CPDD Board of Directors
Anna Rose Childress, PhD, President
Linda J. Porrino, PhD, Past-President
Scott E. Lukas, PhD, President-Elect
Martin W. Adler, PhD, Executive Officer
Sharon L. Walsh, PhD, Interim Treasurer
Patrick M. Beardsley, PhD
Lawrence S. Brown, MD, MPH
Theodore J. Cicero, PhD
Sandra D. Comer, PhD
Andrew Coop, PhD

Linda B. Cottler, PhD, MPH
Richard De La Garza, II, PhD
David A. Fiellin, MD
Leonard L. Howell, PhD
Mary Jeanne Kreek, MD
Geoffrey K. Mumford, PhD
Edward V. Nunes, MD
Richard A. Rawson, PhD
Roger D. Spealman, PhD
Eric C. Strain, MD

CPDD Scientific Program Committee
Sandra D. Comer, PhD, Chair
Sari Izenwasser, PhD, Past Chair
Martin W. Adler, PhD, ex officio
Ellen B. Geller, MA, ex officio
Adam Bisaga, MD
Alan J. Budney, PhD
Howard D. Chilcoat, ScD
Rebecca Craft, PhD
Patrick M. Flynn, PhD

Leonard Howell, PhD
Cynthia Kuhn, PhD
Michelle R. Lofwall, MD
Lance R. McMahon, PhD
Janet L. Neisewander, PhD
Jennifer W. Tidey, PhD
Ellen M. Unterwald, PhD
Elise Weerts, PhD

INRC Program Committee
Co-Chairs
Sari Izenwasser, PhD (USA)
Ellen Unterwald, PhD (USA)

Members
John Traynor, PhD (USA)
Kelly Standifer, PhD (USA)
Brigitte Kieffer, PhD (France)
Craig Stevens, PhD (USA)
Steven Husbands, PhD (UK)

INRC Executive Committee
John Traynor, PhD, President
Lakshmi Devi, PhD, Past-President
Jean Bidlack, PhD, Treasurer
Eric Simon, PhD, Past-Treasurer
Craig Stevens, PhD, Information

Members
Lih-Chu Chiou, PhD (Taiwan)
Mark Connor, PhD (Australia)
Louis Gendron, PhD (Canada)
Susan Ingram, PhD (USA)
Shiro Kishioka, MD, PhD (Japan)
Ian Kitchen, PhD (UK)
Graeme Milligan, PhD (UK)
Ingrid Nylander, PhD (Sweden)
Ellen Unterwald, PhD (USA)

Local Organizing Committee
Sari Izenwasser, PhD
Jean Bidlack, PhD, INRC Treasurer
Laura Bohn, PhD
Amy Starosciak, PhD
Dean Wade, BA
PRE-MEETING SATELLITES

**NIDA: Fundamental Genetics in Drug Abuse and Addiction**
Chair by Minda R. Lynch and Joni L. Rutter

**International Women’s Fourth Meeting and Conference:**
*Drug Use, Abuse, and Dependence in Young Women: Promising Interventions and Treatments*
Chair by Frances E. Ashe-Goins and Wendee Wechsberg

**The 15th Annual NIDA International Forum: Building International Collaborative Research on Drug Abuse**
Chair by Steven Gust

**Addiction Studies Program for Journalists (ASPJ)**
(By Invitation Only)

**The International Study Group Investigating Drugs as Reinforcers (ISGIDAR)**
Chair by S. Barak Caine

**11th Annual Meeting Center for Substance Abuse Treatment (CSAT)**

---

**CPDD/INRC REGISTRATION**
3rd Floor Registration Conference Center

**CPDD OPENING RECEPTION (Cash Bar)**
GREAT HALL 1-3

---

**Saturday, June 18**
1:00 PM - 5:00 PM

**Sunday, June 19**
7:30 AM - 11:30 AM
1:00 PM - 5:00 PM

**Monday, June 20**
7:30 AM - 11:30 AM
1:00 PM - 5:00 PM

**Tuesday, June 21**
7:30 AM - 11:30 AM
1:00 PM - 5:00 PM

**Wednesday, June 22**
8:00 AM - 11:30 AM
2:00 PM - 6:00 PM

**Thursday, June 23**
7:30 AM - 11:30 AM
2:30 PM - 5:00 PM

**Friday, June 24**
8:30 AM - 12:00 Noon

---

**Saturday, June 18**
7:00 PM - 9:00 PM
(Pre-registrants can pick up badges only)
Sunday, June 19, 2011

CSAT Travel Awards Breakfast  Room 214
(By Invitation Only)  7:30 - 8:30 AM

Plenary Session  Atlantic Ballroom
8:30 - 10:45 AM

8:30  Welcome, CPDD President Anna Rose Childress
     In Memoriam

8:40  Presentation of the Marian W. Fischman Award to Bertha K. Madras
     Introduction by Mary Jeanne Kreek and Gregory Miller

8:45  Marian W. Fischman Award Lecture: Public Health and Drug Policy-Challenges for Neuroscience
     Bertha K. Madras, Harvard Medical School New England Regional
     Primate Research Center, Southborough, MA

9:30  Presentation of the CPDD/NIDA Media Award to Justin Hunt
     Introduction by Marc Kaufman

9:35  Presentation of the J. Michael Morrison Award to Steven W. Gust
     Introduction by Robert Balster

9:40  Presentation of the Joseph Cochin Young Investigator Award to
     Thomas Prisinzano
     Introduction by Kenner Rice

9:45  (Posthumous) Presentation of the Mentorship Award to Stephen G. Holtzman
     Introduction by Heather Kimmel

9:50  Presentation of the Nathan B. Eddy Award to Michael J. Kuhar
     Introduction by F. Ivy Carroll

9:55  Nathan B. Eddy Award Lecture: Uncensored Reflections on a Research Career:
     MUs, DATs, CARTs and Beyond
     Michael J. Kuhar, Yerkes National Primate Center of Emory University,
     Atlanta, GA

Public Policy Forum  Atlantic Ballroom
11:00 AM - 1:00 PM

Chairs: Martin Y. Iguchi and William Dewey

Update from the Hill and Friends of NIDA
     William Dewey, Virginia Commonwealth University, Richmond, VA

Punishment can work: A report on Hawaii’s Project HOPE
     Angela Hawken, Pepperdine University, Malibu, CA

Creation of a substance use and abuse institute
     Susan Weiss, David Shurtleff, NIDA, Bethesda, MD

BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS
Late-Breaking Research News

Regency 1
1:00 – 2:00 PM

Chair: Sandra Comer

1:00  
A randomized controlled trial of N-acetylcysteine in cannabis-dependent adolescents: Main findings  
K.M. Gray, M.J. Carpenter, N.L. Baker, S.M. DeSantis, A.L. McRae-Clark,  
K.T. Brady, Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC

1:05  
Drugs of abuse enhance HIV-1 infectivity in dendritic cells by suppressing miR-155 and 20a  
J. Napuri, Z.M. Saiyed, N. Gandhi, A. Yndart, M. Agudelo, V.B. Pichili,  
T. Samikkannu, M.P.N Nair, Institute of NeuromImune Pharmacology, Herbert Wertheim College of Medicine, Florida International University, Miami, FL

1:10  
Depot-naltrexone treatment modulates brain fMRI response to visual cues in heroin-dependent patients  
D.D. Langleben, K. Ruparel, J.W. Loughead, E. Busch, J. Cornish,  
A.R. Childress, C.P. O’Brien, University of Pennsylvania School of Medicine and the Philadelphia VA Medical Center, Philadelphia, PA

1:15  
Zolpidem enhances idling of the brain: Upregulation of resting state network activity  
S.C. Licata, S.B. Lowen, L.D. Nickerson, G. H. Trksak, R.R MacLean,  
S.E. Lukas, Behavioral Psychopharmacology Research Laboratory and Brain Imaging Center, McLean Hospital/Harvard Medical School, Belmont, MA

1:20  
Cav1.2 L-type Ca2+ channels mediate cocaine-induced plasticity in the nucleus accumbens, a long-term adaptation dependent on ventral tegmental area Cav1.3 channels  
K. Schierberl, J. Hao, C. Inturrisi and A. Rajadhyaksha, Weill Cornell Graduated School of Biomedical Sciences, New York, NY

1:25  
Subregion specific striatal activity during reward and disappointment  
R. Salas, P. Baldwin, P.R. Montague, R. De La Garza, II, Menninger Department of Psychiatry, Baylor College of Medicine, Houston, TX,  
Department of Neuroscience, Baylor College of Medicine, Houston, TX,  
Virginia Tech Carillion Institute, Roanoke, VA, Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX
1:30  **Dopamine D1 receptor antagonism in the orbitofrontal cortex prevents drug context-induced cocaine-seeking behavior in rats**  
H.C. Lasseter, X. Xie, A.M. Wells, AR. Newsome, A. Reittinger, R.A. Fuchs, Department of Psychology, University of North Carolina at Chapel Hill, Chapel Hill, NC

1:35  **The effects of oral naltrexone on oral d-amphetamine and smoked cocaine in humans**  

1:40  **Age-specific risk of starting to engage in extra-medical use of opioid analgesic medicines: United States, 2004-2008**  
E.A. Meier, J.P. Troost, J.C. Anthony, Department of Epidemiology, Michigan State University, East Lansing, MI

1:45  **High prevalence of prescription opioid use preceding heroin use in three west coast cities**  
R.A. Pollini, C. Banta-Green, L. Jenkins, E. Teshale, R. Garfein, School of Medicine, University of California San Diego, La Jolla, CA, Alcohol and Drug Abuse Institute, University of Washington, Seattle, WA, Multnomah County Health Department, Portland, OR, Centers for Disease Control and Prevention, Atlanta, GA

1:50  **Menthol preference among smokers: Association with TRPA1 variants**  
G.R. Uhl, D. Walther, C. Johnson, F.M. Behm, J.E. Rose, Molecular Neurobiology, NIH IRP (NIDA) Baltimore MD, Center for Nicotine and Smoking Cessation Research, Duke University, Durham NC

1:55  **ADHD symptoms predict affective functioning in smokers with and without PTSD**  
J.T. Mitchell, E.E. Van Voorhees, F.J. McClimate, S.H. Kollins, P.S. Calhoun, J.C. Beckham, Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, NC, Veterans Affairs Medical Center, Durham, NC, Mid-Atlantic Mental Illness Research Education and Clinical Center, Durham, NC, VA Center for Health Services Research in Primary Care, Durham, NC
Symposium I
Regency 1
2:15 - 4:15 PM

PRENATAL COCAINE EXPOSURE IN ANIMALS AND HUMANS:
SEX DIFFERENCES ACROSS THE LIFESPAN

Chairs: Cora Lee Wetherington and Samia D. Noursi

2:15  Differential effects of prenatal cocaine and environment on reward in male and female adolescent rats
Diana Dow-Edwards, State University of New York, Downstate Medical Center, Brooklyn, NY

2:45  Long-term behavioral and neuropharmacological consequences to prenatal cocaine exposure in male and female rhesus monkeys
Michael A. Nader, Wake Forest University School of Medicine, Winston-Salem, NC

3:15  Prenatal cocaine exposure: Multi-domain outcomes in inner-city male and female adolescents
Emmalee S. Bandstra, University of Miami Miller School of Medicine, Miami, FL

3:45  Prenatal cocaine exposure, early adversity, and stress reactivity: Sex differences
Linda C. Mayes, Yale University School of Medicine, New Haven, CT

Oral Communications 1
Regency 3
2:15 - 4:15 PM

WEEDING OUT THE ROOT OF THE PROBLEM:
THC AND CANNABINOIDs

Chairs: Lisa M. Schrott and Erin A. McClure

2:15  Upregulation of endocannabinoids attenuates the pro-emetic effects of opiates

2:30  Increased sensitivity of female C57Bl6 mice to paclitaxel-induced neuropathic pain and place-conditioning

2:45  THC effects on locomotor activity and elevated plus maze behavior during dosing and during spontaneous withdrawal in adolescent rats
L. C. Harte-Hargrove, D. Dow-Edwards, SUNY Downstate, New York, NY

3:00  Effects of the cannabinoid JWH-018, a primary component of K2/Spice, in rhesus monkeys
L. R. McMahon1, D. R. Schulze1, B. C. Ginsburg2, 1Pharmacology, University of Texas Health Science Center, San Antonio, TX, 2Psychiatry, University of Texas Health Science Center, San Antonio, TX

3:15  Characterizing smoking topography of cannabis in heavy users
E. A. McClure, M. L. Stitzer, R. Vandrey, Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD

3:30  GABA modulation of the discriminative-stimulus effects of THC in humans
J. Lile, T. Kelly, L. Hays, University of Kentucky College of Medicine, Lexington, KY

3:45  Galantamine’s effects on cognitive function in marijuana users
D. E. Sugarman1,2, J. Poling1,2, M. Sofuoglu1,2, 1Psychiatry, Yale University, New Haven, CT, 2VA Connecticut Healthcare System, West Haven, CT
THC impairs, and amphetamine facilitates, memory encoding preferentially for emotionally salient stimuli
M. E. Ballard¹, D. A. Gallo², H. de Wit¹, ¹Psychiatry and Behavioral Neuroscience, University of Chicago, Chicago, IL, ²Psychology, University of Chicago, Chicago, IL

Oral Communications 2

GENETICS: CODE READ

Chairs: Gregory M. Miller and Amy Janes

2:15 GABRA2 genotype influences risk for substance abuse via effects in the nucleus accumbens
M. Heitzeg, B. Weiland, S. Villafuerte, W. Yau, P. Samudra, M. Burmeister, J. Zubieta, R. Zucker, The University of Michigan, Ann Arbor, MI

2:30 Maternal cannabis dependence and offspring early substance involvement: Results from Australian children of twins
M. Waldron¹,², A. C. Heath², N. G. Martin¹, ¹Indiana University, Bloomington, IN, ²Washington University School of Medicine, St. Louis, MO, ³Queensland Institute of Medical Research, Brisbane, QLD, Australia

2:45 Association between CHRNA5 genetic variation and brain reactivity to smoking images in women smokers
A. Janes¹, J. W. Smoller², S. P. David¹, B. D. Frederick¹, S. Haddad², A. Basu², M. Fava², A. E. Evins², M. J. Kaufman¹, ¹McLean Hospital/ Harvard Medical School, Belmont, MA, ²Massachusetts General Hospital, Boston, MA, ³Stanford School of Medicine, Stanford, CA

3:00 Investigating a genetic marker of vulnerability for stimulant abuse

3:15 Effects of methamphetamine abuse and serotonin transporter gene variants on aggression and emotion-processing neurocircuitry
D. E. Payer¹, E. L. Nurmi¹, S. A. Wilson¹, J. T. McCracken¹, E. D. London¹²³, ¹Psychiatry and Biobehavioral Sciences, UCLA, Los Angeles, CA, ²Molecular and Medical Pharmacology, UCLA, Los Angeles, CA, ³Brain Research Institute, UCLA, Los Angeles, CA

3:30 Hypermethylation of specific CpG dinucleotides in the Oprm1 gene promoter region in rats exposed to heroin
D. A. Nielsen¹, L. Maili², M. Levy³, M. Huang¹, S. Hamon³, F. Leri³, ¹Menninger Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, TX, ²Psychiatry and Behavioral Sciences, University of Texas Health Science Center at Houston, Houston, TX, ³Laboratory of Statistical Genetics, The Rockefeller University, New York, NY

3:45 Advancing the rhesus monkey model for opioid research: Discovery of a novel nonsynonomous variant in the kappa opioid receptor gene
G. M. Miller, B. K. Madras, E. J. Vallender, New England Primate Research Center, Harvard Medical School, Southborough, MA

4:00 How susceptible is the alcoholism protection effect of ALDH2 exon 12 SNP to epidemiologic variations?
R. K. Price¹, G. Widner¹, S. Balan¹, E. L. Spitznagel², ¹Department of Psychiatry, Washington University School of Medicine, St. Louis, MO, ²Mathematics, Washington University, Saint Louis, MO
Oral Communications 3

WHAT’S UP WITH DOWNERS AND INHALANTS?

Chairs: Scott Bowen and Bradford D. Fischer

2:15  Physical dependence following acute benzodiazepine administration: Role of $\alpha_1$GABA$_A$ receptors
B. D. Fischer$^1$, L. P. Teixeira$^1$, O. Namjoshi$^2$, M. L. Van Linn$^2$, Z. Wang$^2$, J. M. Cook$^2$, J. K. Rowlett$^1$, $^1$Harvard Medical School/NEPRC, Southborough, MA, $^2$University of Wisconsin, Milwaukee, WI

2:30  Receptor sub-type selectivity affects subjective and cognitive effects of GABA modulators in humans: A comparison of lorazepam and a novel GABA-$\alpha_2$/GABA-$\alpha_3$ selective modulator
K. A. Schoedel$^1$, J. Frey$^2$, B. Chakraborty$^1$, M. Romach$^1$, E. Sellers$^{1,3}$, $^1$Kendle Early Stage - Toronto, Toronto, ON, Canada, $^2$AstraZeneca, Wilmington, DE, $^3$DL Global Partners Inc, Toronto, ON, Canada

2:45  GABA-B receptor positive modulators: Differential enhancement of the discriminative stimulus effects of baclofen and gamma-hydroxybutyrate
W. Koek$^{1,2}$, C. P. France$^{2,1}$, K. Cheng$^3$, K. C. Rice$^3$, $^1$Psychiatry, UTHSCSA, San Antonio, TX, $^2$Pharmacology, UTHSCSA, San Antonio, TX, $^3$Chemical Biology Research Branch, NIDA & NIAAA, Bethesda, MD

3:00  GHB in adolescent rat inhibits contextual fear conditioning
R. Sircar$^{1,2}$, K. Ishiwari$^1$, $^1$Neuroscience, The Feinstein Institute for Medical Research, Manhasset, NY, $^2$Psychiatry & Behavioral Sciences, Albert Einstein College of Medicine, Bronx, NY

3:15  Twelve months of nightly zolpidem does not produce withdrawal symptoms on drug discontinuation: A prospective placebo-controlled study
T. Roehrs$^{1,2}$, S. Randall$^1$, E. Harris$^1$, R. Maan$^1$, T. Roth$^{1,2}$, $^1$Henry Ford Health System, Detroit, MI, $^2$Psychiatry & Behavioral Neuroscience, Wayne State University School of Medicine, Detroit, MI

3:30  Assessing the discriminative stimulus effects of Soma
T. Carbonaro, M. J. Forster, M. B. Gatch, Pharmacology & Neuroscience, UNT Health Science Center, Fort Worth, TX

3:45  Development of tolerance in mice during carisoprodol treatment
J. D. Nguyen, T. Carbonaro, M. B. Gatch, T. R. Birchfield, M. J. Forster, Pharmacology & Neuroscience, UNT Health Science Center, Fort Worth, TX

4:00  Adenylyl cyclases types 1 and 8 alter behavioral responses to toluene
S. Bowen$^{3,4}$, L. Susick$^2$, J. Lowing$^2$, A. Conti$^{1,2}$, $^1$Research & Development Service, John D. Dingell VA Medical Center, Detroit, MI, $^2$Neurosurgery, Wayne State University, Detroit, MI, $^3$Psychology, Wayne State University, Detroit, MI, $^4$Obstetrics & Gynecology, Wayne State University, Detroit, MI

BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS
Sunday, June 19, 2011

Primm-Singleton Travel Awardees Meeting

Room 320
5:30 - 7:30 PM

Workshop I

Regency 1
8:00 - 10:00 PM

17TH ANNUAL CONTINGENCY MANAGEMENT WORKING GROUP

Chairs: Kelly E. Dunn and Kathryn A. Saulsgiver

Workshop II

Regency 3
8:00 - 10:00 PM

MEDIA TRAINING

Chairs: Kathleen Brady and Martin Y. Iguchi

Workshop III

Diplomat 1-2
8:00 - 10:00 PM

ASSESSING AND MONITORING RISK FOR PRESCRIPTION OPIOID ABUSE ACROSS DIVERSE POPULATIONS

Chairs: Andrea Barthwell and Lynn Webster

Managing and identifying risks in patients treated for drug addiction
Andrea Barthwell, EMGlobal LLC, Arlington, VA

Developing surveys to determine the rates of prescription opioid misuse, abuse and pseudo-addiction in chronic pain patients
Beatrice Setnik, King Pharmaceuticals, Inc., Cary, NC

Assessing and mitigating risk in pain patients
Lynn Webster, Lifetree Clinical Research and Pain Clinics, Salt Lake City, UT

Workshop IV

Diplomat 4-5
8:00 - 10:00 PM

FRONTIERS IN SYSTEMS MODELING:
BRIDGING SCIENCE AND POLICY

Chairs: Alison Ritter and Georgiy Bobashev

Primary prevention of HCV among injecting drug users and population - impact and role of opiate substitution treatment, needle and syringe distribution, and HCV antiviral treatment
Matthew Hickman, University of Bristol, Bristol, United Kingdom

Longitudinal estimates from cross-sectional data: The use of agent-based models to estimate HIV risk of drug using and sexual behaviour
Georgiy Bobashev, RTI International, Research Triangle Park, NC

An ontology-based social model of recreational poly-drug use
Pascal Perez, University of Wollongong, NSW, NSW, Australia

Discussant
Allison Ritter, University of New South Wales, Randwick, NSW, Australia
Poster Session I
(Breakfast)
Odd-numbered posters manned first hour;
Even-numbered, second hour

Set-up time begins Sunday 12:00 NOON
Must be removed by Monday 12:00 NOON

HIV I

1 Methadone with or without counseling: Impact on HIV-risk behaviors
   S. M. Kelly1, J. H. Jaffe1,2, K. E. O’Grady3, D. Gandhi2, R. P. Schwartz1, ¹Friends Research
   Institute, Baltimore, MD, ²University of Maryland, School of Medicine, Baltimore, MD, ³University
   of Maryland, College Park, College Park, MD

2 HIV sero-status, knowledge, and injection behaviors among methadone maintenance treatment
   clients in urban vs. rural settings of Kunming, Yunnan
   Y. Chang1, J. Hsieh1, J. Li2, Y. Hser1, R. Rawson1, ¹UCLA, Los Angeles, CA, ²Yun Nan
   Institute on Drug Abuse, Kunming, China

3 HIV risk and treatment among opiate injectors
   K. F. Corsi, S. Min, M. S. Royer, R. E. Booth, Psychiatry, University of Colorado Denver,
   Denver, CO

4 Naltrexone+behavioral intervention compared to usual care: Drug use and HIV risk outcomes
   in men with drug-free female partners
   D. Otiashvili1, I. Kirtadze1, K. E. O’Grady2, H. E. Jones1, ¹Addiction Research Center, Union
   Alternative Georgia, Tbilisi, Georgia, ²Department of Psychology, University of Maryland, ³Research
   Triangle Institute International, Research Triangle Park, NC

5 High risk HIV behaviors in prescription opioid, iv heroin, and non-iv heroin users
   B. Thornton, M. Hillhouse, S. Schroeder, W. Ling, ULCA Integrated Substance Abuse
   Programs, Los Angeles, CA

6 Unhealthy alcohol and illicit drug use are associated with decreased quality of HIV care
   P. T. Korthuis1, K. L. Kraemer2, K. A. McGinnis2, M. Skanderson2, A. C. Justice1, ³Research
   Triangle Institute International, Research Triangle Park, NC

7 A randomized trial evaluating the effectiveness of a hepatitis care coordination model in
   methadone maintenance treatment
   C. L. Masson1, K. L. Delucchi1, D. C. Perlman2, C. Mc Knight2, J. Hall1, C. Young2, J. Ferrara1, ¹Psychiatry,
   University of California San Francisco, San Francisco, CA, ²Beth Israel Medical Center, New York, NY

8 Hepatitis and HIV knowledge in methadone patients
   S. E. Larros1, C. L. Masson1, M. Khalili2, J. Hall1, A. Jordan2, J. L. Sorensen1, D. Perlman2, ¹Psychiatry,
   University of California San Francisco, San Francisco, CA, ²Beth Israel Medical Center, New York, NY

9 HCV-therapy in opioid-dependent, substituted patients in Germany
   S. M. Apelt, Certum Consulting Scientific Research, Oberbergkirchen, Germany
10 Socially-rooted resilience among IDUs: The protective factors that may help long-term IDUs remain HIV uninfected and help other injectors stay safe

11 Intranasal drug use as a component in “combined” prevention of hepatitis C virus transmission among injecting drug users: New York City, 2005 – 2010
D. C. Des Jarlais1, K. Arasteh1, H. Hagan3, C. McKnight1, S. Semaan2, D. Perlman1, 1Baron Edmond de Rothschild Chemical Dependency Institute, Beth Israel Medical Center, New York, NY, 2National Center for HIV/AIDS, STD & TB Prevention, Centers for Disease Control and Prevention, Atlanta, GA, 3School of Nursing, New York University, New York, NY

12 Treatment engagement and re-engagement strategies for syringe exchangers
M. S. Kidorf, V. King, J. Peirce, R. Brooner, Psychiatry, Johns Hopkins, Baltimore, MD

13 The effect of traditional masculinity in response to an HIV risk reduction intervention for substance-abusing men
J. Wilson, Psychology, University of Cincinnati, Cincinnati, OH

