

Substance Abuse Division

Herbert Kleber, MD, Division Chief

Department of Psychiatry, Columbia University College of Physicians and Surgeons

New York State Psychiatric Institute

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Overview

Research in this Division, which began in 1992, focuses on antecedents and consequences of substance use and abuse, with particular emphasis on the development and testing of novel approaches to the treatment of substance abuse. Resources include non-human primate studies; separate human research laboratories for studying heroin and prescription opioid analgesics, methamphetamine, marijuana, nicotine, alcohol, and pain, all located in NYSPI; a cocaine human research laboratory located in the Irving Center Institute for Clinical and Translational Studies; an outpatient clinical research service (STARS) for treatment trials for new medications; a novel residential laboratory for studying a variety of workplace and other drug-related issues; and a regional Node in the National Institute on Drug Abuse (NIDA) Clinical Trials Network creating research affiliations with four major community-based treatment providers in the New York Metropolitan area. Considered one of the leaders in the country in the field, the Division has been so recognized for almost a decade by being in the top three in the country in the U.S. News & World Report's rankings.

The Substance Abuse Division is supported by a number of NIH R01's as well as by a NIDA Medication Development Center that supports research using both laboratory models of substance abuse, imaging studies, and traditional clinical trials research. A major strength of the Division is the ability to conduct initial safety and effectiveness studies using human laboratory models, with the results obtained then used to design larger scale clinical trials. Other projects include brain imaging research that is mapping neuroreceptors (particularly of serotonin and dopamine) in response to cocaine and heroin administration. Recently, the Division added a novel clinical cognitive laboratory for the study of cognitive functioning in substance abusers and its relations to treatment outcome within the regional Node in the NIDA Clinical Trials Network.

Overall, the Division has approximately 127 employees including twenty-three MD or PhD faculty, seven faculty with K awards, and over forty grants (including one Center and Postdoctoral Training Grant) and contracts.

Staff

Joshua Berman, MD, Assistant Professor
Adam Bisaga, MD, Psychiatrist II
Kenneth Carpenter, PhD, Research Scientist IV
Sandra Comer, PhD, Research Scientist VI
Suzette Evans, PhD, Research Scientist VI
Richard Foltin, PhD, Research Scientist VII
Erik Gunderson, MD, Research Scientist VI
Margaret Haney, PhD, Research Scientist VI
Carl Hart, PhD, Research Scientist V
David Hurst, Administrator
Herbert Kleber, MD, Director, Research Scientist VIII
Frances Levin, MD, Research Scientist VII
Jeanne Manubay, MD, Research Associate
John Mariani, MD, Psychiatrist II
Diana Martinez, MD, Psychiatrist II
Edward Nunes, MD, Psychiatrist II
Wilfrid Raby, MD, PhD, Medical Specialist II
Stephanie Collins Reed, PhD, Assistant Professor of Clinical Neurobiology
Eric Rubin, MD, PhD, Medical Specialist II
Shabnam Shakibaie Smith, MD Psychiatrist II
Maria Sullivan, MD, PhD, Psychiatrist II
Nehal Vadhan, PhD, Assistant Professor of Clinical Psychology
Suzanne Vosburg, PhD, Research Scientist III
Jeffrey J. Wilson, MD, Assistant Professor

Current Research

Medications Development Research Center (PI, Kleber, Co-PI, Evans)
As part of Dr. Kleber's Medications Development Center grant, the Division has a mechanism for supporting pilot studies to promote research opportunities for research fellows and junior faculty in the Division. Since the inception of this Center grant in 1994, forty-eight pilot studies have been funded. These pilot studies have been instrumental in obtaining grant funding, including eleven R01's, eleven K Awards, one NARSAD award, and one R-21. These funded pilot studies have also resulted in twenty-five peer-reviewed publications, and over fifty-eight presentations at scientific conferences, both national and international. Currently, there are nine ongoing pilot studies.

