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 2014 Staff Report to the Director.*

RESEARCH HIGHLIGHTS

Parental THC Exposure Leads to Compulsive Heroin-Seeking and Altered Striatal Synaptic Plasticity in the Subsequent Generation Szutorisz H, Dinieri JA, Sweet E, Egervari G, Michaelides M, Carter JM, Ren Y, Miller ML, Blitzer RD, Hurd YL. Neuropsychopharmacology 2014.
Recent attention has been focused on the long-term impact of cannabis exposure, for which experimental animal studies have validated causal relationships between neurobiological and behavioral alterations during the individual's lifetime. Here, the authors show that adolescent exposure to Δ^9-tetrahydrocannabinol (THC), the main psychoactive component of cannabis, results in behavioral and neurobiological abnormalities in the subsequent generation of rats as a consequence of parental germline exposure to the drug. Adult F1 offspring that were themselves unexposed to THC displayed increased work effort to self-administer heroin, with enhanced stereotyped behaviors during the period of acute heroin withdrawal. On the molecular level, parental THC exposure was associated with changes in the mRNA expression of cannabinoid, dopamine, and glutamatergic receptor genes in the striatum, a key component of the neuronal circuitry mediating compulsive behaviors and reward sensitivity. Specifically, decreased mRNA and protein levels, as well as NMDA receptor binding were observed in the dorsal striatum of adult offspring as a consequence of germline THC exposure. Electrophysiologically, plasticity was altered at excitatory synapses of the striatal circuitry that is known to mediate compulsive and goal-directed behaviors. These findings demonstrate that parental history of germline THC exposure affects the molecular characteristics of the striatum, can impact offspring phenotype, and could possibly confer enhanced risk for psychiatric disorders in the subsequent generation.

Synaptic Depression Via Mglur1 Positive Allosteric Modulation Suppresses Cue-Induced Cocaine Craving Loweth JA, Scheyer AF, Milovanovic M, LaCrosse AL, Flores-Barrera E, Werner CT, Li X, Ford KA, Le T, Olive M F, Szumlinski KK, Tseng KY, Wolf ME. Nat Neurosci. 2014: 17(1): 73-80.
Cue-induced cocaine craving is a major cause of relapse in abstinent addicts. In rats, cue-induced craving progressively intensifies (incubates) during withdrawal from extended-access cocaine self-administration. After ~1 month of withdrawal, incubated craving is mediated by Ca(2+)-permeable AMPA receptors (CP-AMPARs) that accumulate in the nucleus accumbens (NAc). The authors found that decreased mGluR1 surface expression in the NAc preceded and enabled CP-AMPAR accumulation. Thus, restoring mGluR1 transmission by administering repeated injections of an mGluR1 positive allosteric modulator (PAM) prevented CP-AMPAR accumulation and incubation, whereas blocking mGluR1 transmission at even earlier withdrawal times accelerated CP-AMPAR accumulation. In studies conducted after prolonged withdrawal, when CP-AMPAR levels and cue-induced craving are high, the authors found that systemic administration of an mGluR1 PAM attenuated the expression of incubated craving by reducing CP-AMPAR transmission in the NAc to control levels. These results suggest a strategy in which recovering addicts could use a systemically active compound to protect against cue-induced relapse.

Designer Receptors Show Role For Ventral Pallidum Input To Ventral Tegmental Area In Cocaine Seeking Mahler SV, Vazey EM, Beckley JT, Keistler CR, McGlinchey EM, Kaufling J, Wilson SP, Deisseroth K, Woodward JJ, Aston-Jones G. Nat Neurosci. 2014 Apr; 17(4): 577-585.
The ventral pallidum is centrally positioned within mesocorticolimbic reward circuits, and its dense projection to the ventral tegmental area (VTA) regulates neuronal activity there. However, the ventral pallidum is a heterogeneous structure, and how this complexity affects its role within wider reward circuits is unclear. The authors found that projections to VTA from the rostral ventral pallidum (RVP), but not the caudal ventral pallidum (CVP), were robustly Fos activated during cue-induced reinstatement of cocaine seeking-a rat model of relapse in addiction. Moreover, designer receptor-mediated transient inactivation of RVP neurons, their terminals in VTA or functional connectivity between RVP and VTA dopamine neurons blocked the ability of drug-associated cues (but not a cocaine prime) to reinstate cocaine seeking. In contrast, CVP neuronal inhibition blocked cocaine-primed, but not cue-induced, reinstatement. This double

dissociation in ventral pallidum subregional roles in drug seeking is likely to be important for understanding the mesocorticolimbic circuits underlying reward seeking and addiction.

Targeted Expression Of μ -Opioid Receptors In A Subset Of Striatal Direct-Pathway Neurons Restores Opiate Reward Cui Y, Ostlund SB, James AS, Park CS, Ge W, Roberts KW, Mittal N, Murphy NP, Cepeda C, Kieffer BL, Levine MS, Jentsch JD, Walwyn WM, Sun YE, Evans CJ, Maidment NT, Yang X W. Nat Neurosci. 2014; 17(2): 254-261.
μ-opioid receptors (MORs) are necessary for the analgesic and addictive effects of opioids such as morphine, but the MOR-expressing neuronal populations that mediate the distinct opiate effects remain elusive. Here the authors devised a new conditional bacterial artificial chromosome rescue strategy to show, in mice, that targeted MOR expression in a subpopulation of striatal direct-pathway neurons enriched in the striosome and nucleus accumbens, in an otherwise MOR-null background, restores opiate reward and opiate-induced striatal dopamine release and partially restores motivation to self administer an opiate. However, these mice lack opiate analgesia or withdrawal. The authors used Cre-mediated deletion of the rescued MOR transgene to establish that expression of the MOR transgene in the striatum, rather than in extrastriatal sites, is needed for the restoration of opiate reward. This study demonstrates that a subpopulation of striatal direct-pathway neurons is sufficient to support opiate reward-driven behaviors and provides a new intersectional genetic approach to dissecting neurocircuit-specific gene function in vivo.

Nicotinic Receptors Regulate the Dynamic Range Of Dopamine Release In Vivo Koranda JL, Cone JJ, McGehee DS, Roitman MF, Beeler JA, Zhuang X. J Neurophysiol 2014; 111(1): 103-111.
Nicotinic acetylcholine receptors (nAChRs) are expressed presynaptically on dopamine axon terminals, and their activation by endogenous acetylcholine from striatal cholinergic interneurons enhances dopamine release both independently of and in concert with dopamine neuron activity. Acute nAChR inactivation is believed to enhance the contrast between low- and high-frequency dopamine cell activity. Although these studies reveal a key role for acute activation and inactivation of nAChRs in striatal microcircuitry, it remains unknown if chronic inactivation/desensitization of nAChRs can alter dopamine release dynamics. Using in vivo cyclic voltammetry in anaesthetized mice, the authors examined whether chronic inactivation of nAChRs modulates dopamine release across a parametric range of stimulation, varying both frequency and pulse number. Deletion of β2*nAChRs and chronic nicotine exposure greatly diminished dopamine release across the entire range of stimulation parameters. In addition, they observed a facilitation of dopamine release at low frequency and pulse number in wild-type mice that is absent in the β2* knockout and chronic nicotine mice. These data suggest that deletion or chronic desensitization of nAChRs reduces the dynamic range of dopamine release in response to dopamine cell activity, decreasing rather than increasing contrast between high and low dopamine activity.

Functional Status of the Serotonin 5-HT2C Receptor (5-HT2CR) Drives Interlocked Phenotypes That Precipitate Relapse-Like Behaviors In Cocaine Dependence Anastasio NC, Stutz SJ, Fox RG, Sears RM, Emeson RB, DiLeone RJ, O'Neil RT, Fink LH, Li D, Green TA, Moeller FG, Cunningham KA. Neuropsychopharmacology 2014; 39(2): 370-382.
Relapse vulnerability in cocaine dependence is rooted in genetic and environmental determinants, and propelled by both impulsivity and the responsivity to cocaine-linked cues ('cue reactivity'). The serotonin (5-hydroxytryptamine, 5-HT) 5-HT2C receptor (5-HT2CR) within the medial prefrontal cortex (mPFC) is uniquely poised to serve as a strategic nexus to mechanistically control these behaviors. The 5-HT2CR functional capacity is regulated by a number of factors including availability of active membrane receptor pools, the composition of the 5-HT2CR macromolecular protein complex, and editing of the 5-HT2CR pre-mRNA. The one-choice serial reaction time (1-CSRT) task was used to identify impulsive action phenotypes in an outbred rat population before cocaine self-administration and assessment of cue reactivity in the form of lever presses reinforced by the cocaine-associated discrete cue complex during forced abstinence. The 1-CSRT task reliably and reproducibly identified high impulsive (HI) and low impulsive (LI) action phenotypes; HI action predicted high cue reactivity. Lower cortical 5-HT2CR membrane protein levels

concomitant with higher levels of 5-HT2CR:postsynaptic density 95 complex distinguished HI rats from LI rats. The frequency of edited 5-HT2CR mRNA variants was elevated with the prediction that the protein population in HI rats favors those isoforms linked to reduced signaling capacity. Genetic loss of the mPFC 5-HT2CR induced aggregate impulsive action/cue reactivity, suggesting that depressed cortical 5-HT2CR tone confers vulnerability to these interlocked behaviors. Thus, impulsive action and cue reactivity appear to neuromechanistically overlap in rodents, with the 5-HT2CR functional status acting as a neural rheostat to regulate, in part, the intersection between these vulnerability behaviors.

Epigenetic Priming Of Memory Updating During Reconsolidation To Attenuate Remote Fear Memories Graff J, Joseph NF, Horn ME, Samiei A, Meng J, Seo J, Rei D, Bero AW, Phan TX, Wagner F, Holson E, Xu J, Sun J, Neve RL, Mach RH, Haggarty SJ, Tsai LH. Cell. 2014; 156(1-2): 261-276.
Traumatic events generate some of the most enduring forms of memories. Despite the elevated lifetime prevalence of anxiety disorders, effective strategies to attenuate long-term traumatic memories are scarce. The most efficacious treatments to diminish recent (i.e., day-old) traumata capitalize on memory updating mechanisms during reconsolidation that are initiated upon memory recall. Here, the authors show that, in mice, successful reconsolidation-updating paradigms for recent memories fail to attenuate remote (i.e., month-old) ones. They find that, whereas recent memory recall induces a limited period of hippocampal neuroplasticity mediated, in part, by S-nitrosylation of HDAC2 and histone acetylation, such plasticity is absent for remote memories. However, by using an HDAC2-targeting inhibitor (HDACi) during reconsolidation, even remote memories can be persistently attenuated. This intervention epigenetically primes the expression of neuroplasticity-related genes, which is accompanied by higher metabolic, synaptic, and structural plasticity. Thus, applying HDACis during memory reconsolidation might constitute a treatment option for remote traumata.

Transcriptome-wide Discovery of microRNA Binding Sites in Human Brain Boudreau RL, Jiang P, Gilmore BL, Spengler RM, Tirabassi R, Nelson JA, Ross CA, Xing Y, Davidson BL. Neuron. 2014; 81(2): 294-305.
The orchestration of brain function requires complex gene regulatory networks that are modulated, in part, by microRNAs (miRNAs). These noncoding RNAs associate with argonaute (Ago) proteins in order to direct posttranscriptional gene suppression via base pairing with target transcripts. In order to better understand how miRNAs contribute to human-specialized brain processes and neurological phenotypes, identifying their targets is of paramount importance. Here, the authors address the latter by profiling Ago2:RNA interactions using HITS-CLIP to generate a transcriptome-wide map of miRNA binding sites in human brain. They uncovered ~ 7,000 stringent Ago2 binding sites that are highly enriched for conserved sequences corresponding to abundant brain miRNAs. This interactome points to functional miRNA:target pairs across >3,000 genes and represents a valuable resource for accelerating our understanding of miRNA functions in brain. The authors demonstrate the utility of this map for exploring clinically relevant miRNA binding sites that may facilitate the translation of genetic studies of complex neuropsychiatric diseases into therapeutics.

Adolescent Risk Taking, Cocaine Self-Administration, and Striatal Dopamine Signaling. Mitchell MR, Weiss VG, Beas BS, Morgan D, Bizon JL, Setlow B. Neuropsychopharmacology 2014; 39(4): 955-962.
Poor decision making and elevated risk taking, particularly during adolescence, have been strongly linked to drug use; however the causal relationships among these factors are not well understood. To address these relationships, a rat model (the Risky Decision-making Task; RDT) was used to determine whether individual differences in risk taking during adolescence predict later propensity for cocaine self-administration and/or whether cocaine self-administration causes alterations in risk taking. In addition, the RDT was used to determine how risk taking is modulated by dopamine signaling, particularly in the striatum. Results from these experiments indicated that greater risk taking during adolescence predicted greater intake of cocaine during acquisition of self-administration in adulthood, and that adult cocaine self-administration in turn caused elevated risk taking that was present following 6 weeks of abstinence. Greater adolescent risk taking was associated with lower striatal D2 receptor mRNA expression, and pharmacological activation of D2/3

receptors in the ventral, but not dorsal, striatum induced a decrease in risk taking. These findings indicate that the relationship between elevated risk taking and cocaine self-administration is bi-directional, and that low striatal D2 receptor expression may represent a predisposing factor for both maladaptive decision making and cocaine use. Furthermore, these findings suggest that striatal D2 receptors represent a therapeutic target for attenuating maladaptive decision making when choices include risk of adverse consequences.

Cell Death By Pyroptosis Drives CD4 T-Cell Depletion In HIV-1 Infection Doitsh G, Galloway NLK, Geng X, Yang Z, Monroe KM, Zepeda O, Hunt PW, Hatano H, Sowinski S, Munoz-Arias I, Greene WC. Nature 2014; 505(7484): 509-514.
The pathway causing CD4 T-cell death in HIV-infected hosts remains poorly understood although apoptosis has been proposed as a key mechanism. The authors now show that caspase-3-mediated apoptosis accounts for the death of only a small fraction of CD4 T cells corresponding to those that are both activated and productively infected. The remaining over 95% of quiescent lymphoid CD4 T cells die by caspase-1-mediated pyroptosis triggered by abortive viral infection. Pyroptosis corresponds to an intensely inflammatory form of programmed cell death in which cytoplasmic contents and pro-inflammatory cytokines, including IL-1β, are released. This death pathway thus links the two signature events in HIV infection-CD4 T-cell depletion and chronic inflammation-and creates a pathogenic vicious cycle in which dying CD4 T cells release inflammatory signals that attract more cells to die. This cycle can be broken by caspase 1 inhibitors shown to be safe in humans, raising the possibility of a new class of 'anti-AIDS' therapeutics targeting the host rather than the virus.

Molecular Control Of Δ-Opioid Receptor Signalling Fenalti G, Giguere PM, Katritch V, Huang XP, Thompson AA, Cherezov V, Roth BL, Stevens RC. Nature 2014; 506(7487): 191-196.
Opioids represent widely prescribed and abused medications, although their signal transduction mechanisms are not well understood. Here the authors present the 1.8Å high-resolution crystal structure of the human δ-opioid receptor (δ-OR), revealing the presence and fundamental role of a sodium ion in mediating allosteric control of receptor functional selectivity and constitutive activity. The distinctive δ-OR sodium ion site architecture is centrally located in a polar interaction network in the seven-transmembrane bundle core, with the sodium ion stabilizing a reduced agonist affinity state, and thereby modulating signal transduction. Site-directed mutagenesis and functional studies reveal that changing the allosteric sodium site residue Asn131 to an alanine or a valine augments constitutive β-arrestin-mediated signalling. Asp95Ala, Asn310Ala and Asn314Ala mutations transform classical δ-opioid antagonists such as naltrindole into potent β-arrestin-biased agonists. The data establish the molecular basis for allosteric sodium ion control in opioid signalling, revealing that sodium-coordinating residues act as 'efficacy switches' at a prototypic G-protein-coupled receptor.

Multilevel Modulation Of A Sensory Motor Circuit During C. Elegans Sleep and Arousal Cho JY, Sternberg PW. Cell 2014; 156(1-2): 249-260.
Sleep is characterized by behavioral quiescence, homeostasis, increased arousal threshold, and rapid reversibility. Understanding how these properties are encoded by a neuronal circuit has been difficult, and no single molecular or neuronal pathway has been shown to be responsible for the regulation of sleep. Taking advantage of the well-mapped neuronal connections of Caenorhabditis elegans and the sleep-like states in this animal, he authors demonstrate the changed properties of both sensory neurons and downstream interneurons that mediate sleep and arousal. The ASH sensory neuron displays reduced sensitivity to stimuli in the sleep-like state, and the activity of the corresponding interneurons in ASH's motor circuit becomes asynchronous. Restoration of interneuron synchrony is sufficient for arousal. The multilevel circuit depression revealed provides an elegant strategy to promote a robust decrease in arousal while allowing for rapid reversibility of the sleep state.