14 Cultural consideration in treating ethnic minority MSM
S. Larkins1, B. Rutkowski1, R. Rawson1, T. Freese1, T. Durham2, A. Skinstad2, J. Aiello4, E. Talboy3, 1Integrated Substance Abuse Programs, University of California, Los Angeles, Los Angeles, CA, 2Danya Institute, Silver Spring, MD, 3University of Iowa, Iowa City, IA, 4Ireta, Pittsburgh, PA

15 Culturally tailoring the Real Men Are Safe HIV prevention intervention
M. A. Hatch-Maillette1, D. A. Calsyn1, A. K. Burlew2, J. Wilson2, B. Beadnell1, L. Wright1, 1University of Washington, Seattle, WA, 2University of Cincinnati, Cincinnati, OH

16 HIV risk behaviors among gay and bisexual men over a weekend vacation
M. Fisher1, R. Ramchand1, M. Y. Iguchi1,2, K. Becker2, 1RAND, Arlington, VA, 2RAND, Santa Monica, CA

17 Interconnection among substance use, depression and HIV behavior in substance abuse treatment patients
S. Tross1, D. Feaster2, S. Erickson3, R. Duan2, Z. Gomez2, T. Kyle2, K. Malotte4, E. Nunes1, L. Metsch1, 1New York State Psychiatric Institute, New York, NY, 2University of Miami Miller School of Medicine, Miami, FL, 3University of California—Los Angeles, Los Angeles, CA, 4California State University—Long Beach, Long Beach, CA

18 Predictors of HIV status among low-income MSMW in three cities
A. J. Ober1, M. Y. Iguchi1,2, S. Berry3, T. Fain3, P. M. Gorbach4, R. Heimer5, L. J. Oullet6, S. Shoptaw7, W. A. Zule8, 1Integrated Substance Abuse Programs, UCLA David Geffen School of Medicine, Los Angeles, CA, 2Community Health Sciences, UCLA School of Public Health, Los Angeles, CA, 3RAND Corporation, Santa Monica, CA, 4Epidemiology, UCLA School of Public Health, Los Angeles, CA, 5Yale University School of Public Health, New Haven, CT, 6University of Illinois Chicago School of Public Health, Chicago, IL, 7Family Medicine, UCLA David Geffen School of Medicine, Los Angeles, CA, 8Research Triangle Institute, Raleigh-Durham, NC

19 Demographic and sex-related factors associated with 4 drug use behaviors in women at risk for HIV
20 Variability in self-esteem as a predictor of risky sexual attitudes in a community sample of female African American drug users
   J. L. Duvall¹, C. B. Oser², M. Staton-Tindall³, J. R. Havens¹, C. G. Leukefeld¹, ¹Behavioral Science, University of Kentucky, Lexington, KY, ²Sociology, University of Kentucky, Lexington, KY, ³Social Work, University of Kentucky, Lexington, KY

21 Apathy as a moderator of the association between social disorganization and sex with men involved in drug dealing
   L. J. Floyd, Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

POLYDRUG I

22 Evidence of preference for higher sucrose solutions in psychoactive substance subjects
   A. V. Cardoso¹, M. C. Rosa¹,², J. P. Costa¹, D. V. Pires¹, M. B. Campos¹, C. M. Gomes¹, S. B. Slavutzyk², F. H. Kessler², E. F. Ferreira¹, F. Pechansky², ¹Universidade Federal de Minas Gerais, Belo Horizonte, Brazil, ²Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil

23 Impulsivity analysis between substance dependence and sugar dependence subjects
   N. C. Marchi¹,²,³, M. C. Rosa¹,², L. Von Diemen¹, T. M. Bastos¹, M. D. Borges¹,³, F. A. Gonçalves¹, C. M. Gomes², S. M. Slavutzyk¹, F. H. Kessler¹, E. F. Ferreira², F. Pechansky¹, ¹Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil, ²Universidade Federal de Minas Gerais, Belo Horizonte, Brazil, ³Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre, Brazil

24 Negative reinforcement learning is impaired in adults with substance dependence
   L. L. Thompson¹, E. Claus², S. Mikulich-Gilbertson¹, M. Banich³, T. Crowley¹, J. Tanabe¹, ¹UCD School of Medicine, Aurora, CO, ²Mind Research Network, Albuquerque, NM, ³University of CO, Boulder, CO

25 Exercise and nutrition profiles in patients with substance use disorders
   P. Dillon, D. Wilson, D. Svikis, Virginia Commonwealth University, Richmond, VA

26 Eating behaviors and relapse among physicians recovering from substance use disorders
   M. Ruffalo, L. J. Merlo, Psychiatry, University of Florida, Gainesville, FL

27 Factor structure of the Spanish version of the CSSA in primary cocaine-dependent patients and methadone-maintained cocaine-dependent patients
   J. C. Pérez de los Cobos¹, J. Trujols¹, N. Síñol¹, L. Vasconcelos², P. Fernandez¹, A. Larrabeiti¹, ¹Addictive Behaviors Unit, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain, ²Fundación Hospital Sant Pere Claver, Barcelona, Spain

28 Can clinical trial adverse events predict pharmacological response?
   M. K. Romach, N. Levy-Cooperman, E. M. Sellers, K. A. Schoedel, Kendle Early Stage - Toronto, Toronto, ON, Canada

29 Willingness to quit smoking among substance abuse recovering patients
   L. Webb, S. Kedia, K. Ward, G. Relyea, Social and Behavioral Sciences, University of Memphis, Memphis, TN

30 Poly-drug and marijuana use among adults who use methamphetamine
   A. Raihan, K. Lovinger, D. Christou, P. Sheaff, D. Herbeck, M. Brecht, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

31 Ask your mother: Parental reports on ADHD, life stress and family history of alcohol abuse
   T. Moore¹, L. Keyser-Marcus², D. Svikis¹, ¹Psychology, VCU, Richmond, VA, ²Psychiatry, Virginia Commonwealth University, Richmond, VA
32 Children of treated substance-abusing mothers  
Y. Hser, E. Evans, D. Huang, N. Messena, UCLA Integrated Substance Abuse Programs, Los Angeles, CA

33 Children’s exposure to violence in substance-abusing homes  
K. Klostermann1,2, M. Kelley2, L. Pusateri1,2, T. Mignone3, 1Old Dominion University Research Foundation, Old Dominion University, Norfolk, VA, 2Department of Psychology, Old Dominion University, Norfolk, VA, 3Western York Health Care System, Buffalo, NY

34 Drug use relapse after first treatment among emerging adults  
E. Evans, L. Li, M. Brecht, Y. Hser, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

35 Fear of being killed by an intimate partner: The impact of substance abuse  
A. Tuller, M. Lin, R. Sage, S. Griffing, L. Madry, Urban Resource Institute, Brooklyn, NY

36 Drug use among poor African-American veterans: A secondary analysis of data from the National Survey on Drug Use and Health  
P. Vazan, A. Golub, Institute for Special Populations Research, NDRI, New York, NY

37 Sociodemographic and clinical predictors of treatment retention and substance use outcomes  
R. Walker, T. Carmody, M. H. Trivedi, University of Texas Southwestern Medical Center, Dallas, TX

38 Cognitive behavioral therapy and substance-using minorities: A meta-analysis  
A. Jemal, L. Windsor, Rutgers University, New Brunswick, NJ

39 Randomized controlled trial of CRAFT vs. treatment entry training alone for family members of treatment-resistant individuals  
K. C. Kirby1,2, L. A. Benishek1,2, C. M. Carpenedo1, K. L. Dugosh1,2, E. Bresani1, 1Treatment Research Institute, Philadelphia, PA, 2School of Medicine, University of Pennsylvania, Philadelphia, PA

40 Quality vs. quantity of coping skills following computerized CBT  
B. D. Kiluk, C. Nich, T. Babuscio, K. M. Carroll, Psychiatry, Yale University School of Medicine, West Haven, CT

41 What is happening in group? Coded observations of treatment-as-usual in outpatient group counseling  
D. J. Knoblach1, A. C. Brooks1, C. E. Nick1, D. Carise2,3, K. C. Kirby1,3, 1Treatment Research Institute, Philadelphia, PA, 2Phoenix House, New York, NY, 3University of Pennsylvania Department of Psychiatry, Philadelphia, PA

42 Impact of first-week monetary incentives in a community substance abuse treatment program  
S. J. Lookatch1, M. Tuten1, H. Fitzsimons1, H. Jones1,2, 1School of Medicine, Department of Psychiatry, Johns Hopkins University, Baltimore, MD, 2Research Triangle Institute International, Durham, NC

43 Client transfers as a continuity of care measure  
D. Urada, R. A. Rawson, A. J. Ober, J. Fan, V. J. Pearce, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

44 Regulatory compliance of residential treatment clinics in west central Mexico  
J. K. Cunningham1, O. Campollo1,3, F. Diaz1, C. M. Prado1, 1Family and Community Medicine, University of Arizona, Tucson, AZ, 2Center of Studies on Alcohol and Addictions, University of Guadalajara, Guadalajara, Mexico, 3Smoking Cessation Clinic, Hospital Civil de Guadalajara, Guadalajara, Mexico, 4Planning, State Council for Addictions of Jalisco (CECAJ), Zapopan, Mexico
Residential treatment services in west central Mexico: Resources and needs
O. Campollo1,2, F. Diaz2, C. M. Prado3, J. K. Cunningham4, 1Center of Studies on Alcohol and Addictions, University of Guadalajara, Guadalajara, Mexico, 2Tobacco Cessation Clinic, Hospital Civil Guadalajara, Guadalajara, Mexico, 3Planning, State Council for Addictions of Jalisco, Guadalajara, Mexico, 4Family and Community Medicine, University of Arizona, Tucson, AZ

Mindfulness-based psychotherapy for cannabis or cocaine dependence
E. Dakwar, J. P. Mariani, E. V. Nunes, F. R. Levin, Division on Substance Abuse, Columbia University, New York, NY

Development of a new drum therapy treatment protocol for American Indians/Alaska Natives with substance use disorders
D. L. Dickerson, Integrated Substance Abuse Programs (ISAP), UCLA, Los Angeles, CA

Effectiveness of two-stage training for brief interventionists in a multi-site trial
M. P. Bogenschutz1, A. A. Forcehimes1, C. Sanchez1, D. M. Donovan2, C. Dunn2, J. S. Baer2, K. Wilson3, R. N. Mandler3, H. I. Perl1, T. B. Moyers1, 1CASAA, U. New Mexico, Albuquerque, NM, 2U. Washington, Seattle, WA, 3NIDA, Rockville, MD

Preliminary findings from two studies of long-term recovery management for persons with stimulant or opiate dependence
G. S. Brigham1,2, R. G. Carlson3, B. M. Booth4, R. Falck3, 1Department of Psychiatry, University of Cincinnati, Columbus, OH, 2Research Institute, Maryhaven, Columbus, OH, 3Boonshoft School of Medicine, Wright State University, Dayton, OH, 4Department of Psychiatry, University of Arkansas for Medical Sciences, Little Rock, AR

Predictors of non-prescribed use of prescription stimulants, sedatives, and opioids
E. C. Katz, J. Freedlander, Psychology, Towson University, Towson, MD

Reactivity to laboratory-induced stress among individuals with prescription opioid dependence
S. E. Back1, S. M. DeSantis2, S. R. Shaftman2, L. M. Singleton1, J. L. Eaddy1, K. T. Brady1,3, 1Psychiatry, Medical University of South Carolina, Charleston, SC, 2Biostatistics, Bioinformatics & Epidemiology, Medical University of South Carolina, Charleston, SC, 3Ralph H. Johnson Veterans Affairs Memorial Hospital, Charleston, SC

Heroin use is a risk factor for injecting prescription opioids
A. Rosenblum1, C. Fong1, M. Parrino2, 1ITSR, NDRI, New York, NY, 2AATOD, New York, NY

Intranasal abuse potential of Immediate-release Oxycodone (Acurox®; IROA) formulated to deter abuse
R. L. Rolleri1, J. Faulkner3, K. A. Schoedel2, G. C. Pixton1, N. Chen2, A. Bass1, E. M. Sellers2, 1King Pharmaceuticals, Inc., Cary, NC, 2Clinical Pharmacology, Kendle Early Stage - Toronto, Toronto, ON, Canada

Assessment of the ease with which prescription opioid abusers prepare a TRF versus a non-TRF for abuse
S. K. Vosburg1, J. D. Jones1, J. M. Manubay1, J. B. Ashworth2, D. Shapiro3, S. D. Comer1, 1Substance Abuse, Columbia University/NYS Psychiatric Institute, New York, NY, 2Grünenenthal GmbH, Aachen, Germany, 3Johnson and Johnson Pharmaceuticals, Titusville, NJ

Mitigation of morphine-induced respiratory depression when morphine sulfate and naltrexone hydrochloride extended release capsules are crushed and injected
L. Webster1, V. Goli2, M. J. Lamson3, E. Carter4, 1Lifetree Clinical Research® and Pain Clinic, Salt Lake City, UT, 2King Pharmaceuticals®, Inc., Cary, NC, 3King Pharmaceuticals R&D, Inc., Cary, NC, 4King Pharmaceuticals®, Inc., Cary, NC
56 Predictors of outcome in the multi-site CTN Prescription Opioid Addiction Treatment Study
R. Weiss1,2, J. Potter3,1,2, M. Griffin1,2, H. Connery1,2, W. Ling4, 1McLean Hospital, Belmont, MA, 2Harvard Medical School, Boston, MA, 3University of Texas Health Science Center, San Antonio, TX, 4UCLA, Los Angeles, CA

57 Public health impact of injecting prescription opioids

58 Levels of knowledge about the risks and safe use of OxyContin® among prescribers of OxyContin®
A. T. Kline, J. Downing, H. Chilcoat, P. M. Coplan, Purdue Pharma, Stamford, CT

59 The effect of family factors on prescription stimulant use in youth aged 10-15
L. E. Rapp, L. B. Cottler, S. Bradford, A. Ben-Abdallah, EPRG, Washington University School of Medicine, St. Louis, MO

60 Weight control, depression and gambling associated with risk of nonmedical prescription stimulant use among pre-teen and teen girls
C. L. Striley, S. Bradford, L. B. Cottler, Psychiatry, Washington University, St. Louis, MO

61 Psychiatric medication-seeking beliefs and behaviors among college students
A. M. Stone, L. J. Merlo, Psychiatry, University of Florida, Gainesville, FL

62 Pill recognition and prescription stimulant brand name identification in N-MAPSS
L. B. Cottler, S. E. Bradford, C. W. Striley, Psychiatry, Washington University School of Medicine, St. Louis, MO

63 Use of Rx stimulants for a reason other than prescribed: How operationalization affects prevalence rates for non-medical use in adolescents
S. E. Bradford, L. B. Cottler, A. Ben Abdallah, Psychiatry, Washington Univ. in St. Louis, Saint Louis, MO

64 Prevalence, sources, motivations and diversion of psychoactive prescription medications among a university sample in Lebanon
L. Ghandour1, D. Elsayed1, S. Martins2, 1Epidemiology and Population Health, American University of Beirut, Beirut, Lebanon, 2Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

65 Predictors of severe prescription drug abuse among college students using the RADARS® System College Survey
A. Wheat1, C. Buchholtz1, J. Davis1, R. C. Dart1,2, 1Rocky Mountain Poison & Drug Center - DHHA, Denver, CO, 2University of Colorado Denver - School of Medicine, Aurora, CO

66 Predictors of moderate, substantial or severe problems associated with drug abuse in college students reporting recent non-medical opioid use
J. Davis1, C. Buchholtz1, A. Wheat1, B. Bucher Bartelson1, R. C. Dart1,2, 1Rocky Mountain Poison & Drug Center - DHHA, Denver, CO, 2University of Colorado Denver - School of Medicine, Aurora, CO

67 Prescription opioid misuse: Two motivational patterns?
M. J. Wunsch1, Y. Hodgkins2, K. Shaver2, K. Nakamoto1, R. D. Brown2, 1Virginia Tech, Blacksburg, VA, 2Carilion Clinic, Roanoke, VA

68 Patterns of prescription medication diversion among drug dealers
K. Rigg, S. P. Kurtz, H. L. Surratt, Center for Drug & Alcohol Studies, University of Delaware, Coral Gables, FL
69 Prescription drug diversion by pharmacists: Mechanisms and areas for prevention
   L. J. Merlo1,2, S. M. Cummings2, L. B. Cottler1,1, Psychiatry, University of Florida, Gainesville, FL, Psychiatry, Washington University, St. Louis, MO

70 Diversion and abuse of buprenorphine: Physician survey
   C. Johanson1,2, C. Arfken2, C. Schuster1,2, Psychiatry and Behavioral Neurosciences, Wayne State University, Chicago, IL, CRS Associates, Chicago, IL

71 Physicians' role in buprenorphine diversion reduction
   A. Yang1, C. Arfken2, C. E. Johanson2,3, Psychiatry & Behavior Neuroscience, University of Chicago, Chicago, IL, Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI, CRS Associates, LLC, Chicago, IL

72 You've got drugs: Estimating illicit or internet sales of prescription opioids
   C. Wright1, R. K. Lanier1, K. D. Gibson2, J. L. Loescher1, Rock Creek Pharmaceuticals, Inc., Gloucester, MA, Gibson Consulting, Somerville, MA

73 Internet discussion endorsing or discouraging abuse of prescription opioids: The Endorsement Ratio
   E. C. McNaughton, T. A. Cassidy, R. A. Black, S. H. Budman, S. F. Butler, Inflexxion, Inc., Newton, MA

STIMULANTS: HUMAN I

74 Relationship between executive functioning and intelligence implications for addictions treatment
   A. M. Horton1, C. R. Reynolds2, Neuropsychology Section, Psych Associates of Maryland, Bethesda, MD, Educational Psychology, Texas A&M University, College Station, TX

75 Eight weeks of citicoline treatment does not affect sleep or cognitive function in non-abstinent cocaine-dependent adults
   B. K. Bracken1,2, D. M. Penetar1,2, J. Rodolico1,2, E. T. Ryan1, S. E. Lukas1,2, McLean Hospital, Belmont, MA, Harvard Med Sch, Boston, MA

76 Cognitive functioning, mental health and substance use severity in adults with a history of methamphetamine use
   D. Herbeck, C. Canamar, M. Brecht, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

77 A randomized trial of the adjunct use of D-Cycloserine to facilitate cognitive behavioral therapy outcomes in a cocaine-dependent population
   A. Kennedy1,2, R. Gross1, N. Whitfield3, K. Drexler1,3, C. Kilts1,2, Psychiatry and Behavioral Sciences, Emory University College of Medicine, Atlanta, GA, Psychiatric Research Institute, University of Arkansas for Medical Sciences, Little Rock, AR, Atlanta Veteran’s Administration Medical Center, Atlanta, GA

78 The noradrenergic α1 receptor antagonist doxazosin attenuates cocaine-induced craving in non-treatment-seeking, cocaine-dependent volunteers
   T. Newton, R. De La Garza, II, R. Bennett, G. Brown, T. Kosten, C. Haile, J. Mahoney, Psychiatry, Baylor College of Medicine, Houston, TX

79 Oral cocaine reduce “craving” in cocaine-dependent patients
   T. Llosa, L. Llosa, Psychiatry, Coca Medica, Lima, Peru

80 Varenicline for the treatment of methamphetamine dependence: A pilot study
   A. Swanson1, S. Shoptaw1,2, K. Heinzerling1, Family Medicine, UCLA, Los Angeles, CA, Dept of Psychiatry and Biobehavioral Sciences, UCLA, Los Angeles, CA
81  *d-Amphetamine and atomoxetine for methamphetamine abuse*
   C. R. Rush, W. W. Stoops, J. A. Lile, P. E. Glaser, L. R. Hays, College of Medicine, University of Kentucky, Lexington, KY

82  *D-amphetamine withdrawal paradigm in methamphetamine dependence*
   M. J. Mancino, J. McGaugh, J. Thostenson, D. K. Williams, A. Oliveto, Psychiatry, University of Arkansas for Medical Sciences, Little Rock, AR

83  *Modafinil: A controlled trial for cocaine dependence*
   R. Malcolm, S. LaRowe, K. Huebner, K. Barnes, L. DeVane, J. Donovan, K. Barth, R. Woolson, Psychiatry & Behavioral Sciences, Medical University of South Carolina, Charleston, SC

84  *Escitalopram attenuates modafinil’s therapeutic action in cocaine-dependent volunteers*
   R. De La Garza, T. Newton, C. Haile, S. Mehtani, J. J. Mahoney, III, R. Hawkins, Psychiatry, Baylor College of Medicine, Houston, TX

85  *Effects of buprenorphine tapering schedule on cocaine use among opioid-dependent treatment-seekers*
   T. Shutter, J. A. Lindsay, T. Kosten, Mental Health, Baylor College of Medicine, Houston, TX

86  *Cortisol secretion profile and treatment outcomes in a trial of mirtazapine for depressed cocaine-dependent patients*
   L. Sanfilippo, W. N. Raby, E. V. Nunes, Columbia University, New York City, NY

87  *Aripiprazole effects on cocaine pharmacodynamics and cocaine self-administration in humans*
   M. R. Lofwall, P. A. Nuzzo, S. L. Walsh, Psychiatry, University of Kentucky (UK), Lexington, KY

88  *The influence of bupropion pretreatment on cocaine self-administration*

89  *Increased serum brain-derived neurotrophic factor is predictive of cocaine relapse outcomes: A prospective study*
   C. D’Sa, H. Fox, A. Hong, R. J. Dileone, R. Sinha, Psychiatry, Yale University, New Haven, CT

90  *The Obsessive Compulsive Cocaine Scale: Assessment of factor structure, reliability, and convergent validity*
   B. Jardin, S. D. LaRowe, B. Hall, R. J. Malcolm, Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC

91  *Using ecological momentary assessment to predict next day methamphetamine use*
   G. P. Galloway, M. J. Baggott, J. R. Coyle, J. Mendelson, Addiction Pharmacology, California Pacific Medical Center Research Institute, San Francisco, CA

92  *Does alexithymia explain variation in cue-elicited craving reported by drug-dependent individuals?*
   E. J. Santa Ana, M. E. Saladin, S. D. LaRowe, A. N. Simpson, B. K. Tolliver, K. L. Price, A. L. McRae-Clark, K. T. Brady, Ralph H. Johnson Veterans Affairs Medical Center, Charleston, SC
93 Relationship between extinction of attentional bias to cocaine-related stimuli and the severity of cocaine dependence
S. Liu¹, S. D. Lane¹, J. M. Schmitz¹, K. A. Cunningham², F. G. Moeller¹, ¹Psychiatry, University of Texas Health Science Center at Houston, Houston, TX, ²Pharmacology and Toxicology and Center for Addiction Research, University of Texas Medical Branch, Galveston, TX

94 Immediate rewards improve outcomes for methamphetamine addiction: A behavioral economic analysis of a contingency management treatment program
K. Ling¹, T. Krishnamurti¹, S. Shoptaw¹², ¹Family Medicine, UCLA DGSOM, Los Angeles, CA, ²Psychiatry and Biobehavioral Sciences, UCLA DGSOM, Los Angeles, CA, ³Carnegie Mellon University, Pittsburgh, PA

95 Cocaine behavioral economics: From the naturalistic environment to the controlled laboratory setting
C. L. Steinmiller, M. K. Greenwald, Psychiatry & Behavioral Neurosciences, Wayne State University, Detroit, MI

96 Effect of contingency management analogs on cocaine behavioral economic demand in the laboratory setting
M. Greenwald, D. M. Ledgerwood, C. L. Steinmiller, Wayne State University, Detroit, MI

97 Contingency management for cocaine addicts: Neuropsychological outcomes
G. García-Fernández, O. García-Rodriguez, R. Secades-Villa, S. Fernández-Artamendi, J. Fernández-Hermida, Department of Psychology, University of Oviedo, Oviedo, Spain

98 Individual characteristics and response to contingency management treatment for cocaine addiction
R. Secades-Villa¹, E. Sánchez-Hervás², O. García-Rodriguez¹, G. García-Fernandez¹, S. Fernández Artamendi¹, J. R. Fernández-Hermida¹, ¹Psychology, University of Oviedo, Oviedo, Spain, ²Dept 10, State Health Agency, Valencia, Spain

99 Delay discounting as a predictor of treatment response among cocaine-dependent outpatients
Y. Washio¹, S. T. Higgins¹², S. H. Heil¹², T. L. McKerchar², G. J. Badger³, J. M. Skelly⁴, R. L. Dantona¹, ¹Psychiatry, University of Vermont, Burlington, VT, ²Psychology, University of Vermont, Burlington, VT, ³Psychology, Jacksonville State University, Jacksonville, AZ, ⁴Medical Biostatistics, University of Vermont, Burlington, VT

100 Future, past, probability, and social discounting by active methamphetamine users
R. Yi¹, A. E. Carter², R. D. Landes³, ¹Psychology, University of Maryland, College Park, MD, ²Psychiatry, University of Arkansas for Medical Sciences, Little Rock, AR, ³Biostatistics, University of Arkansas for Medical Sciences, Little Rock, AR