Novel Medication Approaches for Substance Abuse

The Division has several studies underway that are exploring new treatments for substance abuse:

- A laboratory model of heroin abuse: Dr. Nancy Comer has developed a laboratory model of heroin abuse to evaluate new medications for opioid abuse and dependence, as well as improving outcome and acceptability of existing medications such as methadone and naltrexone. Her current research focus is to evaluate the relative abuse liability of heroin and prescription opioid medications such as fentanyl, oxycodone, buprenorphine, and morphine. The effectiveness of buprenorphine maintenance in reducing the reinforcing effects of the prescription opioids is also being examined. In addition to the above, recent pre-clinical data suggest that glial activation may alter opioid-induced responses. A study is currently underway to examine the ability of AV411, a glial cell activation inhibitor, to alleviate opioid withdrawal symptoms. Research fellow Dr. Ziva Cooper, under the supervision of Dr. Comer, is leading the study.
- Cocaine addiction: Dr. Diana Martinez is using PET to measure the dopamine type 2 receptor and levels of endogenous dopamine in cocaine addiction. The results show that long-term cocaine dependence is associated with a generalized decrease in dopamine type 2 receptors in addition to a decrease in levels of endogenous dopamine compared to healthy control subjects.
- Co-morbid depression and substance abuse: Dr. Edward Nunes and Dr. Wilfred Raby explore pharmacological treatments for depressed cocaine abusers, currently assessing the efficacy of mirtazapine. This study is currently being conducted at STARS. The project also includes stress and its relationship to depression and drug use.
- Marijuana withdrawal: Two groups are exploring treatments for marijuana withdrawal. Dr. Margaret Haney and colleagues have tested the ability of potential treatment medications to decrease marijuana withdrawal and relapse in daily marijuana smokers. To date, a combination of dronabinol, a cannabinoid agonist, and lofexidine, an alpha-2 noradrenergic agonist, were most effective in decreasing symptoms of marijuana withdrawal and decreasing relapse to marijuana use. In the past year, Dr. Haney has shown that neither the GABAB receptor agonist, baclofen, nor mirtazepine, an antidepressant that increases synaptic norepinephrine and serotonin levels, robustly influenced marijuana withdrawal or relapse. An ongoing study is investigating the effects of quetiapine in daily marijuana smokers.
- Dr. Frances Levin is leading a 12-week, double blind, placebo-controlled treatment trial conducted at STARS. Participants receive either active medication (dronabinol) or matching placebo in a “fixed flexible” dose schedule with gradual dose titration. The specific aims of this research are to determine whether dronabinol is superior to placebo in promoting abstinence and reducing marijuana withdrawal symptoms. We expect to

complete this study in the upcoming year and have been surprised by the large number of cannabis-dependent individuals interested in a pharmacologic treatment intervention.

Inpatient Laboratory Research With Human Participants

- **Residential Laboratory:** In their on-going characterization of drug use by the workforce, Dr. Carl Hart and colleagues, are examining the effects of the "club drug" 3,4-methylenedioxymethamphetamine (MDMA) and methamphetamine on cognitive performance, mood, speech and measures of sleep. Workplace-related consequences of acute and repeated dosing of these popular club drugs are being investigated.
- **Methamphetamine Research Laboratory:** This laboratory, led by Dr. Hart, studies the behavioral pharmacology of intranasal methamphetamine in humans in an effort to better understand methamphetamine dependence and increase the available treatment options. Findings from a recently completed study in this lab indicated that a single dose administration of intranasal methamphetamine produced orderly effects on psychological and physiological measures with a rapid onset of effects. Ongoing studies are characterizing the effects of intranasal methamphetamine following repeated doses, a manner in which the drug is reportedly used outside of the lab.
- **Opioid Research Laboratory:** Although buprenorphine clearly is effective in the treatment of opioid dependence, several epidemiological and clinical case studies have reported that buprenorphine itself may have abuse liability. The goal of this study was to compare the reinforcing effects of intravenously-delivered buprenorphine and the buprenorphine/naloxone combination in individuals who were physically dependent on buprenorphine. The results demonstrated that the reinforcing effects of buprenorphine/naloxone were significantly lower than buprenorphine alone, although both drugs did have abuse liability under these conditions (supported by Schering-Plough). A NIDA-funded study is being conducted in the laboratory to examine the effectiveness, safety, and duration of action of an implantable form of naltrexone. This research is a logical extension of Dr. Sandra Comer's previous work with a month-long preparation of depot naltrexone that was shown to be effective and safe in both laboratory and clinical settings (Comer, et al., 2002; Comer, et al., 2006; Sullivan, et al., 2006).
- **Marian W. Fischman Cocaine Laboratory:** Four NIDA-funded grants support this research: "I.V. Cocaine Abuse Treatment: A Laboratory Analysis" (Dr. Richard Foltin); "Sex Differences in Stress & Impulsivity in Cocaine Abusers" (Dr. Suzette Evans); "Translational Approach to Models in Relapse" (Dr. Richard Foltin); and "Laboratory Analysis of Cocaine