Long-Acting Integrase Inhibitor Protects Macaques From Intrarectal Simian/Human Immunodeficiency Virus Andrews CD, Spreen WR, Mohri H, Moss L, Ford S, Gettie A, Russell-Lodrigue K, Bohm RP, Cheng-Mayer C, Hong Z, Markowitz M, Ho DD. Science. 2014; 343(6175): 1151-1154.
GSK1265744 (GSK744) is an integrase strand-transfer inhibitor that has been formulated as a long-acting (LA) injectable suitable for monthly to quarterly clinical administration. GSK744 LA was administered at two time points 4 weeks apart beginning 1 week before virus administration, and macaques were challenged weekly for 8 weeks. GSK744 LA, at plasma concentrations achievable with quarterly injections in humans, protected all animals against repeated low-dose challenges. In a second experiment, macaques were given GSK744 LA 1 week before virus administration and challenged repeatedly until infection occurred. Protection decreased over time and correlated with the plasma drug levels. With a quarterly dosing schedule in humans, these results suggest that GSK744 LA could potentially decrease adherence problems associated with daily preexposure prophylaxis (PrEP).

Independent Optical Excitation Of Distinct Neural Populations Klapoetke NC, Murata Y, Kim SS, Pulver SR, Birdsey-Benson A, Cho YK, Morimoto TK, Chuong AS, Carpenter EJ, Tian Z, Wang J, Xie Y, Yan Z, Zhang Y, Chow BY, Surek B, Melkonian M, Jayaraman V, Constantine-Paton M, Wong GKS, Boyden ES. Nat Methods. 2014; 11(3): 338-346.
Optogenetic tools enable examination of how specific cell types contribute to brain circuit functions. A long-standing question is whether it is possible to independently activate two distinct neural populations in mammalian brain tissue. Such a capability would enable the study of how different synapses or pathways interact to encode information in the brain. Here the authors describe two channelrhodopsins, Chronos and Chrimson, discovered through sequencing and physiological characterization of opsins from over 100 species of alga. Chrimson's excitation spectrum is red shifted by 45 nm relative to previous channelrhodopsins and can enable experiments in which red light is preferred. The authors show minimal visual system-mediated behavioral interference when using Chrimson in neurobehavioral studies in Drosophila melanogaster. Chronos has faster kinetics than previous channelrhodopsins yet is effectively more light sensitive. Together these two reagents enable two-color activation of neural spiking and downstream synaptic transmission in independent neural populations without detectable cross-talk in mouse brain slice.

GENSAT BAC Cre-Recombinase Driver Lines To Study The Functional Organization Of Cerebral Cortical and Basal Ganglia Circuits Gerfen CR, Paletzki R, Heintz N. Neuron 2013; 80(6): 1368-1383.
Recent development of molecular genetic techniques are rapidly advancing understanding of the functional role of brain circuits in behavior. Critical to this approach is the ability to target specific neuron populations and circuits. The collection of over 250 BAC Cre-recombinase driver lines produced by the GENSAT project provides a resource for such studies. Here the authors provide characterization of GENSAT BAC-Cre driver lines with expression in specific neuroanatomical pathways within the cerebral cortex and basal ganglia.

Opioid Receptor-Triggered Spinal Mtorc1 Activation Contributes To Morphine Tolerance and Hyperalgesia Xu JT, Zhao JY, Zhao X, Ligons D, Tiwari V, Atianjoh FE, Lee CY, Liang L, Zang W, Njoku D, Raja SN, Yaster M, Tao YX. J Clin Invest 2014; 124(2): 592-603.
The development of opioid-induced analgesic tolerance and hyperalgesia is a clinical challenge for managing chronic pain. Adaptive changes in protein translation in the nervous system are thought to promote opioid tolerance and hyperalgesia; however, how opioids drive such changes remains elusive. Here, the authors report that mammalian target of rapamycin (mTOR), which governs most protein translation, was activated in rat spinal dorsal horn neurons after repeated intrathecal morphine injections. Activation was triggered through μ opioid receptor and mediated by intracellular PI3K/Akt. Spinal mTOR inhibition blocked both induction and maintenance of morphine tolerance and hyperalgesia, without affecting basal pain perception or locomotor functions. These effects were attributed to the attenuation of morphine-induced increases in translation initiation activity, nascent protein synthesis, and expression of some known key tolerance-associated proteins, including neuronal NOS (nNOS), in dorsal horn. Moreover, elevating spinal mTOR activity by knocking down the mTOR-negative regulator TSC2 reduced morphine analgesia, produced pain

hypersensitivity, and increased spinal nNOS expression. These findings implicate the μ opioid receptor-triggered PI3K/Akt/mTOR pathway in promoting morphine-induced spinal protein translation changes and associated morphine tolerance and hyperalgesia. These data suggest that mTOR inhibitors could be explored for prevention and/or reduction of opioid tolerance in chronic pain management.

Effects of Anonymous Peer Observation on Adolescents' Preference for Immediate Rewards. Weigard A, Chein J, Albert D, Smith A, Steinberg L. Dev Sci. 2014 Jan; 17(1): 71-78.
Research suggests that the presence of peers influences adolescent risk-taking by increasing the perceived reward value of risky decisions. While prior work has involved observation of participants by their friends, the current study examined whether observation by an anonymous peer could elicit similarly increased reward sensitivity. Late adolescent participants completed a delay discounting task either alone or under the belief that performance was being observed from a neighboring room by an unknown viewer of the same gender and age. Even in this limited social context, participants demonstrated a significantly increased preference for smaller, immediate rewards when they believed that they were being watched. This outcome challenges several intuitive accounts of the peer effect on adolescent risk-taking, and indicates that the peer influence on reward sensitivity during late adolescence is not dependent on familiarity with the observer. The findings have both theoretical and practical implications for our understanding of social influences on adolescents' risky behavior.

A Controlled Family Study of Cannabis Users With and Without Psychosis Proal AC, Fleming J, Galvez-Buccollini JA, Delisi LE. Schizophr Res. 2014 Jan; 152(1): 283-288.
Cannabis is one of the most highly abused illicit drugs in the world. Several studies suggest a link between adolescent cannabis use and schizophrenia. An understanding of this link would have significant implications for legalization of cannabis and its medicinal value. The present study aims to determine whether familial morbid risk for schizophrenia is the crucial factor that underlies the association of adolescent cannabis use with the development of schizophrenia. Consecutively obtained probands were recruited into four samples: sample 1: 87 non-psychotic controls with no drug use; sample 2: 84 non-psychotic controls with cannabis use; sample 3: 32 patients with a schizophrenia spectrum psychosis with no drug use; sample 4: 76 patients with schizophrenia spectrum psychosis with cannabis use. All cannabis using subjects used this drug during adolescence, and no other substance, with the exception of alcohol. Structured interviews of probands and family informants were used to obtain diagnostic information about probands and all their known relatives. There was an increased morbid risk for schizophrenia in relatives of the cannabis using and non-using patient samples compared with their respective non-psychotic control samples ($p=.002$, $p<.001$ respectively). There was no significant difference in morbid risk for schizophrenia between relatives of the patients who use or do not use cannabis ($p=.43$). The results of the current study suggest that having an increased familial morbid risk for schizophrenia may be the underlying basis for schizophrenia in cannabis users and not cannabis use by itself.

Robust Changes in Reward Circuitry during Reward Loss in Current and Former Cocaine Users during Performance of a Monetary Incentive Delay Task Patela KT, Stevens KT, Med SA, Musk C, Thomas AD, Potenza MN, Pearlson GD. Biol Psychiatry. 2013 Oct; 74(7): 529–537.
Abnormal function in reward circuitry in cocaine addiction could predate drug use as a risk factor, follow drug use as a consequence of substance-induced alterations, or both. The authors used a functional magnetic resonance imaging monetary incentive delay task (MIDT) to investigate reward-loss neural response differences among 42 current cocaine users, 35 former cocaine users, and 47 healthy subjects who also completed psychological measures and tasks related to impulsivity and reward. The authors found various reward processing-related group differences in several MIDT phases. Across task phases we found a control > current user > former user activation pattern, except for loss outcome, where former compared with current cocaine users activated ventral tegmental area more robustly. The authors also found regional prefrontal activation differences during loss anticipation between cocaine-using groups. Both groups of cocaine users scored higher than control subjects on impulsivity, compulsivity and reward-punishment sensitivity factors.

In addition, impulsivity-related factors correlated positively with activation in amygdala and negatively with anterior cingulate activation during loss anticipation. Compared with healthy subjects, both former and current users displayed abnormal brain activation patterns during MIDT performance. Both cocaine groups differed similarly from healthy subjects, but differences between former and current users were localized to the ventral tegmental area during loss outcome and to prefrontal regions during loss anticipation, suggesting that long-term cocaine abstinence does not normalize most reward circuit abnormalities. Elevated impulsivity-related factors that relate to loss processing in current and former users suggest that these tendencies and relationships may pre-exist cocaine addiction.

FAAH Selectively Influences Placebo Effects Peciña M, Martínez-Jauand M, Hodgkinson C, Stohler CS, Goldman D, Zubieta JK. Mol Psychiatry. 2014 Mar; 19(3): 385-391.
Endogenous opioid and cannabinoid systems are thought to act synergistically regulating antinociceptive and reward mechanisms. To further understand the human implications of the interaction between these two systems, the authors investigated the role of the common, functional missense variant Pro129Thr of the gene coding fatty acid amide hydrolase (FAAH), the major degrading enzyme of endocannabinoids, on psychophysical and neurotransmitter (dopaminergic, opioid) responses to pain and placebo-induced analgesia in humans. FAAH Pro129/Pro129 homozygotes, who constitute nearly half of the population, reported higher placebo analgesia and more positive affective states immediately and 24h after placebo administration; no effects on pain report in the absence of placebo were observed. Pro129/Pro129 homozygotes also showed greater placebo-induced μ-opioid, but not D2/3 dopaminergic, enhancements in neurotransmission in regions known involved in placebo effects. These results show that a common genetic variation affecting the function of the cannabinoid system is serving as a probe to demonstrate the involvement of cannabinoid and opioid transmitters on the formation of placebo effects.

Elevation of Dopamine Induced by Cigarette Smoking: Novel Insights From a [(11)C]-(+)-PHNO PET Study in Humans Le Foll B, Guranda M, Wilson AA, Houle S, Rusjan PM, Wing VC, Zawertailo L, Busto U, Selby P, Brody AL, George TP, Boileau I. Neuropsychopharm. 2014 Jan; 39(2): 415-424.
Positron emission tomography (PET) has convincingly provided in vivo evidence that psychoactive drugs increase dopamine (DA) levels in human brain, a feature thought critical to their reinforcing properties. Some controversy still exists concerning the role of DA in reinforcing smoking behavior and no study has explored whether smoking increases DA concentrations at the D3 receptor, speculated to have a role in nicotine's addictive potential. Here, the authors used PET and [(11)C]-(+)-PHNO ([(11)C]-(+)-4-propyl-3,4,4a,5,6,10b-hexahydro-2H-naphtho[1,2-b][1,4]oxazin-9-ol) to test the hypothesis that smoking increases DA release (decreases [(11)C]-(+)-PHNO binding) in D2-rich striatum and D3-rich extra-striatal regions and is related to craving, withdrawal and smoking behavior. Ten participants underwent [(11)C]-(+)-PHNO scans after overnight abstinence and after smoking a cigarette. Motivation to smoke (smoking topography), mood, and craving were recorded. Smoking significantly decreased self-reported craving, withdrawal, and [(11)C]-(+)-PHNO binding in D2 and D3-rich areas (-12.0 and -15.3%, respectively). The authors found that motivation to smoke (puff rate) predicted magnitude of DA release in limbic striatum, and the latter was correlated with decreased craving and withdrawal symptoms. This is the first report suggesting that, in humans, DA release is increased in D3-rich areas in response to smoking. Results also support the preferential involvement of the limbic striatum in motivation to smoke, anticipation of pleasure from cigarettes and relief of withdrawal symptoms. The authors propose that due to the robust effect of smoking on [(11)C]-(+)-PHNO binding, this radiotracer represents an ideal translational tool to investigate novel therapeutic strategies targeting DA transmission.

Altered Neural Processing of the Need to Stop in Young Adults at Risk for Stimulant Dependence Harlé KM, Shenoy P, Stewart JL, Tapert SF, Yu AJ, Paulus MP. The Journal of Neuroscience. 2014 Dec; 34(13): 4567–4580.
Identification of neurocognitive predictors of substance dependence is an important step in developing approaches to prevent addiction. Given evidence of inhibitory control deficits in substance abusers

(Monterosso et al., 2005; Fu et al., 2008; Lawrence et al., 2009; Tabibnia et al., 2011), the authors examined neural processing characteristics in human occasional stimulant users (OSU), a population at risk for dependence. A total of 158 nondependent OSU and 47 stimulant-naive control subjects (CS) were recruited and completed a stop signal task while undergoing functional magnetic resonance imaging (fMRI). A Bayesian ideal observer model was used to predict probabilistic expectations of inhibitory demand, P(stop), on a trial-to-trial basis, based on experienced trial history. Compared with CS, OSU showed attenuated neural activation related to P(stop) magnitude in several areas, including left prefrontal cortex and left caudate. OSU also showed reduced neural activation in the dorsal anterior cingulate cortex (dACC) and right insula in response to an unsigned Bayesian prediction error representing the discrepancy between stimulus outcome and the predicted probability of a stop trial. These results indicate that, despite minimal overt behavioral manifestations, OSU use fewer brain processing resources to predict and update the need for response inhibition, processes that are critical for adjusting and optimizing behavioral performance, which may provide a biomarker for the development of substance dependence.

Attenuated Insular Processing During Risk Predicts Relapse in Early Abstinent Methamphetamine-Dependent Individuals Gowin JL, Harlé KM, Stewart JL, Wittmann M, Tapert SF, Paulus MP. Neuropsychopharmacology. 2013 Dec. [Epub ahead of print DOI: 10.1038/npp.2013.333].
There is some evidence that neuroimaging can be used to predict relapse among abstinent methamphetamine-dependent (MD) individuals. However, it remains unclear what cognitive and neural processes contribute to relapse. This investigation examined whether insula activation during risk-taking decisions-a process shown to be disrupted in MD-is able to predict susceptibility for relapse. Sixty-eight MD enrolled in a treatment program during early abstinence completed a risk-taking task during functional magnetic resonance imaging. Sixty-three of the sixty-eight individuals were followed up 1 year after the study. Of these, 18 MD reported relapse. The 45 abstinent MD showed patterns of insula activation during risky decisions that resembled those found in prior studies of healthy controls, consisting of lower insula activation during safe decisions paired with higher activation during risky decisions. In contrast, the 18 relapsed MD showed similar insula activation during safe and risky decisions. An increase in one standard deviation in the difference in insula activation between risky and safe choices was associated with a 0.34 odds ratio for relapse at any given time. A median split of insula activation (difference between risky and safe) showed that individuals in the bottom half were two times more likely to relapse. In addition, a model that included several other brain regions increased prediction accuracy compared with insula-based model alone. These results suggest that failure to differentially activate the insula as a function of risk is a part of an altered risk-processing network associated with an increased susceptibility to relapse.

HIV Transmission From Drug Injectors To Partners Who Do Not Inject, and Beyond: Modelling The Potential For A Generalized Heterosexual Epidemic In St. Petersburg, Russia Mills HL, White E, Colijn C, Vickerman P, Heimer R. Drug Alcohol Depend. 2013; 133(1): 242-247.
HIV infection is prevalent among drug injectors in St. Petersburg and their non-injecting heterosexual partners (PIDUs). There are fears that sexual transmission of HIV from IDUs to PIDUs may portend a self-sustaining, heterosexual epidemic in Russia. The present model combines a network model of sexual partnerships of IDUs and non-IDUs to represent sexual transmission of HIV and a deterministic model for parenteral transmission among IDUs. Behavioral parameters were obtained from a survey of St. Petersburg IDUs and their sexual partners. The authors based their model fits on two scenarios for PIDU prevalence in 2006 (5.6% and 15.1%, calculated excluding and including HCV co-infected PIDUs respectively) and compared predictions for the general population HIV prevalence. Results indicate that sexual transmission could sustain a non-IDU HIV epidemic. The model indicates that general population prevalence may be greater than current estimates imply. Parenteral transmission drives the epidemic and the PIDU bridge population plays a crucial role transferring infection to non-IDUs. The model indicates that the high PIDU prevalence is improbable because of the high risk behavior this implies; the lower prevalence is possible. The model implies that transmission through PIDUs will sustain a heterosexual epidemic, if prevalence among IDUs and PIDUs is as high as survey data suggest. The authors postulate that current estimates of population

prevalence underestimate the extent of the HIV epidemic because they are based on the number of registered cases only. Curtailing transmission among injectors and PIDUs will be vital in controlling heterosexual transmission.