101 Inter-temporal choice among methamphetamine-dependent volunteers: Comparison of immediately available money vs. methamphetamine
J. H. Yoon, C. S. Nerumalla, Y. Omar, G. S. Brown, R. De La Garza, II, T. F. Newton, Psychiatry and Behavioral Research, Baylor College of Medicine, Houston, TX

102 On the rapid devaluation of consumable commodities in cocaine addicts: Cross-commodity discounting of sex vs. money
D. P. Jarmolowicz¹, W. K. Bickel¹, R. D. Landes², D. R. Christensen³, L. Jackson², B. A. Jones⁴, ¹Virginia Tech Carilion Research Institute, Roanoke, VA, ²University of Arkansas for Medical Sciences, Little Rock, AR, ³University of Melbourne, Melbourne, VIC, Australia, ⁴Kent State University, Ashtabula, Ashtabula, OH
LITERATURE REVIEWS

103 Vouchers, prizes and clinic privileges as reinforcement for abstinence: A review of the efficacy of contingency management applications
B. J. Hartzler¹, S. Lash², J. Roll⁴, ¹Alcohol & Drug Abuse Institute, University of Washington, Seattle, WA, ²Veteran’s Affairs Medical Center, Salem, VA, ³Psychiatry and Neurobehavioral Medicine, University of Virginia, Charlottesville, VA, ⁴Program of Excellence in Addictions, Washington State University, Pullman, WA

104 Motivational interviewing: A review of coding systems
J. K. Manuel¹, J. M. Houck², T. B. Moyers³, ¹Department of Psychiatry, University of California, San Francisco, San Francisco, CA, ²Department of Psychology, University of New Mexico, Albuquerque, NM

105 Do gambling-induced disorders exist?
M. Fatséas¹, E. Bosc¹, C. Denis², M. Auriacombe¹, ¹Addiction Psychiatry (UMSR-CNRS), Universite Victor Segalen Bordeaux 2, Bordeaux, France, ²Addiction Treatment Center, CHCP et CHU, Bordeaux, France

106 Screening, brief intervention, and referral to treatment for drug- and alcohol-related health problems in emergency departments: Review of outcomes, implementations, and feasibility
D. J. Fischer¹, D. M. Donovan², M. P. Bogenschutz¹, A. A. Forcehimes¹, ¹CASAA, University of New Mexico, Albuquerque, NM, ²U. Washington, Seattle, WA

107 Alcohol and drug treatment outcome studies methodological review (2005-2010)
S. Robinson, S. Arcidiacono, D. Tzall, L. Sobell, M. Sobell, Nova Southeastern University, Fort Lauderdale, FL

108 Contraceptive adherence and method choice among women with drug and alcohol problems: A systematic review
M. Terplan¹, K. Hladky¹, M. Chisolm¹, S. Tristan², ¹Obstetrics, Gynecology and Reproductive Sciences, University of Maryland Baltimore, Baltimore, MD, ²Obstetrics and Gynecology, New York University, New York City, NY, ³Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD

109 Issues faced by female injection drug users: A review of the literature
L. E. Pennington, Social Work, New York University, New York, NY

110 Treatment of MDMA(ecstasy)-associated hyponatremia (MDMA-AH)
A. J. Siegel, McLean Hospital, Belmont, MA

111 Sex differences in drug abuse
J. Perry, M. Kuhar, Behavioral Neuroscience, Yerkes National Primate Research Center, Atlanta, GA

SEX, GENDER DIFFERENCES

112 ERK and CREB are associated with cocaine-induced conditioned place preference
S. K. Nygard¹, R. Hazim¹, S. Kendall¹, M. H. Eltareb¹, J. C. Blank¹, A. Klambatsen¹, V. Quinones-Jenab¹, S. Jenab¹, ¹Psychology, Hunter College, CUNY, New York, NY, ²Graduate School and University Center, CUNY, New York, NY

113 Effect of sex in selecting between food and cocaine
K. A. Kerstetter¹, M. Ballis¹, A. E. Carr¹, A. Behrens¹, T. E. Kippin¹, ¹Psychology, University of California at Santa Barbara, Santa Barbara, CA, ²Neuroscience Research Institute, University of California at Santa Barbara, Santa Barbara, CA

114 Sex differences in response to gaboxadol modification of cocaine-induced behaviors
N. Siegal, D. Dow-Edwards, Physiology / Pharmacology, SUNY Downstate College of Medicine, Brooklyn, NY
Adolescent male and female rats show enhanced responding to sucrose reward in a Pavlovian conditioning paradigm
L. M. Robertson¹, N. B. Senese², B. A. Marcus², A. J. Waldman², J. M. Gulley¹,²
¹Neuroscience, Univ. Illinois Urbana-Champaign, Champaign, IL, ²Psychology, Univ. Illinois Urbana-Champaign, Champaign, IL

Litter gender composition alters maternal behavior in rats
T. A. Kosten, Y. Hao, W. Huang, D. A. Nielsen, Psychiatry, Baylor College of Medicine, Houston, TX

Sex differences in the effects of early life stress on addiction-related cognitive deficits
A. Elton, C. Kilts, University of Arkansas for Medical Sciences, Little Rock, AR

Chronic marijuana use is associated with gender-dependent alterations in cortical microstructure
R. M. Gonzales, G. King, H. Nakama, T. Ernst, L. Chang, Department of Medicine, University of Hawaii, Honolulu, HI

Gender and cannabis use: Is there evidence of ‘telescoping’?
K. M. Zumberg, L. H. Lundahl, Psychiatry and Behavioral Neuroscience, Wayne State University School of Medicine, Detroit, MI

Gender-specific relationship between distress tolerance and HPA axis response to stress among adolescents
S. B. Daughters, S. M. Gorka, K. Marks, J. M. Richards, Behavioral and Community Health, University of Maryland, College Park, MD

Relationship between estradiol and mood in women smokers
C. E. Schiller, M. E. Saladin, K. M. Gray, S. R. Shaftman, S. A. McCullough, E. M. Klintworth, J. H. Olsen, K. J. Hartwell, M. J. Carpenter, Psychiatry, Medical University of South Carolina, Charleston, SC

The relationship between gender and expectancies for the process of smoking cessation
P. Hendricks¹,², S. M. Hall², ¹Health Behavior, University of Alabama at Birmingham, Birmingham, AL, ²Psychiatry, University of California, San Francisco, San Francisco, CA

Gender differences in exercise patterns for persons enrolled in community-based SUD treatment and recovery programs
L. Islam¹, P. Dillon³, D. Wilson², L. Keyser-Marcus¹, T. Rieckmann¹, S. Ondersma⁵, D. Svikis¹, ¹Institute for Drug and Alcohol Studies, Virginia Commonwealth University, Richmond, VA, ²Internal Medicine, Virginia Commonwealth University, Richmond, VA, ³Center for Translational Science, Virginia Commonwealth University, Richmond, VA, ⁴Public Health, Oregon Health and Sciences University, Portland, OR, ⁵Psychiatry, Wayne State University, Detroit, MI

Neurocognitive functioning among patients receiving treatment for substance use disorders: sociodemographic and drug use characteristics
M. L. Copersino¹, D. J. Schretlen², S. E. Lukas¹, G. Fitzmaurice¹, J. Sokoloff², R. D. Weiss¹, ¹McLean Hospital/Harvard Medical School, Belmont, MA, ²Johns Hopkins School of Medicine, Baltimore, MD

Understanding drug use trajectories leading to injection initiation among female sex workers who inject drugs
M. D. Morris¹, A. Vera¹, G. Martinez², L. Lozada², S. A. Strathdee¹, ¹Division of Global Public Health, University of California San Diego, La Jolla, CA, ²Patronato Pro-COMUSIDA AC, Tijuana, Mexico
126 Gender differences and similarities in sexual risk behavior: Implications for assessment and intervention in substance abuse treatment settings
K. M. Peavy, E. A. Wells, B. Hartzler, D. A. Calsyn, University of Washington, Seattle, WA

127 Gender differences in methadone-maintained cocaine users
S. Mulpur, J. Lindsay, T. Kosten, Baylor College of Medicine, Houston, TX

128 Gender differences in risk factors for new-onset nonmedical use of opioids, heroin and other drugs: Findings from NESARC
P. H. Smith, J. S. Masci, G. G. Homish, K. E. Leonard, Community Health and Health Behavior, SUNY at Buffalo, Buffalo, NY, Psychiatry, SUNY at Buffalo, Buffalo, NY, Research Institute on Addictions, SUNY at Buffalo, Buffalo, NY

129 Gender differences in 30-year trajectories of heroin and other drug use and health outcomes
C. Grella, K. Lovinger, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

130 Gender differences in health and perceptions of drug misuse among prescription opioid misusers
K. B. Nickel, A. Ben Abdallah, C. C. O’Leary, C. W. Striley, K. S. Leung, L. B. Cottler, Psychiatry, Washington University School of Medicine, St. Louis, MO

NICOTINE

131 Nicotine modulates expression of dynamin 1 in rat brain and in SH-SY5Y cells
Q. Xu, M. Li, Biological Science and Bioengineering, Institute of Beijing Jiaotong University, Beijing, China, Psychiatry and Neurobehavioral Sciences, University of Virginia, Charlottesville, VA

132 The roles of nicotinic and muscarinic cholinergic receptors in cost-benefit decision making
I. A. Mendez, J. C. Damborsky, U. Winzer-Serhan, J. L. Bizon, B. Setlow, Department of Psychology, Texas A&M University, College Station, TX, Department of Neuroscience and Experimental Therapeutics, Texas A&M University Health Science Center, College Station, TX, Department of Psychiatry, University of Florida College of Medicine, Gainesville, FL

133 Effects of varenicline and reinforcing abstinence with an alternative nondrug reinforcer alone and in combination on nicotine self-administration in rats
M. G. LeSage, Medicine, Minneapolis Medical Research Foundation, Minneapolis, MN

134 Smoking reinforcement is associated with inhibitory control performance in adult regular smokers
S. H. Kollins, F. J. McClernon, J. S. English, B. O’Brien, Duke University Medical Center, Durham, NC

135 Reinforcing effects of nicotine in nicotine non-users
A. N. Duke, R. R. Griffiths, Behavioral Pharmacology Research Unit, Johns Hopkins University School of Medicine, Baltimore, MD

136 Abuse liability assessment of electronic cigarettes in cigarette smokers
A. R. Vansickel, T. Eissenberg, Virginia Commonwealth University, Richmond, VA

137 E-cigarette abuse liability: Subjective and behavioral effects of short-term switching
V. W. Rees, J. K. Noel, G. N. Connolly, Center for Global Tobacco Control, Harvard School of Public Health, Boston, MA

138 Impulsivity, stress and depression among cigarette smokers in community corrections: Relation to suicidal behavior
C. McCullumsmith, A. Perkins, C. B. Clark, K. Cropsey, UAB, Birmingham, AL

139 Impulsivity and symptoms of ADHD and ODD/CD in daily-smoking adolescents
G. Kong, T. Liss, D. Cavallo, A. Liss, S. Krishnan-Sarin, Yale University School of Medicine, New Haven, CT
140 Impulsiveness of tobacco and street drug addiction: Delay discounting among community corrections participants who are dependent on legal and illicit substances
   A. C. Perkins, B. Clark, S. Hardy, N. Katiyar, K. Cropsey, Psychiatry, University of Alabama, Birmingham, Birmingham, AL

141 Baseline delay discounting predicts response to a behavioral smoking intervention among opioid-maintained patients
   K. A. Saulsgiver, K. Dunn, S. Sigmon, S. Heil, S. Higgins, Psychiatry, University of Vermont, Burlington, VT

142 Education and reinforcing efficacy of cigarettes predict rates of delay discounting among smokers
   E. T. Mueller¹, W. K. Bickel¹, R. D. Landes², B. P. Kowal³, R. Yi⁴, ¹Virginia Tech Carilion School of Medicine, Roanoke, VA, ²University of Arkansas for Medical Sciences, Little Rock, AR, ³University of Arkansas at Little Rock, Little Rock, AR, ⁴University of Maryland, College Park, MD

143 Prize-based contingency management and standard treatment for smoking cessation
   D. M. Ledgerwood¹, C. L. Arfken¹, N. M. Petry², S. M. Alessi², ¹Department of Psychiatry and Behavioral Neurosciences, Wayne State School of Medicine, Detroit, MI, ²Calhoun Cardiology Center, University of Connecticut Health Center, Farmington, CT

144 Contingency management for smoking cessation: Do prizes help methadone patients quit?
   B. Knezevic, A. A. Wiedemann, M. K. Greenwald, D. M. Ledgerwood, Wayne State University, Detroit, MI

145 A 12-week contingency management intervention to promote smoking cessation in opioid-maintained individuals
   M. E. Patrick, K. Saulsgiver, S. Sigmon, S. Higgins, University of Vermont, Burlington, VT

146 Acceptability and efficacy of Internet-based contingency management to promote smoking cessation
   B. R. Raiff¹, A. Rojewski², J. Dallery¹,², ¹National Development Research Institutes, New York, NY, ²University of Florida, Gainesville, FL

147 An Internet-based group contingency management program to promote smoking cessation
   S. Meredith¹, M. Grabinski², J. Dallery¹,³, ¹University of Florida, Gainesville, FL, ²Red 5 Group, New York, NY, ³National Development and Research Institutes, Inc., New York, NY

148 Smoking cessation RCT based on CBPR. Difficult but feasible. And better
   F. A. Wagner, P. Sheikhattari, M. Bolden, D. Wall, L. Bleich, Prevention Sciences Research Center, Morgan State University, Baltimore, MD

149 Differences in parenting in smokers vs. non-smokers during pregnancy
   M. Tandon, X. Si, J. Luby, Psychiatry, Washington University School of Medicine, St.Louis, St.Louis, MO

EPIDEMIOLOGY I

150 Characterization of smoking motives between African-American and European-American smokers
   J. Z. Ma², M. D. Li¹, T. J. Payne³, ¹Psychiatry, University of Virginia, Charlottesville, VA, ²Public Health Sciences, University of Virginia, Charlottesville, VA, ³ACT Center, University of Mississippi Medical Center, Jackson, MS

151 Epidemiological evidence of an alcohol dependence process phenotype observable soon after drinking onset
   D. A. Barondess, J. C. Anthony, Epidemiology, Michigan State University, East Lansing, MI
152 Are perceived neighborhood environment characteristics associated with the likelihood of smoking and alcohol use?
N. Jitnarin1,2, K. M. Heinrich3, C. K. Haddock1, J. Hughey4, L. A. Berkel4, W. C. Poston1,
1NDRI, New York, NY, 2Public Health Solutions, New York, NY, 3Kansas State University,
Manhattan, KS, 4University of Missouri-Kansas City, Kansas City, MO

153 Neighborhood perceptions association with depression
R. J. Evans-Polce1, C. Latkin1, A. Hulbert2, 1Health, Behavior, and Society, Johns Hopkins
School of Public Health, Baltimore, MD, 2Oncology, Johns Hopkins Medical Institution,
Baltimore, MD

154 Smoking rates significantly elevated in drug-dependent study populations
K. Hartwell1,2, A. Simpson1, D. Friedrich3, R. Lewis4, S. Thomas1, A. McRae-Clark1, S. Back1,
K. Brady1,2, 1MUSC, Charleston, SC, 2Ralph H Johnson V AMC, Charleston, SC, 3Cornell
University, Ithaca, NY, 4SC Dept Health and Environmental Control, Columbia, SC

155 Smokeless tobacco use and onset of cigarette smoking: A case-crossover study
J. P. Troost, J. C. Anthony, Epidemiology, Michigan State University, East Lansing, MI

156 A case-crossover approach to gateway research: First cigar to first blunt smoking
B. Fairman, J. C. Anthony, Epidemiology, Michigan State University, East Lansing, MI

157 The prevalence of THC among drivers in a medical marijuana state
T. Kelley-Baker, R. B. Voas, M. Johnson, J. Lacey, Pacific Institute for Research and Evaluation,
Calverton, MD

158 Young adults’ anonymous self reports of marijuana use online are reliable and valid
D. Ramo, S. M. Hall, J. J. Prochaska, Psychiatry, UC San Francisco, San Francisco, CA

159 Perceptions of benefits and risks of methamphetamine use
J. C. Maxwell, Addiction Research Institute, University of Texas at Austin, Austin, TX

160 WITHDRAWN

161 Factors influencing study effort in young, low-income women in a longitudinal cohort study
H. Wu1, L. Maurer1, M. Morgado1, C. Holzer1, C. Arcari1, L. Cottler2, J. Grady1, 1University of
Texas Medical Branch, Galveston, TX, 2University of Washington, St. Louis, MO

162 Burden of substance abuse in elderly prostate cancer patients
S. Chhatre1, D. Metzger1, G. Woody1, R. Jayadevappa2, 1Psychiatry, University of
Pennsylvania, Philadelphia, PA, 2Medicine, University of Pennsylvania, Philadelphia, PA

163 Hepatitis C among homeless clients of Health Care for the Homeless primary care clinics
L. Gelberg1, A. J. Strehlow5, M. J. Robertson2, S. Zerger3, C. R. Rongey4, L. E. Arangua1,
E. Farrell6, A. O’Sullivan7, 1Family Medicine, UCLA, Los Angeles, CA, 2Alcohol Research
Group, Public Health Institute, Emeryville, CA, 3Center for Social Innovation, Needham, MA,
4San Francisco Veterans Affairs Medical Center, UCSF, San Francisco, CA, 5School of
Nursing, UCLA, Los Angeles, CA, 6Clinica Family Health Services, Thornton, CO, 7Health
Care For The Homeless, Phoenix, AZ

164 Patterns of recreational use of GBL, impact on prevention policy - In situ survey
S. Balester Mouret, M. Benchaar, P. Batel, UTAMA, CHU Beaujon - Hôpitaux de Paris,
Clichy, France

165 Community and drug use among gay men: The role of neighborhoods and networks
B. C. Kelly1, R. M. Carpiano2, A. Easterbrook3, J. T. Parsons4, 1Sociology, Purdue University,
West Lafayette, IN, 2Sociology, University of British Columbia, Vancouver, BC, Canada,
3Psychology, City University of New York, New York, NY
Monday, June 20, 2011

166  *Use of over-the-counter codeine in Australia*
J. Cassar¹, L. Burns¹, S. Arora², B. De Graaff², B. Phillips¹, R. Bruno², S. Neilsen³, ¹National Drug and Alcohol Research Centre, New South Wales, NSW, Australia, ²University of Tasmania, Tasmania, TAS, Australia, ³Turning Point Alcohol and Drug Centre, Eastern Health, Melbourne, VIC, Australia

167  *Assessment of individual differences in the rewarding and aversive effects of 10 mg/kg morphine*
A. Verendeev, A. L. Riley, Psychology, American University, Washington, DC

**Symposium II**

**Regency 1**

**10:00 AM - 12:00 NOON**

**NALTREXONE IN THE TREATMENT OF OPIOID ADDICTION: CURRENT RESEARCH AND NOVEL APPLICATIONS**

**Chairs:** Kenneth Silverman and Sandra D. Comer

**10:00  Naltrexone maintenance for opioid dependence: A decade of NIDA-funded clinical trials**
Maria A. Sullivan, New York State Psychiatric Institute, Columbia University, New York, NY

**10:24  Naltrexone in Russia: Oral, implantable, and injectable**
Evgeny Krupitsky, Bekhterev Research Psychoneurological Institute, St. Petersburg, Russian Federation

**10:48  Naltrexone for prevention of relapse in parolees with a history of opioid addiction**
Charles O’Brien, University of Pennsylvania, Philadelphia, PA

**11:12  Employment-based reinforcement of naltrexone adherence: A maintenance treatment for heroin addiction**
Kenneth Silverman, Johns Hopkins University School of Medicine, Baltimore, MD

**11:36  Implications of using sustained-release naltrexone in various populations: Critical issues**
Sandra D. Comer, New York State Psychiatric Institute, Columbia University, New York, NY

**Symposium III**

**Regency 3**

10:00 - 11:00 AM

**PLASTICITY IN REWARD CIRCUITS DURING ADOLESCENCE: EFFECTS OF EARLY DRUG EXPOSURE**

**Chairs:** Sari Izenwasser and Kathleen Kantak

**10:00  Cognitive functioning of rats exposed to self-administered cocaine during adolescence vs. adulthood**
Kathleen Kantak, Boston University, Boston, MA

**10:20  Enrichment differentially alters stimulant reward and dopamine markers in male and female adolescents**
Sari Izenwasser, University of Miami Miller School of Medicine, Miami, FL

**10:40  Neurobehavioral changes exhibited in adulthood after cannabinoid exposure during adolescence**
Emilio Ambrosio, University for Distance Learning (UNED), Madrid, Spain

**BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS**
Oral Communications 4

DRUGS AND PREGNANCY

Chairs: Margaret S. Chisolm and Loretta Finnegan

11:15 Cigarette smoking and neonatal abstinence syndrome in opioid-dependent agonist-maintained pregnant patients on methadone vs. buprenorphine
M. S. Chisolm¹, S. P. Acquavita¹, K. Kaltenbach², B. Winklbaur³, S. H. Heil⁴, P. R. Martin⁵, S. M. Stine⁶, M. Coyle⁷, J. S. Leoutsakos¹, L. M. Jansson¹, M. Tuten¹, H. Jones¹, ¹Johns Hopkins University, Baltimore, MD, ²Thomas Jefferson University, Philadelphia, PA, ³Medical University of Vienna, Vienna, Austria, ⁴University of Vermont, Burlington, VT, ⁵Vanderbilt University, Nashville, TN, ⁶Wayne State University, Detroit, MI, ⁷Brown University, Providence, RI

11:30 Pre-conception markers of dual risk for alcohol and smoking exposed pregnancy: Tools for primary prevention
J. E. Hettema, K. S. Ingersoll, Psychiatry and Neurobehavioral Sciences, University of Virginia, Charlottesville, CA

11:45 Delay discounting predicts smoke status during pregnancy

12:00 An indirect self-report screener for identification of drug use in pregnant women
C. Smith¹, S. J. Ondersma², A. Unser¹, D. Wooten¹, D. S. Svikis¹, ¹Psychology, Virginia Commonwealth University, Richmond, VA, ²Psychiatry, Wayne State University, Detroit, MI

Oral Communications 5

OUTSIDE THE BOX: NEW APPROACHES TO THERAPEUTICS

Chairs: David M. Penetar and Judson Brewer

10:00 The isoflavone puerarin reduces alcohol intake in heavy drinkers
D. M. Penetar, L. H. Toto, S. L. Farmer, S. E. Lukas, Behavioral Psychopharmacology Research Lab, McLean Hospital/Harvard Medical School, Belmont, MA

10:15 Mindfulness Training for smoking cessation: Results from a randomized controlled trial
J. Brewer, S. Mallik, T. Babuscio, C. Nich, H. Johnson, C. Deleone, C. Minnix-Cotton, S. Byrne, A. Weinstein, H. Kober, K. Carroll, B. Rounsaville, Psychiatry, Yale University School of Medicine, New Haven, CT

10:30 Collegiate Recovery Communities: Student membership and prospective outcomes
A. K. Baker¹, A. B. Laudet², K. Harris¹, ¹Center for the Study of Addiction & Recovery, Texas Tech University, Lubbock, TX, ²C-STAR, NDRI, New York City, NY

10:45 Mentorship for alcohol problems
K. Tracy¹, M. Burton¹, A. Miescher¹, M. Galanter¹, T. Babuscio², T. Frankforter², C. Nich², B. Rounsaville², ¹New York University School of Medicine, New York, NY, ²Yale University School of Medicine, New Haven, CT
Symposium IV

EPIDEMIOLOGY OF CHRONIC PAIN AND CLINICAL MANAGEMENT AMONG INDIVIDUALS WITH A SUBSTANCE USE DISORDER

Chairs: Lara Dhingra and Carmen L. Masson

11:15 Epidemiology of pain in a methadone maintenance treatment population: Demographic and medical correlates of pain experience
Lara Dhingra, Beth Israel Medical Center and Albert Einstein College of Medicine, New York, NY

11:35 Clinical aspects of risk management for opioid therapy to improve chronic pain in patients with substance use disorders
Steve Passik, Vanderbilt University Medical Center, Nashville, TN

11:55 Funding opportunities and research portfolio on chronic pain and prescription opioid abuse at the National Institute on Drug Abuse
Richard Denisco, National Institute on Drug Abuse, Bethesda, MD

Oral Communications 6

CRACK IN THE ANIMAL HOUSE: PRECLINICAL STIMULANTS

Chairs: Karen K. Szumlinski and Brid Áine Nic Dhonnchadha

10:00 Roles of hippocampal and amygdalar cAMP and cGMP in extinction of cocaine-induced conditioned place preference
Y. Itzhak, S. A. Liddie, A. Paz, K. L. Anderson, Psychiatry & Behavioral Sciences, University of Miami Miller School of Medicine, Miami, FL

10:15 The hypocretin/orexin system regulates dopamine responses to cocaine
R. A. España, D. C. Roberts, S. R. Jones, Physiology and Pharmacology, Wake Forest University Health Sciences, Winston Salem, NC