Abstinence" (Dr. Richard Foltin). In addition, three K-training awards (Drs. Nehal Vadhan, Kenneth Carpenter, Stephanie Collins Reed) are also conducted, at least partially, in the laboratory. The goal is to better understand cocaine abuse and its treatment. We have been evaluating the efficacy of modafinil and aripiprazole to alter the subjective and reinforcing effects of cocaine. We are also continuing behavioral studies on changes in the motivation to smoke cocaine during a cocaine "binge," and on how environmental conditions affect the development of sensitization to smoke cocaine. We continue to refine new procedures for modeling relapse to cocaine use, and evaluating medication specifically for relapse prevention. We are also continuing a long-term study comparing the subjective and reinforcing effects of cocaine under controlled laboratory conditions, in groups of abstinent cocaine abusers with symptoms (most likely substance-induced) of major depression, or no psychiatric comorbidity. We recently received funding to evaluate new medications for relapse prevention.

- **Clinical Trials Network Node:** The Long Island Node of the NIDA Clinical Trials Network, led by Dr. Edward Nunes, has completed eight clinical trials at affiliated community-based treatment sites in which over 400 participants were randomized. These clinical trials include a multisite trial of Motivational Enhancement Therapy for Spanish speaking patients, a multisite trial of buprenorphine for treatment of opiate dependence, a multisite trial of cognitive behavioral therapy and nicotine replacement for smoking cessation among patients in treatment for drug dependence, a trial of algorithmic treatment with buprenorphine and behavioral interventions for prescription opioid dependence, and trials of methylphenidate for adolescents and adults with nicotine dependence and attention deficit hyperactivity disorder (ADHD).

The Node is also leading two nationwide multisite randomized controlled trials (N = 400 each), one of Seeking Safety a cognitive behavioral intervention for drug dependent patients with PTSD (Dr. Denise Hien, Lead Investigator), and one of a skills based HIV risk reduction intervention for women in drug dependence treatment (Dr. Susan Tross, Lead Investigator); both have been completed and are in data analysis. The latter study showed that a 6-session skills-based group intervention was superior to an educational control in reducing HIV risk behavior among women in drug treatment and that local clinicians at community-based treatment programs could effectively carry out the intervention. Dr. Tross will be working with NIDA to develop a training program for disseminating this intervention widely throughout treatment programs in the field.

The Node has recently been selected to lead a multi-site clinical trial of a computerized cognitive-behavioral intervention for drug dependence in

collaboration with its developer, Dr. Lisa Marsch from NDRI. In addition, the Node provides a platform for a number of projects funded by R01s and other funding sources, including a study on training clinicians in Motivational Interviewing and a study of naltrexone to prevent relapse among individuals on parole or probation (described below).

- **Motivational Interviewing Training Project:** Funded by a NIDA R01 to Dr. Edward Nunes this is a randomized trial comparing three different methods of training substance abuse clinicians in the skill of motivational interviewing—workshop alone, versus workshop plus one of two supervision methods. A supervision method designed specifically for this project involves supervisors listening live to the trainees' interviews over the telephone, and giving real time feedback. Data collection is completed and data analysis is underway. Dissemination of new evidence-based treatments into community-based treatment is an important public health imperative, and this is among the first randomized trials examining different training/dissemination methods. Prior studies, mainly from other branches of medicine, have shown that lectures, workshops and other didactic exercises do not succeed in teaching clinicians new skills, and supervision and feedback are needed. Preliminary analyses show that the supervision methods, particularly the condition that provided immediate feedback, produced superior skill at Motivational Interviewing among the clinician-participants compared to those who received only Workshop training. Future directions may include further testing of current supervision methods among community-based substance abuse treatment personnel and testing of the methods for training of physicians in Motivational Interviewing.

- **Imaging Studies:** Dr. Diana Martinez's research uses PET to image dopamine receptors and dopamine transmission in addiction. Her current studies include three studies in human subjects and one in non-human primates. The human studies are: 1) imaging dopamine transmission in heroin addiction and investigating the correlation between neurobiology and heroin self-administration; 2) imaging the effect of a behavioral treatment for cocaine dependence on dopamine transmission; and 3) imaging dopamine depletion in cocaine dependence. Dr. Martinez is also a close collaborator on two other projects: one is the imaging of dopamine transmission in Bulimic patients (conducted with Dr. Allegra Broft in the eating disorders group) and the other is imaging the effects of alcohol on parameters of dopamine transmission (conducted with Dr. Anissa Abi-Dargham in the Division of Translational Imaging). Dr. Martinez has completed studies characterizing a new radiotracer to label the kappa receptor, and has begun studies with this radiotracer in human participants.