Driving After Drug or Alcohol Use by US High School Seniors, 2001–2011 O'Malley PM, Johnston LD. Am J Public Health. 2013; 103:2027–2034. doi:10. 2105/AJPH.2013.301246.
The authors examined prevalence, trends, and correlates of driving or riding after use of drugs or alcohol among US high school seniors from 2001 to 2011. Data come from Monitoring the Future, an annual survey of nationally representative samples of high school seniors. The authors used logistic regressions with data from more than 22 000 respondents to examine multivariate associations with demographic and lifestyle factors. Large numbers of US high school seniors put themselves and others at great risk of harm by driving after using marijuana or other illicit drugs or drinking alcohol or by riding in a vehicle whose driver had used marijuana, other illicit drugs, or alcohol. Driving after drinking has declined in recent years, but driving after use of marijuana has increased. A higher percentage of students reported driving after using marijuana than after having 5 or more alcoholic drinks. Risky driving and riding behaviors differed little between demographic subgroups but considerably according to lifestyle factors. The authors conclude that stronger efforts are needed to combat adolescent driving under the influence of illicit drugs.

Association Between Cannabis Use, Psychosis, and Schizotypal Personality Disorder: Findings From The National Epidemiologic Survey On Alcohol and Related Conditions Davis GP, Compton MT, Wang S, Levin FR, Blanco C. Schizophr Res. 2013; 151(1-3): 197-202.
Studies to date showing an association between cannabis use and schizophrenia-spectrum disorders are of relatively small sample sizes with limitations in generalizability. The present study addresses this gap by examining the relationship between cannabis use and psychotic-like symptoms in a large representative community sample. Data were derived from the 2004-2005 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC, Wave 2), a large, nationally representative sample of 34,653 adults from the United States population. The authors evaluated the association between lifetime cannabis use, psychosis, and schizotypal personality features. The prevalence of psychosis and schizotypal personality disorder increased significantly with greater cannabis use in a dose-dependent manner. The associations between cannabis use and psychosis were 1.27 (95% CI 1.03-1.57) for lifetime cannabis use, 1.79 (95% CI 1.35-2.38) for lifetime cannabis abuse, and 3.69 (95% CI 2.49-5.47) for lifetime cannabis dependence. There was a similar dose-response relationship between the extent of cannabis use and schizotypal personality disorder (OR=2.02 for lifetime cannabis use, 95% CI 1.69-2.42; OR=2.83 for lifetime cannabis abuse, 95% CI 2.33-2.43; OR=7.32 for lifetime cannabis dependence, 95% CI 5.51-9.72). Likelihood of individual schizotypal features increased significantly with increased extent of cannabis use in a dose-dependent manner. This is the first population-based study to examine the association between lifetime cannabis use, psychosis, and schizotypal personality traits. These results add to evidence that cannabis use may be a risk factor for psychosis liability.

Initial Reactions To Tobacco and Cannabis Smoking: A Twin Study Agrawal A, Madden PAF, Bucholz KK, Heath AC, Lynskey MT. Addiction. 2014 April; 109(4): 663-671.
Initial subjective reactions to cannabis and tobacco, broadly classified as positive or negative; have previously been explored for their associations with onset and maintenance of subsequent abuse/dependence. The authors examine (i) the factorial architecture of self-reported initial reactions to cannabis and tobacco; (ii) whether these factors associate with concurrently reported age at onset of DSM-IV diagnosis of nicotine dependence and cannabis abuse/dependence; and (iii) estimate heritable variation in and co-variation between the factors. Factorial and exploratory structural equation modeling was conducted to examine the factor structure of initial reactions. Cox proportional hazards modeling was employed to examine their association with time to onset of diagnosis of DSM-IV nicotine dependence and cannabis abuse/dependence. Classical twin modeling, using univariate and multivariate models, was used to parse variance in each factor (and the covariance between factors) to their additive genetic, shared environmental and non-shared

environmental sources. General population sample of Caucasian female twins aged 18-32 years, with a life-time history of tobacco [n=2393] and cannabis [n=1445] use. Self-report of initial subjective reactions to tobacco (cigarettes) and cannabis the first time they were used and time to onset of life-time history of DSM-IV diagnosis of abuse (cannabis) and dependence (cannabis or nicotine).Factors representing putatively positive and negative reactions to cannabis and tobacco emerged. Initial reactions to tobacco were associated with onset of DSM-IV diagnosis of nicotine dependence and cannabis abuse/dependence while initial reactions to cannabis were associated with onset of DSM-IV diagnosis of cannabis abuse/dependence alone. Genetic factors played a moderate role in each factor (heritability of 27-35%, P<0.05), with the remaining variance attributed to individual-specific environment. Co-variation across the factors indexing positive and negative initial reactions was attributable to genetic sources (0.18-0.58, P<0.05) and to overlapping individual-specific environmental factors (-0.16 to 0.36, P<0.05).Initial subjective reactions to tobacco are associated with onset of DSM-IV diagnosis of nicotine dependence and cannabis abuse/dependence while initial subjective reactions to cannabis are only associated with onset of diagnosis of DSM-IV cannabis abuse/dependence. Genetic and environmental factors underpin the overlap across the factors representing initial reactions, both positive and negative.

Youth Problem Behaviors 8 Years After Implementing The Communities That Care Prevention System: A Community-Randomized Trial Hawkins JD, Oesterle S, Brown EC, Abbott RD, Catalano RF. JAMA Pediatr. 2014; 168(2): 122-129.
Community-based efforts to prevent adolescent problem behaviors are essential to promote public health and achieve collective impact community wide. The objective of this study was to test whether the Communities That Care (CTC) prevention system reduced levels of risk and adolescent problem behaviors community wide 8 years after implementation of CTC. A community-randomized trial was performed in 24 small towns in 7 states, matched within state, assigned randomly to a control or intervention group in 2003. All fifth-grade students attending public schools in study communities in 2003-2004 who received consent from their parents to participate (76.4% of the eligible population) were included. A panel of 4407 fifth graders was surveyed through 12th grade, with 92.5% of the sample participating at the last follow-up. A coalition of community stakeholders received training and technical assistance to install CTC, used epidemiologic data to identify elevated risk factors and depressed protective factors for adolescent problem behaviors in the community, and implemented tested and effective programs for youths aged 10 to 14 years as well as their families and schools to address their community's elevated risks. Main outcomes and measures obtained included levels of targeted risk; sustained abstinence, and cumulative incidence by grade 12; and current prevalence of tobacco, alcohol, and other drug use, delinquency, and violence in 12th grade. By spring of 12th grade, students in CTC communities were more likely than students in control communities to have abstained from any drug use (adjusted risk ratio [ARR] =1.32; 95% CI, 1.06-1.63), drinking alcohol (ARR=1.31; 95% CI, 1.09-1.58), smoking cigarettes (ARR=1.13; 95% CI, 1.01-1.27), and engaging in delinquency (ARR=1.18; 95% CI, 1.03-1.36). They were also less likely to ever have committed a violent act (ARR=0.86; 95% CI, 0.76-0.98). There were no significant differences by intervention group in targeted risks, the prevalence of past-month or past-year substance use, or past-year delinquency or violence. The authors conclude that using the CTC system continued to prevent the initiation of adolescent problem behaviors through 12th grade, 8 years after implementation of CTC and 3 years after study-provided resources ended, but did not produce reductions in current levels of risk or current prevalence of problem behavior in 12th grade.

Real-time fMRI Links Subjective Experience with Brain Activity during Focused Attention Garrison KA1, Scheinost D, Worhunsky PD, Elwafi HM, Thornhill TA 4th, Thompson E, Saron C, Desbordes G, Kober H, Hampson M, Gray JR, Constable RT, Papademetris X, Brewer JA. Neuroimage. 2013 Nov 1; 81: 110-118.
Recent advances in brain imaging have improved the measure of neural processes related to perceptual, cognitive and affective functions, yet the relation between brain activity and subjective experience remains poorly characterized. In part, it is a challenge to obtain reliable accounts of participant's experience in such

studies. Here the authors addressed this limitation by utilizing experienced meditators who are expert in introspection. They tested a novel method to link objective and subjective data, using real-time fMRI (rt-fMRI) to provide participants with feedback of their own brain activity during an ongoing task. They provided real-time feedback during a focused attention task from the posterior cingulate cortex, a hub of the default mode network shown to be activated during mind-wandering and deactivated during meditation. In a first experiment, both meditators and non-meditators reported significant correspondence between the feedback graph and their subjective experience of focused attention and mind-wandering. When instructed to volitionally decrease the feedback graph, meditators, but not non-meditators, showed significant deactivation of the posterior cingulate cortex. The authors were able to replicate these results in a separate group of meditators using a novel step-wise rt-fMRI discovery protocol in which participants were not provided with prior knowledge of the expected relationship between their experience and the feedback graph (i.e., focused attention versus mind-wandering). These findings support the feasibility of using rt-fMRI to link objective measures of brain activity with reports of ongoing subjective experience in cognitive neuroscience research, and demonstrate the generalization of expertise in introspective awareness to novel contexts.

Toward Empirical Identification of a Clinically Meaningful Indicator of Treatment Outcome: Features of Candidate Indicators and Evaluation of Sensitivity to Treatment Effects and Relationship to One Year Follow Up Cocaine Use Outcomes Carol KM, Kiluk, BD, Nich C, DeVito EE, Decker S, LaPaglia D, Duffey D, Babuscio TA, Ball SA. Drug and Alcohol Dependence. 2014 Apr; 137C: 3-19.
Selection of an appropriate indictor of treatment response in clinical trials is complex, particularly for the various illicit drugs of abuse. Most widely used indicators have been selected based on expert group recommendation or convention rather than systematic empirical evaluation. Absence of an evidence-based, clinically meaningful index of treatment outcome hinders cross-study evaluations necessary for progress in addiction treatment science. Fifteen candidate indicators used in multiple clinical trials as well as some proposed recently are identified and discussed in terms of relative strengths and weaknesses (practicality, cost, verifiability, sensitivity to missing data). Using pooled data from five randomized controlled trials of cocaine dependence (N=434), the indicators were compared in terms of sensitivity to the effects of treatment and relationship to cocaine use and general functioning during follow-up. Commonly used outcome measures (percent negative urine screens; percent days of abstinence) performed relatively well in that they were sensitive to the effects of the therapies evaluated. Others, including complete abstinence and reduction in frequency of use, were less sensitive to effects of specific therapies and were very weakly related to cocaine use or functioning during follow-up. Indicators more strongly related to cocaine use during follow-up were those that reflected achievement of sustained periods of abstinence, particularly at the end of treatment. These analyses did not demonstrate overwhelming superiority of any single indicator, but did identify several that performed particularly poorly. Candidates for elimination included retention, complete abstinence, and indicators of reduced frequency of cocaine use.

Preclinical Characterization Of An Anti-Methamphetamine Monoclonal Antibody For Human Use
Stevens MW, Tawney RL, West CM, Kight AD, Henry RL, Owens SM, Gentry WB. MAbs. 2014 Mar; 6(2): 547-555.
Ch-mAb7F9, a human-mouse chimeric monoclonal antibody (mAb) designed to bind (+)-methamphetamine (METH) with high affinity and specificity, was produced as a treatment medication for METH abuse. In these studies, the authors present the preclinical characterization that provided predictive evidence that ch-mAb7F9 may be safe and effective in humans. In vitro ligand binding studies showed that ch-mAb7F9 is specific for and only binds its target ligands (METH, (+)-amphetamine, and 3,4-methylenedioxy-N-methylamphetamine) with high affinity. It did not bind endogenous neurotransmitters or other medications and was not bound by protein C1q, thus it is unlikely to stimulate in vivo complement-dependent cytotoxicity. Isothermal titration calorimetry potency studies showed that METH binding by ch-mAb7F9 is efficient. Pharmacokinetic studies of METH given after ch-mAb7F9 doses in rats demonstrated the in vivo application of these in vitro METH-binding characteristics. While METH had little effect on ch-mAb7F9 disposition, ch-mAb7F9 substantially altered METH disposition, dramatically reducing the volume of

distribution and clearance of METH. The elimination half-life of METH was increased by ch-mAb7F9, but it was still very fast compared with the elimination of ch-mAb7F9. Importantly, the rapid elimination of unbound METH combined with previous knowledge of mAb:target ligand binding dynamics suggested that ch-mAb7F9 binding capacity regenerates over time. This finding has substantial therapeutic implications regarding the METH doses against which ch-mAb7F9 will be effective, on the duration of ch-mAb7F9 effects, and on the safety of ch-mAb7F9 in METH users who use METH while taking ch-mAb7F9. These results helped to support initiation of a Phase 1a study of ch-mAb7F9.

Controlled-Deactivation Cannabinergic Ligands Sharma R, Nikas SP, Paronis CA, Wood JT, Halikhedkar A, Guo JJ, Thakur GA, Kulkarni S, Benchama O, Raghav JG, Gifford RS, Järbe TU, Bergman J, Makriyannis A. J Med Chem. 2013 Dec; 56(24): 10142-10157.
The authors report an approach for obtaining novel cannabinoid analogues with controllable deactivation and improved druggability. Their design involves the incorporation of a metabolically labile ester group at the 2'-position on a series of (-)-Δ(8)-THC analogues. The authors have sought to introduce benzylic substituents α to the ester group which affect the half-lives of deactivation through enzymatic activity while enhancing the affinities and efficacies of individual ligands for the CB1 and CB2 receptors. The 1'-(S)-methyl, 1'-gem-dimethyl, and 1'-cyclobutyl analogues exhibit remarkably high affinities for both CB receptors. The novel ligands are susceptible to enzymatic hydrolysis by plasma esterases in a controllable manner, while their metabolites are inactive at the CB receptors. In further in vitro and in vivo experiments key analogues were shown to be potent CB1 receptor agonists and to exhibit CB1-mediated hypothermic and analgesic effects.

Maintenance Treatment With Varenicline For Smoking Cessation In Patients With Schizophrenia and Bipolar Disorder: A Randomized Clinical Trial Evins AE, Cather C, Pratt SA, Pachas GN, Hoeppner SS, Goff DC, Achtyes ED, Ayer D, Schoenfeld DA. JAMA. 2014 Jan; 311(2): 145-154.
It is estimated that more than half of those with serious mental illness smoke tobacco regularly. Standard courses of pharmacotherapeutic cessation aids improve short-term abstinence, but most who attain abstinence relapse rapidly after discontinuation of pharmacotherapy. The goal of this study was to determine whether smokers diagnosed with schizophrenia and bipolar disease have higher rates of prolonged tobacco abstinence with maintenance pharmacotherapy than with standard treatment. Randomized, double-blind, placebo-controlled, parallel-group, relapse-prevention clinical trial conducted in 10 community mental-health centers. Of 247 smokers with schizophrenia or bipolar disease recruited from March 2008-April 2012, 203 received 12-weeks' open-label varenicline and cognitive behavioral therapy and 87 met abstinence criteria to enter the relapse prevention intervention. Participants who had 2 weeks or more of continuous abstinence at week 12 of open treatment were randomly assigned to receive cognitive behavioral therapy and double-blind varenicline (1 mg, 2 per day) or placebo from weeks 12 to 52. Participants then discontinued study treatment and were followed up to week 76. Seven-day rate of continuous abstinence at study week 52, the end of the relapse-prevention phase, confirmed by exhaled carbon monoxide. Secondary outcomes were continuous abstinence rates for weeks 12 through 64 based on biochemically verified abstinence and weeks 12 through 76, based on self-reported smoking behavior. Sixty-one participants completed the relapse-prevention phase; 26 discontinued participation (7 varenicline, 19 placebo) and were considered to have relapsed for the analyses; 18 of these had relapsed prior to dropout. At week 52, point-prevalence abstinence rates were 60% in the varenicline group (24 of 40) vs 19% (9 of 47) in the placebo group (odds ratio [OR], 6. 2; 95% CI, 2. 2-19. 2; P<. 001). From weeks 12 through 64, 45% (18 of 40) among those in the varenicline group vs 15% (7 of 47) in the placebo group were continuously abstinent (OR, 4. 6; 95% CI, 1. 5-15. 7; P=. 004), and from weeks 12 through 76, 30% (12 of 40) in the varenicline group vs 11% (5 of 47) in the placebo group were continuously abstinent (OR, 3. 4; 95% CI, 1. 02-13. 6; P=. 03). There were no significant treatment effects on psychiatric symptom ratings or psychiatric adverse events. Among smokers with serious mental illness who attained initial abstinence with standard treatment, maintenance pharmacotherapy with varenicline and cognitive behavioral therapy improved prolonged tobacco abstinence rates compared with cognitive behavioral therapy alone after 1 year of treatment and at 6 months after treatment discontinuation. clinicaltrials.gov Identifier: NCT00621777.

Extended Release Naltrexone Injection Is Performed In The Majority Of Opioid Dependent Patients Receiving Outpatient Induction: A Very Low Dose Naltrexone And Buprenorphine Open Label Trial
Mannelli P, Wu LT, Peindl KS, Swartz MS, Woody GE. Drug Alcohol Depend. 2014 Feb; [Epub ahead of print].
The approval of extended release injectable naltrexone (XR-NTX; Vivitrol(®)) has introduced a new option for treating opioid addiction, but studies are needed to identify its place within the spectrum of available therapies. The absence of physiological opioid dependence is a necessary and challenging first step for starting XR-NTX. Outpatient detoxification gives poor results and inpatient detoxification is either unavailable or too brief for the physiological effects of opioids to resolve. Here the authors present findings from an open label study that tested whether the transition from opioid addiction to XR-NTX can be safely and effectively performed in an outpatient setting using very low dose naltrexone and buprenorphine. Twenty treatment seeking opioid addicted individuals were given increasing doses of naltrexone starting at 0. 25mg with decreasing doses of buprenorphine starting at 4mg during a 7-day outpatient XR-NTX induction procedure. Withdrawal discomfort, craving, drug use, and adverse events were assessed daily until the XR-NTX injection, then weekly over the next month. Fourteen of the 20 participants received XR-NTX and 13 completed weekly assessments. Withdrawal, craving, and opioid or other drug use were significantly lower during induction and after XR-NTX administration compared with baseline, and no serious adverse events were recorded. Outpatient transition to XR-NTX combining upward titration of very low dose naltrexone with downward titration of low dose buprenorphine was safe, well tolerated, and completed by most participants. Further studies with larger numbers of subjects are needed to see if this approach is useful for naltrexone induction.