10:30 Interaction between 5-HT2A receptor blockade and 5-HT2C receptor activation on spontaneous and cocaine-induced locomotion
L. A. Pockros1, N. Pentkowski1, A. Berger1, M. Ostos1, S. Conway1, J. Neisewander1, 1School of Life Sciences, Arizona State University, Tempe, AZ, 2Psychology, Arizona State University, Tempe, AZ

10:45 Long-term cocaine self-administration by rhesus monkeys results in increased expression of 1 subunits of the GABAA receptor
N. M. Shinday1,2, S. Westmoreland1, W. Yao1,2, J. K. Rowlett1,2, 1New England Primate Research Center-Harvard Medical School, Southborough, MA, 2Univ of Massachusetts, Amherst, MA

11:00 Involvement of V1b and kappa opioid receptors in HPA hyperactivity during acute withdrawal from chronic cocaine exposure in rodents
Y. Zhou1, Y. Litvin2, E. Butelman1, A. Ho1, D. Pfaff2, M. J. Kreek1, 1Biology of Addictive Diseases, Rockefeller University, NY, NY, 2Neurobiology Behavior, Rockefeller University, New York, NY
11:15  Functional studies of cocaine-induced increases in prefrontal cortex mGluR1, PI3K and PKC epsilon expression for cocaine-seeking in mice  
K. K. Szumlinski, J. A. Courson, A. W. Ary, Psychology, University of California, Santa Barbara, Santa Barbara, CA

11:30  c-Fos and AMPA receptor expression following cocaine cue extinction learning  
B. Áine Nic Dhonnchadha, B. Lovascio, N. Shrestha, C. Kirkman, A. Lin, H. Y. Man, K. Leite-Morris, G. B. Kaplan, K. M. Kantak, Boston University, Boston, MA, VA Boston Healthcare, Boston, MA

11:45  Brain-region specific changes in serotonin 2C receptor and phospholipase D signaling track with a distinct behavioral phenotype expressed in conditioned hyperactivity to cocaine  
B. Krishnan, N. C. Anastasio, R. G. Fox, S. J. Stutz, K. A. Cunningham, Center for Addiction Research, Department of Pharmacology and Toxicology, UTMB, Galveston, TX

**Animals in Research Forum**

*Atlantic Ballroom*

**12:15 - 2:00 PM**

**Chairs:** Nancy A. Ator and Toby K. Eisenstein

12:15  Animal research: Why is public support waning?  
Richard K. Nakamura, National Institute of Mental Health, Bethesda, MD

12:40  Species selection for preclinical abuse liability assessment studies  
Robert L. Balster, Virginia Commonwealth University, Richmond, VA

1:05  Regulatory and PHS policy issues that affect preclinical drug abuse research: How can we avoid regulatory creep?  
Nancy A. Ator, Johns Hopkins University, Baltimore, MD

1:30  Defending self and science from animal rights terrorists  
Edyth D. London, University of California, Los Angeles, Los Angeles, CA

**Oral Communications 7**

*Regency 1*

**2:00 - 4:00 PM**

**OLD DOG, NEW TRICKS: NOVEL TREATMENTS FOR COCAINE DEPENDENCE**

**Chairs:** Sara Jane Ward and Justin J. Anker

2:00  The GLT-1 activator ceftriaxone attenuates behavioral and neurochemical effects of cocaine in rodents  

2:15  Long-term blockade of cocaine seeking in rats treated with a cocaine hydrolase viral vector  
J. J. Anker, University of Minnesota, Minneapolis, MN

2:30  32,476: A low addictive slow-onset long-acting dopamine transporter inhibitor that inhibits cocaine’s actions in rats  
Z. Xi, X. Li, J. Li, X. Peng, R. Srivastava, M. Froimowitz, E. Gardner, Intramural Research Program, National Institute on Drug Abuse, Baltimore, MD, University of Massachusetts Lowell, Lowell, MA
2:45  *The long-acting alpha-1 antagonist, doxazosin, alters cocaine’s effects in rats*
H. Yanli, C. Haile, W. Huang, T. A. Kosten, Psychiatry, Baylor College of Medicine, Houston, TX

3:00  *Topiramate for the treatment of comorbid alcohol and cocaine dependence*

3:15  *Extended-release mixed amphetamine salts and topiramate increase abstinence rates in cocaine-dependent individuals*
J. J. Mariani1,2, W. Cheng1, M. Pavlicova1, A. Bisaga1,2, E. V. Nunes1,2, D. Brooks2, F. R. Levin1,2, 1Psychiatry/Division on Substance Abuse, Columbia University, New York, NY, 2Psychiatry/Division on Substance Abuse, New York State Psychiatric Institute, New York, NY

3:30  *Modafinil and d-amphetamine for the treatment of cocaine dependence*
J. Schmitz1, C. Green1, F. G. Moeller1, D. Herin2, J. Grabowski2, 1University of Texas Medical School at Houston, Houston, TX, 2University of Minnesota, Minneapolis, MN

3:45  *A clinical trial of N-acetylcysteine for cocaine dependence*
S. LaRowe1,3, P. W. Kalivas2, R. J. Malcolm1, 1Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC, 2Neurosciences, Medical University of South Carolina, Charleston, SC, 3Charleston VAMC, Charleston, SC

**Oral Communications 8**

**DOUBLE TROUBLE: PSYCHIATRIC COMORBIDITY**

Chairs: Staci A. Gruber and Jessica M. Peirce

2:00  *Psychological distress and depression / anxiety diagnosis among patients in substance abuse treatment centers in seven countries of Latin America and one in the Caribbean: Policy and program implications*
E. Merchán-Hamann1, L. Basso-Musso2, L. Domenech3, O. Jones-Willis4, O. V. Kulakova5, M. G. Wright6, E. Vásquez-Espinosa6, E. Leal1, P. Reid1, R. Prieto-López1, M. García-Estrada1, R. Mann6, B. Brands6, C. Strike6, J. Sapag6, 1Collective Health, University of Brasilia, Brasilia, Brazil, 2Sch. of Nursing, U. of Valparaiso, Valparaiso, Chile, 3Fac. Medicine, University of the Republic, Montevideo, Uruguay, 4Fac. Nursing, U. Panama, Panama, Panama, 5Fac. Med. Sciences, UNAN - León, León, Nicaragua, 6International Health, CAMH, Toronto, ON, Canada, 7CICAD, OAS, Washington, DC

2:15  *Life stressors and substance use among Israeli adolescents*
M. Schiff1, R. Pat-Horenczyk2, R. Benbenishty3, D. Brom2, 1School of Social Work and Social Welfare, Hebrew University, Jerusalem, Israel, 2Israel Center for the Treatment of Psychotrauma, Herzog Hospital, Jerusalem, Israel, 3School of Social Work, Bar Ilan University, Ramat Gan, Israel

2:30  *Lifetime stress is associated with increased daily use of cocaine and nicotine, and elevated ASI and BDI scores, in cocaine-dependent participants*
J. J. Mahoney, III, A. Aziziye, S. Harrison, T. Newton, R. De La Garza, II, Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, TX

2:45  *PTSD predicts treatment-seeking and drug use in syringe exchange participants*
J. M. Peirce, R. K. Brooner, V. L. King, M. S. Kidorff, Johns Hopkins University School of Medicine, Baltimore, MD
Monday, June 20, 2011

3:00  *Marijuana and mood: A role in bipolar disorder*  
S. A. Gruber, K. Sagar, M. K. Dahlgren, S. E. Lukas, Cognitive and Clinical Neuroimaging Core, McLean Hospital/Harvard Medical School, Belmont, MA

3:15  *Mood/anxiety disorders and their longitudinal association with non-medical prescription opioid use and prescription opioid use disorder*  
S. S. Martins¹, M. Fenton², K. M. Keyes², C. Blanco², H. Zhou¹, C. L. Storr³, ¹Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, ²Columbia University, New York City, NY, ³University of Maryland School of Nursing, Baltimore, MD

3:30  *Depression and abstinence in effectively treated cocaine dependence with other mental disorders*  
J. B. Milby¹, K. Crouch¹, D. Wallace², J. Schumacher¹, S. Mennemeyer¹, ¹Univ of Alabama at Birmingham, Birmingham, AL, ²RTI International, Research Triangle Park, NC

3:45  *Searching for a neurobiological basis for self-medication theory in ADHD comorbid with substance use disorders: An in vivo study of dopamine transporters using 99mTc-TRODAT-1 SPECT*  
C. M. Szobot¹, N. Junior¹, C. Shih², M. Hoexter², C. Anselmi¹, F. Pechansky¹, R. Bressan², L. Rohde¹, ¹Federal University of Rio Grande do Sul, Porto Alegre, Brazil, ²Laboratório Interdisciplinar de Neurociências Clínicas (LiNC). Department of Psychiatry, Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil

**Oral Communications 9**

DOWN ON THE PHARM: OPIOID PHARMACOLOGY

**Diplomat 1-2**  
2:00 - 4:00 PM

Chairs: Sharon L. Walsh and Daniel Roche

2:00  *Sex differences in HPA axis response to naltrexone: Preliminary evidence for the influence of estradiol*  
D. Roche¹, H. Kim², A. C. King¹, ¹Psychiatry, University of Chicago, Chicago, IL, ²Obstetrics/Gynecology, University of Chicago, Chicago, IL

2:15  *Treatment with a glial modulator attenuates opioid tolerance and dependence in opioid-dependent volunteers*  
Z. D. Cooper¹, K. W. Johnson², S. K. Vosburg¹, M. A. Sullivan¹, J. Manubay¹, D. Martinez¹, J. D. Jones¹, P. Saccone¹, S. D. Comer¹, ¹Psychiatry, SURC, Columbia University, New York, NY, ²Medicinova, San Diego, CA

2:30  *Effects of the NK-1 antagonist, aprepitant, on response to oxycodone in humans*  
S. L. Walsh¹,²,³, M. A. Heilig⁴, P. A. Nuzzo¹, M. R. Lofwall¹,²,³, ¹Center on Drug and Alcohol Research, University of Kentucky (UK), Lexington, KY, ²Behavioral Science, UK, Lexington, KY, ³Psychiatry, UK, Lexington, KY, ⁴National Institute on Alcohol Abuse and Alcoholism, Bethesda, MD

2:45  *The discriminative stimulus effects of tramadol in drug-experienced humans*  
E. C. Strain, A. N. Duke, G. E. Bigelow, Johns Hopkins University SOM, Baltimore, MD

3:00  *Interactions between the serotonin receptor agonist 1-(2,5-dimethoxy-4-methylphenyl)-2-aminopropane (DOM) and heroin: I.v. self administration*  
C. P. France¹,², J. X. Li¹, W. Koek¹,², ¹Pharmacology, University of Texas Health Science Center, San Antonio, TX, ²Psychiatry, University of Texas Health Science Center, San Antonio, TX
Monday, June 20, 2011

3:15 Effects of intra-accumbal ΔFosB overexpression on extinction of opiate conditioned place preference  
G. B. Kaplan¹, S. C. Heinrichs¹, K. A. Leite-Morris¹, V. Vialou², W. Y. Fan¹,  
E. J. Nestler², Psychiatry, Boston University/VA, Boston, MA, Fishberg  
Dept. of Neuroscience, Mount Sinai Medical Center, New York, NY

3:30 Influence of estrogen on morphine reward  
L. I. Perrotti, S. A. Morris Bobzean, Psychology, University of Texas at  
Arlington, Arlington, TX

3:45 Functional interaction between HIV-gp120 in the brain and opioid medications  
K. Benamar, J. Palma, A. Cowan, E. B. Geller, M. W. Adler, CSAR,  
Temple University, School of Medicine, Philadelphia, PA

Symposium V

DRUG-RELATED ATTENTIONAL BIAS AND CUE REACTIVITY:  
NEUROPSYCHOLOGICAL MECHANISMS AND CLINICAL RELEVANCE

Chairs: Lee Hogarth and Mohammed Shoaib

2:00 Associative basis of cue effects on intentional drug choice: Implications for the treatment of addiction  
Lee Hogarth, University of Nottingham, University Park, United Kingdom

2:25 Reliability of modified Stroop and visual probe tasks to assess cognitive biases for smoking-related cues  
Sally Adams, University of Bristol, Bristol, United Kingdom

2:50 Mechanisms for counteracting drug-related attentional biases and their relevance to abstinence  
Hugh Garavan, University of Vermont, Burlington, VT

3:15 Responses to drug-related and emotional cues in heroin users: Implications for treatment  
Dan Lubman, Turning Point Alcohol and Drug Centre, Eastern Health, Monash University, Fitzroy, VIC, Australia

3:40 Animal models of drug cue reactivity and their role in developing pharmacotherapies for addiction  
Mohammed Shoaib, Institute of Neuroscience, Medical School, Newcastle University, Newcastle Upon Tyne, United Kingdom

President’s Lecture

Presentation of the Distinguished Service Award  
4:15 - 5:15 PM  
We Must Be of One Mind for Research  
Patrick L. Kennedy, Next Chapter LLC, Absecon, NJ
Monday, June 20, 2011

Pre- and Post-Doc Networking Event Room 307
5:30 - 7:00 PM

Workshop V Regency 1
8:00 - 10:00 PM

CONTINGENCY MANAGEMENT FOR ADOLESCENT SUBSTANCE ABUSE/ SASATE BUSINESS MEETING

Chairs: Catherine Stanger and Michael L. Dennis

Family-based contingency management for adolescent substance abuse
Catherine Stanger, UAMS Center for Addiction Research, Little Rock, AR

Management principles to develop high-school-based tobacco interventions
Suchitra Krishnan-Sarin, Yale University School of Medicine, New Haven, CT

Lessons learned in transporting CM to community-based practitioners
Michael R. McCart, Medical University of South Carolina, Charleston, NC

Contingency management interventions: Clinical, research, and dissemination challenges
Alan J. Budney, UAMS Center for Addiction Research, Little Rock, AZ

Society of Adolescent Substance Abuse Treatment Effectiveness (SASATE) business meeting
Michael Dennis, Chestnut Health Systems, Normal, IL

Workshop VI Regency 3
8:00 - 10:00 PM

CAREER DEVELOPMENT: A PERSPECTIVE FROM JUNIOR AND SENIOR RESEARCHERS

Chairs: Gerald McLaughlin and Scott Chen

Workshop VII Diplomat 1-2
8:00 - 10:00 PM

NIDA MEDICATIONS DEVELOPMENT WORKSHOP 2011

Chairs: David McCann and Phil Skolnick

Abstinence: A new look at an old endpoint
David McCann, Division of Pharmacotherapies and Medical Consequences of Drug Abuse, NIDA, Bethesda, MD

Medication non-compliance: What can we do about it?
Phil Skolnick, Division of Pharmacotherapies and Medical Consequences of Drug Abuse, NIDA, Bethesda, MD

What's in the pipeline?
Jane Acri, Division of Pharmacotherapies and Medical Consequences of Drug Abuse, NIDA, Bethesda, MD
Navigating through procedural and regulatory aspects described in the FDA draft guidance on abuse potential testing  
   Beatriz Rocha, Merck Research Laboratories, Ann Arbor, MI
Talking with the FDA controlled substance staff about preclinical evaluation of abuse potential issues as indicated in the draft guidance  
   Mary Jeanne Kallman, Covance Laboratories Inc., Greenfield, IN
Talking with the FDA controlled substance staff about design and interpretation of the clinical evaluation of abuse potential of drugs  
   Marta Sokolowska, Grunenthal USA, Bedminster, NJ
Talking with Industry – FDA controlled substance staff feedback  
   Silvia Calderon, Food and Drug Administration, Silver Spring, MD
NIDA International Forum Poster Session

Great Hall 5-6 Foyer
8:00 – 10:00 PM

Chair: Steven W. Gust

Basic Science

Disposition of CB1 agonist JWH-018 in the mouse following inhalation of the herbal incense “Buzz”
D. Amira^1,2, J.L. Poklis^1, L.E. Wise^1, J.M. Wiebelhaus^1, A. Poklis^1. ^1Hubert H. Humphrey Fellowship Program and Departments of Pharmacology, Toxicology, and Pathology, Virginia Commonwealth University, United States; ^2Laboratory of Toxicology, Emergency Assistance Center-Tunis, Tunisia

Changes in the cannabinoid (CB1) receptor expression level and G-protein activation in the kainic acid model of epilepsy
A. Borsodi^1, E. Bojnik^1, E. Turunc^2, G. Armagan^2, L. Kanit^2, S. Benyhe^1, A. Yalcin^2. ^1Hungarian Academy of Sciences, Hungary; ^2Ege University, Turkey

Comparative gene expression profiling analysis of lymphoblastoid cells in heroin addicts
C.H. Chen^1, D.L. Liao^2, M.C. Cheng^3, S.H. Hsu^1, C.H. Lai^1, H.J. Tsai^1. ^1National Health Research Institutes, Taiwan; ^2Bali Psychiatric Center, Department of Health, Taiwan; ^3Yuli Mental Health Research Center, Yuli Veterans Hospital, Taiwan

Craving and severity of cannabis dependence modulate brain responses to cannabis cues
J. Cousijn^1, A.E. Goudriaan^2, K.R. Ridderinkhof^1, W. van den Brink^2, D.J. Veltman^2, R.W. Wiers^1. ^1University of Amsterdam, Netherlands; ^2Academic Medical Centre, Netherlands

Synergistic analgesic response of a morphine-fentanyl combination: Correlation with mu-opioid receptor internalization
S. Cruz^1, A. Silva-Moreno^1, M. Leon-Olea^2. ^1Cinvestav, Mexico; ^2National Institute of Psychiatry, Mexico

Calcium signaling underlying nicotine’s suppressive effect on Toll-like receptor 3 and Toll-like receptor 4 pathways
W.Y. Cui^1, J. Wang^2, R. Polanowska-Grabow^2, J.J. Saucerman^2, J. Gu^1, S. Chang^4, M.D. Li^2. ^1Peking University, China; ^2Departments of Psychiatry and Neurobehavioral Sciences, Biomedical Engineering, University of Virginia, United States; ^4Institute of NeuroImmune Pharmacology, Seton Hall University, United States

Neuropharmacological and toxicological effects of inhaling a local Egyptian glue in comparison with toluene in rats
A. Elkoussi, M. Abdelraheim, M. Shaker. College of Medicine, University of Assiut, Egypt

Growth-restricted piglets: A natural occurring animal model of intrauterine growth restriction in humans?
E.T. Gieling, R.E. Nordquist, F.J. van der Staay. Faculty of Veterinary Medicine, Department of Farm Animal Health, Utrecht University, Netherlands; Emotion and...
Cognition Program, Netherlands; Rudolf Magnus Institute for Neuroscience, University Medical Center Utrecht, Netherlands

**Neuroimaging heavy cannabis users versus sporadic users and nonusers: Working memory and decisionmaking**
A. Goudriaan¹, J. Cousijn¹, L. Porrino², D. Veltman¹, W. van den Brink¹, R. Wiers¹.
¹Academic Medical Center, University of Amsterdam, Netherlands; ²Wake Forest University, United States

**Quantitative electroencephalogram and trimensional personality questionnaire factors in substance abusers**
M.W. Huang¹,², P.Y. Lo², Y.T. Chen³, K.S. Cheng². ¹Chia-Yi Veterans Hospital, Taiwan; ²Institute of Biomedical Engineering, National Cheng Kung University, Taiwan; ³Department of Electrical Engineering, Southern Taiwan University, Taiwan

**Transgenic pig models for studying neurodegenerative diseases**
L. Lai, D. Yang, C.E Wang, B. Zhao, W. Li, Z. Ouyang, Z. Liu, Y. Zhao, H. Yang, N. Fan, J. Song, J. Tian, S.H. Li, X.J. Li. Guangzhou Institutes of Biomedicine and Health, Chinese Academy of Sciences, China; Emory University, United States

**Structural magnetic resonance imaging of piglet brain development from postnatal day 1 through 28**
R.E. Nordquist¹,²,³, E.C. Zeinstra¹,³, L. van Dijk¹,³, K. van der Marel⁴, A. van der Toorn⁴, F.J. van der Staay¹,²,³, R.M. Dijkhuizen⁴. ¹Emotion and Cognition Response Program, Utrecht University, Netherlands; ²Rudolf Magnus Institute for Neuroscience, University Medical Center Utrecht, Netherlands; ³Department of Farm Animal Health, Utrecht University, Netherlands; ⁴Image Sciences Institute, University Medical Center Utrecht, Netherlands

**N-acetylcysteine changes glutamate levels in cocaine-dependent subjects: An open-label magnetic resonance spectroscopy study**
L. Schmaal, A.E. Goudriaan, D.J. Veltman, W. van den Brink. Department of Psychiatry, Academic Medical Center, Netherlands

**Searching for a neurobiological basis for self-medication theory in attention deficit/hyperactivity disorder comorbid with substance use disorders: An in vivo study of dopamine transporters using ⁹⁹mTc-TRODAT-1 SPECT**
C. Szobot¹, N. Silva Jr.²,³, M.C. Shih⁴, M.Q. Hoexter⁴, C.E. Anselmi², F. Pechansky¹, R.A. Bressan⁴, L.A. Rohde⁵. ¹Federal University of Rio Grande do Sul, Brazil; ²Laboratory of Nuclear Medicine, Hospital Complex Santa Casa, Brazil; ³Child and Adolescent Psychiatric Division, Hospital de Clínicas de Porto Alegre, Brazil; ⁴Interdisciplinary Laboratory of Neuroimaging and Cognition, Federal University of São Paulo, Brazil; ⁵National Institute for Developmental Psychiatry, Brazil
**Association study of the β-arrestin 2 gene (ARRB2) with opioid and cocaine dependence in a European American sample**
M. Vaswani1,2, L.M. Ambrose-Lanci1, T.K. Clarke1, A. Zeng1, T.N. Ferraro1, F.W. Lohoff1, W.H. Berrettini1. 1Center for Neurobiology and Behavior, University of Pennsylvania School of Medicine, United States; 2All India Institute of Medical Sciences, India

**TCM-9811 may be a potential anti-inflammatory neuroprotective agent to decrease neuron insult from drug abuse**
Y.W. Wang1, Y.F. Chen1, S.L. Chang2. 1China Medical University, Taiwan; 2Seton Hall University, United States

**Nicotine modulates expression of dynamin 1 in rat brain and in SH-SY5Y cells**
Q. Xu1, M.D. Li2. 1Institute of Biological Science and Bioengineering, Beijing Jiaotong University, China; 2Department of Psychiatry and Neurobehavioral Sciences, University of Virginia, United States

**Reinforcing effects of cocaine in COMT knockout mice**
E. Zvartau1, L. Mus1, O. Dravolina1, A. Bespalov1, M. Käenmäki2, R. Talka2, O. Salminen2, R.K. Tuominen2, P.T. Männistö2. 1Valdman Institute of Pharmacology, St. Petersburg Pavlov State Medical University, Russia; 2Faculty of Pharmacy, University of Helsinki, Finland

---

**Epidemiology**

**Prescription drug abuse trends among school and university students in Gaza (Palestinian Authority)**
M.F. AlAfifi1, M. Sakka2, R. Afifi1. 1Substance Abuse Research Center, Palestinian Territory; 2AlAzhar University, Palestinian Territory

**Size estimation of injection drug users in Chiang Mai Province, Northern Thailand, using network scale-up methods**
A. Aramrattana1, K. Thaikla1, K. Yodreurn2, S. Wongchai2, W. Wongtip2, C. Chariyalertsak2, S. Wisurarut2. 1Chiang Mai University, Thailand; 2Chiang Mai Public Health Office, Ministry of Public Health, Thailand

**Are vocational students at high risk for drug use and problem behaviors?**
S. Assanangkornchai. Prince of Songkla University, Thailand

**Consumption of licit and illicit psychoactive drugs and its impact on the educational, family, economic, and legal problems in university students**
F. Bautista-Perez2, E.E. Mendoza2. 1Universidad Evangélica de El Salvador, El Salvador; 2Universidad Capitan General Gerardo Barrios, El Salvador

**Drug-defined crimes among inmates of a city jail in Eastern Visayas, Philippines**
T. Cajano1, J. Pascual2, I. Escartin1. 1Department of Health, Philippines; 2University of the Philippines, Philippine General Hospital, Philippines
Knowledge of sexual practices and beliefs about HIV/AIDS among drug users in a Central America suburban community
M. Chacón-Ortiz¹, R. Achí¹, M. Comerford², K. Barrantes¹, C. McCoy². ¹Institute of Health Research, University of Costa Rica, Costa Rica; ²Comprehensive Drug Research Center, University of Miami, United States

HIV serostatus, knowledge, and injection behaviors among methadone maintenance treatment clients in urban versus rural settings of Kunming, Yunnan
Y.J. Chang¹, J. Hsieh¹, J. Li², Y.I. Hser¹. ¹University of California, Los Angeles, United States; ²Yun Nan Institute on Drug Abuse, China

Level of crime predicts differential mortality risk prior to opioid maintenance treatment
T. Clausen, A. Bukten. University of Oslo, Norway

GABRA2 and parental control in relation to adolescent substance use: The TRAILS Study
H. Creemers¹, R. Veenstra², F. van Oort³, F. Verhulst³, W. Vollebergh⁴, H. Ormel², A. Huizink¹, D. Dick⁵, J. Meyers⁵. ¹University of Amsterdam, Netherlands; ²University of Groningen, Netherlands; ³Erasmus Medical Center, Netherlands; ⁴Utrecht University, Netherlands; ⁵Virginia Commonwealth University, United States