Outpatient Laboratory Research with Human Participants

- **Women's Research:** Dr. Suzette Evans is the Director of the Women's Research Center in the Division on Substance Abuse, with Dr. Stephanie Collins Reed as the Co-Director and Dr. Frances Levin as the Medical Director. The primary research focus is related to women's health issues specifically related to substance abuse and the menstrual cycle. Dr. Evans has had a grant since 1995 to conduct human laboratory studies to assess vulnerability to drug and alcohol abuse in subgroups of women at increased risk for substance abuse problems. Over the last several years Dr. Evans and Dr. Reed have been conducting a series of studies on stress response and the effects of alcohol and d-amphetamine on measures of impulsivity in various groups of women, including women with childhood sexual abuse and women with bulimia nervosa. They are collaborating with Dr. Timothy Walsh, Director of the Eating Disorder Unit on this project, and are also collaborating with Dr. Mary Jeanne Kreek, at Rockefeller University, to assess genetic associations in these women. They are also assessing the effects of d-amphetamine on measures of impulsivity in male and female cocaine abusers. Lastly, they are assessing the effects of progesterone administration on the response to d-amphetamine in women.

- **Marijuana:** Dr. Margaret Haney is the Director of Marijuana Research in the Division on Substance Abuse, with Dr. Adam Bisaga as the Medical Director. Although laboratory animal data suggest that opioid antagonists block the effects of cannabinoids, the data in daily marijuana smokers show that a range of naltrexone doses (12, 25, 50, 100 mg) increased the intoxicating effects of smoked marijuana (6.2% THC). These data suggest that naltrexone would not be useful for the treatment of marijuana dependence, and suggest that long-term cannabis use may alter the interaction between endogenous opioids and cannabinoids.

- **Pain:** Dr. Sullivan and Dr. Comer are carrying out a combined laboratory study and clinical trial to examine the growing problem of prescription opioid abuse among chronic pain patients. Participants diagnosed with moderate pain initially are admitted to the hospital and transitioned from their baseline prescription opioid to a standing daily dose of buprenorphine/naloxone (Bup/Nx). In the human subjects laboratory, participants have the opportunity to self-administer oxycodone and subjective, analgesic, physiologic, and performance effects are measured. Subsequently, patients are followed on an outpatient basis while maintained on Bup/Nx. A major goal of this study is to determine which variables collected in the laboratory most reliably predict subsequent relapse to opioid abuse. In addition, the utility of Bup/Nx in treating patients diagnosed with both chronic pain and substance abuse will be assessed. This is the first study to date examining opioid self-administration in persons with pain who have a history of opioid abuse and

could provide important information about prescription opioid abuse liability in pain patients and a laboratory model for predicting likelihood to relapse. These questions are of immediate clinical relevance to the treatment of chronic pain with opioid therapy.

In addition to examining the problem of prescription opioid abuse among chronic pain patients, Dr. Comer has completed studies examining the abuse liability of prescription opioids in normal, healthy volunteers compared to prescription opioid abusers. Participants were given the opportunity to self-administer orally delivered oxycodone in both the presence and absence of experimental pain. Prescription opioid abusers self-administered oxycodone regardless of pain condition, while normal, healthy volunteers only self-administered oxycodone in the presence of experimentally induced pain.

This outcome was obtained even though both groups of participants reported equivalent levels of positive subjective responses. These data substantiate the clinical observation that non-drug abusers only use prescription opioids when clinically indicated whereas substance abusers use them under a wider variety of conditions. Future research will attempt to elucidate the etiology of this effect. In addition to the above, Dr. Comer also is conducting studies to examine abuse-deterrent formulations of opioids.

One of the most commonly abused prescription opioids is OxyContin. Abusers can easily crush the tablet, thereby releasing large amounts of drug for a quick high. In response to this problem, several drug companies have begun to develop abuse-deterrent or tamper-resistant formulations. In a current study, participants are asked to manipulate tablets that are designed to resist tampering in an effort to understand how abusers tamper with prescription opioids and how effective the abuse-deterrent medications may be.