Changes in HIV Incidence among People Who Inject Drugs in Taiwan following Introduction of a Harm Reduction Program: A Study of Two Cohorts Huang Y-F, Yang J-Y, Nelson KE, Kuo H-S, Lew-Ting C-Y, et al. PLoS Med 2014;11(4): e1001625. doi:10.1371/journal.pmed.1001625.
Harm reduction strategies for combating HIV epidemics among people who inject drugs (PWID) have been implemented in several countries. However, large-scale studies using sensitive measurements of HIV incidence and intervention exposures in defined cohorts are rare. The aim of this study was to determine the association between harm reduction programs and HIV incidence among PWID. The study included two populations. For 3,851 PWID who entered prison between 2004 and 2010 and tested HIV positive upon incarceration, The authors tested their sera using a BED HIV-1 capture enzyme immunoassay to estimate HIV incidence. Also, they enrolled in a prospective study a cohort of 4,357 individuals who were released from prison via an amnesty on July 16, 2007. The authors followed them with interviews at intervals of 6–12 mo and by linking several databases. A total of 2,473 participants who were HIV negative in January 2006 had interviews between then and 2010 to evaluate the association between use of harm reduction programs and HIV incidence. The authors used survival methods with attendance at methadone clinics as a time-varying covariate to measure the association with HIV incidence. They used a Poisson regression model and calculated the HIV incidence rate to evaluate the association between needle/syringe program use and HIV incidence. Among the population of PWID who were imprisoned, the implementation of comprehensive harm reduction programs and a lower mean community HIV viral load were associated with a reduced HIV incidence among PWID. The HIV incidence in this population of PWID decreased from 18.2% in 2005 to 0.3% in 2010. In an individual-level analysis of the amnesty cohort, attendance at methadone clinics was associated with a significantly lower HIV incidence (adjusted hazard ratio: 0.20, 95% CI: 0.06–0.67), and frequent users of needle/syringe program services had lower HIV incidence (0% in high NSP users, 0.5% in non NSP users). In addition, no HIV seroconversions were detected among prison inmates. The authors conclude that although their data are affected by participation bias, they strongly suggest that comprehensive harm reduction services and free treatment were associated with reversal of a rapidly emerging epidemic of HIV among PWID.

Expansion of HAART Coverage Is Associated with Sustained Decreases in HIV/AIDS Morbidity, Mortality and HIV Transmission: The "HIV Treatment as Prevention" Experience in a Canadian Setting Montaner JS, Lima VD, Harrigan PR, Lourenço L, Yip B, et al. PLoS ONE 2014; 9(2): e87872. doi:10.1371/journal.pone.0087872.

There has been renewed call for the global expansion of highly active antiretroviral therapy (HAART) under the framework of HIV treatment as prevention (TasP). However, population-level sustainability of this strategy has not been characterized. The authors used population-level longitudinal data from province-wide registries including plasma viral load, CD4 count, drug resistance, HAART use, HIV diagnoses, AIDS incidence, and HIV-related mortality. They fitted two Poisson regression models over the study period, to relate estimated HIV incidence and the number of individuals on HAART and the percentage of virologically suppressed individuals. HAART coverage, median pre-HAART CD4 count, and HAART adherence increased over time and were associated with increasing virological suppression and decreasing drug resistance. AIDS incidence decreased from 6.9 to 1.4 per 100,000 population (80% decrease, $p = 0.0330$) and HIV-related mortality decreased from 6.5 to 1.3 per 100,000 population (80% decrease, $p = 0.0115$). New HIV diagnoses declined from 702 to 238 cases (66% decrease; $p = 0.0004$) with a consequent estimated decline in HIV incident cases from 632 to 368 cases per year (42% decrease; $p = 0.0003$). Finally, the authors' models suggested that for each increase of 100 individuals on HAART, the estimated HIV incidence decreased 1.2% and for every 1% increase in the number of individuals suppressed on HAART, the estimated HIV incidence also decreased by 1%. These results show that HAART expansion between 1996 and 2012 in BC was associated with a sustained and profound population-level decrease in morbidity, mortality and HIV transmission. These findings support the long-term effectiveness and sustainability of HIV treatment as prevention within an adequately resourced environment with no financial barriers to diagnosis, medical care or antiretroviral drugs. The 2013 Consolidated World Health Organization Antiretroviral Therapy Guidelines offer a unique opportunity to further evaluate TasP in other settings, particularly within generalized epidemics, and resource-limited setting, as advocated by UNAIDS.

Effects Of Early Versus Delayed Initiation Of Antiretroviral Treatment On Clinical Outcomes Of HIV-1 Infection: Results From The Phase 3 HPTN 052 Randomised Controlled Trial Grinsztejn B, Hosseinipour, MC, Ribaudo HJ, Swindells S et al. The Lancet Infectious Diseases.1 April 2014; 14(4): 281-290.DOI: 10.1016/S1473-3099(13)70692-3

Use of antiretroviral treatment for HIV-1 infection has decreased AIDS-related morbidity and mortality and prevents sexual transmission of HIV-1. However, the best time to initiate antiretroviral treatment to reduce progression of HIV-1 infection or non-AIDS clinical events is unknown. The authors reported previously that early antiretroviral treatment reduced HIV-1 transmission by 96%. They aimed to compare the effects of early and delayed initiation of antiretroviral treatment on clinical outcomes. The HPTN 052 trial is a randomised controlled trial done at 13 sites in nine countries. The authors enrolled HIV-1-serodiscordant couples to the study and randomly allocated them to either early or delayed antiretroviral treatment by use of permuted block randomisation, stratified by site. Random assignment was unblinded. The HIV-1-infected member of every couple initiated antiretroviral treatment either on entry into the study (early treatment group) or after a decline in CD4 count or with onset of an AIDS-related illness (delayed treatment group). Primary events were AIDS clinical events (WHO stage 4 HIV-1 disease, tuberculosis, and severe bacterial infections) and the following serious medical conditions unrelated to AIDS: serious cardiovascular or vascular disease, serious liver disease, end-stage renal disease, new-onset diabetes mellitus, and non-AIDS malignant disease. Analysis was by intention-to-treat. This trial is registered with ClinicalTrials.gov, number NCT00074581. 1763 people with HIV-1 infection and a serodiscordant partner were enrolled in the study; 886 were assigned early antiretroviral treatment and 877 to the delayed treatment group (two individuals were excluded from this group after randomisation). Median CD4 counts at randomisation were 442 (IQR 373—522) cells per μL in patients assigned to the early treatment group and 428 (357—522) cells per μL in those allocated delayed antiretroviral treatment. In the delayed group, antiretroviral treatment was initiated at a median CD4 count of 230 (IQR 197—249) cells per μL. Primary clinical events were reported in 57 individuals assigned to early treatment initiation versus 77 people allocated to delayed antiretroviral

treatment (hazard ratio 0.73, 95% CI 0.52—1.03; p=0.074). New-onset AIDS events were recorded in 40 participants assigned to early antiretroviral treatment versus 61 allocated delayed initiation (0.64, 0.43—0.96; p=0.031), tuberculosis developed in 17 versus 34 patients, respectively (0.49, 0.28—0.89, p=0.018), and primary non-AIDS events were rare (12 in the early group *vs* nine with delayed treatment). In total, 498 primary and secondary outcomes occurred in the early treatment group (incidence 24.9 per 100 person-years, 95% CI 22.5—27.5) versus 585 in the delayed treatment group (29.2 per 100 person-years, 26.5—32.1; p=0.025). 26 people died, 11 who were allocated to early antiretroviral treatment and 15 who were assigned to the delayed treatment group. Early initiation of antiretroviral treatment delayed the time to AIDS events and decreased the incidence of primary and secondary outcomes. The clinical benefits recorded, combined with the striking reduction in HIV-1 transmission risk previously reported, provides strong support for earlier initiation of antiretroviral treatment. Funding: NIAID.

Do Metropolitan HIV Epidemic Histories and Programs For People Who Inject Drugs and Men Who Have Sex With Men Predict AIDS Incidence and Mortality Among Heterosexuals? Friedman SR, West BS, Tempalski B, Morton CM, Cleland CM, Des Jarlais DC, Hall HI, Cooper HLF. Annals of Epidemiology 2014; 24(4): 304–311.

The authors focus on a little-researched issue—how human immunodeficiency virus (HIV) epidemics and programs in key populations in metropolitan areas affect epidemics in other key populations. They consider (1) How are earlier epidemics among people who inject drugs (PWID) and men who have sex with men (MSM) related to later AIDS incidence and mortality among heterosexuals?; (2) Were prevention programs targeting PWID or MSM associated with lower AIDS incidence and mortality among heterosexuals?; and (3) Was the size of the potential bridge population of noninjecting drug users (NIDUs) in a metropolitan area associated with later AIDS incidence and mortality among heterosexuals? Using data for 96 large U.S. metropolitan areas, Poisson regression assessed associations of population prevalences of HIV-infected PWID and MSM (1992); NIDU population prevalence (1992–1994); drug use treatment coverage for PWID (1993); HIV counseling and testing coverage for MSM and for PWID (1992); and syringe exchange presence (2000) with CDC data on AIDS incidence and mortality among heterosexuals in 2006–2008, with appropriate socioeconomic controls. Population density of HIV+ PWID and of NIDUs were positively related, and prevention programs for PWID negatively related to later AIDS incidence among heterosexuals and later mortality among heterosexuals living with AIDS. HIV+ MSM population density and prevention programs for MSM were not associated with these outcomes. The authors conclude that efforts to reduce HIV transmission among PWID and NIDUs may reduce AIDS and AIDS-related mortality among heterosexuals. More research is needed at metropolitan area, network, and individual levels into HIV bridging across key populations and how interventions in one key population affect HIV epidemics in other key populations.

Cocaine Enhances HIV-1 Infectivity In Monocyte Derived Dendritic Cells By Suppressing MicroRNA-155 Napuri J, Pilakka-Kanthikeel S, Raymond A, Agudelo M, Yndart-Arias A, Saxena SK, Nair M. PLoS One. 2013; 8(12): e83682.

Cocaine and other drugs of abuse increase HIV-induced immunopathogenesis; and neurobiological mechanisms of cocaine addiction implicate a key role for microRNAs (miRNAs), single-stranded non-coding RNAs that regulate gene expression and defend against viruses. In fact, HIV defends against miRNAs by actively suppressing the expression of polycistronic miRNA cluster miRNA-17/92, which encodes miRNAs including miR-20a. IFN-g production by natural killer cells is regulated by miR-155 and this miRNA is also critical to dendritic cell (DC) maturation. However, the impact of cocaine on miR-155 expression and subsequent HIV replication is unknown. The authors examined the impact of cocaine on two miRNAs, miR-20a and miR-155, which are integral to HIV replication, and immune activation. Using miRNA isolation and analysis, RNA interference, quantitative real time PCR, and reporter assays we explored the effects of cocaine on miR-155 and miR-20 in the context of HIV infection. Here they demonstrate using monocyte-derived dendritic cells (MDCCs) that cocaine significantly inhibited miR-155 and miR-20a expression in a dose dependent manner. Cocaine and HIV synergized to lower miR-155 and miR-20a in MDDCs by 90%.

Cocaine treatment elevated LTR-mediated transcription and PU. 1 levels in MDCCs. But in context of HIV infection, PU. 1 was reduced in MDDCs regardless of cocaine presence. Cocaine increased DC-SIGN and and decreased CD83 expression in MDDC, respectively. Overall, the authors show that cocaine inhibited miR-155 and prevented maturation of MDDCs; potentially, resulting in increased susceptibility to HIV-1. These findings could lead to the development of novel miRNA-based therapeutic strategies targeting HIV infected cocaine abusers.

Variants In HAVCR1 Gene Region Contribute To Hepatitis C Persistence In African Americans Wojcik G, Latanich R, Mosbruger T, Astemborski J, Kirk GD, Mehta SH, Goedert JJ, Kim AY, Seaberg EC, Busch M, Thomas DL, Duggal P, Thio CL. J Infect Dis. 2014 Feb; 209(3): 355-359.
To confirm previously identified polymorphisms in HAVCR1 that were associated with persistent hepatitis C virus (HCV) infection in individuals of African and of European descent, the authors studied 165 subjects of African descent and 635 subjects of European descent. Because the association was only confirmed in subjects of African descent (rs6880859; odds ratio, 2.42; P =.01), they then used 379 subjects of African descent (142 with spontaneous HCV clearance) to fine-map HAVCR1. rs111511318 was strongly associated with HCV persistence after adjusting for IL28B and HLA (adjusted P = 8. 8 × 10(-4)), as was one 81-kb haplotype (adjusted P =.0006). The HAVCR1 genomic region is an independent genetic determinant of HCV persistence in individuals of African descent.

Gender Disparities in HIV Treatment Outcomes Following Release from Jail: Results from a Multicenter Study Meyer JP, Zelenev A, Wichersham J, Williams C, Teixeira P, Altice F. Am J Public Health. 2014; 104: 434–441. doi: 10.2105/AJPH.2013. 301553.
The authors assessed gender differences in longitudinal HIV treatment outcomes among HIV-infected jail detainees transitioning to the community. Data were from the largest multisite prospective cohort study of HIV-infected released jail detainees (n=1270)-the Enhancing Linkages to HIV Primary Care and Services in Jail Setting Initiative, January 2008 and March 2011, which had 10 sites in 9 states. The authors assessed baseline and 6-month HIV treatment outcomes, stratifying by gender. Of 867 evaluable participants, 277 (31.9%) were women. Compared with men, women were more likely to be younger, non-Hispanic White, married, homeless, and depressed, but were similar in recent alcohol and heroin use. By 6 months post-release, women were significantly less likely than men to experience optimal HIV treatment outcomes, including (1) retention in care (50% vs 63%), (2) antiretroviral therapy prescription (39% vs 58%) or optimal antiretroviral therapy adherence (28% vs 44%), and (3) viral suppression (18% vs 30%). In multiple logistic regression models, women were half as likely as men to achieve viral suppression. HIV-infected women transitioning from jail experience greater comorbidity and worse HIV treatment outcomes than men. Future interventions that transition people from jail to community-based HIV clinical care should be gender-specific.

Concurrent Life-Course Trajectories of Employment and Marijuana-Use: Exploring Interdependence of Longitudinal Outcomes Hara M, Huang DYC, Weiss RE, Hser Y-I. J Subst Abuse Treat. 2013; 45(5): 426-432.
This study analyzes data on 7661 individuals who participated in the 1979 National Longitudinal Survey of Youth (NLSY79) to estimate trajectories of employment and marijuana-use over a 17-year period. Bivariate random intercept and slope modeling is applied to examine concurrently the cross-correlation between the two concurrent longitudinal trajectories from age 23 to 39. Parameter estimates indicate baseline level (at age 23) of employment to be negatively correlated with marijuana, suggesting marijuana-use is associated with lower workforce productivity at age 23. The longitudinal employment slope is positively correlated with employment intercept for both males and females, indicating that survey participants with higher levels of employment at age 23 are more likely to have a positive impact on employment trajectory over time. For males, however, the employment slope is also significantly correlated with marijuana intercept (r=-0.07), indicating marijuana-use in early adulthood may uniquely lower workforce productivity over age.

Internet-delivered Treatment for Substance Abuse: A Multi-site Randomized Controlled Clinical Trial
Campbell AN, Nunes EV, Matthews AG, Stitzer M, Miele GM, Polsky D, Turrigiano E, Walters S, McClure EA, Kyle TL, Wahle A, Van Veldhuisen P, Goldman B, Babcock D, Stabile PQ, Winhusen T, Ghitza UE. Am J Psychiatry. 2014 Apr 4. [Epub ahead of print].
Computer-delivered interventions have the potential to improve access to quality addiction treatment care. The objective of this study was to evaluate the effectiveness of the Therapeutic Education System (TES), an Internet-delivered behavioral intervention that includes motivational incentives, as a clinician-extender in the treatment of substance use disorders. Adult men and women (N=507) entering 10 outpatient addiction treatment programs were randomly assigned to receive 12 weeks of either treatment as usual (N=252) or treatment as usual plus TES, with the intervention substituting for about 2 hours of standard care per week (N=255). TES consists of 62 computerized interactive modules covering skills for achieving and maintaining abstinence, plus prize-based motivational incentives contingent on abstinence and treatment adherence. Treatment as usual consisted of individual and group counseling at the participating programs. The primary outcome measures were abstinence from drugs and heavy drinking (measured by twice-weekly urine drug screens and self-report) and time to dropout from treatment. Compared with patients in the treatment-as-usual group, those in the TES group had a lower dropout rate (hazard ratio=0.72, 95% CI=0.57, 0.92) and a greater abstinence rate (odds ratio=1.62, 95% CI=1.12, 2.35). This effect was more pronounced among patients who had a positive urine drug or breath alcohol screen at study entry (N=228) (odds ratio=2.18, 95% CI=1.30, 3.68). The authors conclude that internet-delivered interventions such as TES have the potential to expand access and improve addiction treatment outcomes. Additional research is needed to assess effectiveness in non-specialty clinical settings and to differentiate the effects of the community reinforcement approach and contingency management components of TES.