Epidemiology of coca leaf chewing: Mental health survey evidence from the rural Andean Highlands of Peru, 2008
V. Cruz¹, J. Saavedra¹, J.C. Anthony². ¹Office of Epidemiology, Peruvian National Institute of Mental Health, Peru; ²Michigan State University, United States

The SACENDU Project: Monitoring alcohol and drug abuse trends in South Africa
S. Dada¹, A. Pfüddemann¹, A. Bhana², C. Parry³. ¹Alcohol and Drug Abuse Research Unit, Medical Research Council, South Africa; ²Child, Youth, Family and Social Development Program, Human Sciences Research Council, South Africa

Drug use in rural China
Q. Deng¹, Q. Tang², M. Chawarski³, R. Schottenfeld³, W. Hao¹. ¹Mental Health Institute of Central South University, China; ²The Fifth People’s Hospital of Nanning, China; ³Yale University, United States

Digital screening of psychoactive drugs in Nigeria
E. Ehikhamenor, H. Obianwu. University of Benin/Savan, Nigeria

Drug use among Moroccan youth students: MedSPAD national survey
F. El Omari, J. Toufiq. Arrazí Psychiatric Hospital, Morocco
Differences in smoking prevalence in the same population when using different surveillance tools in eight countries
O. El Shahawy1,2, L. Haddad2,3. 1General Medical Management, Ain Shams University, Egypt; 2Institute for Drug and Alcohol Studies, Virginia Commonwealth University, United States; 3School of Nursing, Virginia Commonwealth University, United States

Street youth background and its contribution to an injection drug use career
K. Eritsyan, V. Odinokova, L. Safiullina, M. Rusakova. NGO “Stellit,” Russia

Perceived coercion among individuals who drive under the influence of alcohol and drugs: Testing the “rolling consent” approach applied to a nationwide telephone survey
S. Faller1, J.M. Webster2, J. Protas1, C. Machado1, D.B. Bumaguin1, P.V. Duarte3, R. De Boni1, F. Pechansky1. 1Center for Drug and Alcohol Studies, Federal University of Rio Grande do Sul, Brazil; 2Center on Drug and Alcohol Research, University of Kentucky, United States; 3Brazilian National Secretariat for Policies on Drugs, Brazil

Hepatitis C virus among homeless clients of Health Care for the Homeless primary care
L. Gelberg1, A.J. Strehlow1, M.J. Robertson2, S. Zerger3, C.R. Rongey4, L.E. Arangua1, E. Farrell5, A. O'Sullivan6. 1University of California, Los Angeles, United States; 2Alcohol Research Group, Public Health Institute, United States; 3Center for Social Innovation, United States; 4San Francisco Veterans Affairs Medical Center, University of California, San Francisco, United States; 5Clinica Family Health Services, United States; 6Health Care for the Homeless, United States

Exploring the impact of underage entry into sex work: Associations between underage sex work and HIV/sexually transmitted infections, substance use, and violence in two Mexican border cities
S. Goldenberg1, R. Lozada2, H. Staines3, A. Vera1, D. Abramovitz1, T.P. Patterson1, A. Raj4, S.A. Strathdee1. 1University of California, San Diego, United States; 2Patronato Pro-COMUSIDA, Mexico; 3Faculty of Medicines, Autonomous University of the City of Juárez, Mexico; 4Department of Community Health Sciences, Boston University, United States

10 years of regional inequalities in deaths by diagnosis of mental and behavioral disorders due to psychoactive substance use: A view of the Brazilian public health data
V. Gonçalves, S. Faller, D. Benzano, R. De Boni, F. Pechansky. Center for Drug and Alcohol Studies, Federal University of Rio Grande do Sul, Brazil

Smoking and periodontal disease among patients of the Bethania Clinic of the Social Security System of the Republic of Panama
G. Gonzalez. Social Security, Panama

BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS
Utility and cost-effectiveness of hepatitis C antiviral therapy for prevention among injecting drug user populations
M. Hickman¹, N.K. Martin¹, P. Vickerman¹, G.R. Foster², S.J. Hutchinson³, D.J. Goldberg⁴. ¹University of Bristol, United Kingdom; ²Queen Mary, University of London, Barts and the London School of Medicine, United Kingdom; ³Health Protection Scotland, United Kingdom

Nonmedical prescription drug use among Israeli school dropouts
R. Isralowitz¹, A. Reznik¹, M. Kron². ¹Regional Alcohol and Drug Abuse Resources Center, Israel; ²Migal/Lifta Adolescent Drug Treatment Program, Israel

Preliminary investigation of the AUDIT and DUDIT versus biomarkers of alcohol and drug use among HIV-infected clinic attendees in Cape Town, South Africa
R. Kader¹, C. Parry¹, S. Seedar², R. Koch³, L. Rowland¹, S. Dada¹. ¹Medical Research Council, South Africa; ²Department of Psychiatry, University of Stellenbosch, South Africa; ³Virginia Commonwealth University, United States

Drug use and sexual behavior of injecting drug users in Indonesia
O. Kamil¹, R. Tambunan¹, H. Erlan¹, I. Praptoharjo², I. Irwanto¹, S. Lenggogeni¹. ¹HIV/AIDS Research Center, Atma Jaya University, Indonesia; ²Health Policy Administration Department, University of Illinios, United States

Perception of drinking, smoking, and narcotic drug use behavior of secondary school students in Thailand, 2009
D. Kanchanasuwan, S. Assanangkornchai, U. Pattanasattayawong. Prince of Songkla University, Thailand

Association between alcohol, tobacco, and other drug use and bullying among secondary school students in Nakuru District, Kenya
M. Kariuki, O.J. Samsom. Egerton University, Kenya

Correlation between antiretroviral therapy initiation during incarceration and enrollment in HIV care among newly released inmates in Odessa Region, Ukraine
T. Kiriazova¹, O. Neduzhko². ¹Future Without AIDS, Ukraine; ²Odessa Medical University, Ukraine

Neonatal neurobehavior of New Zealand infants exposed to methamphetamine predicts cognitive development at age 1 year
L. LaGasse³, T. Woulde², M. Hinckley¹, B.M. Lester¹, S. Della Gotta¹. ¹Center for the Study of Children at Risk, Brown Alpert Medical School, Women and Infants Hospital, United States; ²University of Auckland, New Zealand

Relationship between social network factors, HIV, and hepatitis C virus among injection drug users in Chennai, India
C. Latkin¹, C. Yang¹, A.K. Srikrishnan², S.S. Solomon², S.H. Mehta¹, D.D. Celentano¹, M.S. Kumar², S. Solomon². ¹Bloomberg School of Public Health, Johns Hopkins University, United States; ²YR Gaitonde Centre for AIDS Research and Education, India
Does a defense mechanism matter: A preliminary study among substance misusers in Taiwan
C.H. Lee¹, S.K. Lin¹, C.H. Chen², Y.L. Chiu¹, H.C. Liu¹. ¹Taipei City Hospital and Psychiatric Center, Taiwan; ²Taipei Medical University, Shuang-Ho Hospital, Taiwan

Item response analysis on DSM-IV criteria for alcohol, cannabis, cocaine, and opioids
K.S. Leung, A.B. Abdallah, L.B. Cottler. Washington University School of Medicine, United States

Temporal changes of smoking status and motivation among Chinese female heroin-dependent smokers
L. Li¹, Y. Liu¹, Y. Yao², J. Zhao², W. Shen¹, W. Zhou¹. ¹Ningbo Addiction Treatment and Research Center, China; ²Administrative Institute of Education Through Labor of Zhejiang Province, China

Survey of the HIV-infected who inject opium solution in a border ethnic minority village where it abuts Burma (Myanmar)
Y. Li¹, Y.Q. Yang², S.G. Zhang³, H.Y. Bi³, L. Duo⁴, H. Liu⁵, Hong Li²,⁶. ¹Kunming Medical College, China; ²Nu Jiang State Center for Disease Control, China; ³Lusui Center for Disease Control, China; ⁴Yunnan Red Cross Hospital, China; ⁵Institute of Human Virology, Sun Yat-sen University, China; ⁶Yunnan Center for Disease Control and Prevention, China

Household survey shows increasing cannabis and cocaine use in Bolivia
R. Lopez. Universidad Mayor de San Andres, Bolivia

Drug use resilience and its determinants among school adolescents in Bogota, Colombia
C. Lopez-Quintero, Y. Neumark. Braun School of Public Health and Community Medicine, Hebrew University of Jerusalem, Israel

Sexual risk behavior in women with substance abuse disorders
D. Molina¹, G. Rivero², S. Colina². ¹State Hospital Dr. Pedro Iturbe, Venezuela; ²Rafael Urdaneta University, Venezuela

Depression, suicidal behavior, and substance use among high school students in Thailand
A. Muekthong, S. Assanangkornchai, N. Sam-angsri. Psychiatric Department, Prince of Songkla University, Thailand

R. Muga¹,², M. Torrens²,³, F. Bolao²,⁴, E. Martínez¹, A. Sanvisens¹; S. Pérez-Hoyos⁵, G. Vallecillo²,³, F. Fonseca²,³, D. Fuster¹,², J. Tor¹,². ¹Hospital Universitari Germans Trias i Pujol, Spain; ²Universitat Autònoma de Barcelona, Spain; ³Hospital del Mar, Spain; ⁴Hospital Universitari de Bellvitge, Spain; ⁵Universitat de Barcelona, Spain; ⁶Hospital Vall d’Hebrón, Spain
Genetic and environmental contributions to cannabis withdrawal and abuse/dependence in a national adult twin sample
N. Nat1, A. Agrawal2, H.E. Creemers1, A.C. Huizink1, N.G. Martin3, M.T. Lynskey2.
1University of Amsterdam, Netherlands; 2Washington University School of Medicine, United States; 3Queensland Institute of Medical Research, Australia

Seeking online information about drugs/alcohol/tobacco by Jewish and Arab schoolchildren in Israel: Who does, who doesn’t, and who wants to?
Y. Neumark1, C. Lopez-Quintero2, B. Feldman2, L. Flum2, R. Shtarkshali2. 1Hebrew University-Hadassah, Israel; 2Braun School of Public Health and Community Medicine, Hebrew University of Jerusalem, Israel

Preliminary success from evaluation of a pilot program results in scaling up a methadone maintenance program in Vietnam

Correlations of drug use and personal, familial, peer, community, and stress factors among young adults in Vietnam: Differences in males and females
V.T. Nguyen. Ministry of Labor, Invalids and Social Affairs, Department for Social Vice Prevention, Vietnam

Persistent versus nonpersistent patterns of marijuana use in adolescents: Are there protective factors that distinguish these subgroups of users?
A.R. Noto1, T. de Castro Amato1, S.S. Martins2. 1Federal University of São Paulo, Brazil; 2Bloomberg School of Public Health, Johns Hopkins University, United States

Cannabis use and crime among young offenders in a correctional center in south-western Nigeria
A. Ogunwale. Neuropsychiatric Hospital, Nigeria

Use of substance and prescription medication among working class females in Lagos, Nigeria
C. Okonkwo1, F. Jinadu1, R. Lawal1, B. Ola2, A. Gabriel1, T. Akinola1. 1Federal Neuropsychiatric Hospital, Nigeria; 2Lagos State University Teaching Hospital, Nigeria

Rates of experimental and regular substance use in Uruguay boy and girls: Comparison of 2003 and 2009 survey results
G. Olivera1,3, D. Svikis2, H. Suarez2. 1Hubert H. Humphrey Fellowship Program, Institute for Drug and Alcohol Studies, Virginia Commonwealth University, United States; 2Addiction and Women’s Health, Advancing Research and Evaluation Program, Virginia Commonwealth University, United States; 3National Drug Assembly, Presidency of Uruguay, Observatory of Drug Demand Reduction Area, Uruguay
Alcohol, smoking, and illicit substance use among secondary school students in northeastern Thailand

S. Paileeklee, B. Jindawong. Faculty of Medicine, Khon Kaen University, Thailand

Association between post-traumatic stress disorder, sexual risk behaviors, and drug use among Brazilian club drug users

G. Pasa¹, L. Remy¹, D. Benzano¹, S. Kurtz², H. Surratt², F. Pechansky¹. ¹Center for Drug and Alcohol Studies, Federal University of Rio Grande do Sul, Brazil; ²Center for Drug and Alcohol Studies, University of Delaware–Florida, United States

Rapid assessment and response of drug use and HIV in Thailand: Songkhla Province

U. Pattanasattayavong, S. Assanangkornchai. Faculty of Medicine, Prince of Songkla University, Thailand

Age of sexual initiation, psychiatric symptoms, and sexual risk behavior among ecstasy and LSD users in Porto Alegre, Brazil: A preliminary analysis

F. Pechansky¹, L. Remy¹, H. Surratt², T. Botter¹, M. Rocha¹, L. Von Diemen¹, D.B. Bumaguin¹, J.A. Inciardi². ¹Center for Drug and Alcohol Studies, Federal University of Rio Grande do Sul, Brazil; ²Center for Drug and Alcohol Studies, University of Delaware–Florida, United States

Amphetamine-type stimulant use and sexually transmitted infection risk behavior among young people in Vientiane Capital and Vientiane Province, Lao People’s Democratic Republic

C. Phimphachanh¹, S. Menorath², V. Sychareun², S. Manivong¹, A. Phengsavanh³, A. Fischer³, N. Chanlivong¹, N. Thomson³, B. Santavasy³, R. Power³. ¹Center for HIV/AIDS and STI, Laos; ²University of Health Sciences, Laos; ³Burnet Institute, Australia; ⁴Chiang Mai University, Thailand

A prospective study of methamphetamine use as a predictor of high school nonattendance in Cape Town, South Africa

A. Pluddemann¹, A.J. Flisher², R. McKetin³, C. Parry¹, C. Lombard¹. ¹Medical Research Council of South Africa, South Africa; ²University of Cape Town, South Africa; ³University of New South Wales, Australia

HPA axis reactivity to social stress and adolescent cannabis use: The TRAILS Study

A. Prince van Leeuwen¹,², H.E. Creemers¹,², K. Greaves-Lord², F.C. Verhulst², J. Ormel³, A.C. Huizink¹,²,⁴. ¹Research Institute of Child Development and Education, University of Amsterdam, Netherlands; ²Department of Child and Adolescent Psychiatry, Erasmus University, Netherlands; ³Interdisciplinary Center for Psychiatric Epidemiology, University of Groningen, Netherlands; ⁴The Netherlands Research Institute for Addiction, Netherlands

How to find ecstasy users? Adapting methods to sample club drug users in a Brazilian setting

L. Remy¹, H. Surratt², S. Kurtz², F. Pechansky¹. ¹Center for Drug and Alcohol Studies, Federal University of Rio Grande do Sul, Brazil; ²Center for Drug and Alcohol Studies, University of Delaware–Florida, United States
Characteristics of heroin abusers enrolled in a methadone maintenance program in metropolitan Barcelona, Spain, 1991–2008
I. Rivas¹, E. Faure¹, E. Martinez², M. Rubio¹, A. Sanvisens², T. Muñoz¹, R. Muga².
¹Municipal Center for Substance Abuse Treatment, Spain; ²Hospital Universitari Germans Trias i Pujol, Spain

Evidence of preference for higher sucrose solutions in psychoactive substance subjects
M.A. Rosa¹, A. Cardoso¹, J.P. Costa¹, D. Pires¹, M. Campos¹, C. Gomes¹, S. Slavutzky², F. Kessler², E. Ferreira¹, F. Pechansky². ¹Federal University of Minas Gerais, Brazil; ²Federal University of Rio Grande do Sul, Brazil

HIV prevalence and risk among women drug users in Argentina, Brazil, and Uruguay (1998–2004)
D. Rossi¹, G. Ralón¹, W. Teixeira², F. Bastos³, L. Latorre⁴, M. Vila⁵, S. Friedman⁶.
¹Intercambios Civil Association, Argentina; ²Federal University of Minas Gerais, Observatory for Urban Health, Brazil; ³Oswaldo Cruz Foundation, FIOCRUZ, Brazil; ⁴Instituto de Investigación y Desarrollo Social, Uruguay; ⁵Intercambios Civil Association, Argentina; ⁶National Development and Research Institutes, United States

Study on reasons of cross-border HIV infection among Burma’s (Myanmar’s) injecting drug users in Ruili
Y. Ruan¹, L. Duo², Y. Lin¹, H.M. Xue², L.H. Yang², J.R. Zhong², L. Deng², X. Ji².
¹Kunming Medical University, China; ²Yunnan Red Cross Hospital, HIV/AIDS Asia Regional Project Office, China

Drug use patterns among Russian female sex workers
M. Rusakova, Virginia Commonwealth University, United States; NGO “Stellit,” Russia; St. Petersburg State University, Russia

Prevalence of illicit substance use among high school students in Thailand
N. Sam-angsri, S. Assanangkornchai, A. Muekthong, U. Pattanasattayawong. Psychiatric Department, Prince of Songkla University, Thailand

Increasing drug abuse problems in juveniles in India and opportunities for intervention
S. Sharma¹, G. Sharma². ¹Institute of Human Behaviour and Allied Sciences, India; ²Safdarjung Hospital, India

Study of women with concurrent substance use and mental health disorders in Canada
U. Sharma. Brockville Mental Health Center, Canada

Trends of shisha (water pipe) use among females in Gaza Strip (Palestine Authority)
M. Shehada¹, M. Sakka², R. Afifi¹. ¹Substance Abuse Research Center, Palestinian Territory; ²AlAzhar University, Palestine Authority

Early-onset substance use and risk for use of illicit drugs in Kathmandu, Nepal
A. Sinha. Bloomberg School of Public Health, Johns Hopkins University, United States
Initial assessment of risky behaviors among injecting drug users at five methadone clinics in Jakarta, Indonesia
H. Susami¹, A. Nurhidayat¹, D. Utami¹, R. Sarasvita², M. Chawaski³, D. Metzger⁴, G. Woody⁴. ¹Addiction and AIDS Research Center, Indonesia; ²Indonesia Ministry of Health, Indonesia; ³Yale University, United States; ⁴University of Pennsylvania, United States

Drug use, voluntary HIV testing, and seroprevalence: Trends over the period 1999–2009 among clients attending a reference drug use treatment center in Rio De Janeiro, Brazil
P.R. Telles-Dias. State University of Rio de Janeiro, Brazil

Household survey for size estimation of injecting drug users in Chiang Mai during 2010 using network scale-up methods
K. Thaikla, A. Aramratana. Research Institute for Health Sciences, Chiang Mai University, Thailand

Assessing executive function in cocaine-dependent patients using the Autobiographical Episode Interview—an exploratory study
F. Vallejo Reyes¹, D. Lewis², P.A. Somoza², E.C. Somoza²,³. ¹Pontificia Universidad Católica de Valparaiso, Chile; ²University of Cincinnati, United States; ³Cincinnati Veterans Administration Medical Center, United States

Inhalant abuse among Roma youth in Slovakia: Links with discrimination and marginalization
P. Vazan. National Development and Research Institutes, United States

Drug use prevalence and drug use harm estimation among Russian students
A. Yakovleva¹, K. Eritsyan²,³, O. Levina²,³, Z. Bodanovskaya¹,², M. Rusakova¹,². ¹Sociological Institute of Russian Academy of Science, Russia; ²NGO “Stellit,” Russia; ³St. Petersburg State University, Russia

Prevalence of alcohol, tobacco, and illegal substance use among ninth-grade students in Izmir, Turkey
U. Yildiz, H. Coskunol, Z. Yuncu, A.E. Altintoprak, C. Aydin. Ege University, Institute on Drug Abuse, Turkey

Drug-related mortality in the Czech Republic: Novel methods for estimation and their results
T. Zabransky¹, V. Mravcik², P. Chomynova². ¹Charles University, Prague, Czech Republic; ²Czech National Monitoring Centre for Drugs and Drug Addiction, Czech Republic

Methadone substitution therapy for heroin addiction: A treatment program assessment in Colombia
M.A. Zapata¹, L.F. Giraldo². ¹CES University, Colombia; ²Center of Attention and Integral Rehabilitation of Mental Health, Colombia
Differences in use patterns of injection stimulants in Ukraine, Czech Republic, and Georgia
O. Zeziulin\textsuperscript{1}, R. Booth\textsuperscript{2}, K. Dumchev\textsuperscript{3}, T. Zabransky\textsuperscript{4}, D. Otiashvili\textsuperscript{5}. \textsuperscript{1}Vinnitsa Regional Narcological Dispensary, Ukraine; \textsuperscript{2}Health Sciences Center, University of Colorado, United States; \textsuperscript{3}World Health Organization Country Office, Ukraine; \textsuperscript{4}Centre for Addictology, Charles University Prague, Czech Republic; \textsuperscript{5}Addiction Research Center, Union Alternative Georgia, Georgia

Psychological characteristics of Chinese female methamphetamine abusers in compulsory detoxification centers
W. Zhou\textsuperscript{1}, W. Shen\textsuperscript{1}, Y. Liu\textsuperscript{2}, Y. Zhang\textsuperscript{3}, L. Li\textsuperscript{1}, Y. Yao\textsuperscript{4}, J. Zhao\textsuperscript{4}. \textsuperscript{1}Laboratory of Behavioral Neuroscience, Ningbo Addiction Research and Treatment Center, China; \textsuperscript{2}School of Medicine, Ningbo University, China; \textsuperscript{3}Department of Obstetrics and Gynecology, Ningbo First Hospital, China; \textsuperscript{4}Administrative Institute of Education Through Labor of Zhejiang Province, China

Other

Iraq (Ministry of Health)—U.S. (Substance Abuse and Mental Health Services Administration) collaboration to address the substance abuse problem in Iraq
R. Aqrawi\textsuperscript{1}, W. Mitchell\textsuperscript{2}, S. Sadik\textsuperscript{3}. \textsuperscript{1}Ministry of Health, Iraq; \textsuperscript{2}Substance Abuse and Mental Health Services Administration, United States; \textsuperscript{3}International Medical Corps, Iraq

Experiences hosting the joint International Programme in Addiction Studies
B. Buisman-Pijlman, R. Irvine. The University of Adelaide, Australia

Asian regional network of addiction clinical researchers workshop
V.B. Kasinather\textsuperscript{1}, R.S. Schottenfeld\textsuperscript{2}, M.C. Chawarski\textsuperscript{2}, M. Mazlan\textsuperscript{1}. \textsuperscript{1}Centre for Drug Research, Universiti Sains Malaysia, Malaysia; \textsuperscript{2}Yale University School of Medicine, United States

1-year follow-up of participants in the Virginia Commonwealth University Hubert H. Humphrey Fellowship Program in Substance Abuse Prevention, Treatment, and Policy
J.R. Koch, L. Leonchuk, R.L. Balster, A. Brelan, C. O’Keeffe. Institute for Drug and Alcohol Studies, Virginia Commonwealth University, United States

Drug research experiences: Multicountry comparison
C. McCoy\textsuperscript{1}, M. Zhao\textsuperscript{2}, R. Achi\textsuperscript{3}, J. Shultz\textsuperscript{1}. \textsuperscript{1}University of Miami, United States; \textsuperscript{2}Shanghai Jiaotong University School of Medicine, China; \textsuperscript{3}University of Costa Rica, Costa Rica

Health education strategies and policies to reduce drug-related harm among university students: The case of Sweden and Portugal
L. Serrano\textsuperscript{1}, J. Carstensen\textsuperscript{2}. \textsuperscript{1}Linkoping University, Sweden; \textsuperscript{2}Division of Health and Society, Department of Medical and Health Sciences, Sweden
Education of family physicians and nurses on substance abuse in Kosovo
Z. Tahiri, R. Ismajli, V. Zeqiri. Center for Development of Family Medicine of Kosova, Kosovo

Prevention
A disability-adjusted cannabis withdrawal scale reveals withdrawal symptoms associated with relapse
D. Allsop¹, M.M. Norberg¹, A. Budney², J. Copeland¹. ¹University of New South Wales, Australia; ²University of Arkansas for Medical Sciences, United States

Comprehensive community HIV prevention and care among drug users in Myanmar
H. Aung¹,². ¹Hubert H. Humphrey Fellowship Program, Johns Hopkins University, United States; ²Myanmar Anti-Narcotics Association, Myanmar

Adolescent cigarette smoking in Mexico: A decisionmaking model for initiation and continuous use
M. Bermudez-Parsai¹, B. Nuño-Gutierrez². ¹Arizona State University, United States; ²Mexican Social Security Institute, University of Guadalajara, Mexico

Alcohol and drug use among HIV-infected drinkers in Russia
E. Blokhina¹, E. Krupitsky², D. Cheng³, A. Raj³, A. Walley³, S. Coleman³, C. Bridden³, C. Chaisson³, J. Samet³. ¹St. Petersburg Pavlov State Medical University, Russia; ²St. Petersburg Bekhterev Psychoneurological Scientific Research Institute, Russia; ³Schools of Public Health and Medicine, Boston University, United States

