [NIDA research shines light on a potential target for cocaine addiction](#)

March 27, 2013 - [Genes linked to hepatitis C viral clearance could lead to personalized treatments](#)

April 3, 2013 - [NIH study sheds light on how to reset the addicted brain](#)

HONORS AND AWARDS

Grantee Honors and Awards

Dr. Tor Wager, University of Colorado at Boulder, was selected to receive the Cognitive Neuroscience Society's Young Investigator Award at their annual meeting held April 13-16, 2013 in San Francisco, CA.

Dr. James Sorensen, co-director of the Western States Node and Professor of Psychiatry at the University of California, San Francisco is the recipient of The College on Problems of Drug Dependence (CPDD) Mentorship

Award for 2013. Dr. Sorensen will receive the award at CPDD's 75th Annual Meeting in San Diego, California, June 15-20, 2013.

STAFF CHANGES

New Appointments/Transfers

Dr. Mark Swieter is serving as Acting Director, Office of Extramural Affairs (OEA).

Stephanie Older, J.D., has been named Deputy Branch Chief, Public Information and Liaison Branch (PILB), Office of Science Policy and Communications (OSPC).

Sheri Grabus, Ph.D., has been named Acting Press Officer, PILB, OSPC.

Drs. Cora Lee Wetherington and **Samia Noursi** have recently moved from the Division of Basic Neuroscience and Behavioral Research (DBNBR) to join the Division of Clinical Neuroscience and Behavioral Research (DCNBR) where they will continue to advance NIDA's Women and Sex/Gender Research Program.

New Employees

Kate Bent, RN, PhD, CNS, joined NIDA on February 25, 2013 as the new Deputy Director of the Office of Extramural Affairs (OEA). Before coming to NIDA, Dr. Bent was at the NIH Center for Scientific Review (CSR) where she was Senior Advisor to the Director, responsible for advising on strategic planning, budget, analysis, integration, and policy. Prior to that, she served as the Chief of CSR's Healthcare Delivery and Methodologies (HDM) Integrated Review Group. She came to NIH from the Department of Veterans Affairs central office in Washington, D.C., where she served as Scientific Program Manager for health services research in the Office of Research and Development. Previously, Dr. Bent held a clinical research position at the Denver VA Medical Center, where her work focused on transitions and caring for patients with complex chronic conditions. She held a faculty appointment at the University of Colorado Health Sciences Center, where she taught Health Policy and Applied Epidemiology. Dr. Bent, a past president of the Council on Nursing and Anthropology, has published extensively in areas of clinical research, theory, health policy, public health, and translation and implementation of research. Dr. Bent earned her Ph.D. from the University of Colorado at Denver and is an advanced practice registered nurse with specializations in complex illness and home and community health.

Gregg Friedman joined NIDA on March 11, 2013 as the new Chief Information Officer and Chief of the Information and Resource Management Branch within the Office of Management. Prior to coming to NIDA, Gregg was a Project Manager and Leader in the NIH Business System (NBS) Office where over the past 5 years he has overseen systems architecture and enterprise software delivery across the organization. Prior to that, he served as a Senior Business Consultant in the Oracle Solutions Group at BearingPoint, Inc., and provided integral expertise and leadership on the implementation and stabilization for the HHS Program Support Center's Unified Financial Management System. Gregg earned a MIS and Finance degree in Business Administration from the George Washington University, holds Project Management Professional and Contract Officer certifications, and brings over 10 years of combined experience in project management, strategic analysis, systems architecture and integration, and premier service support.

Christopher Belt joined the Office of Acquisitions' Consolidated Station Support/Simplified Acquisitions Branch as a Supervisory Contract Specialist and Branch Chief on March 11, 2013. Prior to coming to NIDA, Christopher was with the NIH Clinical Center.

Mario Gray joined the Office of Acquisitions' Consolidated Station Support/Simplified Acquisitions Branch as a Contract Specialist on February 10, 2013. Mario holds a BA with majors in Political Science and Economics. Prior to coming to NIDA he served with the Food and Drug Administration.

Nathaniel Fredericks joined NIDA's Management Analysis Branch within the Office of Management as a Management Analyst on February 24, 2013. Prior to coming to NIDA he served with the HHS Program Support Center.