Real-Time Tracking Of Neighborhood Surroundings and Mood In Urban Drug Misusers: Application Of A New Method To Study Behavior In Its Geographical Context Epstein DH, Tyburski M, Craig IM, Phillips KA, Jobes ML, Vahabzadeh M, Mezghanni M, Lin JL, Furr-Holden CD, Preston KL. Drug Alcohol Depend. 2014 Jan 1; 134: 22-29. doi: 10.1016/j.drugalcdep. 2013.09.007. Epub 2013 Sep 14.
Maladaptive behaviors may be more fully understood and efficiently prevented by ambulatory tools that assess people's ongoing experience in the context of their environment. To demonstrate new field-deployable methods for assessing mood and behavior as a function of neighborhood surroundings (geographical momentary assessment; GMA), the authors collected time-stamped GPS data and ecological momentary assessment (EMA) ratings of mood, stress, and drug craving over 16 weeks at randomly prompted times during the waking hours of opioid-dependent polydrug users receiving methadone maintenance. Locations of EMA entries and participants' travel tracks calculated for the 12 before each EMA entry were mapped. Associations between subjective ratings and objective environmental ratings were evaluated at the whole neighborhood and 12-h track levels. Participants (N=27) were compliant with GMA data collection; 3711 randomly prompted EMA entries were matched to specific locations. At the neighborhood level, physical disorder was negatively correlated with negative mood, stress, and heroin and cocaine craving (ps<.0001-.0335); drug activity was negatively correlated with stress, heroin and cocaine craving (ps .0009-.0134). Similar relationships were found for the environments around respondents' tracks in the 12h preceding EMA entries. The results support the feasibility of GMA. The relationships between neighborhood characteristics and participants' reports were counterintuitive and counter-hypothesized, and challenge some assumptions about how ostensibly stressful environments are associated with lived experience and how such environments ultimately impair health. GMA methodology may have applications for development of individual- or neighborhood-level interventions.

Cocaine Dysregulates Opioid Gating of GABA Neurotransmission in the Ventral Pallidum Kupchik YM, Scofield MD, Rice KC, Cheng K, Roques BP, Kalivas PW. J Neurosci. 2014; 34(3): 1057-1066.
The ventral pallidum (VP) is a target of dense nucleus accumbens projections. Many of these projections coexpress GABA and the neuropeptide enkephalin, a δ and μ opioid receptor (MOR) ligand. Of these two, the MOR in the VP is known to be involved in reward-related behaviors, such as hedonic responses to

palatable food, alcohol intake, and reinstatement of cocaine seeking. Stimulating MORs in the VP decreases extracellular GABA, indicating that the effects of MORs in the VP on cocaine seeking are via modulating GABA neurotransmission. Here, the authors use whole-cell patch-clamp on a rat model of withdrawal from cocaine self-administration to test the hypothesis that MORs presynaptically regulate GABA transmission in the VP and that cocaine withdrawal changes the interaction between MORs and GABA. They found that in cocaine-extinguished rats pharmacological activation of MORs no longer presynaptically inhibited GABA release, whereas blocking the MORs disinhibited GABA release. Moreover, MOR-dependent long-term depression of GABA neurotransmission in the VP was lost in cocaine-extinguished rats. Last, GABA neurotransmission was found to be tonically suppressed in cocaine-extinguished rats. These substantial synaptic changes indicated that cocaine was increasing tone on MOR receptors. Accordingly, increasing endogenous tone by blocking the enzymatic degradation of enkephalin inhibited GABA neurotransmission in yoked saline rats but not in cocaine-extinguished rats. In conclusion, these results indicate that following withdrawal from cocaine self-administration enkephalin levels in the VP are elevated and the opioid modulation of GABA neurotransmission is impaired. This may contribute to the difficulties withdrawn addicts experience when trying to resist relapse.

Pain-related Depression of the Mesolimbic Dopamine System in Rats: Expression, Blockade by Analgesics, and Role of Endogenous κ-opioids Leitl MD, Onvani S, Bowers MS, Cheng K, Rice KC, Carlezon WA Jr, Banks ML, Negus SS. Neuropsychopharmacology 2014; 39(3): 614-624.
Pain is often associated with depression of behavior and mood, and relief of pain-related depression is a common goal of treatment. This study tested the hypothesis that pain-related behavioral depression is mediated by activation of endogenous κ-opioid systems and subsequent depression of mesolimbic dopamine release. Adult male Sprague-Dawley rats were implanted with electrodes targeting the medial forebrain bundle (for behavior studies of intracranial self-stimulation (ICSS)) or with cannulae for microdialysis measures of nucleus accumbens dopamine (NAc DA). Changes in ICSS and NAc DA were examined after treatment with a visceral noxious stimulus (intraperitoneal injection of dilute lactic acid) or an exogenous κ-agonist (U69593). Additional studies examined the sensitivity of acid and U69593 effects to blockade by two analgesics (the nonsteroidal antiinflammatory drug ketoprofen and the μ-opioid agonist morphine) or by the κ-antagonist norbinaltorphimine (norBNI). The effects of acid were also examined on mRNA expression for prodynorphin (PDYN) and κ-opioid receptors (KORs) in mesocorticolimbic brain regions. Both acid and U69593 depressed ICSS and extracellular levels of NAc DA. Pain-related acid effects were blocked by ketoprofen and morphine but not by norBNI. The U69593 effects were blocked by norBNI but not by ketoprofen, and were only attenuated by morphine. Acid did not significantly alter PDYN or KOR in NAc, but it produced a delayed increase in PDYN in prefrontal cortex. These results support a key role for the mesolimbic DA system, but a more nuanced role for endogenous κ-opioid systems, in mediating acute pain-related behavioral depression in rats.

Similar Roles of Substantia Nigra and Ventral Tegmental Dopamine Neurons in Reward and Aversion Ilango A, Kesner AJ, Keller KL, Stuber GD, Bonci A, Ikemoto S. J Neurosci. 2014 Jan 15; 34(3): 817-822. doi: 10.1523/Journal of Neuroscience.1703-13.2014.
Dopamine neurons in the ventral tegmental area (VTA) are implicated in affective functions. However, it is unclear to what extent dopamine neurons in substantia nigra pars compacta (SNc) play such roles. TH-Cre transgenic mice received adeno-associated viral vectors encoding channelrhodopsin2 (ChR2), halorhodopsin (NpHR), or control vector into the VTA or SNc, resulting in selective expression of these opsins in dopamine neurons. Mice with ChR2 learned instrumental responding to deliver photostimulation into the VTA or SNc and also sought for the compartment where they received photostimulation (i.e., operant place preference). Operant place preference scores were highly correlated with self-stimulation responses. In contrast, mice with NpHR avoided the compartment where they received photostimulation into the VTA, SNc, or dorsal striatum, whereas control mice did not. These observations suggest that the excitation and inhibition of SNc dopamine neurons elicit positive and negative affective effects, respectively, similar to those of VTA dopamine neurons.

Large Scale Brain Network Coupling Predicts Acute Nicotine Abstinence Effects on Craving and Cognitive Function Lerman C, Gu H, Yang Y, Ruparel K, Stein, EA. JAMA Psychiatry 2014 Mar 12. doi: 10.1001/jamapsychiatry.2013.4091. [Epub ahead of print].

Interactions of large-scale brain networks may underlie cognitive dysfunctions in psychiatric and addictive disorders. To test the hypothesis that the strength of coupling among 3 large-scale brain networks—salience, executive control, and default mode—will reflect the state of nicotine withdrawal (vs smoking satiety) and will predict abstinence-induced craving and cognitive deficits and to develop a resource allocation index (RAI) that reflects the combined strength of interactions among the 3 large-scale networks. A within-subject functional magnetic resonance imaging study in an academic medical center compared resting-state functional connectivity coherence strength after 24 hours of abstinence and after smoking satiety. The authors examined the relationship of abstinence-induced changes in the RAI with alterations in subjective, behavioral, and neural functions. They included 37 healthy smoking volunteers, aged 19 to 61 years, for analyses. The main outcome measures were inter-network connectivity strength (primary) and the relationship with subjective, behavioral, and neural measures of nicotine withdrawal during abstinence vs smoking satiety states (secondary). The RAI was significantly lower in the abstinent compared with the smoking satiety states (left RAI, P = .002; right RAI, P = .04), suggesting weaker inhibition between the default mode and salience networks. Weaker inter-network connectivity (reduced RAI) predicted abstinence-induced cravings to smoke ($r = -0.59$; P = .007) and less suppression of default mode activity during performance of a subsequent working memory task (ventromedial prefrontal cortex, $r = -0.66$, P = .003; posterior cingulate cortex, $r = -0.65$, $p = .001$). Alterations in coupling of the salience and default mode networks and the inability to disengage from the default mode network may be critical in cognitive/affective alterations that underlie nicotine dependence.

NIH/HHS POLICY UPDATES

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

2014

March 28	Maintaining Confidentiality in NIH Peer Review
March 20	NIH Policy for Managing Conflict of Interest in the Peer Review of Concepts and Proposals for Research and Development Contract Projects
March 20	Notice of Extension of Eligibility for PA-14-150 "Ruth L. Kirschstein National Research Service Award (NRSA) Individual Predoctoral MD/PhD or Other Dual-Doctoral Degree Fellowship (Parent F30)"
March 14	NIH Extramural Grant Systems Upgrade for Unicode Compatibility Means Memorial Day Weekend Downtime
March 14	Adjustments to May 25-28, 2014 Grant Application Due Dates
March 11	Request for Information: Invitation to Comment on Proposed Guidance Regarding Significant Changes to Ongoing Animal Activities
March 7	Notice of Implementation of Pilot Program for Enhancement of Employee Whistleblower Protections
March 7	Notice of Reissuance of the Ruth L. Kirschstein National Research Service Award (NRSA) Individual Fellowship Funding Opportunity Announcements
March 5	Notice of Online Data Submission and Access to the National Institutes of Health (NIH) database of Genotypes and Phenotypes (dbGaP)
March 4	NIH Will Open the Research Performance Progress Report (RPPR) for All Type 5 Non-SNAP Progress Reports on April 25, 2014
February 27	Notice of Additional Legislative Mandate in Effect for FY2014 Restricting Pornography on Computer Networks
February 18	Notice of Intent to Publish the Reissuance of the Ruth L. Kirschstein National Research Service Awards for Individual Predoctoral MD/PhD and Other Dual Doctoral Degree Fellows (Parent F30)" Funding Opportunity Announcement
February 18	Notice of Intent to Publish the Reissuance of the Ruth L. Kirschstein National Research Service Awards for Individual Predoctoral Fellows (Parent F31)" Funding Opportunity Announcement
February 18	Notice of Intent to Publish the Reissuance of the Ruth L. Kirschstein National Research Service Awards (NRSA) for Individual Postdoctoral Fellows (Parent F32)" Funding Opportunity Announcement
February 18	Notice of Intent to Publish the Reissuance of the Ruth L. Kirschstein National Research Service Awards (NRSA) for Individual Senior Fellows (Parent F33)" Funding Opportunity Announcement
February 18	Notice of Intent to Publish the Reissuance of the Ruth L. Kirschstein National Research Service Awards for Individual Predoctoral Fellowships to Promote Diversity in Health-Related Research (Parent F31 - Diversity)" Funding Opportunity Announce
February 18	Registration Now Open for the 2014 NIH Regional Seminar on Program Funding and Grants Administration in Baltimore, MD
February 10	Ruth L. Kirschstein National Research Service Award (NRSA) Stipends,

	Tuition/Fees and Other Budgetary Levels Effective for Fiscal Year 2014
February 10	Notice of Salary Limitation on Grants, Cooperative Agreements, and Contracts
February 10	Notice of Legislative Mandates in Effect for FY2014
February 10	NIH Fiscal Policy for Grant Awards FY 2014
February 7	Notice of Revised Term of Award for All Recovery Act Awards to Repeal Section 1512 Reporting Requirement Effective February 1, 2014
February 6	Timetable for Next Round Resubmission of New Investigator R01 Applications Changed for October 2014 Council
February 5	NIH Implements Option for Applicants to Switch between the SBIR/STTR programs and the SBIR Direct to Phase II pilot of the SBIR/STTR Reauthorization Act of 2011
February 5	New Requirements in the Funding Opportunity Announcement PAR-14-073 "Shared Instrumentation Grant Program (S10)"
January 30	Updated Electronic Application Forms (FORMS-C) Now Available for Administrative Supplement (non-competing Type 3), Successor-in-Interest (Type 6), and Change of Grantee Organization (Type 7) Applications
January 30	NIH Reminds Applicants to Use Updated Electronic Application Forms (FORMS-C) for F, K, T and D Submissions with Due Dates on/after January 25, 2014 - Correction

CONGRESSIONAL AFFAIRS
(Prepared April 25, 2014)

APPROPRIATIONS

The President's budget request for NIDA for FY 2015 is $1.023 billion. This compares to a 2014 "enacted" level of $1.016 billion. For NIH, the President requested $30.362 billion, a 0.7% increase over the 2014 level.

CONGRESSIONAL HEARINGS/MEETINGS

Past

On February 25, 2014, NIDA Director Dr. Nora Volkow met with Congressman William Foster (D-IL) at his request. He is especially concerned about the rise of opiate abuse and addiction in his district.

On March 20, 2014, NIDA Deputy Director Dr. Wilson Compton participated in a staff briefing sponsored by the Senate Caucus for International Narcotics Control. The topic: opiate abuse and addiction. Other federal agencies participated, including ONDCP, SAMHSA, FDA, and DEA.

On April 2, 2014, NIDA Director Dr. Nora Volkow testified in front of the House Appropriations Committee, Subcommittee on Commerce, Science, Justice and Related Agencies. This was the budget hearing for the Drug Enforcement Administration. Subcommittee Chairman Frank Wolf (R-VA) invited Dr. Volkow to testify on the science of addiction, what we know and understand about addiction as a brain disease. With the current popular interest in marijuana and opiates issues, Chairman Wolf asked Dr. Volkow to focus some attention on those specific topics. He was extremely appreciative of her testimony, evidenced by a letter he sent to the President recommending to him that he meet with Dr. Volkow on these issues.

On April 22, 2014, NIH Director Dr. Francis Collins and NIDA Director Dr. Nora Volkow delivered keynote addresses to the third annual National Rx Drug Abuse Summit. Dr. Collins and Dr. Volkow were both personally invited by House Appropriations Chairman Harold Rogers (R-KY) to be part of this event. This was the first year Dr. Collins participated; Dr. Volkow has been a keynote speaker for each of the three years.

On April 23, 2014, NIDA Deputy Director Wilson Compton participated in a briefing sponsored by the Senate Committee on Health, Education, Labor and Pensions. Topic: Prescription Drug Abuse. At the request of the Committee, Dr. Compton focused on NIDA's role in addressing this issue. Other participating agencies included CDC and SAMHSA.

On April 24, 2014, NIDA Deputy Director Dr. Wilson Compton participated in a congressional briefing focused on the intersection of hepatitis C and opioid abuse, especially in young people. This briefing was organized by the Harm Reduction Coalition and the National Alliance of State & Territorial AIDS Directors.

On April 29, 2014, the Senate Appropriations Committee held a hearing on Driving Innovation Through Federal Investments. NIH Director Dr. Francis Collins testified.

On April 29, 2014, the House Energy and Commerce Subcommittee on Oversight and Investigations held a hearing on heroin and prescription drug abuse. NIDA Director Dr. Nora Volkow testified, along with other witnesses from SAMHSA and CDC.

On April 29, 2014, Senators Sheldon Whitehouse (D-RI) and Rob Portman (D-OH) sponsored the first in a series of Capitol Hill addiction forums. The first one is titled Addiction Forum: Overview of Addiction in the Criminal Justice System. Dr. Redonna Chandler, Acting Director, Division of Epidemiology, Services and Prevention Research, NIDA, presented as part of the opening panel. Dr. Chandler is a recognized national expert on this topic, having spent years working with DOJ and others to disseminate evidenced-based research.

On April 30, 2014, the Senate Veterans Affairs Committee held a hearing on overmedication, and the particular role of opioids in this discussion. Dr. Josephine Briggs, Director, NCCAM, testified along with representatives from the Department of Veterans Affairs and the Army.

Future expected events

On May 9**,** 2014, at the request of the Congressional Hepatitis Caucus, NIDA Deputy Director Dr. Wilson Compton will participate in a briefing entitled Hepatitis on the Hill. Also invited to participate are HRSA and the Office of the Assistant Secretary for Health.