Harm reduction knowledge and practice among prison uniformed personnel in Albania
A. Boci. STOP AIDS, Albania

Workplace substance abuse and substance-related HIV prevention programs suitable for a South African setting: A systematic review
N. Burnhams¹, A. Musekiwa¹, C. Parry¹,², L. London³. ¹Medical Research Council, South Africa; ²Department of Psychiatry, University of Stellenbosch, South Africa; ³University of Cape Town, South Africa

Adaptation of interventions to address alcohol and other drug use, sexual risk behavior, and gender-based violence in Cape Town, South Africa
T. Carney¹, W.M. Wechsberg², F.A. Browne², B. Myers¹, T. Kline². ¹Medical Research Council, South Africa; ²RTI International, United States

Reasons for stopping using or not using MDMA (ecstasy) in the electronic music context
A. Comis, A.R. Noto. Universidad Federal de Sao Paulo, Brazil
Family and acquaintances of illicit drug users: Community perspectives on laws and public policies in Western Rio De Janeiro, Brazil
J. Da Silva, B. Brands, E. Adlaf, N. Giesbrecht, L. Simich, M.G.M. Wright. 1Anna Nery School of Nursing, Federal University of Rio de Janeiro, Brazil; 2Centre for Addiction and Mental Health, University of Toronto, Canada; 3Inter-American Drug Abuse Control Commission, Organization of American States, United States

Implementation of prevention of diseases with crack users in Brazil: Barriers and achievements
A. Domanico, M. Malta. 1Núcleo de Estudos Para A Prevencao da AIDS, Brazil; 2Oswaldo Cruz Foundation, FIOCRUZ, Brazil

Assessment of development of babies exposed to drugs intrauterine in Brazil
F. Driemeier, G. Cunha, M.L. Zavaschi, J. Dreyer, M.R. Iorra, R. Riesgo. 1Hospital Materno Infantil Presidente Vargas, Brazil; 2Center for Drug and Alcohol Research, Federal University of Rio Grande do Sul, Brazil

Effectiveness of psychosocial intervention for heroin dependence in methadone maintenance treatment in Shanghai
J. Du, M. Zhao. Shanghai Mental Health Center, Jiaotong University School of Medicine, China

Gender differences in early age of onset of alcohol and tobacco use as a risk factor

Attitudes toward drug dealers and the prevalence of sex with drug dealers among young adult African American females
L. Floyd. Bloomberg School of Public Health, Johns Hopkins University, United States

A survey of harm reduction interventions in pharmacies in the Czech Republic
R. Gabrhelik, L. Šťastná, M. Miovský. 1Bloomberg School of Public Health, Johns Hopkins University, United States; 2Charles University, Czech Republic

Secondhand smoke exposure among nonsmoking married women in Jordan
L. Haddad, S. Al-Zyoud, N.A. Baker, H. Gharaibeh. 1Virginia Commonwealth University, United States; 2Hashemite University, Jordan; 3Jordan University of Science and Technology, Jordan

Reduction in initiation of injecting drugs in Albania
E. Hallkaj. STOP AIDS, Albania

Training needs for combating the HIV/AIDS epidemic in Indonesia
M. Hidayat, A. Nurhidayat, H. Susami, D. Utami, D. Metzger. 1Drug Dependence Hospital-RSKO Jakarta, Indonesia; 2Addiction and AIDS Research Centre, Indonesia; 3Indonesian HIV/AIDS Counselor Association, Indonesia; 4University of Pennsylvania, United States
The first educational materials on tobacco, alcohol, and marijuana for children in Kosovo
R. Ismajli. Kosova Health Foundation, Kosovo

Substance abuse among migrant workers of the Thai-Laos border, Thailand
S. Jaichuang1, M. Kanato2, A. Ratanasiri2. 1Public Health Office, Ministry of Public Health, Thailand; 2Khon Kaen University, Thailand

HIV-1 incidence of injecting drug users in Yuxi Prefecture, Yunnan Province of China
L.G. Jinxian-Zhao. Yuxi Center for Disease Control and Prevention, China

Prevalence of substance abuse among residents of Karachi: Reasons and cost of using substances
L. Khowaja. Aga Khan University, Pakistan

Consumption patterns and dependence on nicotine, alcohol, and the abuse of drugs in Uganda
F. Kiwalabye. YCWU, Uganda

Health-seeking behavior among injecting drug users in Bekasi
S. Lenggogeni, E. Bong, O. Kamil, L. Hidajat, I. Irwanto. HIV/AIDS Research Center, Atma Jaya University, Indonesia

Methamphetamine use among HIV-negative drug users in methadone maintenance therapy clinics in Yunnan, China
H. Liu1, L. Duo2, C. Wang1, J. Zhang1, B. Lu1, X. Haomin2, Y. Chang3, X. Shi4, J. Cao1, M. Song1, X. Zhang1, H. Li5, S. Ivanov6, A. Iwamoto7. 1Sun Yat-sen University, China; 2HIV/AIDS Asia Regional Project, Yunnan Office, China; 3Yunnan Provincial No 2 People’s Hospital, China; 4Guangzhou Medical University, China; 5Yunnan Centers for Disease Control and Prevention, China; 6Bloomberg School of Public Health, Johns Hopkins University, United States; 7The Institute of Medical Science, University of Tokyo, Japan

Preventing substance abuse in fetal alcohol spectrum disorder-affected youth

Mixed-methods study on relapse management experiences among peer group counselors for opiate dependence
M. Maarefvand1, H. Ekhtiari2, M. Eghlima1, A. Deilamizadeh3. 1University of Social Welfare and Rehabilitation, Iran; 2Iranian National Center for Addiction Studies, Tehran University of Medical Sciences, Iran; 3Rebirth Charity, Iran

Amphetamine-type stimulant use and HIV/sexually transmitted infection risk behavior among young female sex workers in Phnom Penh, Cambodia
L. Maher1, P. Phlong2, J. Mooney-Somers1, S. Keo3, E. Stein4, M.C. Couture4, K. Page4. 1National Centre in HIV Epidemiology and Clinical Research, Australia; 2Royal University of Fine Arts, Cambodia; 3Cambodian Women’s Development Agency, Cambodia; 4University of California, San Francisco, United States
Updated curricula on tobacco, alcohol, and drug use needed for students of high schools of Kosova
I. Miftari. Center for Development of Family Medicine of Kosovo, Kosovo

Risk for HIV infection among injecting drug users and needs assessment for health care services in Kosovo
D. Muçaj. Hubert H. Humphrey Fellowship Program, Virginia Commonwealth University, United States; Medico-Psychotherapeutic Centre “Labyrinth,” Kosovo

Drug and sexual risk behaviors among impoverished women in Puerto Rico: An exploratory analysis of women living in public housing
L. Norman, L. Cintron, C. Alvarez. Ponce School of Medicine and Health Sciences, United States

Smoking as a risk factor for anxiety among hypertensive patients
M.A. Ojo. Virginia Commonwealth University, United States; Federal Neuropsychiatric Hospital, Nigeria

Behavioral risks of injection drug users and HIV/AIDS in Nigeria
A. Onigbanjo-Williams, B. Mancha. Bloomberg School of Public Health, Johns Hopkins University, United States

Aggression and prenatal stress in pigs

Findings from a 3-year follow-up study of the first substance abuse prevention and treatment project at an institute of higher education in Israel
M. Schori¹, E. Lawental². ¹School of Social Policy and Practice, University of Pennsylvania, United States; ²Tel-Hai Academic College, Israel

Quality of life in crack, cocaine, and other psychoactive substance abusers seeking treatment in four Brazilian capitals
A.O. Sordi, F. Kreische, F. Pechansky, F. Kessler. Center for Drug and Alcohol Research, Federal University of Rio Grande do Sul, Brazil

Psychosocial predictors of cannabis abuse among Iranian high school students
F. Taremian¹, M.S. Meigooni², A. Jazayeri³. ¹Zanjan University of Medical Sciences, Iran; ²SAMA Tehran High School, Iran; ³University of Welfare and Rehabilitation Sciences, Iran

Social demography and behavior patterns of serodiscordant couples in St. Petersburg, Russia
O. Toussova¹, Wendee Wechsberg². ¹The Biomedical Center, Russia; ²RTI International, United States
What is the impact of hepatitis C virus-related service providing and seeking behaviors among methadone maintenance treatment clinics?
Z. Wang, J. Du, M. Zhao. Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, China

A comparative look at psychosocial risk factors associated with female versus male adolescent substance use
P. Whitehorne-Smith, K.A.D. Morgan, W. De La Haye. University of the West Indies, Jamaica

Substance use disorders and psychiatric conditions in postpartum women who use methamphetamine: A cross-cultural comparison
T.A. Wouldes, L.L. LaGasse, C. Derauf, E. Newman, L.M. Smith, R. Shah, A.M. Arria, S.D. Grotta, T. Wilcox, B.M. Lester. 1University of Auckland, New Zealand; 2Warren Alpert Medical School, Brown University, United States; 3John A. Burns School of Medicine, University of Hawaii, United States; 4The University of Tulsa, United States; 5Los Angeles Biomedical Institute at Harbor, University of California, Los Angeles Medical Center, United States; 6David Geffen School of Medicine, University of California, Los Angeles, United States; 7Blank Hospital Regional Child Protection Center, Iowa Health, United States; 8Center for Substance Abuse Research, University of Maryland, United States

Treatment

HIV and sexually transmitted diseases’ knowledge among patients in substitution therapy in Bucharest, Romania

Patterns of memory impairments in a sample of active heroin users in Penang, Malaysia
S.A. Alamdari, V.B. Kasinather, M. Chawarski. 1Centre for Drug Research, Universiti Sains Malaysia, Malaysia; 2Yale University, United States

SUPPORT Study—hepatitis C virus therapy in opioid-dependent, substituted patients in Germany: Are there predictors for high retention?
S.M. Apelt, M. Nowak, M. Muthwill, P. Sandow, A. Hummel, M. Backmund. 1Certum Consulting Scientific Research, Germany; 2Independent Practice, Germany

Pharmacotherapy with buprenorphine and behavioral therapy for reducing other drug use in opioid-dependent study participants
M.A. Bardi, M. Hillhouse, W. Ling. Integrated Substance Abuse Programs, University of California, Los Angeles, United States
Evidence-based multimedia toolkits improve counselor adherence in group counseling with minimal training: Preliminary results
A. Brooks¹, G. DiGuiseppi¹, A. Laudet², D. Knoblach¹, D. Carise³, K. Kirby¹. ¹Treatment Research Institute, United States; ²National Development and Research Institutes, United States; ³Phoenix House, United States

Residential treatment services in west central Mexico: Resources and needs
O. Campollo¹, F. Díaz², C.M. Prado², J. Cunningham³. ¹University of Guadalajara, Mexico; ²The State Council Against Addiction in Jalisco, Mexico; ³University of Arizona, United States

Methodological issues in studying treatment dose: An example from the National Institute on Drug Abuse Clinical Trials Network
A. Chakrabarti¹, M.L. Griffin²,³, G.M. Fitzmaurice²,⁴, G.E. Woody⁵, R.D. Weiss²,³. ¹Sikkim Manipal Institute of Medical Sciences, India; ²McLean Hospital, United States; ³Harvard Medical School, United States; ⁴Harvard School of Public Health, United States; ⁵Treatment Research Institute, University of Pennsylvania, United States

Effect of naltrexone and buprenorphine on smoking in opioid-dependent subjects
B. Chatterjee, R. Jain, S. Jhanjee. All India Institute of Medical Sciences, India

Randomized controlled trial on the effectiveness of supplemental counseling sessions in the prevention of relapse among patients in compulsory treatment programs for heroin addiction in Shanghai
H. Chen¹, W. Ling², M. Hillhouse², M. Zhao¹. ¹Shanghai Mental Health Center, Jiaotong University School of Medicine, China; ²Integrated Substance Abuse Programs, University of California, Los Angeles, United States

Contingency management: Sociodemographic profile, diagnosis, and results of patients seen in a mental health service
R.A. da Paz. Hubert H. Humphrey Fellowship Program, Virginia Commonwealth University, United States

Spontaneous recovery from problematic substance abuse among aboriginal peoples in Canada
C. Dell, A. Tempier. University of Saskatchewan, Canada

Drug use during pregnancy in South Brazil
J. Dreyer¹, G. Cunha¹, C. Campos¹, C. Estrela¹, E. Lança¹, F. Driemeier¹, G. Costa¹, M.L. Zavaschi², M.R. Iorraj, R. Riesgo², B. Lester³. ¹Hospital Materno Infantil Presidente Vargas, Brazil; ²Universidade Federal do Rio Grande do Sul, Brazil; ³Brown Center for Study of Children at Risk, Brown University, United States
Routine opioid substitution therapy program data document low HIV prevalence among injection drug users in Ukraine
K. Dumchev¹, Y. Kobyshecha¹, S. Dvoryak², O. Chernova², I. Grishayeva³, L. Vlasenko³, I. Veretko⁴. ¹World Health Organization Country Office, Ukraine; ²Ukrainian Institute on Public Health Policy, Ukraine; ³Clinton Health Access Initiative, Ukraine; ⁴Vinnitsya Regional Narcological Dispensary, Ukraine

Four settings of opioid agonist maintenance treatment in Ukraine
S. Dvoriak. Ukrainian Institute on Public Health Policy, Ukraine

Treatment outcome predictors in a patient-tailored flexible dose-duration methadone detoxification program
H. Ekhtiari, A. Dezfouli, B. Zamanian, A. Mokri. Neurocognitive Laboratory, Iranian National Center for Addiction Studies, Tehran University of Medical Sciences, Iran

Multicentric study on challenges and advantages of using addiction clinic management software with automated dispensing
M. Faiaznoori, M.S.H. Ekhtiari. Neurocognitive Laboratory, Iranian National Center for Addiction Studies, Tehran University of Medical Sciences, Iran

Cocaine-dependent patients seeking treatment: Retention and abstinence rates
F. Fonseca¹, R. Martínez-Riera¹,², D. Martínez-Sanvisens¹,², P. Samos¹, P. Rossi¹,², C. Castillo¹,², M. Torrens¹,²,³. ¹Institute of Neuropsychiatry and Addictions, Parc de Salut Mar, Spain; ² Substance Use Disorders Research Group, Parc de Salut Mar, Spain; ³Department of Psychiatry, Universitat Autònoma de Barcelona, Spain

Contingency management for cocaine addicts: Neuropsychological outcomes

Is virtual reality the best approach for cue exposure treatment?
O. García-Rodríguez¹, I. Pericot-Valverde², M. Ferrer-García², R. Secades-Villa¹, J. Gutiérrez-Maldonado². ¹University of Oviedo, Spain; ²University of Barcelona, Spain

United Nations Office on Drugs and Crime Treatnet II: Working toward evidence-based drug dependence treatment and care—capacity-building cascade: Pre-post assessment and training satisfaction data
G. Gerra¹, E. Saenz¹, G. Campello¹, A. Busse¹, S. Ibanez de Benito², S. Karimova³, I. Palacios⁴, J. Tomas-Rossello⁵, B. Shaumarov⁶, C. Amghar¹. ¹United Nations Office on Drugs and Crime—Headquarters, Austria; ²United Nations Office on Drugs and Crime—East Africa; ³United Nations Office on Drugs and Crime—Central Asia; ⁴United Nations Office on Drugs and Crime—Peru; ⁵United Nations Office on Drugs and Crime—South East Asia
A case-control study of factors associated with drug treatment and rehabilitation completion and success
R.J. Go, S. Buensalido, J. Chavez, T. Go, M.L. Nitorreda, M.C. Veloso. Ateneo de Manila University, Philippines

Evaluation of the nonresidential drug court program in Montego Bay, Jamaica
K. Goulbourne. Western Regional Health Authority, Jamaica

Dental health status of methadone/buprenorphine maintenance patients in Iran
H. Hoseyny1, S. Momtazi2. 1Garb Health Center, Iran; 2Zabjan University of Medical Sciences, Iran

Self-managed change from problematic cannabis use
J. Howard1, J. Copeland1, A. Kwong2, A. Arcuri1. 1National Cannabis Prevention and Information Centre, Australia; 2University of New South Wales, Australia

Feto-maternal outcome of pregnancy in women maintained on methadone but using illicit substances
J. Igboekwu1, Kim Wolff2. 1Ravenswood Medium Secure Hospital, United Kingdom; 2Institute of Psychiatry, Kings College, United Kingdom

“Ready or unready?”: Factors related to motivation for change among drug dependents admitted in a government drug treatment and rehabilitation center in metropolitan Manila, Philippines
M.T. Inigo1, J.C. Pascual2, C.G. Quingking2. 1Department of Health, Philippines; 2College of Medicine, University of the Philippines, Philippines

Medication-assisted treatment—approaches and essential actions for scale-up in the politically unfavorable environment in Ukraine
Z. Islam, S. Filippovych. International HIV/AIDS Alliance

Pattern of urinalysis results for patients prescribed with dextropropoxyphene in opioid-dependent subjects: Do patients really comply?
R. Jain, R.D. Pattanayak. All India Institute of Medical Sciences, India

Clinical outcome of drug-exposed children at 12 months: A first analysis of a follow-up program in Brazil
E. Lança1, J. Dreyer1, G. Cunha1, C. Campos1, C. Estrela1, F. Driemeier1, G. Costa1, M.L. Zavaschi2, M.R. Iorra1, R. Riesgo2, B. Lester3. 1Hospital Materno Infantil Presidente Vargas, Brazil; 2Federal University of Rio Grande do Sul, Brazil; 3Brown Center for Study of Children at Risk, Brown University, United States
The minipig as an animal model to study antidepressant pharmacology by positive emission tomography
A.M. Landau, S. Dyve, A. Kristian, O. Alstrup, S. Jakobsen, M. Simonsen, A. Møller, P. Videbech, G. Wegener, A. Gjedde, D.J. Doudet. PET Center, Aarhus University Hospital, Denmark

Prospective patterns and correlates of quality of life among women in substance abuse treatment
A. Laudet1, M.O. Min2, E. Tracy2, H. Kim3, S. Brown2, L. Singer2, M.K. Jun2. 1Center for the Study of Addictions and Recovery, National Development and Research Institutes, United States; 2Case Western Reserve University, United States

Evaluating the impacts of methadone maintenance treatment on heroin abusers in Taiwan: An 18-month follow-up study
T.S. Lee. National Taiwan Normal University, Taiwan

Combined scopolamine and chlorpromazine treatment for heroin dependence: A randomized trial
S. Liu1, W. Zhou1, F. Zhang1, L. Li1, J. Zhang1, Q. Wang2, D. Gui1, Y. Liu3, D. Cai2, W. Li1, Y. Liu1, W. Shen1. 1Ningbo Addiction Research and Treatment Center, China; 2Addiction Treatment Center, Zhejiang Qingchun Hospital, China; 3Medical School of Ningbo University, China

Alcohol as a risk factor for intravenous drug users in their remote period of abstinence
B. Lobodov. Senter “Semya,” Russia

Therapeutic interventions for volatile substance misuse
S. MacLean1, J. Cameron2, A. Harney2, N. Lee3,4. 1University of Melbourne, Australia; 2Turning Point Alcohol and Drug Centre, Australia; 3Psychiatry and Psychological Medicine, Monash University, Australia; 4National Centre for Education and Training on Addictions, Flinders University, Australia

Temporal changes in initiation of injection use in heroin users in Malaysia, 1968 to 2010
M. Mazlan1, R. Schottenfeld2, M. Chawarski2, E. Tejani2. 1Substance Abuse Research Center, Malaysia; 2Yale University School of Medicine, United States

Recovery rates of addicts in residential treatment centers
M.M. Joseph. Kenyatta University, Kenya

Psychological distress and depression/anxiety diagnosis among patients in substance abuse treatment centers in seven countries of Latin America and one in the Caribbean: Policy and program implications
E. Merchán-Hamann1, E. Leal2, L. Basso-Musso3, P. Reid4, O. Kulakova5, E. Vásquez-Espinoza5, O. Jones-Willis5, R. Prieto-López5, D. Domenech5, M. García-Estrada5, R. Mann10, B. Brands10, C. Strike10, L. Simich10, J. Sapag10, M.G.M. Wright11. 1University of Brasilia, Brazil; 2Federal University of Rio de Janeiro, Brazil; 3University of Valparaiso, Chile; 4University of the West Indies, Mona Campus, Jamaica; 5National Autonomous
University of Leon, Nicaragua; 6University of Panama, Panama; 7Iberoamerican University, Mexico; 8University of the Republic, Uruguay; 9University of San Carlos, Guatemala; 10Centre for Addiction and Mental Health, University of Toronto, Canada; 11Inter-American Drug Abuse Control Commission, Organization of American States, United States

**Drug abuse background and mental health status of a sample of methadone/buprenorphine maintenance patients in Iran**
S. Momtazi1, N. Musavinasab1, B. Daneshvar2, A. Moradi2, I. Omidi3. 1Zanjan University of Medical Sciences and Substance Abuse Prevention and Treatment Office, Iran; 2Agonsit Treatment Center, Iran; 3Private Researcher, Canada

**A comparison of buprenorphine taper outcomes between prescription opioid and heroin users**
S. Nielsen, M. Hillhouse, A. Hasson, C. Thomas, W. Ling. Integrated Substance Abuse Programs, University of California, Los Angeles, United States

**Naltrexone plus behavioral intervention compared with usual care: Drug use and HIV risk outcomes in men with drug-free female partners**
D. Otiashvili1, I. Kirtadze1, K.E. O’Grady2, H.E. Jones3. 1Addiction Research Center, Union Alternative Georgia, Georgia; 2University of Maryland, College Park, United States; 3RTI International, United States

**Contextualizing drug use in China: Gender differences in family relationship and social network among drug users**
C.Y. Peng1, J. Hsieh1, J. Li2, M. Zhao3, Y.I. Hser1, R. Rawson1. 1University of California, Los Angeles, United States; 2Yun Nan Institute on Drug Abuse, China; 3Shanghai Mental Health Center, Shanghai Jiaotong University School of Medicine, China

**Methadone maintenance and opiate addicts’ positive and negative affects in outpatient and in prison treatment programs**
P. Piray, H. Ekhtiari, F. Mirzaei, O. Rezaei, M.A. Ahmadi, A. Mokri. Neurocognitive Laboratory, Iranian National Center for Addiction Studies, Tehran University of Medical Sciences, Iran

**Validation and factor structure of the SOCRATES Questionnaire among substance abusers in a therapeutic community**
C.G. Quingking1, M.A. Inigo2. 1School of Medicine, University of the Philippines, Philippines; 2Department of Health, Philippines

**Impact of inpatient research participation on subsequent heroin use patterns**
P. Roux1,2, C. Tindall1, J. Murray1, S.K. Vosburg1, P. Saccone1, M.A. Sullivan1, J.M. Manubay1, Z.D. Cooper1, J.D. Jones1, R.W. Foltin1, S.D. Comer1. 1Substance Use Research Center, Columbia University, United States; 2French National Institute of Health and Medical Research, France
An Iranian women’s drug clinic: Reports from women about their journey into drugs
S. Salimi1, B. Nassirimanesh2, S. Mohsenifar4, D. Allsop3, A. Mokri1, K. Dolan3. 1Iranian National Center for Addiction Studies, Tehran University of Medical Sciences, Iran; 2University of British Columbia, Canada; 3National Drug and Alcohol Research Centre, University of New South Wales, Australia

Client and social characteristics of methadone maintenance treatment in Indonesia
R. Sarasvita1, R. Ali2, B. Utomo3. 1Indonesia Ministry of Health, Indonesia; 2University of Adelaide, Australia; 3University of Indonesia, Indonesia

Individual characteristics and response to contingency management treatment for cocaine addiction
R. Secades-Villa1, E. Sánchez-Hervás2, O. García-Rodríguez1, G.G. Fernandez1, S.F. Artamendi1, J.R. Fernández-Hermida1. 1University of Oviedo, Spain; 2Valencia State Health Agency, Spain

Benzodiazepine use at program admission and treatment outcomes among patients in methadone maintenance treatment programs in Israel
L. Shabtai1, M. Schiff2, R. Benbenishty3. 1Association for Public Health, Israel; 2Hebrew University School of Social Work and Social Welfare, Israel; 3Bar Ilan University, School of Social Work, Israel

Feasibility of providing educational counseling for heroin abusers participating in needle-syringe programs
Z. Shamandi1, V.B. Kasinather1, M. Chawarski2. 1Centre for Drug Research, Universiti Sains Malaysia, Malaysia; 2School of Medicine, Yale University, United States

Creation of a computerized database for the Therapeutic Justice Program in Sao Paulo, Brazil
M.S. Sobrinho. Hubert H. Humphrey Fellowship Program, Virginia Commonwealth University, United States; Sao Paulo Public Attorney North Area Office, Brazil

The health-related quality of life for drug abusers test: A validation study of the English version in Australia
R. Sud1, J. Emerson1, E. Shafaei1, O. Lozano2, C. Zubaran1. 1University of Western Sydney, Australia; 2University of Huelva, Spain