William Etti joined NIDA's Management Analysis Branch within the Office of Management as a Management Analyst on February 24, 2013. William holds Master of Science in Management and Master of Business Administration degrees from the University of Maryland and has 12 years of work experience at the NIH in multiple aspects of business operations. Prior to coming to NIDA, he worked at the Clinical Center, Office of Purchasing and Contracts.

Raymond Hawkins, Jr. joined NIDA's Administrative Management Branch (AMB) under the NIDA Office of Management as a Management Analyst on March 11, 2013. Ray holds a BS in Financial Economics with a minor in Public Administration from the University of Maryland, Baltimore County (UMBC) and an MBA in Management from the University of Maryland, University College (UMUC). Prior to coming to NIDA, Ray served as the primary senior contracting officer to several NIH Office of the Director (OD) programs (e.g., NIH Business Systems Office), where he was responsible for the strategic planning, managing, oversight and justification of various contract requirements in the areas of: professional consulting support services, enterprise-wide business management solutions and information technology (IT) support systems.

Andrea McGee joined the Office of Acquisitions' Consolidated Station Support/Simplified Acquisitions Branch as a Lead Contract Specialist on April 21, 2013. Andrea holds a BA in Public Administration. Prior to coming to NIDA she worked for the Clinical Center as a Contract Specialist, Invoice Specialist and the Back-up Purchase Card Coordinator.

Dr. Mark Verdecia joined the Optogenetics and Transgenic Technology Core facility at the IRP and oversees the Protein Discovery and Engineering program.

Dr. Mark Henderson was appointed as a Research Fellow in the Glia-Neuron Interactions (GNI) lab at the IRP.

Departures

Dr. Meena Hiremath, OEA, left NIDA March 23, 2013 to become the Director of NHLBI's Office of Extramural Policy and Training. Meena began her career at NIDA as a Scientific Review Officer for NIDA-F, the Health Services Review Committee. She subsequently became the NIDA Receipt and Referral Officer, and in that position she was instrumental in working with NIDA colleagues to develop the referral decision tree to make referral more reliable, transparent and efficient. She also was the staff liaison for two important Council workgroups, the Diversity and Health Disparities Council Review Work Group and the Adoption of NIDA's Evidence-based Treatments in Real World Settings Work Group, where her organizational and writing skills were much appreciated by the Council workgroup members and staff.

Idella Simpson, a Contract Specialist in the Office of Acquisitions' Consolidated Station Support/Simplified Acquisitions Branch transferred to NIMH on March 23, 2013.

James Deloso, an IT Specialist in NIDA's Information Resources Management Branch within the Office of Management left NIDA on April 6, 2013 to take a position with the Department of State.

Lisa Gerring, an Extramural Support Assistant in DPMCDAs resigned from her position at NIDA on April 19, 2013.

Joseph Tam Lung, a Contract Specialist in the Office of Acquisitions' Contracts Management Branch left NIDA on April 20, 2013 for a position in DHHS/ASPR.

Retirements

Susan Schlossberg retired on January 31, 2013 after 23 years of Federal service, the last 20 of which were with NIDA. Sue began her career at NIMH, transferred to ADAMHA's Office of the Administrator, and then returned to assume several positions at NIMH including Executive Assistant to the Deputy Director and later, Executive Assistant to the NIMH Acting Director. Sue came to NIDA in 1994 where she skillfully managed the day-to-day administrative operations within the Office of the Director. Over the past two decades she has also served as Staff Assistant to several NIDA Directors with resourcefulness and outstanding dedication. During her tenure at NIDA, Sue received multiple professional awards including the NIDA Directors Award in 2011, which recognized her impact on enhancing the organizational operations of the Office of the Director. In addition to the significant administrative contributions she has made while at NIDA, Sue has also used her creative talents to help promote the Institute's mission in many other ways, most notably in the design of graphics for NIDA's "Principles of Drug Abuse Treatment" booklet as well as other drug abuse treatment-related materials.

Anne Jarrett, OEA, retired from Federal service on February 28, 2013. Anne Jarrett worked at NIDA for 12 years, first within the OD, and for the last 6 years, in the Office of Extramural Affairs. While in OEA, she served as Program Analyst and special assistant to the Director of OEA. Anne was known for her tenacity, organizational skills, and willingness to take on new tasks, such as organizing the Certificates of Confidentiality, working with members of the Advisory Council on travel and related matters, and serving as office manager.