On May 14, 2014, the Senate Caucus on International Narcotics control will hold a hearing on the Causal Role Prescription Drug Abuse has had on the Increased Use of Heroin in the United States. Dr. Nora Volkow, Director, NIDA, will testify. Other expected witnesses include: Michael Botticelli, Acting Director, Office of National Drug Control Policy; Dr. H. Westley Clark, Director, Substance Abuse and Mental Health Services Administration; and Dr. Andrew Kolodny, Chief Medical Officer, Phoenix House.

On June 19, 2014, the House Oversight and Government Reform Subcommittee on Government Operations will hold a hearing on marijuana. Dr. Nora Volkow, Director, NIDA, will testify. This is the third in a series of hearings held by this Subcommittee on this topic. Also scheduled to testify is Dr. Douglas Throckmorton of FDA.

SOME 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, 2013, 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, 2013, 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 1263 – On March 19, 2013, Representative Doris Matsui (D-CA) introduced the Excellence in Mental Health Act, to increase access to community behavioral health services for all Americans and to improve Medicaid reimbursement for community behavioral health services. The bill was referred to the Committee on Energy and Commerce. See also S 264,
S 265.

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, and Judiciary. See also S 621. [NOTE: The FDA has recommended to HHS the reclassification of hydrocodone combination products as Schedule II controlled substances.]

HR 1366 – On March 21, 2013, Representative Stephen Lynch (D-MA) introduced the Stop Oxycontin Abuse Act of 2013, to direct the Commissioner of Food and Drugs to modify the approval of any drug containing controlled-release oxycodone hydrochloride to limit such approval to use for the relief of severe-only instead of moderate-to-severe pain, and for other purposes. The bill was referred to the Committee on Energy and Commerce.

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.

HR 3717 – On December 12, 2013, Representative Tim Murphy (R-PA) introduced the Helping Families in Mental Health Crisis Act of 2013, to make available needed psychiatric, psychological, and supportive services for individuals diagnosed with mental illness and families in mental health crisis, and for other purposes. The bill was referred to the House Committees on: Energy and Commerce; Judiciary; Energy and the Workforce; Ways and Means; and Science, Space and Technology.

HR 4046 – On February 11, 2014, Representative Steven Cohen (D-TN) introduced the Unmuzzle the Drug Czar Act, to strike provisions that prohibit the Director of the Office of National Drug Control Policy from studying the legalization of marijuana, that require the Director to oppose any attempt to legalize marijuana, and for other purposes. The bill was referred to the Committees on Oversight and Government Reform, Judiciary, and Energy and Commerce.

HR 4169 – On March 4, 2014, Donna Edwards (D-MD) introduced the Stop Overdose Stat (S.O.S.) Act, to prevent deaths occurring from drug overdoses. The bill would create a new CDC grant program focused on overdose prevention; create a new CDC grant program to improve fatal and nonfatal drug overdose surveillance and reporting capabilities; create a national task force that would develop a plan to reduce drug overdose deaths (NIDA explicitly included in this); and focus on overdose prevention research at NIDA (the bill authorizes $5 million dollars a year for the next few years to do this work). The bill was referred to the Committee on Energy and Commerce, Subcommittee on Health.

HR 4241 – On March 13, 2014, Representative Stephen Lynch (D-MA) introduced the Act to Ban Zohydro, to withdraw approval for the drug Zohydro ER and prohibit the Food and Drug Administration from approving such drug unless it is reformulated to prevent abuse. The bill was referred to the Committee on Energy and Commerce. See S. 213443024

S 237 – On February 7, 2013, Senator Lisa Murkowski (R-AK) introduced the Advancing FASD 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 264 – On February 7, 2013, Senator Debbie Stabenow (D-MI) introduced the Excellence in Mental Health Act, to expand access to community mental health centers and improve the quality of mental health care for all Americans. The bill was referred to the Committee on Health, Education, Labor, and Pensions. See also S 265, HR 1263

NOTE: On March 31, 2014, Congress passed the Protecting Access to Medicare Act (H.R. 4302), which included a demonstration program based on the Excellence in Mental Health Act. The Excellence Act will increase Americans' access to community mental health and substance use treatment services while improving Medicaid reimbursement for these services.

S 265 – On February 7, 2013 Senator Jack Reed (D-RI) introduced Community-Based Mental Health Infrastructure Improvements Act, to amend the Public Health Service Act to provide grants for community-based mental health infrastructure improvement. The bill was referred to the Committee on Health, Education, Labor and Pensions. See also S 264, HR 1263

S 348 – On February 14, 2013, 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. [NOTE: The FDA has recommended to HHS the reclassification of hydrocodone combination products as Schedule II controlled substances.]

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.

S 1277 – On July 10, 2013, Senator Barbara Boxer (D-CA) introduced the Combating Prescription Drug Abuse Act, to establish a commission for the purpose of coordinating efforts to reduce prescription drug abuse, and for other purposes. The bill was referred to the Committee on Health, Education, Labor and Pensions.

S 2134 -- On March 13, 2014, Senator Joe Manchin (D-WV) introduced the Act to Ban Zohydro, to withdraw approval for the drug Zohydro ER and prohibit the Food and Drug Administration from approving such drug unless it is reformulated to prevent abuse. The bill was referred to the Committee on Health, Education, Labor and Pensions. See HR 4241.

PROGRAM ACTIVITIES/FOAS

New NIDA RFAs

On April 4, 2014, NIDA issued an RFA entitled **Avenir Award Program for Research on Substance Abuse and HIV/AIDS (DP2**) **RFA-DA-15-007**. Avenir means future in French, and this award looks toward the future by supporting early stage investigators proposing highly innovative studies. The award will support those in an early stage of their career who may lack the preliminary data required for an R01 grant, but who propose high impact research and who show promise of being tomorrow's leaders in the field. NIDA has developed two Avenir Award Programs, one for HIV/AIDS research and the other for genetics or epigenetics studies. The Avenir Award Program for Research on Substance Abuse and HIV/AIDS will support creative individuals who wish to pursue innovative research at the nexus of substance abuse and HIV/AIDS. The Avenir Award Program for Research on Substance Abuse and HIV/AIDS will support research approaches for substance using populations with or at risk for HIV/AIDS that may lead to improved preventive interventions, improved therapies and/or long term retention in care, and ultimately, eradication of HIV. Open date: October 12, 2014. Application due date(s): November 12, 2014, November 12, 2015, November 14, 2016, by 5:00 PM local time of applicant organization. AIDS application due date(s): November 12, 2014, November 12, 2015, November 14, 2016, by 5:00 PM local time of applicant organization.

On March 27, 2014, NIDA issued an RFA entitled **Avenir Award Program for Genetics or Epigenetics of Substance Abuse (DP2) RFA-DA-15-006.** Avenir means future in French, and this award looks toward the future by supporting early stage investigators proposing highly innovative studies. The award will support those in an early stage of their career who may lack the preliminary data required for an R01 grant, but who propose high impact research and who show promise of being tomorrow's leaders in the field. NIDA has developed two Avenir Award Programs, one for HIV/AIDS research and the other for genetics or epigenetics studies. The Genetic Avenir Award program supports early stage investigators proposing highly innovative studies that open new areas of research for the genetics or epigenetics of addiction. The award will support those in an early stage of their career who may lack the preliminary data required for an R01 grant, but who propose high impact research and who show promise of being tomorrow's leaders in the field of genetics or epigenetics of substance abuse. Open date: July 18, 2014. Application due date(s): August 18, 2014, August 18, 2015, August 18, 2016, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

On February 13, 2014, NIDA issued an RFA entitled **NIDA Avant-Garde Award Program for HIV/AIDS and Drug Use Research (DP1) RFA-DA-15-004.** The NIDA Avant-Garde Award Program for HIV/AIDS Research supports individual scientists of exceptional creativity who propose high-impact research that will open new areas of HIV/AIDS research and/or lead to new avenues for prevention and treatment of HIV/AIDS among drug abusers. The term “avant-garde” is used to describe highly innovative approaches that have the potential to be transformative. The proposed research should reflect approaches and ideas that are substantially different from those already being pursued by the investigator or others. The NIDA Avant-Garde award supports innovative, basic research that may lead to improved preventive interventions or therapies; creative, new strategies to prevent disease transmission; novel approaches to improve disease outcomes; and creative approaches to eradicating HIV or improving the lives of those living with HIV. Open date: June 29, 2014. Application due date(s): July 29, 2014, July 29, 2015, July 29, 2016, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

On February 5, 2014, NIDA issued an RFA entitled **Advancing Exceptional Research on HIV/AIDS and Substance Abuse (R01) RFA-DA-15-005.** This FOA 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 Avant-Garde award supports individuals who conduct high-risk, high-reward research and does not require a detailed research plan. Applications submitted under this FOA are expected to have a detailed research plan and preliminary data. This FOA 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. The nexus with substance abuse should be clearly described. This FOA is open to both individual researchers and research teams and is not limited to any one area of research on HIV and substance use. Open date: June 30, 2014. Application due date(s): July 31, 2014, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

On January 31, 2014, NIDA issued an RFA entitled **Medications Development Centers of Excellence Cooperative Program (U54) RFA-DA-15-003.** This FOA solicits Specialized Center Cooperative Agreement (U54) applications to provide support for Medications Development Centers of Excellence (MDCE) with emphasis solely on clinical research directed towards the identification, evaluation, and development of safe and effective medications and biologics for treatment of substance use disorders (SUDs). Research may focus on both currently approved or novel investigational products. Centers may have a translational project to reinforce rationale of medications for testing. Any preclinical work proposed must be specifically devoted to the reinforcement of rationale of medications planned for clinical testing during the life of the project. Open date: n/a. Application due date(s): April 25, 2014. AIDS application due date(s): Not Applicable.

New NIDA Program Announcements

On March 26, 2014, NIDA issued PAs entitled **Effects of Cannabis Use and Cannabinoids on the Developing Brain (R21) PA-14-162, (R01) PA-14-163, (R03) PA-14-164.** This Funding Opportunity Announcement (FOA) encourages applications from institutions and organizations that propose to study the effects and functional consequences of cannabis and cannabinoid exposures on the developing brain, from pre-, peri-, post-natal development through young adulthood in animal models and humans. Topics of interest pertaining to this PA include, but are not limited to: molecular and cellular mechanisms of cannabis/cannabinoid effects on the developing brain; long term functional consequences of cannabis/cannabinoid exposure on learning and memory, cognitive and emotional development. Open date: May 5, 2014 (R01), May 16, 2014 (R21 and R03). Application due date(s): Standard dates apply, by 5:00 PM local time of applicant organization AIDS application due date(s): Standard AIDS dates apply, by 5:00 PM local time of applicant organization.

On March 3, 2014, NIDA, in collaboration with NIDDK, issued PAs entitled **Prevention and Treatment of Substance Using Populations with or at Risk for HCV (R34) PA-14-135, (R21) PA-14-136, (R01) PA-14-137.** This Funding Opportunity Announcement outlines priority areas for high impact clinical and basic research for at-risk substance using populations, including those infected with or at risk for HIV. In particular, this FOA encourages research focused on prevention and treatment of Hepatitis C Virus (HCV) to reduce new infections and identify and treat existing infections more effectively. This FOA is informed by priority areas in the 2011 HHS Action Plan, Combating the Silent Epidemic of Viral Hepatitis: Action Plan for the Prevention, Care and Treatment of Viral Hepatitis. Open date: May 5, 2014 (R01), May 16, 2014 (R21 and R34). Application due date(s): Standard dates apply, by 5:00 PM local time of applicant organization AIDS application due date(s): Standard AIDS dates apply, by 5:00 PM local time of applicant organization.

On February 20, 2014, NIDA issued PAs entitled **Synthetic Psychoactive Drugs and Strategic Approaches to Counteract Their Deleterious Effects (R03) PAR-14-104, (R21) PAR-14-105, (R01) PAR-14-106.** The purpose of this Funding Opportunity Announcement (FOA) is to support research to deepen our knowledge of the use of synthetic psychoactive drugs, their mechanisms of action, their health

effects, and development of prevention strategies and strategies to treat patients in emergency departments and long range treatment. Open date: May 5, 2014 (R01), May 16, 2014 (R03 and R21). Application due date(s): Standard dates apply, by 5:00 PM local time of applicant organization AIDS application due date(s): Standard AIDS dates apply, by 5:00 PM local time of applicant organization.

On February 4, 2014, NIDA issued PAs entitled **Neuroimmune Signaling and Function in Substance Use Disorders (R01) PA-14-084, (R21) PA-14-083.** The purpose of this Funding Opportunity Announcement (FOA) is to encourage the submission of research project grant applications that propose to examine the molecular, cellular, circuit, and behavioral responses to neuroimmune signaling within the central nervous system (CNS) as it pertains to the initiation, escalation, and maintenance of, and the neurological consequences resulting from, substance use disorders (SUDs), and to abstinence and withdrawal from, and subsequent relapse of, drug use. The goal of this understudied area of research is to determine the extent to which neuroimmune responses contribute to or protect against current and future risk and consequences of SUDs. Open date(s): May 5, 2014 (R01), May 16, 2014 (R21). Application due date(s): Standard dates apply, by 5:00 PM local time of applicant organization AIDS application due date(s): Standard AIDS dates apply, by 5:00 PM local time of applicant organization.

New FOAs Issued by the NIH Roadmap

On April 18, 2014, the NIH Common Fund issued a Roadmap RFA entitled **Undiagnosed Diseases Gene Function Research (R21) RFA-RM-14-005.** The purpose of this Exploratory/Developmental Research Funding Opportunity 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). Responsive applications will propose to investigate the underlying genetics, biochemistry and/or pathophysiology of newly diagnosed diseases in association with the respective gene variant(s) identified through the UDN. In recent years, gene function studies combined with genetic and genomic analyses and metabolic studies have greatly improved diagnoses of these very rare diseases and advanced scientific knowledge of the underlying pathogenesis. This initiative is funded through the NIH Common Fund, which supports cross-cutting programs that are expected to have exceptionally high impact. Open date: May 23, 2014. Application due date(s): June 23, 2014, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

On February 12, 2014, the NIH Common Fund issued a Roadmap RFA entitled **Limited Competition: Renewal Applications for Technology Development for New Affinity Reagents Against the Human Proteome (U01) RFA-RM-14-002.** The purpose of the NIH Common Fund Protein Capture Reagents Program (PCRP) aims to develop over time the capacity to generate a community resource of high quality renewable affinity reagents for all human proteins (see https://commonfund.nih.gov/proteincapture/). This Funding Opportunity Announcement (FOA) is a component of the PCRP, and it seeks renewal applications to cooperative agreements that were funded through **RFA-RM-10-018.** Novel approaches for producing validated protein affinity reagents have been developed by the presently funded technology centers and have demonstrated potential for substantially reducing cost and increasing throughput. To determine if any of these approaches can be used in a large-scale proteome project, applicants funded through this FOA are expected to demonstrate scalability by generating affinity reagents recognizing at least three hundred human protein targets. Open date: May 25, 2014. Application due date(s): April 25, 2014, by 5:00 PM local time of applicant organization. AIDS application due date(s): Not Applicable.

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

Development of Software and Analysis Methods for Biomedical Big Data in Targeted Areas of High Need (U01) RFA-HG-14-020

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

Early Stage Development of Technologies in Biomedical Computing, Informatics, and Big Data Science (R01) PA-14-155

Extended Development, Hardening and Dissemination of Technologies in Biomedical Computing, Informatics and Big Data Science (R01) PA-14-156

Early Stage Development of Technologies in Biomedical Computing, Informatics, and Big Data Science (R41/R42) PA-14-157

Early Stage Development of Technologies in Biomedical Computing, Informatics, and Big Data Science (R43/R44) PA-14-154

Ruth L. Kirschstein National Research Service Award (NRSA) Individual Predoctoral Fellowship (Parent F31) PA-14-147

Ruth L. Kirschstein National Research Service Award Individual Predoctoral Fellowship to Promote Diversity in Health-Related Research (Parent F31 - Diversity) PA-14-148

Ruth L. Kirschstein National Research Service Award (NRSA) Individual Postdoctoral Fellowship (Parent F32) PA-14-149

Ruth L. Kirschstein National Research Service Award (NRSA) Individual Predoctoral MD/PhD or Other Dual-Doctoral Degree Fellowship (Parent F30) PA-14-150

Behavioral Interventions to Address Multiple Chronic Health Conditions in Primary Care (R01) PA-14-114

Eradication of HIV-1 from Central Nervous System Reservoirs (R01) PA-14-095

HIV Infection of the Central Nervous System (R01) PA-14-094

Bioengineering Research Partnerships (BRP) R01 PAR-14-092

Direct Phase II SBIR Grants to Support Biomedical Technology Development PAR-14-088

Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp) PA-14-077

Successor-in-Interest (Type 6 Parent) PA-14-079

Change of Grantee Organization (Type 7 Parent) PA-14-078

New RFAs Issued by the NIH Blueprint for Neuroscience Research

NIH Blueprint Program for Enhancing Neuroscience Diversity through Undergraduate Research Education Experiences (R25) RFA-NS-14-010

New NIDA Administrative Supplement Program Announcements

On February 26, 2014, NIDA issued an administrative supplement PAR entitled **Additional Research Training Positions for NIDA-Supported NRSA Institutional Training (T32) Grants (Admin Supp) PAR-14-115**. The purpose of this administrative supplement program is to provide funds to support additional training positions on current NIDA-supported institutional Ruth L. Kirschstein National Research Service Award (NRSA) programs to enhance research training capacity in NIDA mission-critical areas. Mission-critical areas include, but are not limited to, genetics and epigenetics, computational neuroscience, HIV/AIDS, medications development, marijuana/ cannabinoid and tobacco/nicotine and health care reform/delivery innovations. Duration of supplement support is one to two years, depending on the number of years remaining on the parent T32 grant. Applications were due March 21, 2014 by 5:00 PM local time of applicant organization. Earliest start dates for awards is July 1, 2014.