Association of functional COMT Val108/Met polymorphism with smoking cessation in a randomized, double-blind, and placebo-controlled nicotine replacement therapy trial
H. Sun1, S. Guo3,4, D. Chen5, F. Yang1, Y. Zou1, X. Di1, Y. Cao1, T. Kosten6, L. Lu2, X.Y. Zhang1,6. 1Beijing Hui-Long-Guan Hospital, China; 2National Institute on Drug Dependence, Peking University, China; 3National Drug Treatment Center, Beijing Anding Hospital Affiliated Capital University of Medical Sciences, China; 4Singapore Institute of Mental Health, Woodbridge Hospital, Singapore; 5Department of Epidemiology and Statistics, Peking University School of Public Health, China; 6Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, United States
Compulsory drug treatment program in Thailand
O. Sungkhawanna. Virginia Commonwealth University, United States

Practices and attitudes of addiction treatment providers in the Russian Federation
M. Torban1,2, R. Heimer2, E. Krupitsky1, R. Ilyuk1. 1St. Petersburg Bekhterev Psychoneurological Scientific Research Institute, Russia; 2Yale University School of Public Health, United States

Efficacy of antidepressants in opioid dependence and implications of comorbid depression: Systematic review and meta-analysis
M. Torrens1,2,3, F. Fonseca1, D. Martínez-Sanvisens1,2, R. Martínez-Riera1,2, P. Rossi1,2, C. Castillo1,2. 1Institute of Neuropsychiatry and Addictions, Parc de Salut Mar, Spain; 2Department of Psychiatry, Universitat Autònoma de Barcelona, Spain

Challenges in implementing methadone services in primary health care and prisons in Jakarta, Indonesia
D.S. Utami1, R. Sarasvita2, D. Purwaning1, P. Sandy1. 1Drug Dependence Hospital-RSKO Jakarta, Indonesia; 2Indonesian Ministry of Health, Indonesia

A brain-imaging study of nicotine-induced dopamine release in cigarette smokers in treatment with bupropion using [11C] raclopride in positron emission tomography
A. Weinstein1, J. Greif2, N. Freedman3, E. Mishani3, A. Weizman4, R. Ebstein5, R. Chisin3, M. Bocher3. 1Hadassah Medical Organization, Israel; 2Tel Aviv Sourasky Medical Center, Israel; 3Hadassah Hospital, Israel; 4Geha Hospital, Israel; 5Herzog Hospital, Israel

Impulsive personality traits, affective state, and cognitive performance of heroin-dependent individuals in Guangdong, China
H. Zeng1, T. Lee2, M. Chawarski3, R. Schottenfeld3, X. Wu1. 1Jinan University School of Medicine, China; 2University of Hong Kong, Hong Kong; 3Yale University, United States

Sigma-1 receptor antagonist BD1047 enhances social interaction-induced reallocation of behavior away from cocaine
G. Zernig, M. Fritz, S. Klement, R. El Rawas, A. Saria. Medical University Innsbruck, Austria

Contingency management at a methadone maintenance treatment clinic in Shanghai, China
H. Zhang1,2, H. Jiang3, J. Du3, A. Dong1, J. Wang1, M. Chawarski2, R. Schottenfeld2, M. Zhao3, Y.I. Hser4. 1Shanghai Yangpu Mental Health Center, China; 2Yale University, United States; 3Shanghai Mental Health Center, China; 4Integrated Substance Abuse Programs, University of California, Los Angeles, United States

Predicting factors for methadone maintenance treatment retention among heroin-dependent patients in Shanghai, China
M. Zhao1, H. Jiang1, J. Du1, H. Zhang2. 1Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, China; 2Shanghai Yangpu District Mental Health Center, China
Tuesday, June 21, 2011

**Poster Session II**  
**Great Hall 3-6**  
**(Breakfast)**  
**8:00 - 10:00 AM**

Odd-numbered posters manned first hour;  
Even-numbered, second hour

Set-up time begins Monday 1:00 P.M.  
Must be removed by Tuesday 12:00 NOON

---

**PROGRAM DESCRIPTION**

1. *Evolutionary implications for animal models in addiction research*  
   E. J. Vallender, C. G. Sweeney, L. M. Ogawa, G. M. Miller, Harvard Medical School - NEPRC, Southborough, MA

2. *On-going real time analysis of drug use, mental health problems and health care utilization of veterans vs. non-veterans*  

3. *A programmatic treatment engagement intervention for homeless veterans with co-occurring mental health and substance abuse problems*  
   D. Smelson1,3,2, A. Kline4,5, C. Bruzios6, S. Rodrigues1, M. Losonczy4,2, L. Sawh1,3,  
   G. Gonzalez3, D. Ziedonis1, Edith Nourse Rogers Memorial Veterans Hospital, Bedford, MA,  
   2VA National Center on Homelessness Among Veterans, Philadelphia, PA, 3Psychiatry, University of Massachusetts Medical School, Worcester, MA, 4VA New Jersey Health Care System, Lyons, NJ, 5Psychiatry, University of Medicine and Dentistry-Robert Wood Johnson Medical School, New Brunswick, NJ, 6Rutgers University, New Brunswick, NJ

4. *Recent drug behaviors among a sample of HIV-positive adults in Miami, FL*  
   C. Spadola, M. Nair, FIU, Miami, FL

5. *Adoption of a rapid HIV testing and counseling program facilitates state-wide implementation*  
   B. W. Holmes1, L. Haynes2, J. Korte2, K. Brady2, 1NIDA Clinical Trials Network, Lexington Richland Alcohol and Drug Abuse Council, Columbia, SC, 2Department of Psychiatry, Medical University of South Carolina, Charleston, SC

6. *HIV risk reduction counselor training for a randomized clinical trial*  
   L. Haynes1, T. Matheson2, K. Brady1, L. Metsch3, 1Medical University of SC, Charleston, SC,  
   2San Francisco Dept of Public Health, San Francisco, CA, 3University of Miami, Miami, FL

7. *The Women’s Recovery Group Study: Challenges and strategies for therapist training, adherence and subject recruitment in a 2-site group therapy trial*  
   S. F. Greenfield1,2, G. Bailey3, H. Connery1,2, M. Crisafulli1, C. Freid1,2, J. Kaufman1,  
   M. Rapoza3, J. Rodolico1,2, K. Schlebecker3, 1McLean Hospital, Belmont, MA, 2Harvard Medical School, Boston, MA, 3SSTAR, Fall River, MA

8. *TOWAR: A comprehensive training on women’s addiction and recovery for drug courts*  
   S. Nemes1, N. Messina2, B. Kearley1, 1Social Solutions International Inc, Olney, MD, 2ISAP, UCLA, Los Angeles, CA

---

**BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS**
9 Development of a Native American substance abuse treatment program for inmates in South Dakota
M. Baron1, A. H. Skinstad2,3, E. Goodteacher4, W. Dougherty5, K. Summers3, 1Educational Administration, University of South Dakota, Vermillion, SD, 2Dept of Community and Behavioral Health, University of Iowa, College of Public Health, Iowa City, IA, 3Prairielands ATTC, Iowa City, IA, 4State Corrections Substance Abuse Program, Yankton, SD, 5State Corrections Substance Abuse Program, Springfield, SD

10 Issues of diversity in workforce development
A. H. Skinstad1,2, K. Winters2, K. Summers2, K. Winters3, 1Dept of Community and Behavioral Health, University of Iowa, College of Public Health, Iowa City, IA, 2Dept of Psychiatry, University of Minnesota, Minneapolis, MN, 3Prairielands ATTC, Iowa City, IA

A. Busse2,3, G. Gerra1, J. Tomas Rossello3, E. Saenz2,1, G. Campello2,1, S. Karimova4, S. Ibanez de Benito4, I. Piacios4, M. R. Stanikzai5, B. Shaumaro5, C. Amghar2,1, 1. Treatnet Mastertrainers2, 2. Treatnet Trainers2, 1Drug Prevention and Health Branch, United Nations Office on Drugs and Crime, Vienna, Austria, 2Prevention, Treatment and Rehabilitation Section, United Nations Office on Drugs and Crime, Vienna, Austria, 3South East Asia, United Nations Office on Drugs and Crime, Bangkok, Thailand, 4East Africa, United Nations Office on Drugs and Crime, Nairobi, Kenya, 5Central Asia, United Nations Office on Drugs and Crime, Tashkent, Uzbekistan, 6Peru, United Nations Office on Drugs and Crime, Lima, Peru, 7Afghanistan, United Nations Office on Drugs and Crime, Kabul, Afghanistan

12 The Missouri Screening, Brief Intervention and Referral to Treatment program: Six-month outcomes
R. E. Adkins, B. E. Keehn, J. G. Noel, M. G. Hile, D. Cho, R. E. Claus, Behavioral Health Division, MO Institute of Mental Health, St. Louis, MO

13 Addict'prev: A motivational website dedicated to drug use and abuse prevention for students in a French area
P. Courty1,2,4, A. Gagne2, A. Perreve2, L. Gerbaud2,3,4, 1SATIS, University Hospital, Clermont Ferrand, France, 2University Health Prevention Center, Clermont Ferrand, France, 3Department of Public Health, University Hospital, Clermont Ferrand, France, 4Paedi EA 4281, IUFM d’Auvergne, Chamalieres, France

14 NIDA CTN Electronic Medical Records Project: Implication of adopting standardized core data elements in health IT systems of drug-abuse treatment providers
U. Ghitza1, R. Lindblad2, R. Gore-Langton2, S. Sparenborg1, B. Tai1, 1National Institute on Drug Abuse, Bethesda, MD, 2The EMMES Corporation, Rockville, MD

15 Establishment of inter-observer reliability using the Finnegan neonatal abstinence scoring tool
K. D’Apolito, School of Nursing, Vanderbilt University, Nashville, TN

16 Current drug scheduling reviews reported by the Drug Enforcement Administration
S. R. Tella, C. Prioleau, M. D. Walker, S. G. Ghozland, C. A. Sannerud, Office of Diversion Control, Drug Enforcement Administration, Springfield, VA

17 Manufacture and analysis of reduced nicotine cigarettes for NIDA Drug Supply Program
K. Davis1, P. G. Pande1, S. Sabharwal1, B. Thomas1, M. Moynihan2, 1RTI International, RTP, NC, 222nd Century Ltd, Williamsville, NY

18 Designer drugs, synthetic cannabinoids and their related products spice, K2 and many others
T. L. Boos, D. P. Pressley, M. D. Walker, L. L. Wong, C. M. Sannerud, Office of Diversion Control, Drug Enforcement Administration, Springfield, VA
DRUG INTERACTIONS

19 Effects of chronic nicotine use on cocaine use
J. L. Miner1,2, P. V. Roebke1,2, D. J. Brooks1,2, J. J. Mariani1,2, F. R. Levin1,2, 1Substance Abuse, New York State Psychiatric Institute, New York, NY, 2Psychiatry, Columbia University, New York, NY

20 Impact of cocaine use on methadone and buprenorphine concentrations in HIV-infected and uninfected patients
J. M. Tetraul1, E. F. McCance-Katz2, A. T. Dinh1, D. E. Moody3, B. Lurie1, M. Jackson1, D. A. Fiellin1, L. E. Sullivan1, 1Internal Medicine, Yale Univ, New Haven, CT, 2Psychiatry, UCSF, San Francisco, CA, 3Toxicology, Univ of Utah, Salt Lake City, UT

21 Interaction of alcohol and HIV
E. F. McCance-Katz, S. Prathikanti, G. Beatty, J. Arenander, E. Rosenfeld, P. Lum, University of California, San Francisco, San Francisco, CA

22 Acute and residual interactive effects of repeated administration of oral methamphetamine and alcohol in humans
M. G. Kirkpatrick1,2, E. W. Gunderson2, F. R. Levin2, R. W. Foltin2, C. L. Hart1,2, 1Columbia University, Department of Psychology, New York, NY, 2Division on Substance Abuse and Department of Psychiatry, Columbia University, New York, NY

23 Heterogeneity in treatment response for cocaine dependence: A Bayesian sub-group analysis incorporating historical data
C. E. Green1,2, J. Schmitz3, J. Lindsay4, C. Pedroza1, S. Lane2, R. Agnelli4, K. Kjome2, F. Moeller2, 1Pediatrics, UTHSC, Houston, TX, 2Psychiatry, UTHSC, Houston, TX, 3Psychiatry, Houston VA, Houston, TX, 4Technical Support, SAS, Inc., Cary, TX

24 The impact of cocaine vaccine (TA-CD) on opiate use in methadone-maintained, opiate- and cocaine-dependent participants
D. I. Shorter1,2, J. A. Lindsay1,2, J. R. Springer1, T. R. Kosten1,2, 1Department of Psychiatry, Houston VAMC, Houston, TX, 2Menninger Department of Psychiatry, Baylor College of Medicine, Houston, TX

25 Self-administration of cocaine and remifentanil by monkeys under concurrent access conditions
K. Freeman, W. L. Woolverton, Psychiatry and Human Behavior, The University of Mississippi Medical Center, Jackson, MS

26 Dopamine transmission following acute and chronic “speedball” administration
L. P. Pattison, S. McIntosh, V. Grinevich, E. A. Budygin, S. E. Hemby, Wake Forest University School of Medicine, Winston Salem, NC

27 Rifampin, but not rifabutin, treatment may be associated with opiate withdrawal in buprenorphine maintenance therapy
V. A. Gruber1, D. E. Moody2, S. Prathikanti1, G. Friedland1, J. Arenander1, P. M. Rainey4, E. F. McCance-Katz1, 1University of California, San Francisco, San Francisco, CA, 2University of Utah, Salt Lake City, UT, 3Yale University, New Haven, CT, 4University of Washington, Seattle, WA

28 Nicotine preexposure in adulthood alters the aversive, physiological and reinforcing effects of alcohol
J. A. Rinker1, E. D. Singley2, A. Thorsell2, M. Heilig2, A. L. Riley1, 1Psychology, American University, Washington, DC, 2NIAAA/NIH, Bethesda, MD

29 Effects of buspirone on the reinforcing effects of cocaine and cocaine + nicotine polydrug combinations in rhesus monkeys
N. Mello, J. Newman, Alcohol and Drug Abuse Research Center, McLean Hospital/Harvard Medical School, Belmont, MA
30 Recreational drugs modulate the discriminative stimulus effects of LSD
M. B. Gatch, T. Carbonaro, Pharmacology & Neuroscience, UNT Health Science Center, Fort Worth, TX

31 Novel use of dose equivalence theory to examine cocaine-induced endothelial dysfunction
N. Lamarre, T. Parry, R. J. Tallarida, Pharmacology, Temple University School of Medicine, Philadelphia, PA

STIMULANTS: HUMAN II

32 Individual differences in regional brain activation during a task involving potential monetary loss or gain are associated with striatal dopamine responses to amphetamine
S. J. Coates¹, H. H. Holcomb², J. West², L. Oswald¹, ¹University of Maryland School of Nursing, Baltimore, MD, ²University of Maryland School of Medicine, Baltimore, MD

33 Associations between amphetamine-induced dopamine release and real-time impulsive responding
L. Oswald¹, D. F. Wong², G. S. Wand², S. J. Coates¹, H. Kuwabara², ¹University of Maryland School of Nursing, Baltimore, MD, ²Johns Hopkins University School of Medicine, Baltimore, MD

34 Risk-taking and impulsivity in methamphetamine-dependent and healthy control participants
M. Kohno¹, A. T. Morgan², E. D. London², ³, ³Neuroscience IDP, UCLA, Los Angeles, CA, ²Psychiatry and Biobehavioral Sciences, UCLA, Los Angeles, CA, ³Molecular and Medical Pharmacology, UCLA, Los Angeles, CA, ⁴Brain Research Inst., UCLA, Los Angeles, CA

35 Cigarette smoking as a target for potentiating outcomes for methamphetamine use treatment
M. Brensilver, D. Telesca, A. N. Swanson, K. H. Heinzerling, S. J. Shoptaw, UCLA, Los Angeles, CA

36 Methylphenidate increases cigarette smoking in ADHD diagnosed adults
F. P. Wagner¹, A. R. Vansickel¹, M. M. Poole¹, W. W. Stoops¹, ², P. E. Glaser¹, C. R. Rush¹, ², ³, ²Behavioral Science, University of Kentucky, Lexington, KY, ²Psychology, University of Kentucky, Lexington, KY, ³Psychiatry, University of Kentucky, Lexington, KY

37 Individuals with high attentional bias for cocaine cues and blunted motivation for non-drug rewards may be at risk for long-term cocaine use
C. Robinson¹, S. D. Lane², F. G. Moeller², J. M. Schmitz², A. J. Waters¹, ¹Department of Medical and Clinical Psychology, Uniformed Services University of the Health Sciences, Washington, DC, ²Department of Psychiatry and Behavioral Sciences, University of Texas, Houston, TX

38 N-acetyl-cysteine alters drug-cue enhanced subjective effects of smoked methamphetamine in METH-dependent volunteers
C. N. Haile, R. DeLaGarza, II, J. J. Mahoney, R. Hawkins, C. S. Nerumalla, S. Mehtani, G. Brown, R. Bennett, T. F. Newton, Psychiatry, Baylor College of Medicine, Houston, TX

39 MDMA-induced increases in blood pressure are not mediated by -adrenergic mechanisms and are not due to elevated peripheral vascular resistance
J. Mendelson, M. J. Baggott, L. Li, J. R. Coyle, G. P. Galloway, Addiction and Pharmacology, California Pacific Medical Center Research Institute, San Francisco, CA

40 Trajectories of cocaine and blood pressure over 18 years: The CARDIA study
S. Kertesz¹, ², Y. Khodneva², M. Pletcher³, J. Schumacher², J. Richman², J. Tucker², ¹Birmingham VA Med Ctr, Birmingham, AL, ²U. Ala. Birmingham, Birmingham, AL, ³U. Calif San Francisco, San Francisco, CA
41 **HPA axis response to stress predicts distress tolerance among cocaine users**  
J. M. Richards, J. R. Leonard, N. Eshera, J. Herberholz, C. W. Lejuez, S. B. Daughters,  
University of Maryland, College Park, MD

42 **Association of bulimia nervosa with treatment outcomes of methamphetamine-dependent adults**  
S. Glasner-Edwards, L. J. Mooney, P. Marinelli-Casey, M. Hillhouse, A. Ang, R. A. Rawson,  
Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

43 **Using Facebook to maximize follow-up response rates in a longitudinal study of adults who use methamphetamine**  
F. Bolanos, A. Pham, D. Herbeck, M. Brecht, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

44 **Long-term (13-year) outcomes of treatment of methamphetamine use**  
M. Brecht, D. Herbeck, K. Lovinger, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

45 **Long-term stable abstinence in adults who used methamphetamine**  
D. Christou, P. Sheaff, A. Raihan, K. Lovinger, D. Herbeck, M. Brecht, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

46 **Cocaine-dependent patients seeking treatment: Retention and abstinence rates**  
F. Fonseca¹,² R. Martínez-Riera¹,², D. Martínez-Sanvisens¹,², P. Samos¹, P. Rossi¹,²,  
C. Castillo¹,², M. Torrens¹,²,³, ¹Institut de Neuropsiquiatria i Addiccions (INAD), Parc de Salut  
Mar, Barcelona, Spain, ²Substance Use Disorders Research Group, Neuropsychopharmacology  
Program, IMIM-Par de Salut Mar, Barcelona, Spain, ³Department of Psychiatry, Universitat  
Autònoma de Barcelona, Barcelona, Spain

47 **Quality of life in crack, cocaine and other psychoactive substance abusers who seek treatment in four Brazilian capitals**  
F. Pechansky, A. O. Sordi, F. Kreische, F. Kessler, Center for Drug and Alcohol Research,  
Hospital de Clinicas de Porto Alegre, Porto Alegre, Brazil

48 **Prospective patterns and correlates of quality of life among women in substance abuse treatment**  
A. Laudet², M. Min¹, E. Tracy¹, H. Kim¹, S. Brown¹, M. Jun¹, ¹Mandel School of Applied  
Social Sciences, Case Western Reserve University, Cleveland, OH, ²NDRI, New York, NY

49 **High prevalence of partner violence among HIV-negative, heterosexual, female methamphetamine users**  
J. K. Stockman¹, S. A. Strathdee¹, S. J. Semple², M. D. Ulibarri², J. K. Zians², T. L. Patterson²,  
¹Division of Global Public Health, University of California San Diego, La Jolla, CA,  
²Psychiatry, University of California San Diego, La Jolla, CA

50 **Social exclusion and engagement in risky sexual behavior among female crack cocaine users**  
A. Pickover, C. Kopetz, C. W. Lejuez, Psychology, Center for Addictions, Personality, and  
Emotion Research, University of Maryland, College Park, MD

51 **Longitudinal patterns of social networks of women in substance abuse treatment**  
E. Tracy¹, M. Oh Min¹, H. Kim¹, C. McCarty³, A. Laudet², S. Brown¹, M. Jun¹, ¹Mandel  
School of Applied Social Sciences, Case Western Reserve University, Cleveland, OH, ²NDRI,  
New York, NY, ³University of Florida, Gainesville, FL

52 **Relationship between overall health and cocaine abstinence in cocaine and alcohol dependence treatment**  
J. G. Plebani, A. R. Leshner, A. B. Lipson, K. M. Kampman, Psychiatry, University of  
Pennsylvania, Philadelphia, PA
53 Health conditions, health status and substance use severity among adults who use methamphetamine  
K. Lovinger, D. Herbeck, D. Christou, P. Sheaff, M. Brecht, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

54 Medical care utilization in a methamphetamine-dependent treatment follow-up sample  
S. M. Schroeder, M. Hillhouse, B. Thornton, W. Ling, Neuropsychiatric Institute, University of California Los Angeles, Los Angeles, CA

CAFFEINE

55 Characteristics of a sample of caffeine treatment seekers  
D. P. Evatt¹, L. M. Juliano², J. Cohen¹, R. R. Griffiths¹, ¹Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, ²Psychology, American University, Washington, DC

56 PMS symptom severity and daily caffeine consumption in female college students  
P. Nora², L. Hull¹, J. Draper², P. Dillon², L. Keyser-Marcus², A. Sepulveda², E. McGee³, B. Perry¹, D. Svikis², ¹VCU, Richmond, VA, ²AWHARE, VCU, Richmond, VA, ³Institute for Women's Health, VCU, Richmond, VA, ⁴CTSA, VCU, Richmond, VA

57 Caffeine activation of brain stress regions  
A. J. Morgan¹, E. Stanley², S. B. Harrod¹, J. R. Fadel², ¹Psychology, University of South Carolina, Columbia, SC, ²Pharmacology, Physiology, and Neuroscience, University of South Carolina School of Medicine, Columbia, SC

58 Caffeine alone and in combination with alcohol: Patterns of use and attitudes among U.S. college students  
M. D. Blank, C. O. Cobb, K. G. Jentink, T. Eissenberg, Psychology, Virginia Commonwealth University, Richmond, VA

59 Caffeinated energy drinks in college students linked to higher levels of alcohol, marijuana and tobacco use  
L. C. Hull¹, P. M. Dillon¹, M. M. O’Connell¹, P. Chitnavis¹, D. S. Svikis¹, ¹IDAS, VCU, Richmond, VA, ²IWH, VCU, Richmond, VA

60 Evaluating the acute effects produced by smoking caffeinated tobacco in a waterpipe  
C. O. Cobb¹, A. Shihadeh², A. R. Vansickle¹, M. F. Weaver¹, T. Eissenberg¹, ¹Virginia Commonwealth University, Richmond, VA, ²Mechanical Engineering, American University of Beirut, Beirut, Lebanon

61 Effects of smoking on caffeine intake among individuals with and without schizophrenia  
K. K. Gandhi¹, J. W. Williams¹, S. Kumar¹, N. L. Benowitz², ¹Psychiatry, UMDNJ Robert Wood Johnson Medical School, New Brunswick, NJ, ²University of California, San Francisco, CA

SEROTONIN

62 Knockdown of 5-HT2C receptor in the nucleus accumbens enhances trait impulsivity and confers enhanced sensitivity to non-drug reward  
K. A. Cunningham¹, N. C. Anastasio¹, S. J. Stutz¹, R. Sears³, R. G. Fox¹, J. D. Hommel¹, T. A. Green¹, R. J. DiLeone¹, F. G. Moeller¹, ¹Ctr Addiction Research, UTMB, Galveston, TX, ²Pharm & Tox, UTMB, Galveston, TX, ³Psych, Yale University, New Haven, CT, ⁴Psych & Behav Sci, UTHSC, Houston, TX
Knockdown of serotonin (5-HT) 5-HT2C receptor in the nucleus accumbens decreases compulsive cocaine-seeking behavior
S. J. Stutz1,2, N. C. Anastasio1,2, R. Sears3, R. G. Fox1,2, J. D. Hommel1,2, T. A. Green1,2, R. J. DiLeone1, F. G. Moeller4, K. A. Cunningham1,2, 1Ctr Addiction Res, UTMB, Galveston, TX, 2Pharm & Tox, UTMB, Galveston, TX, 3Psych, Yale University, New Haven, CT, 4Psych & Behav Sci, UTHSC, Houston, TX