- Nicotine: Dr. Bisaga is conducting several studies to elucidate the neurobiology of nicotine dependence in humans and to develop new pharmacotherapies. Laboratory models of smoking cessation and relapse to smoking have been developed, and additional procedures for modeling relapse are being refined. Bupropion, an effective smoking cessation medication reduced smoking behavior in the laboratory model of smoking cessation confirming its predictive validity. Current studies evaluate effects of varenicline in the laboratory model of smoking cessation and effects of bupropion a laboratory model of relapse. Continuing work explores the role of NMDA receptor neurotransmission in effects of nicotine and is assessing therapeutic potential of the NMDA receptor antagonist memantine. Memantine was not effective in the laboratory model of

smoking cessation and currently we are assessing its role in the model of relapse.

- **Clinical Treatment Studies:** The primary clinical research program, the Substance Treatment and Research Service (STARS), is conducted under the leadership of Drs. John Mariani and Frances Levin. After expanding to space at 1775 Broadway in early 2006, STARS now operates 50 hours per week at two locations: the main location is at 166th Street and the satellite location is at new space developed by the psychiatry department near Columbus Circle. Current treatment studies taking place at STARS involve problems with cocaine, marijuana, and opiates, as well as cognitive studies. During the past year five independently funded investigators had eight clinical trials open for enrollment. Approximately 750 potential participants attended an initial screening appointment and approximately 225 participants were enrolled into a clinical trial. With expanded capacity at the Columbus Circle site, and 2 additional new trials expected to begin enrollment, recruitment volume is expected to continue to increase over the next year.

In the research clinic, investigators have successfully adopted Velos eResearch software, a comprehensive electronic system for clinical trials. This system includes the following components: 1) trial management (communication with IRB and study staff), 2) clinical data management (electronic Case Report Forms, data entry and storage), 3) patient registration and management, and 4) NIH reporting. Over a hundred Case Report and other study-specific forms were programmed and five clinical trials are now fully operational in Velos eResearch.

- **Cocaine Treatment Studies:** Dr. Levin is currently conducting two pharmacologic treatment trials for cocaine dependence. One study is a randomized, controlled trial comparing combined pharmacotherapy (topiramate and mixed amphetamine salts-extended release; MAS-ER) for cocaine abusers without additional psychiatric comorbidity. The second study is a multi-site collaborative trial comparing two doses of extended-release amphetamine (MAS-ER) for the treatment of cocaine abusers with adult attention-deficit hyperactivity disorder. Dr. Levin's program at NYSPI serves as the Coordinating Site. Drs. Evans and Levin have a new grant focusing on cocaine treatment for women. This small pilot treatment trial will assess the efficacy of oral micronized progesterone in women seeking treatment for their problems with smoked cocaine.
- **Opioid Treatment Studies:** Drs. Nunes, Sullivan, and Bisaga have been conducting studies that aim to improve effectiveness of naltrexone in the treatment of opioid dependence. This includes studies testing adjunctive use of pharmacotherapies (memantine), behavioral therapies (Behavioral Naltrexone Treatment), or the extended release form of Naltrexone

(Vivitrol). More effective strategies to detoxify from opioids and induct on naltrexone are also being developed.

- **Marijuana Treatment Studies:** In addition to the clinical trial conducted as part of the Medications Development Center, Dr. Levin is conducting a clinical trial comparing venlafaxine to placebo for depressed cannabis-dependent individuals. It is expected that this study will be completed in the next year. In addition to the studies reported here, the Division has numerous other human laboratory and clinical trials involving the various drugs of abuse, which are not described because they are ongoing.
- **Long-Acting Injectable Naltrexone to Prevent Relapse Among Parolees and Probationers with Histories of Drug Dependence.** In a NIDA funded multi-site R01 (Dr. Nunes PI at Columbia/NYSPI site) injectable naltrexone will be tested as a tool to prevent relapse in individuals on parole or probation with either current opioid dependence or a history of opioid dependence and risk of relapse. Injectable naltrexone provides blockade of the effects of heroin or other opioids for a month or more after each injection and has promise for preventing relapse to opioid dependence. A high proportion of prisoners in the United States have drug problems, and the risk of relapse after release from prison or jail is very high. Participants will be randomly assigned to treatment as usual in the community or treatment as usual plus monthly injections of long-acting naltrexone. Participants who are currently opioid dependent will be detoxified on the research inpatient unit prior to naltrexone induction. If shown to be useful in this study, long acting injectable naltrexone could significantly expand the Division's treatment armamentarium for opioid dependence.