On March 5, 2014, NIDA, in collaboration with NIAAA and NCI, issued an administrative supplement PA entitled **Additional Research Training Positions for NIAAA-, NIDA-, NCI-supported NRSA Institutional Training (T32) Grants (Admin Supp) PA-14-116.** The purpose of this administrative supplement program is to provide funds to support additional training positions on NIAAA-, NIDA-, or NCI-supported T32 programs to help meet the goals of Collaborative Research on Addiction at NIH (CRAN). Duration of support is up to three years, depending on the number of years remaining on the parent T32 grant. Applications were due by April 9, 2014, by 5:00 PM local time of applicant organization. Earliest start date is July 1, 2014.

NIDA will be awarding 20 travel awards to NIDA-supported NRSA trainees, NRSA fellows, and Minority Supplement recipients to attend the 2014 CPDD Meeting. The application deadline for these awards was December 19, 2013.

COMMUNICATIONS

PUBLICATIONS/VIDEOS

NIDA Publications and Online Resources

"Heads Up" (Scholastic/NIDA) ***Drugs + Your Body: It Isn't Pretty!*** interactive poster (January 2014): http://www.scholastic.com/drugs-and-your-body/

"Research Report Series: Hallucinogens and Dissociative Drugs" (Revised January 2014) http://www.drugabuse.gov/publications/research-reports/hallucinogens-dissociative-drugs

"Research Report Series: Heroin" (Revised February 2014): http://www.drugabuse.gov/publications/research-reports/heroin

"Marijuana: Facts Parents Need to Know" (Revised March 2014): http://www.drugabuse.gov/publications/marijuana-facts-parents-need-to-know

NIDA Notes
Nineteen new articles and 2 videos (Elizabeth Howell and Joni Rutter, also available as podcasts) have been posted on the *NIDA Notes* homepage. The *NIDA Notes* website has added an RSS feature whereby readers can subscribe to have new articles delivered directly to their browser or email. Three email blasts have been sent to subscribers -- two content updates and one announcing RSS feeds. December - February article views numbered 103,000 which are up, partly as a result of a Google AdWords campaign.

Videos

- **What's New at NIDA:**
  Office of Science Policy and Communication Director's notes for January
  http://youtu.be/jw0eUbvJRyo
- **NDFW Teen MOTS, Part III**
  http://youtu.be/Y_gf4Wpe5xA
- **NDFW Dance Party 2014**
  http://youtu.be/olPg12Cgec4
- **IQ Challenge Videos**
  http://youtu.be/LXixFul6wFk
- **Three (3) NDFW Dance Party Tweets (Images and Videos)**
  http://www.flickr.com/photos/nida-nih/12105064696 http://www.flickr.com/photos/nida-nih/12104779564 http://www.flickr.com/photos/nida-nih/12104687563
- **CEWG-NIDA, Heroin in the Twin Cities**
  http://www.youtube.com/watch?v=8DMlMa-uubI&list=UUfXHx9qyqeB3ezHQnHk8zXA
- **NIDA Research Spotlight: "Sex, Drugs and Facebook"**
  http://youtu.be/Lonhn1BElis
- **NIDA TV Spotlight: Communities That Care**
  http://youtu.be/nmMhCxo4u1w

CTN-Related Publications

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

Data from 29 CTN studies are now available on the NIDA Data Sharing website http://www.nida.nih.gov/CTN/Data.html. Over 2,300 data sets have been downloaded by researchers from 55 countries. These data sets are in compliance with HIPAA and CDISC (Clinical Data Interchange Standards Consortium) standards in support of the interoperability required by the NIH Roadmap. The CTN Data Share is also part of the Neuroscience Information Framework (NIF), which is a dynamic inventory of Web-based neuroscience resources: data, materials, and tools accessible via any computer connected to the Internet.

COMMUNITY AND PRESS EVENTS

NIDA Director Dr. Nora Volkow Speaks at 2014 Clinton Foundation Health Matters Conference
On January 14, 2014, in La Quinta, California, Dr. Nora Volkow participated in a panel discussion on prescription drug abuse and misuse at the Clinton Foundation Health Matters Conference. This conference served as the annual anchor event for the Clinton Health Matters Initiative which works to improve the health and well-being of people across the United States by activating individuals, communities, and organizations to make meaningful contributions to the health of others. The audience was comprised of approximately 450 senior business, healthcare, entertainment and community and sports leaders. The NIDA press office conducted social media outreach.

2014 Chat Day and National Drug Facts Week (NDFW)
NIDA conducted its annual Chat Day (Jan 28) and NDFW (January 27 - February 2, 2014), which included over 1,000 events in 50 states. Approximately 100 high schools registered for Chat Day and close to 2,000 questions were answered by NIDA scientists. NIDA developed and distributed press and promotional materials, cultivated radio and organizational partnerships, pitched to select media, coordinated two Radio Media Tours for English and Spanish speaking audiences, participated in and filmed local events, and promoted the week via traditional and social media outreach.

NIDA Participates in Opening of *Target America Exhibit: Opening Eyes to the Damage Drugs Cause*
On February 11, 2014, NIDA's Redonna Chandler participated in the ribbon cutting ceremony for *Target America Exhibit: Opening Eyes to the Damage Drugs Cause*, an interactive traveling exhibit now housed at the Maryland Science Center that explores the effects of drugs on individuals and society. Dr. Chandler was joined by DEA Administrator Michele Leonhart, SAMSHA Special Assistant to the Director Richard Lucey, Mayor of Baltimore City Stephanie Rawlings-Blake, Special Assistant from the Office of Congressman Elijah Cummings Hope Williams, Chairman & CEO of the DEA Educational Foundation Bill Alden, and President & CEO of the Maryland Science Center Van Reiner. NIDA's Deputy Press Officer, Rachel Wolf, accompanied Dr. Chandler to provide press support during the event.

NIDA Joins ONDCP for Teleconference about Heroin and Opioid Abuse
On February 11th, 2014, NIDA's Deputy Director Dr. Wilson Compton and Director of the Office of National Drug Control Policy Gil Kerlikowske held a media teleconference to discuss recent trends in opioid use in the United States, including heroin and prescription painkiller abuse. During the teleconference, they shared the latest data indicators regarding trends in opioid drug use and the actions currently underway to reduce drug use and its consequences. NIDA's Press Officer, Dr. Sheri Grabus, provided press support for Dr. Compton and promoted the teleconference via live tweets.

NIDA Director Meets with Washington Post Editorial Board
On April 1, 2014, NIDA Director Dr. Nora Volkow met with the Washington Post Editorial Board in Washington, D.C. During the meeting, Washington Post Editorial Board members asked Dr. Volkow about the latest topics relevant to drug abuse research. These included the latest usage, trends, and research on marijuana, heroin, and prescription drug abuse, as well as other areas.

NIDA Director Testifies in front of House Appropriations Committee
On April 2, 2014, NIDA Director Dr. Nora Volkow testified in front of the House Appropriations Committee, Subcommittee on Commerce, Science, Justice and Related Agencies during the budget hearing for the Drug Enforcement Administration. Subcommittee Chairman Frank Wolf (R-VA) invited Dr. Volkow to testify on the science of addiction, what we know and understand about addiction as a brain disease. With the current popular interest in marijuana and opiates issues, Chairman Wolf asked Dr. Volkow to focus some attention on those specific topics.

NIDA Deputy Director Participates in FDA Telebriefing about Naloxone Auto-Injector
On April 3, 2014, NIDA Deputy Director Dr. Wilson Compton participated in an FDA multi-stakeholder telebriefing with other federal partners to highlight the approval of Evzio, a hand-held auto-injector naloxone prescription treatment that can be used by family members or caregivers to reverse opioid overdose.

Press Release

April 24, 2014	***HHS leaders call for expanded use of medications to combat opioid overdose epidemic***

Science Spotlights and Announcements

February 4, 2014	***Medication may help patients with severe mental illness stay smoke-free***
February 26, 2014	***Transition services for drug using, HIV-infected inmates leaving jail should be gender-specific***
February 27, 2014	***NIDA's updated Heroin Research Report now available online***
March 27, 2014	***Targeting delta opioid receptor may reduce pain without causing addiction***
April 3, 2014	***Medication can help prevent relapse in cocaine-dependent males***
April 4, 2014	***Web-based intervention strengthens drug abuse treatment***
April 18, 2014	***Comprehensive prevention programs successful in decreasing HIV rates in people who inject drugs***
April 25, 2014	***NIDA announces new resources for healthcare providers***

Meetings/Conferences

Select Meetings and Conferences in which NIDA played a significant role

NIDA staff delivered two sessions at the **2014 Community Anti-Drug Coalitions of America (CADCA) National Forum** at National Harbor, MD, February 3-6, 2014. Ruben Baler, Ph.D. (NIDA) presented "Where do Addictions Come from?" and Jacqueline Lloyd, Ph.D., (NIDA) chaired a session on "Cultural and Contextual Adaptation of Evidence-Based Prevention Interventions for Real World Community and Practice Settings." The sessions highlighted the ongoing research being conducted by Dr. Jeanne Poduska (American Institutes for Research, Baltimore, MD) on the Good Behavior Game, which is an evidence-based classroom behavior management strategy. Dr. Volkow delivered a plenary address, and Drs. Wilson Compton and Jack Stein participated in a Power Session titled "Science Update from NIDA: Spotlight on Marijuana-Related Research."

On March 13, 2014, NIDA participated in the 15th annual **Brain Awareness Week** activities at the National Museum of Health and Medicine. NIDA staff members Drs. Cathrine Sasek, Roger Sorensen, Rik Kline and Erica Boone led the "**Brain Derby**," an interactive fast-moving game designed to teach children about drugs of abuse and neuroscience, with children from area schools as part of the week-long festivities. NIDA's game was enthusiastically received and the children not only learned new things, but they also had a great time.

On April 24, 2014 NIDA again participated in **Take Your Child to Work Day** by having numerous activities both in the Neuroscience Center and on the main NIH campus. Activities included: **Brains Up Close, Animal Brain Matching, Looking through the Microscope, Hands on Science, Brain Science Coloring Contest, Sharpen Your Brain, Dr. Sciencehead** and **Brain Derby**. In addition, this year NIMH partnered with NIDA to include an activity, **Put on Your Thinking Cap** and Archie Fobbs from the National Museum of Health and Medicine gave an interactive presentation titled **Your Brain – How It Works And What Happens When It's Injured**. A very enthusiastic group of children was able to rotate through the stations and learn about the brain as well as how drugs can impact the brain and body. NIDA and NIMH staff who developed and led the activities included Drs. Cathrine Sasek, Mary Kautz, Sheri Grabus, Dave Thomas, as well as Stephanie Older, Quandra Scudder, Hirsch Davis, Rachel Wolf and Phyllis Quartey-Ampofo.

On April 25-27, 2014, NIDA participated in the 3rd annual **USA Science & Engineering Festival** at the Washington DC Convention Center. The festival, which was designed to re-invigorate the interest of our Nation's youth in science, presented the most exciting, educational and entertaining science available. NIDA staff, led by Dr. Cathrine Sasek, conducted the **Brain Derby** (see above) and other activities to educate youth about what makes the human brain different from the brains of other species, as well as what areas of the brain are involved in and impacted by drugs of abuse.

On February 10-11, 2014, NIDA's Office of Diversity and Health Disparities (ODHD) hosted a two-day **Special Populations Research Development Seminar Series Workshop** at NIDA Headquarters in Rockville, Maryland. Chaired by Flair Lindsey, Program Analyst, this workshop convened 18 new early stage substance abuse investigators and NIDA-supported faculty mentors in an intensive grants development workshop setting. During the workshop, new investigators learned of NIDA's research and funding priorities and the NIH grants submission and review process, met with NIDA program staff and NIDA funded researchers and received feedback on research proposals.

NIDA's Office of Diversity and Health Disparities (ODHD) convened the **NIDA ODHD Translational Research Speaker Series: Promoting Diversity and Moving Toward Health Equity** at NIDA Headquarters in Rockville, Maryland, on Tuesday, March 11, 2014. Featured speaker Dennis M. Donovan, Ph.D., Director Alcohol and Drug Abuse Institute & Professor, Psychiatry and Behavioral Sciences, University of Washington School of Medicine, presented "A Community-Based Participatory Research (CBPR) Perspective on Moving Evidence-Based Drug Treatment Research into Clinical Practice." His presentation provided an overview of issues involved with moving Evidenced Based Practices into community based settings, with an example and issues drawn from the Clinical Trials Network and from work with Native American communities. This was the 5th seminar of the ongoing series, which is coordinated by Flair Lindsey, Program Analyst, ODHD.

NIDA's Office of Diversity and Health Disparities (ODHD) convened a two-day **NIDA Diversity Supplements Workshop** on Thursday and Friday, April 10-11, 2014 at NIDA Headquarters in Rockville, Maryland. The workshop brought together 26 current NIDA and selected NIAAA-supported diversity supplement recipients at the pre-doctoral, postdoctoral, and early career investigator levels, and presented them information and guidance on NIDA research priorities and research funding opportunities to help them transition to independent research careers. Participants met with NIDA and NIAAA program staff and senior officials, and with NIDA-funded investigators, some of whom were former recipients of NIDA diversity supplement funding support. In addition, participants presented posters of research they currently are engaged in through their respective diversity supplements. Pamela Goodlow, Public Health Analyst, ODHD, hosted and coordinated the two-day workshop. Dr. Albert Avila, Acting Director, ODHD, presented "Health Disparities Research at NIDA and the NIH" and "Research Training Opportunities Available through NIDA/NIH."

NIDA's Blending Initiative-Supported Sessions

A Regional Conference was held March 20-21, 2014 in Towson, Maryland by the Mid- Atlantic and Delaware Valley CTN Nodes and the Central East Region ATTC with support from the Blending Initiative. The title of the conference was "Preparing for Change: Emerging Models for Integrated Health Care Delivery."

The Society for Adolescent Health and Medicine (SAHM) Annual Meeting was held March 23-26, 2014 in Austin, Texas. The Blending Initiative sponsored a session titled "Screening and Brief Intervention of Adolescent Substance Use in Primary Care."

The American College of Physicians (ACP) Annual Internal Medicine Conference was held April 10-12, 2014 in Orlando, Florida. The Blending Initiative sponsored a session titled "Motivational Interviewing: Skills to Engage Patients and Initiate the Discussion of Substance Abuse in Internal Medicine."

The Annual Medical-Scientific Conference of the American Society for Addiction Medicine (ASAM) was held April 10-13, 2014 in Orlando, Florida. The Blending Initiative provided support for a session titled "Prescription Stimulant Use and Misuse Among Youth: Review and Practice Implications."

Operation Unite's National Rx Drug Abuse Summit was held April 22-24, 2014 in Atlanta, Georgia. The Blending Initiative provided support for a symposium titled "What's Next for Treatment?"

The Society for the Teachers of Family Medicine (STFM) held its Annual Spring Conference May 3-5, 2014 in San Antonio, Texas. The Blending Initiative sponsored a day-long workshop titled "Empowering Family Medicine Residencies to Address Prescription Opioid Abuse With Office-Based Buprenorphine Treatment."

PLANNED MEETINGS (pending approval)

College on Problems of Drug Dependence (CPDD) Annual Scientific Meeting - San Juan, Puerto Rico, on June 14–19, 2014.
The National Institute on Drug Abuse (NIDA) will sponsor a Grant-Writing and Career Development Workshop at the CPDD Annual Scientific Meeting. The Grant/Career Workshop provides new or junior investigators with information and skills to advance their research careers, with a heavy emphasis on NIDA funding opportunities, grantsmanship, and the grant application process. In addition, NIDA's Blending Initiative will provide support for a session titled "Addiction Treatment Research vs Usual Care: What are the Foreseeable Risks?"

2014 American Psychiatric Association Annual (APA) Meeting – New York, NY, May 3-7, 2014.
NIDA will hold a track of sessions at the APA Annual Meeting. Dr. Nora Volkow is scheduled to deliver the Frontiers of Science Lecture, and hold an interactive session with residents. NIDA staff will chair sessions on a variety of substance abuse related topics including: Cannabis Use and Youth: Risk Assessment and Implications for Clinical Practice, The Role of Substance Use in Violence Against Self and Others, Persistence and Desistance of Comorbid Drug Abuse and Psychiatric Disorders in Adolescence, Biological Approaches To Treat Substance Use Disorders, and Diagnostic and Assessment Considerations for the Treatment of Comorbid Opioid Addiction and Chronic Pain.