Research with Non-human Primates

Under the direction of Drs. Richard Foltin and Suzette Evans, the Division's pre-clinical studies in non-human primates continue with funding supplied by two grants from NIDA. One set of studies is examining variables affecting food seeking and food taking using pharmacological manipulations to determine mechanisms that underlay feeding behavior. This study has an imaging component that extends the Division's capabilities to conducting imaging studies in non-human primates. The second study focuses on developing a novel non-human primate model of relapse to drug taking. This work is being done in parallel with human studies at the Fischman Laboratory thus providing a truly translational approach to developing models for relapse and relapse prevention.

Education & Training

In addition to training medical students, psychiatry residents and fellows, the Division has continued to expand its substance abuse training for medical residents. Each month, four medical residents are spending two days at the substance abuse treatment program at which didactic and experiential learning is provided. After this experience, the medical housestaff spend an afternoon with several faculty members from the Substance Abuse Division and learn about additional pharmacologic and nonpharmacologic treatment strategies for their addicted patients.

Dr. Frances Levin, as the PI of the Research Fellowship in Substance Abuse Disorders, organizes the training for the research fellowship as well as the substance abuse curriculum for first and second year medical students. Drs. Levin coordinates a course for second and third year psychiatric residents. In addition, she and Dr. Gunderson have collaborated to receive CSAT support for curriculum development to teach medical housestaff how to diagnose and manage DSM-IV opioid use disorders among patients receiving prescription opioids for chronic non-malignant pain. The curriculum is case-based and conducted in small groups at the AIM primary care clinic. Dr. Levin continues to serve as the substance abuse course director for the Clinical Practice Course for the first and second year medical students and coordinates the substance abuse section of the pharmacology course for the second year medical students. Various faculty, including Dr. Kleber, give lectures on drugs of abuse for this course.

The purpose of the Addiction Fellowship is to train candidates for careers in clinical research in substance abuse and dependence. The American Council of General Medical Education (ACGME) also certifies the fellowship as an Addiction Psychiatry Residency Program. Interested fellows complete the necessary ACGME program requirements and sit for the boards in addiction psychiatry. These clinical experiences help inform the fellows' future lines of research. This past year we had five Fellows: Benjamin Bryan, MD, Ziva Cooper, PhD, Jennifer Hanner, MD, S. Robert Vorel, MD, PhD, and Soteri Polydorou, MD. In July-October 2008, four fellows joined the Division: David Mysels, MD, Pradeep Atluri, MD, Elias Dakwar, MD, Jermaine Jones, PhD. Drs. Vorel, Polydorou and Hanner graduated from the Fellowship June 30-July 31st, 2007. Drs. Polydorou and Hanner have joined the faculty of New York University Medical Center/Bellevue Hospital and Dr. Vorel is an Assistant Professor within the Division on Substance Abuse and recently submitted a K23 award.

STARS continues to be an important site for training of general psychiatry residents and addiction psychiatry fellows. Patients who are either ineligible for clinical trial participation or who complete a clinical trial and are in need of additional treatment are considered for referral to the NYSPI PGY3 psychiatry resident outpatient clinic. All PGY3 psychiatry residents receive clinical

supervision by Division on Substance Abuse clinical faculty. STARS also continues to provide a training opportunity for clinical psychology graduate students as part of their pre-doctoral internship experience at the NYSPI. STARS is also a training site for NYSPI PGY1 psychiatry residents. PGY 1 residents spend two weeks in the division rotating through a wide-variety of substance use disorder treatment sites. Dr. Mariani supervises training of psychiatry residents and addiction psychiatry fellows, and Dr. Carpenter supervises psychology trainees.

Clinical Services

Buprenorphine Program

In September 2003, Dr. Kleber founded the Buprenorphine Program, one of the first of its kind in the country. The program has grown over the past four years, and is now housed with the Specialty Outpatient Clinics in the Department of Psychiatry. Led by Drs. Kleber, Gunderson, Manubay and Vosburg its objectives are 3-fold: to develop a model for induction stabilization and maintenance or detoxification via the partial agonist, buprenorphine; to develop a new model for training physicians about buprenorphine; and as a site for research and training. It has treated over 500 opioid dependent patients to date with most referred to physicians in the community and approximately 90 remaining at the Program for on-going maintenance. Approximately 50% were using primarily prescription opioids, 40% heroin, and 10% methadone at the time of admission.

The Program remains committed to physician training, and has continued to receive physicians from the U.S. and abroad to observe its methods. The program has led to research project initiation, including setting up a buprenorphine program in Internal Medicine primary care clinic at Columbia University Medical Center. Internal Medicine faculty and housestaff are able to learn about and participate in buprenorphine treatment at this program as well. Dr. Gunderson is a nationally recognized mentor on buprenorphine treatment through the Physicians Clinical Support System, sponsored by the American Society of Addiction Medicine (ASAM) and Center for Substance Abuse Treatment (CSAT) of SAMHSA, and has been studying the effectiveness of buprenorphine treatment of opioid dependence delivered in a naturalistic primary care clinic setting.

Awards/Honors

Dr. Margaret Haney was promoted to a Research Scientist VI.

Dr. Carl Hart received the 2008 Presidential Teaching Award (Columbia University) and became a member of the Executive Planning Committee for the Global Methamphetamine Conference.

Dr. Herbert Kleber received a number of honors during the reporting period, among them:

- He became a member of the Executive Council of the newly formed Betty Ford Institute
- He was elected to the Council of American College of Neuropsychopharmacology
- He became a Consulting Member of the APA Council on Addiction after serving 10 years as member and Vice Chair
- He gave the plenary address at the AMERSA Annual Meeting in November 2007 on Marijuana: Myths and Realities and received their McGovern Award
- The 4th Edition of The American Psychiatric Press Textbook of Substance Abuse Treatment, edited by Galanter M, & Kleber HD, was published in May 2008 and continues to be the leading textbook in the field.
- He was again named one of New York Magazine's Best Doctors® in America in addiction psychiatry.

Dr. Frances Levin received several noteworthy honors this year:

- Vice President, American Academy of Addiction Psychiatry
- Best Doctors® in America
- Who's Who in America.

Dr. Jeanne Manubay received the 2008 NIDA Director's Travel Award to attend the College on Problems of Drug Dependence Conference.

Dr. Edward Nunes was appointed Vice-Chair of the NYSPI Institutional Review Board and was named among New York Magazine's Best Doctors.

Grants

National Institute on Drug Abuse

Dr. Joshua Berman

"Interaction of Stress and Nicotine" (K Award)

Dr. Adam Bisaga

"Memantine Naltrexone Treatment for Opioid Dependence" (R01)

"Developing Medication for Tobacco Addiction: NMDA Agents" (R01)

Dr. Kenneth Carpenter

"An Experimental Model of Human Language and Cognition in Drug Dependence" (K Award)

Dr. Sandra Comer

“Novel Medication Approaches for Substance Abuse – Laboratory Model for Heroin Abuse Medications (Project 1)

“Prescription Opioid Effects in Drug and Non-drug Abusers” (R01)

“Sustained-release Naltrexone for Opioid Dependence: Longitudinal Study in Humans” (R01)

Dr. Suzette Evans

“Vulnerability to Anxiolytic Abuse in Women” (R01)

“Effects of Smoked Heroin Across the Menstrual Cycle (R01)

“Sex Differences in Stress & Impulsivity in Cocaine Abusers” (R01)

“Progesterone Treatment for Cocaine Dependent Women” (R01)

Dr. Richard Foltin

“Anorectic Drugs: Abuse & Behavioral Mechanisms of Action (R01)

“IV Cocaine Abuse Treatment: A Laboratory Model” (R01)

“Laboratory Analysis of Cocaine Abstinence” (R01)

“Translational Approach to Models in Relapse” (R01)

Dr. Erik Gunderson

“Buprenorphine for Opioid Dependence in Primary Care” (K Award)

Dr. Margaret Haney

“Novel Medication Approaches for Substance Abuse – Pharmacological Treatment of Marijuana Dependence (Project 5)”

“Medication Development for Marijuana Relapse” (R01)

Dr. Carl Hart

“Drug Effects on Behavior: Workplace Implications” (R01)

“Intranasal Methamphetamine: A Pharmacotherapy Model” (R01)

Dr. Herbert Kleber

“Novel Medication Approaches for Substance Abuse - Administrative & Educational Cores”

“Improving Drug Abuse Treatment by Research & Training” (K Award)

Dr. Frances Levin

“Treatment of Substance Abuse & Psychiatric Comorbidity” (K Award)

“Research Fellowship in Substance Abuse Disorders”

“Novel Medication Approaches for Substance Abuse – Agonist Treatment for Marijuana Dependence (Project 4)”

“Marijuana Dependence & Depression: Venlafaxine Treatment 5 (R01)

“Marijuana Abusing ADHD Teens: Atomoxetine Treatment (R01)

“Extended Release of Mixed Amphetamine Salts for Adult ADHD and Cocaine Dependence” (R01)

“Combined Pharmacotherapies for Cocaine Dependence” (R01)