2014 American Psychological Association (APA) Annual Meeting – Washington, DC, August 7-10, 2014.
NIDA will co-host the NIDA/NIAAA /APA (Divisions 28&50) Early Career Investigator Poster Session.

GRANTEE HONORS AND AWARDS

Dr. Annette Fleckenstein, University of Utah, was elected president of the American Society for Pharmacology and Experimental Therapeutics. Her term begins July 1, 2014.

Dr. Kenneth Kellar, of Georgetown University's department of pharmacology, and a NIDA-funded grantee, has been named the recipient of the Society for Research in Nicotine and Tobacco's 2015 Langley Award, for his contributions to the field of nicotinic receptor research and addiction. The award will be presented at the Society's February 2015 annual meeting.

Dr. Mary Jeanne Kreek, Patrick E. and Beatrice M. Haggerty Professor, Head, Laboratory of the Biology of Addictive Diseases, and Senior Physician, The Rockefeller University Hospital, was presented with **NIDA's Lifetime Science Award** on May 6, 2014, *"In recognition of your pioneering efforts to bring methadone, the first medication for treating addiction, to the clinic; your seminal contributions to our understanding of addiction vulnerability and the neurobiology of opioid receptors; and your lifelong commitment to mentorship that has ensured the future of high quality addiction research."*

Dr. R. Christopher Pierce, received the Daniel H. Efron Research Award from ACNP (American College of Neuropsychopharmacology) at their meeting in December, 2013. The American College of Neuropsychopharmacology (ACNP) presents the Efron Award to an individual on the basis of outstanding basic research contributions to neuropsychopharmacology.

CTN Delaware Valley Node

The **Christiana Care Health System** is a Community Treatment Provider (CTP) with the Delaware Valley Node. Project Engage is a product of the DVN/Christiana Care collaboration. **Project Engage** is being honored by the Professional Nurse Council in May at their annual meeting for "contributing significantly to the care of our patients and supporting nursing." It aims to identify patients hospitalized on medical/surgical wards that have a substance use problem and use peer counselors to get them into treatment.

CTN Florida Node Alliance

Dr. José Szapocznik, (Co-PI) has been appointed by the Institute of Medicine of the National Academies to the National Research Council Forum on Promoting Children's Cognitive, Affective and Behavioral Health. The newly established forum aims to connect the prevention, treatment and implementation sciences with settings where children receive care, including healthcare facilities, schools, social service and child welfare agencies, the juvenile justice system and other community-based organizations. The forum will develop effective and affordable systems that address children's needs in these settings. Dr. Szapocznik, who is also Director of the Center for Family Studies and the Miami Clinical and Translational Science Institute at the University of Miami, welcomes the opportunity to contribute to a forum that will help improve the health of children.

CTN New England Consortium Node

Nancy Paull, CEO of Stanley Street Treatment & Resources, Inc. (SSTAR) in Fall River, Massachusetts — a Community Treatment Program affiliated with the New England Consortium Node —was recently named a 2014 honoree for the National Council for Behavioral Health's Impact Award. The award is given to recognize organizations and leaders in the behavioral health field, committed to providing community-based treatment to individuals with mental illnesses and substance use disorders. Nancy Paull was selected for a Visionary Leadership award. A celebration for the 2014 honorees will take place on May 6, 2014, in Washington, DC, at the time of the upcoming National Council Conference 2014. You can learn more about this award through the following link, http://www.thenationalcouncil.org/about/awards/.

Dr. Samuel A. Ball, professor of psychiatry at Yale University School of Medicine and an affiliated researcher with the New England Consortium Node and The APT Foundation, was recently named the president and chief executive officer of The National Center on Addiction and Substance Abuse (CASAColumbia®). CASA was founded in 1992 at Columbia University and has a mission to inform Americans of the economic and social costs of addiction and risky substance use and its impact on their lives; and to assess what works in prevention, treatment and disease management. Dr. Ball will retain his affiliation with Yale University School of Medicine and hopes to foster collaborations between CASAColumbia® and the Clinical Trials Network.

Dr. Gene Brody was inducted into the Honor Hall of Recognition by the University of Georgia at Athens College of Family and Consumer Sciences.

Dr. Bruce Schackman has been promoted to Professor of Public Health in the Department of Public Health at Weill Cornell Medical College.

CTN Ohio Valley Node

Dr. Kathy Burlew is being appointed as Fellow of the Graduate School at the University of Cincinnati. Dr. Burlew is the Principal Investigator of The Crossroads Center, a Community Treatment Program in the Ohio Valley Node and a Professor of Psychology at the University of Cincinnati. The Fellows of The Graduate School is an organization that recognizes distinguished researchers and scholars from throughout the University of Cincinnati. In addition to their outstanding individual accomplishments, Fellows are generally among the most experienced and accomplished graduate-student mentors at the University. New Fellows are elected annually by the current Fellows and are then appointed for life by the Board of Trustees. Criteria for election include evidence of outstanding scholarly and/or artistic attainment. The Fellows therefore constitute a significant resource of talent, experience and intellect at the university. Dr. Burlew will be honored at a ceremony in the Spring.

STAFF HIGHLIGHTS

Staff Honors and Awards

Dr. Elizabeth Robertson, DESPR, has been selected to receive the Society for Prevention Research's (SPR) *2014 Presidential Award* for her outstanding contributions to advancing the field of prevention science. The SPR *Presidential Award* is given to an individual or a team of individuals who have made a major specific contribution to prevention science research. This award is a "lifetime achievement" award for a significant body of research or theory in any area related to prevention that has had a major impact on the field. Dr. Robertson will be presented this award at the Annual Awards Presentation on Thursday, May 29, 2014 at the 22nd Annual Meeting of the Society for Prevention Research.

Dr. Guillermo Esber, IRP, was awarded a K99 grant.

Dr. Marilyn Huestis, CDM Chief, IRP, was selected for the new National Commission on Forensic Science that will set the standards for all forensic sciences in the United States.

Dr. Jag Khalsa, DPMCDA, received the ***Lifetime Contributions Award*** from the Society on NeuroImmune Pharmacology, March 26-29, 2014.

Dr. Belinda Sims, DESPR, Prevention Research Branch, received a Meritorious Research Service Commendation for 2013 from the American Psychological Association Board of Scientific Affairs. The commendation recognizes individuals who have made outstanding contributions to psychological science through their service as employees of the federal government or other organizations. Dr. Sims was recognized for her outstanding contributions to psychological science through her service as a research and health science administrator NIDA.

Dr. Dong Wang, IRP, received a travel award for a Janelia Farm Conference on Genetic Manipulation of Neuronal Activity III held May 18-21, 2014.

Dr. Roy Wise, IRP, joined the Program Committee of the Society for Neuroscience.

Dr. Ariane Wohlfarth, Visiting Fellow, IRP, was awarded the 2014 Excellence in Scientific Research NIDA Fellow Award by the NIA and NIDA Women Scientists Advisor Committee..

Staff Changes

New Employees

Gloria Dabbondanza joined the Administrative Management Branch (AMB) on February 10, 2014 as a Program Analyst. She will be the new NIDA HR liaison and will also be responsible for workforce development programs and activities. Prior to joining the NIDA team, Gloria was a Paralegal Specialist for the Civil Rights Division of the Department of Justice, and then moved to the National Heart, Lung, and Blood Institute as a Management Analyst in 2007. She has experience in policy development, budget management, human resource liaison, program evaluation, data management and reporting, editing, and event planning.

Stacey Gills joined NIDA on March 13, 2014 as the Chief of OM's Administrative Management Branch (AMB). Stacey comes to us from the NBS group in the NIH OD where she has been a Change Management Specialist facilitating business system operations and rollouts. Stacey previously served as a Lead Administrative Officer at NCI and a Program Analyst at NIAID, and is experienced at advising senior management on operations, policy, change, and productivity. She holds a degree in Sociology from Towson State University and has received numerous awards recognizing her performance and leadership.

Debasis Goswami joined NIDA on February 24, 2014, as IRMB's Applications Manager within the Office of Management. Debasis comes to us with 20+ years of extensive experience with Program and Project Management handling multiple IT initiatives varying in size and scope spanning geographical boundaries across the world. He has strong hands-on experience in a diverse set of technologies along with a strong sense of focus around Customer Relationship Management. A recent NIH Director's Award recipient, Mr. Goswami comes to NIDA from NIDDK where he supported many different stakeholder communities including Scientific and Grants Management Divisions since 2009. In addition to supporting Administrative Systems at NIDDK, Mr. Goswami also has a strong understanding of and experience in the Pharmaceutical industry focusing on drug development and Clinical Trials of all stages, Regulations, and Data Management. At NIDA, Debasis will play an essential role in managing the Operations & Maintenance and New Project Development activities within our Application Management team supporting NEPS, CMIS, DISCS, CAS, and SharePoint Applications.

Dr. Hiromi Ono joined OEA as a Scientific Review Officer in February 2014. Hiromi received bachelor's degrees in mathematics and sociology from Reed College and master's and doctoral degrees in demographics and sociology from UCLA and UC Berkeley. She was a postdoctoral fellow at the School of Public Affairs, UCLA, an assistant research professor at the University of Michigan, and a tenured associate professor of sociology at Washington State University and her 35 publications address family demography, methodology and related policy issues. Hiromi joined the government as a program officer for the Postsecondary Education and the Improving Education Systems programs at the Institute for Education Sciences, US Department of Education.

Christina Page joined OEA as an Extramural Support Assistant in February 2014. Christina transferred from the Department of Army where she worked as a Patient Representative for Moncrief Army Community Hospital, one of the largest basic trainee locations in the nation. She received her undergraduate degree in Business Administration from Frostburg State University. Christina had previously worked for NINDS as a human resource intern in the Presidential Management Fellows Program and brings experience in employee relations in the public sector with the DHHS and Department of Army as well as private sector experience as a Managed Care Specialist representing Cape Fear Valley Health System in North Carolina.

Dr. Jagadeesh Rao joined NIDA in January 2014 as a Scientific Review Officer. Jagadeesh received bachelor's and master's degrees in biochemistry and a doctoral degree in neurochemistry from the University of Mysore and NIMHANS, India. After a postdoctoral fellow position at the University of Illinois, Jagadeesh was a scientist with Johnson and Johnson in Pennsylvania. He joined NIH's National Institute of Aging as a Research Fellow and was promoted to Staff Scientist. Jagadeesh's 68 publications address neuroinflamation, imaging, neurotransmitter transporters, transduction, behavior and pharmacology, with attention to synaptic plasticity, HIV, and signal transduction related to chronic neurological diseases.

Christine Salaita, MS, RDN, joined NIDA's OEA as a Program Analyst in April 2014. She will assume primary responsibility for NIDA's National Advisory Council activities. Christine came to NIDA from NIDDK, where she was a Program Analyst in the Division of Extramural Activities for 3 ½ years and was responsible for Council activities, end-of-year reporting and helped ensure timely processing and publication of FOAs. Prior to that, Christine completed a 2-year competitive NIH Management Intern program with rotations through multiple Institutes and with the State Department in the Office of the Global AIDS

Coordinator, focused on the administrative management of international and global health initiatives. Her first position at NIH was as a Clinical Research Dietitian in the Department of Nutrition at the Clinical Center where she provided medical nutrition therapy and counseling to patients with immunodeficiency including HIV/AIDS, diabetes, renal disease and transplantation, obesity and sickle cell disease, precepted dietetic interns, co-authored research publications, and presented to outside organizations.

New Appointments/Transfers

Dr. Albert Avila has been selected for the position of Director of NIDA's Office of Diversity and Health Disparities (ODHD). Dr. Avila received his Ph.D. from Georgetown University and completed his postdoctoral training at the National Institute of Dental and Craniofacial Research (NIDCR). At NIDCR, he became the Intramural Training Director and then a Program Officer (PO) directing extramural research training and career development. Dr. Avila came to NIDA's DBNBR where, as a PO, he directed a grant research portfolio in neuroimmunology, psychopharmacology, and HIV as they relate to drug abuse, and fostered a robust research training and career development portfolio for early career investigators. Since June 2013, he has been serving as Acting Director, ODHD. Dr. Avila brings with him an extensive background in research training, career development, and health disparity issues, along with passion and enthusiasm for drug and addition research. Please join me in welcoming Dr. Avila to his new role at NIDA where he will use his outstanding creativity and leadership to increase our ability to recruit and retain the best scientists at the NIH.

Nathaniel Fredericks has been selected for the position of Chief, Management Analysis Branch (MAB) in the NIDA Office of Management. Since joining NIDA in February of 2013, Nathaniel has played a key role in transitioning the Conference Approval function to MAB. He has also guided NIDA's Risk Management program and served as the administrator for the NIDA IT Change Review Board. Nathaniel holds Bachelor's and Master's degrees in accounting from Saint Louis University, and has had a diverse career ranging from positions as the finance director for political campaigns, corporate tax consulting, an internal auditor for St. Louis County Government, and the audit remediation lead for the Division of Payment Management in the Program Support Center of HHS.

Dr. Cheryl Anne Boyce, DCNBR, will serve as the representative for NIDA as an official member of the Interagency Coordinating Committee on Fetal Alcohol Spectrum Disorders (ICCFASD). **Dr. Karen Sirocco**, DCNBR, will serve as the alternate representative.

Dr. Mary Kautz, DCNBR, has been appointed as the NIDA Coordinator for the NIH-FDA Tobacco Regulatory Science Program (TRSP). In this role, she serves as a Liaison between NIDA and NIH TRSP-OD staff to administer grant awards that have been funded by the Food and Drug Administration (FDA) Center for Tobacco Products (CTP) to inform the development and evaluation of regulations on tobacco product manufacturing, distribution, and marketing.

Departures

Dr. Eliane Lazar-Wesley, OEA, moved to the Scientific Review Branch at NIDCD in April 2014. For 11 years Eliane effectively managed many types of reviews as an SRO at NIDA, notably serving as the SRO for NIDA-K, the Training and Career Development Review Committee, and for the Centers reviews.

Cikena Reid, Program Analyst, OEA, moved to the White House Liaison Office at the USDA in March 2014. For the past 5 years, Cikena's primary responsibility was managing the activities of NIDA's National Advisory Council. Notably, she was responsible for introducing the Electronic Council Book into Council operations.

Dr. Mihaela Iordanova, IRP, accepted a Tier II Chair position at Concordia University in Montreal.

Dr. Jim Bjork, DCNBR, has accepted a position as Associate Professor in the Department of Psychiatry of the Virginia Commonwealth University Medical School in Richmond, Virginia, effective July 2014. Jim will also have a part-time appointment at the McGuire VA Hospital in Richmond. In his new position, Jim will continue his neuroimaging research on the functional mechanisms of altered motivation, impulse-control, and decision-making in addiction- both in community and campus populations, as well as in veterans with and without traumatic brain injury. Jim joined NIDA in 2007, after several years conducting neuroimaging research on alcoholic inpatients and their adolescent children at the NIH Clinical Center, as a postdoctoral fellow in the NIAAA Laboratory of Clinical and Translational Studies. Jim intends to continue to be of service to his NIDA colleagues until his July departure, as well as in the future, in the capacity of an extramural researcher.

Retirements

Dr. Elizabeth Robertson retired after 19 years at NIDA. Following an earlier career in research, teaching and federal service at the Department of Agriculture, Dr. Robertson joined NIDA in 1995. She served as the Chief of the Prevention Research Branch (PRB) from 1998 until 2011 and for the last three years has been Senior Advisor for Prevention Research. Dr. Robertson has been a leading advocate of a developmental, life course perspective on drug abuse prevention and she played a major role in fostering prevention services research to maximize the ways that effective prevention services would be available to the public. Dr. Robertson has been an advisor to the White House Office of National Drug Control Policy and a frequent consultant to many government and outside organizations. Dr. Robertson has always been a tireless advocate for prevention and the support of children and families. She developed and guided NIDA's prevention research program for more than 15 years.

In Memoriam

In March 2014, NIDA lost a colleague and friend, **Richard Denisco, M.D., MPH.** Richard joined the Services Research Branch in the Division of Epidemiology, Services, and Prevention Research in September 2005. He received his undergraduate degree from Emory University, his medical degree from the University of Florida, and was board certified in anesthesiology and pain medicine. He worked as an anesthesiologist and pain management specialist for many years. In 2005, he received his MPH from the Bloomberg School of Public Health at Johns Hopkins University. Richard was passionate about improving the lives of those struggling with substance use disorders. Drawing on his unique personal, professional, and medical expertise, he provided leadership for scientific initiatives emphasizing the delivery of smoking cessation, treatment of chronic pain, reduction of prescription drug abuse, and the training of physicians to effectively address addiction. He was an active member of several important NIH and federal groups focused on translating research into policies and practices to improve the lives of individuals. He received many accolades for his work including two NIH Director's awards for projects related to physician education. He gave his time, expertise, and ideas freely to others. He lived a life of noble service always seeking to relieve suffering and improve lives. He will indeed be missed.