Dr. John Mariani

“Anticonvulsant Pharmacotherapy for Sedative-Hypnotic Use Disorders” (K Award)

“Novel Medication Approaches for Substance Abuse – Mesolimbic DA D1/D2 Receptors and Response to Cocaine (Project 2)”

“Kappa Receptor Selective PET Ligands”

“PET Imaging of Mesolimbic Dopamine in Heroin Dependence (R01)

“Imaging the Neurobiology of a Behavioral Treatment for Cocaine” (R01)

Dr. Edward Nunes

“Novel Medication Approaches for Substance Abuse – New Approaches to Cocaine Abuse Medications (Project 3)”

“CU Partners: NY/Long Island Regional Node”

“MI Training: Live Supervision by Tele-Conference (R01)

“Drug Abuse Treatment Development and Research Mentoring (K Award)

Dr. Stephanie Collins Reed

“Sex Differences & Impulsivity: Effect of Drug History & Stimulant Administration” (K Award)

Dr. Maria Sullivan

“Opiate Dependence: Combined Naltrexone/ Behavior Therapy (R01)

“Predictors of Relapse to Prescription Opioid Abuse Among Pain Patients (w/ Diversity Supplement)” (R01)

Dr. Nehal Vadhan

“Neuropsychological Effects of Binge-Smoked Cocaine” (K Award)

Dr. Jeffrey Wilson

“Parent-Child Interactions During Addiction Treatment” (K Award)

Substance Abuse and Mental Health Services Administration

Dr. Erik Gunderson

“Treatment Strategies for Prescription Drug Misuse and Abuse”

Other Awards

Avigen, Inc.

Dr. Sandra Comer

“Effects of AV-411, a Glial Activation Inhibitor, on Opioid Withdrawal Symptoms in Morphine-Maintained Heroin Abusers”

Grunenthal GmbH

Dr. Sandra Comer

“Relationship between Infusion Duration and Reinforcing Effects of Intravenous Oxycodone in Heroin-Dependent Individuals”

“Effect of Tablet Mechanical Stability on Drug Preference and Relative Street Value of Oxycodone Controlled-release (CR) Tablets in Experienced Oxycodone CR Abusers”

Pfizer, Inc.

Dr. Edward Nunes

“Study of Pathological Gamblers”

Schering-Plough

Dr. Sandra Comer

“Reinforcing Effects of Intravenous Buprenorphine versus Buprenorphine/Naloxone in Buprenorphine-maintained Intravenous Drug Users”

TAP Pharmaceuticals

Dr. Herbert Kleber

“Safety, Physiological Effects and Behavioral Effects of A-77000”

Significant Contributions

Dr. Sandra Comer: At equianalgesic doses, oxycodone appears to have greater reinforcing effects than morphine when both drugs are given orally. These data provide empirical support for the epidemiological observation that oxycodone is one of the most commonly abused opioid medications. The data suggest that perhaps the pharmacology of oxycodone, rather than its greater availability on the streets, may mediate its abuse liability.

Dr. Richard Foltin in collaboration with Diana Martinez: Developed a model for studying changes in dopamine binding potential and dopamine D2 receptor binding as a function of binge eating and drug-taking in non-human primates.

Dr. Margaret Haney: Demonstrated that a clinical dose of aripiprazole significantly increased cocaine craving, self-administration and intoxicating effects in cocaine abusers. These data suggest that administering aripiprazole to psychiatric patients who abuse cocaine may result in increased cocaine use.

Dr. Frances Levin: Compared baseline characteristics and treatment outcome between cocaine-dependent patients with major depressive disorder (MDD), those with attention-deficit/hyperactivity disorder (ADHD), and those with cocaine dependence (CD) without comorbid disorders in randomized clinical trials. The diagnosis and treatment of co-occurring disorders such as depression and ADHD may be important components of treatment planning for CD and the baseline level of cocaine use should be included as a covariate in studies evaluating the impact of such treatment.

Dr. John Mariani: Cannabis-dependent individuals have lower rates of past treatment and are less likely to be considering treatment at the time of exposure to clinical trial recruitment methods as compared to those with opioid or cocaine dependence.

Dr. Edward Nunes: Completed a chapter for the new edition of the textbook *Addiction Medicine* that synthesizes his research and others' research on treatment of co-occurring mood disorders among substance-dependent patients and that proposes guidelines for evaluation and treatment. With Dr. Susan Tross, he showed that a skills-based behavioral intervention, delivered by clinicians at community-based drug treatment programs, was effective in reducing HIV risk behavior among women in drug treatment.

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