Peptide disruption of the serotonin (5-HT) 5-HT2C receptor interaction with protein phosphatase and tensin homologue deleted on chromosome 10 (PTEN) is functionally important to the 5-HT2CR signalosome
A. G. McGinnis1,2, S. E. Swinford1,2, N. M. Bremer1,2, N. C. Anastasio1,2, A. Shavkunov1,2, P. K. Seitz1,2, A. Agarov4, R. L. Veselenak3, A. Natarajan6, N. Bourne3, F. Laezza1,2, C. S. Watson1,3, S. R. Gilbertson4, K. A. Cunningham1,2, 1Ctr Addiction Research, UTMB, Galveston, TX, 2Pharm & Tox, UTMB, Galveston, TX, 3Biochem & Mol Bio, UTMB, Galveston, TX, 4Chem, Univ Houston, Houston, TX, 5Assay Dvlpmnt Serv Div, Galveston Ntl Laboratory, UTMB, Galveston, TX, 6Eppley Inst Res Cancer & Allied Diseases, Univ Nebraska Med Center, Omaha, NE

5-HT2C receptor activation attenuates cocaine-induced conditioned place preference and hyperactivity
C. Craige, E. M. Unterwald, Pharmacology, Center for Substance Abuse Research, Temple University School of Medicine, Philadelphia, PA

Repeated intermittent treatment with the selective 5-HT2CR agonist Way 163909 produces behavioral tolerance to its acute hypomotive effects
L. H. Fink1,2, S. J. Stutz1,2, K. A. Cunningham1,2, 1Center for Addiction Research, University of Texas Medical Branch, Galveston, TX, 2Dept of Pharm & Tox, University of Texas Medical Branch, Galveston, TX

A functionally selective serotonin 2 receptor ligand for drug-induced psychooses and schizophrenia
C. Canal, D. Morgan, R. Booth, University of Florida, Gainesville, FL

Characterization of the extracellular vestibule of the human serotonin transporter
L. M. Geffert1, Y. Huang1, T. L. Nolan1,2, M. Indarte2, S. Manepalli2, J. D. Madura2, C. K. Surratt1, 1Pharmaceutical Sciences, Duquesne University, Pittsburgh, PA, 2Chemistry and Biochemistry, Duquesne University, Pittsburgh, PA

The serotonin (5-HT) and estrogen receptor systems dynamically interact to regulate serotonin transporter activity
J. GuptaR1,3, N. M. Bremer1,2, P. K. Seitz1,2, K. A. Cunningham1,2, C. S. Watson1,3, 1Ctr Addiction Research, UTMB, Galveston, TX, 2Pharm & Tox, UTMB Galveston, Galveston, TX, 3Biochem & Molec Bio, UTMB, Galveston, TX

Methamphetamine produces contrasting effects in neurodevelopmental gene expression in adolescent and adult mice: Relevance to adolescent addiction?
B. K. Madras1,2, E. Vallender1, G. Miller1, 1Psychiatry, Harvard Medical School, Southborough, MA, 2Psychiatry, Massachusetts General Hospital, Boston, MA

Reversible and cell-type specific in vivo silencing of CNS neurons using ivermectin-gated chloride channels
C. E. Bass1, P. M. Fuller2, 1Physiology and Pharmacology, Wake Forest University Health Sciences, Winston Salem, NC, 2Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA
<table>
<thead>
<tr>
<th>Page</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>72</td>
<td>Further validation of “neurochemical fingerprinting” to characterize</td>
<td>S. P. Vickers, M. Prow, S. C. Cheetham, D. J. Heal, Renasci Consultancy, Nottingham, United</td>
</tr>
<tr>
<td></td>
<td>drugs with different presynaptic dopaminergic mechanisms: Comparison</td>
<td>Kingdom</td>
</tr>
<tr>
<td></td>
<td>with in vivo microdialysis</td>
<td></td>
</tr>
<tr>
<td>73</td>
<td>Identification of “partial” substrates for the biogenic amine</td>
<td>R. B. Rothman¹, C. L. Lightfoot-Siordia¹, B. E. Blough², J. S. Partilla¹, ¹Clinical</td>
</tr>
<tr>
<td></td>
<td>transporters</td>
<td>Psychopharmacology Section, IRP, NIDA, NIH, Baltimore, MD, ³Chemistry and Life Sciences</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Group, Research Triangle Institute International, Research Triangle Park, NC</td>
</tr>
<tr>
<td>74</td>
<td>D2 receptor partial agonists: Defining the association between</td>
<td>D. J. Heal³, A. C. McCreary¹, K. B. Freeman², B. V. Woolverton², ¹Abbott Healthcare Products</td>
</tr>
<tr>
<td></td>
<td>intrinsic efficacy and reinforcing properties in monkeys</td>
<td>BV, Weesp, Netherlands, ²University of Mississippi Medical Center, Jackson, MO, ³RenaSci</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Consultancy Ltd, Nottingham, United Kingdom</td>
</tr>
<tr>
<td>75</td>
<td>The reinforcing and discriminative stimulus effects of the (+)-(2S,3S)-hydroxymetabolite of bupropion in rhesus monkeys and mice</td>
<td>P. M. Beardsley, Pharmacology &amp; Toxicology, Virginia Commonwealth University, Richmond, VA</td>
</tr>
<tr>
<td>76</td>
<td>Neural regulation of the time course for cocaine cue extinction</td>
<td>J. J. Szalay¹, A. B. Hodges³, K. M. Kantak¹, ¹Psychol and Grad Prog for Neurosci, Boston</td>
</tr>
<tr>
<td></td>
<td>consolidation</td>
<td>²Morgan State Univ., Baltimore, MD</td>
</tr>
<tr>
<td>77</td>
<td>Region-specific changes in zif268 mRNA following cocaine self-</td>
<td>R. M. Bastle¹, E. D. Dickey¹, K. J. Thiel¹, N. S. Pentkowski¹,², R. P. Hammer, Jr.¹,³,</td>
</tr>
<tr>
<td></td>
<td>administration, abstinence, and extinction training</td>
<td>¹Psychology, Arizona State University, Tempe, AZ, ²School of Life Sciences, Arizona State</td>
</tr>
<tr>
<td></td>
<td></td>
<td>University, Tempe, AZ, ³Basic Medical Sciences, University of Arizona-College of Medicine,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Phoenix, AZ</td>
</tr>
<tr>
<td>78</td>
<td>The effects of amphetamine on working memory in rats exposed to the</td>
<td>L. Sherrill¹, A. Sharma¹, A. McClory¹, M. Kang¹, B. Obomanu¹, J. M. Gulley¹,², ¹Psych, Univ</td>
</tr>
<tr>
<td></td>
<td>drug in adolescence compared to adulthood</td>
<td>of Illinois, Urbana-Champaign, Champaign, IL, ²Neurosci Prog, Univ Illinois, Champaign, IL</td>
</tr>
<tr>
<td>79</td>
<td>Adolescent amphetamine exposure alters performance in medial</td>
<td>E. R. Venheim¹, J. M. Gulley¹,², ¹Psychology, Univ. Illinois, Urbana-Champaign,</td>
</tr>
<tr>
<td></td>
<td>prefrontal cortex sensitive tasks</td>
<td>Champaign, IL, ²Neuroscience Program, Univ. Illinois, Urbana-Champaign, Champaign, IL</td>
</tr>
<tr>
<td>80</td>
<td>Armodafinil and other cognitive enhancers increase extracellular</td>
<td>J. R. Sink¹, M. A. Ayestas¹, T. E. Prisinzano², R. B. Rothman¹, M. H. Baumann¹, ¹Translational</td>
</tr>
<tr>
<td></td>
<td>norepinephrine and dopamine in rat prefrontal cortex</td>
<td>Pharmacology Sect., IRP, NIDA, NIH, Baltimore, MD, ²Dept. of Medicinal Chemistry,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>University of Kansas, Lawrence, KS</td>
</tr>
<tr>
<td>81</td>
<td>Dopaminergic regulation of risky decision-making</td>
<td>N. Simon¹, M. R. Mitchell², R. P. Haberman³, J. L. Bizon², B. Setlow², ¹University of</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pittsburgh, Pittsburgh, PA, ²University of Florida, Gainesville, FL, ³The Johns Hopkins</td>
</tr>
<tr>
<td></td>
<td></td>
<td>University, Baltimore, MD</td>
</tr>
<tr>
<td>82</td>
<td>Adolescent risk-taking and cocaine self-administration</td>
<td>M. R. Mitchell, B. Setlow, Psychiatry, University of Florida, College of Medicine,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gainesville, FL</td>
</tr>
<tr>
<td>83</td>
<td>Wheel running affects escalation of cocaine intake in adolescent and</td>
<td>N. Zlebnik¹,², J. J. Anker¹, A. T. Saykao¹, M. E. Carroll¹, ¹Psychiatry, Univ of MN,</td>
</tr>
<tr>
<td></td>
<td>adult female rats</td>
<td>Minneapolis, MN, ²Grad. Prog. in Neuroscience, Univ of MN, Minneapolis, MN</td>
</tr>
<tr>
<td>Page</td>
<td>Title</td>
<td>Authors</td>
</tr>
<tr>
<td>------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>84</td>
<td>Sensory reinforcement as a predictor of cocaine self-administration in rats</td>
<td>A. M. Gancarz, M. A. Kausch, M. Robble, L. J. Beyley, D. R. Lloyd, J. B. Richards</td>
</tr>
<tr>
<td></td>
<td>Research Institute on Addictions, State University of New York at Buffalo, Buffalo, NY</td>
<td></td>
</tr>
<tr>
<td>85</td>
<td>Locomotor activity and behavioral stereotypy during an escalating-dose “binge” pattern of cocaine administration in C57BL/6J mice</td>
<td>J. Rabkin, S. D. Schlossman, Y. Zhang, M. J. Kreek, Rockefeller University, New York, NY</td>
</tr>
<tr>
<td>86</td>
<td>Behavioral and neurocognitive effects of low, escalating doses of methamphetamine administration</td>
<td>D. Morgan, M. Guidi, J. D. Mitzelfelt, M. S. Gold, F. H. Kobaissy, Psychiatry, University</td>
</tr>
<tr>
<td></td>
<td>of Florida, Gainesville, FL</td>
<td></td>
</tr>
<tr>
<td>87</td>
<td>Self-administration of 4-methylmethcathinone (mephedrone; ‘meow meow’) in Wistar and Sprague-Dawley rats</td>
<td>S. M. Aarde, S. A. Vandewater, K. Creehan, B. Vaillencourt, M. J. Wright, M. A. Taffe, CNAD,</td>
</tr>
<tr>
<td></td>
<td>The Scripps Research Institute, La Jolla, CA</td>
<td></td>
</tr>
<tr>
<td>88</td>
<td>Behavioral profiling of stimulants after acute administration in rats using LABORAS™</td>
<td>T. Wolinsky, L. Quinn, D. Virley, V. Castagné, P. Moser, Porsolt, Boulogne-Billancourt, France</td>
</tr>
<tr>
<td>89</td>
<td>Differences in environmental enrichment predict self-administration of a low unit dose of methylphenidate in rats</td>
<td>C. D. Gipson¹, J. A. Marusich², K. M. Alvers³, M. T. Bardo³, ¹Neurosciences, Medical</td>
</tr>
<tr>
<td></td>
<td>University of South Carolina, Charleston, SC, ²Pharmacology and Toxicology, Research Triangle Institute, Research Triangle Park, NC, ³Psychology, University of Kentucky, Lexington, KY</td>
<td></td>
</tr>
<tr>
<td>90</td>
<td>Effect of environmental enrichment on behavioral phenotypes and methamphetamine self-administration in rats</td>
<td>Y. Liu, X. Lv, L. Zhang, C. Zhao, Ningbo University, Ningbo, China</td>
</tr>
<tr>
<td></td>
<td>Sciences, U Miami Sch Medicine, Miami, FL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sciences, Univ Miami Sch Medicine, Miami, FL</td>
<td></td>
</tr>
<tr>
<td>93</td>
<td>Stress-induced reinstatement of conditioned place preference induced by MDMA or cocaine in adolescent mice</td>
<td>A. Vidal-Infer, M. Daza-Losada, M. A. Aguilar, J. Minarro, M. M. Rodríguez-Arias, Psychobiology, School of Psychology, Valencia, Spain</td>
</tr>
<tr>
<td>94</td>
<td>Early methylphenidate treatment differentially affects conditioned and unconditioned cocaine activity</td>
<td>C. A. Crawford, J. D. Johnson, V. Rios, J. M. Valentine, L. R. Horn, V. Y. Greenfield, Psychology, California State University, San Bernardino, San Bernardino, CA</td>
</tr>
<tr>
<td>95</td>
<td>Priming effects of dopamine D1 receptor agonist on the reinstatement of amphetamine-induced conditioned place preference</td>
<td>R. Liao¹,², Y. Chang¹, F. Yang¹, Y. Shen¹, ¹Department of Psychology, National Cheng-Chi University, Taipei, Taiwan, ²Institute of Neuroscience, National Cheng-Chi University, Taipei, Taiwan</td>
</tr>
</tbody>
</table>
96 Neuropeptide Y decreases the expression of cocaine-induced conditioned place preference in rats
M. Suarez1, J. M. DiPirro1, A. C. Thompson2, 1Psychol, Univ at Buffalo, Buffalo, NY, 2Res
Instit on Addictions, Univ at Buffalo, Buffalo, NY, 3Psychol, Buffalo State College,
Buffalo, NY

ADOLESCENTS I

97 Examining the factor structure of a behavioral economic demand curve measure of nicotine
reinforcement in adolescent smokers
L. Bidwell1,2, J. MacKillop3, J. G. Murphy4, J. W. Tidey1,2, S. M. Colby1,2, 1Department of
Psychiatry and Human Behavior, Brown University, Providence, RI, 2Center for Alcohol and
Addiction Studies, Brown University, Providence, RI, 3Department of Psychology, University
of Athens Georgia, Athens, GA, 4Department of Psychology, University of Memphis,
Memphis, TN

98 Parental monitoring and delay discounting: Associated risk factors for adolescent cigarette
smoking
S. Thamotharan1, L. Huynh2, M. Patak3, S. Fields1, P. Pirie2, B. Reynolds3,4, 1Psychology, Texas
A&M University, College Station, TX, 2Health Behavior and Health Promotion, The Ohio
State University, Columbus, OH, 3Research Institute, Nationwide Children’s Hospital,
Columbus, OH, 4Department of Psychology, University of Memphis, Memphis, TN

99 Relationship between weight status and delay discounting in a sample of adolescent cigarette
smokers
S. Fields1, M. Sabet2, A. Peal2, B. Reynolds2,3, 1Psychology, Texas A&M University, College
Station, TX, 2Research Institute, Nationwide Children’s Hospital, Columbus, OH, 3Pediatrics,
The Ohio State University, Columbus, OH

100 Gender differences in early age of onset of alcohol and tobacco use as a risk factor
S. Fernandez-Artamendi, J. R. Fernández-Hermida, R. Secades-Villa, G. García-Fernández,
O. García-Rodríguez, Department of Psychology, University of Oviedo, Oviedo, Spain

101 Pregnant by age 15 and substance use initiation among U.S. adolescent females
University School of Medicine, St. Louis, MO

102 Relationship between pubertal development and alcohol expectation in late childhood
C. Chen1,4, C. Storr2, Y. Chen1, Y. Lin1, W. Chen1, K. Lin4, 1Public Health, National Yang-Ming
University, Taipei, Taiwan, 2Family & Community Health, University of Maryland School of
Nursing, Baltimore, MD, 3Public Health, National Taiwan University, Taipei, Taiwan, 4National
Health Research Institutes, Mioli, Taiwan

103 Onset of abstinence in adolescents treated for marijuana and alcohol use disorders
P. C. Brown, A. Budney, C. Stanger, J. Thostenson, E. Williams, Psychiatric Research Institute,
Center for Addiction Research, University of Arkansas for Medical Sciences, Little Rock, AR

104 Pubertal status as a predictor of increased risk-taking on a laboratory task
A. Collado-Rodriguez, K. Young, A. Tyson, L. MacPherson, C. W. Lejuez, University of
Maryland - College Park, College Park, MD

105 Acute effects of exercise on risk-taking in a sample of adolescent males
A. C. Black, M. I. Rosen, Psychiatry, Yale University, West Haven, CT

106 An examination of predictors of family and individual treatment attendance among substance-
abusing adolescent runaways
N. Slesnick, G. Erdem, J. Collins, D. Bantchevska, H. Katafiasz, The Ohio State University,
Columbus, OH
Deviant socialization mediates transmissible and contextual risk of cannabis use disorder development: A prospective study
L. Kirisci, R. Tarter, T. Ridenour, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA

Sex, age, and symptom-associated changes in brain metabolites of young marijuana users
C. Cloak, L. Chang, T. Ernst, JABSOM, Univ of Hawaii, Honolulu, HI

Sex differences in marijuana use among urban African-American adolescents
E. S. Bandstra1, V. H. Accornero1, L. Xue1, E. Mansoor1, M. S. Glavach1, C. E. Morrow1, J. C. Anthony2, 1Pediatrics, University of Miami Miller School of Medicine, Miami, FL, 2Epidemiology, Michigan State University, East Lansing, MI

Modeling the association of transmissible risk, sexual maturation and peer affiliation on the development of cannabis use disorder: A longitudinal study
M. S. Horner1, R. E. Tarter2, L. Kirisci2, 1School of Medicine, University of Pittsburgh, Pittsburgh, PA, 2Pharmaceutical Sciences, University of Pittsburgh, Pittsburgh, PA

HPA axis reactivity to social stress and adolescent cannabis use: The TRAILS Study
A. Prince van Leeuwen1,2, H. E. Creemers1,2, K. Greaves-Lord2, F. C. Verhulst2, J. Ormel3, A. C. Huizink1,2,4, 1Research Institute of Child Development and Education, University of Amsterdam, Amsterdam, Netherlands, 2Department of Child and Adolescent Psychiatry, Erasmus University Medical Center Sophia Children’s Hospital, Rotterdam, Erasmus MC, Rotterdam, Netherlands, 3Interdisciplinary Center for Psychiatric Epidemiology, Department of Psychiatry, University Medical Center Groningen and University of Groningen, Groningen, Netherlands, 4The Netherlands, Research Institute for Addiction (IVO), Rotterdam, Netherlands

The marijuana-mood association during early-mid adolescence
V. H. Accornero1, J. C. Anthony2, L. Xue1, E. Mansoor1, M. S. Glavach1, E. S. Bandstra1, 1Pediatrics, University of Miami Miller School of Medicine, Miami, FL, 2Epidemiology, Michigan State University, East Lansing, MI

Distress tolerance and negative mood regulation expectancies predict adolescent smoking self-change efforts
J. R. Dahne, K. Geisel, B. Dubose, K. C. Young, W. F. Schreiber, L. MacPherson, Psychology, University of Maryland, College Park, College Park, MD

Estimating treatment effects in the presence of differential follow-up between groups
B. Griffin, R. Ramchand, D. McCaffrey, S. Hunter, A. Morral, RAND Corporation, Arlington, VA

Observed therapist behaviors and their effects on adolescent and family outcomes in Functional Family Therapy for adolescent substance abuse
T. J. Ozechowski, H. B. Waldron, Center for Family and Adolescent Research, Oregon Research Institute, Albuquerque, NM

HIV/AIDS II

Multi-level predictors of relationship power among drug-involved women
A. Campbell1, S. Tross1, M. Hu2, M. Pavlicova2, E. V. Nunes1, 1New York State Psychiatric Institute, Columbia University, New York, NY, 2Columbia University Mailman School of Public Health, New York, NY

Knowledge of HIV transmission through breast milk among drug-dependent pregnant women
J. B. Zur, E. Dunne, W. Latimer, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD
118 WITHDRAWN

119 HIV risk behaviors and intervention efficacy in drug abuse treatment trials
J. E. Korte1, T. Killeen1, K. Magruder2,1, S. Sonne1, K. T. Brady1,2, 1Medical University of South Carolina, Charleston, SC, 2Ralph H. Johnson VA Medical Center, Charleston, SC

120 Relationships between infection-related knowledge, opinions, expertise, and training among clinicians in addiction treatment
L. S. Brown, S. A. Kritz, M. Lin, R. Zavala, T. Charles, Medical Services, Research and Information Technology, Addiction Research and Treatment Corporation, Brooklyn, NY

121 Implementation of an electronic information system to enhance practice at an opioid treatment program: Study design & preliminary assessment of quality and risk management
S. A. Kritz, M. Lin, R. Zavala, L. S. Brown, Medical Services, Research and Information Technology, Addiction Research and Treatment Corporation, Brooklyn, NY

122 Predictors of discussing HIV testing with customers among pharmacy staff registered in the New York State Expanded Syringe Access Program: Preliminary findings from the PHARM-HIV study
S. Amesty1,2, S. Blaney3, A. Rivera4, D. Ompad3, C. Fuller1, 1Center for Family Medicine, Columbia University, New York, NY, 2Department of Population and Family Health, Columbia University, Mailman School of Public Health, New York, NY, 3Center for Urban Epidemiologic Studies, New York Academy of Medicine, New York, NY, 4Department of Epidemiology, Columbia University, Mailman School of Public Health, New York, NY

123 Predictors of Lost-to-Care vs. engaged status among urban HIV clinic patients
A. Pecoraro, G. E. Woody, Psychiatry, University of Pennsylvania, Philadelphia, PA

S. L. Linton, J. Astemborski, G. D. Kirk, S. H. Mehta, Epidemiology, Johns Hopkins University Bloomberg School of Public Health, Baltimore, MD

125 Alcohol and drug use among HIV-infected drinkers in Russia
E. A. Blokhina1, E. M. Krupitsky1,4, D. M. Cheng3, A. Ray3, A. Y. Walley2, S. Coleman3, C. Bridden2, C. Chaisson3, J. H. Samet2,3, 1Boston University School of Medicine, Boston, MA, 2Boston University School of Public Health, Boston, MA, 3St. Petersburg State Pavlov Medical University, Saint-Petersburg, Russian Federation, 4Section of General Internal Medicine, Boston University School of Medicine, Boston, MA, 5Boston University School of Public Health, Boston, MA, 6St. Petersburg Psychoneurological Scientific Research Institute named after Bekhterev, Saint-Petersburg, Russian Federation

126 Risk factors for non-fatal overdose among HIV-infected Russians with heavy alcohol use
A. Y. Walley1, D. M. Cheng3, E. Krupitsky3, A. Raj2, E. Blokhina1, S. Coleman2, C. Bridden1, C. Chaisson3, J. Samet1,2, 1Boston University School of Medicine, Boston, MA, 2Boston University School of Public Health, Boston, MA, 3St. Petersburg State Pavlov Medical University, St. Petersburg, Russian Federation

127 Medication diversion among HIV-positive substance abusers in Miami
H. Surratt1, S. P. Kurtz1, T. J. Cicero2, 1University of Delaware, Coral Gables, FL, 2Washington University, St. Louis, MO

128 Marijuana use among HIV patients
B. McClatchey, C. Arfken, L. Zeman, C. Christensen, J. Cohn, D. Johnson, M. K. Greenwald, Wayne State University, Detroit, MI

129 Cocaine, methamphetamine, alcohol and marijuana enhances HIV infection and disease progression: Role of neurotoxin arachidonic acid
S. Thangavel, P. Khatavkar, P. V. Reddy, M. Agudelo, N. Gandhi, M. Noriega, C. Spadola, M. P. Nair, Immunology, Florida International University, Miami, FL
EPIDEMIOLOGY II

130 Frequency of and response to witnessed overdoses among drug users
A. S. Bohnert1,2, M. Tracy1,3, S. Galea1, 1University of Michigan, Ann Arbor, MI, 2Dept of Veterans Affairs, Ann Arbor, MI, 3Epidemiology, Columbia University, New York, NY

131 Prevalence of substance use: A comparison of adult American Indians of the Northern Plains to the National Household Survey on Drug Abuse
V. O’Keefe1,2, J. Gossage2, K. Venner2,1, P. May2, R. Falcon1, 1Psychology, University of New Mexico, Albuquerque, NM, 2Center on Alcoholism, Substance Abuse, and Addictions (CASAA), Albuquerque, NM

132 The epidemiology of coca leaf chewing: Mental health survey evidence from the rural Andean highlands of Peru, 2008
V. Cruz1,2, J. Saavedra2,3, J. Anthony1, 1Epidemiology, Michigan State University, East Lansing, MI, 2Epidemiology, Peruvian National Institute of Mental Health, Lima, Peru, 3Psychiatry, Universidad Peruana Cayetano Heredia, Lima, Peru

133 Ten years of regional inequalities in deaths by diagnosis of mental and behavioral disorders due to psychoactive substance use: A view of the Brazilian public health data
V. M. Gonçalves, S. Faller, D. Benzano, R. DeBoni, F. Pechansky, Center for Drug and Alcohol Research, Federal University of Rio Grande do Sul, Porto Alegre, Brazil

134 Defining types of opioid and cocaine users based on Latent Class Analysis

135 Drug prevalence results from the 2007 U.S. national roadside survey
J. Lacey1, T. Kelley-Baker1, R. Voas1, E. Romano1, C. Moore2, R. Compton3, A. Berning3, 1ALPS, Pacific Institute for Research and Evaluation, Calverton, MD, 2Immunalysis Corporation, Pomona, CA, 3National Highway Traffic Safety Administration, Washington, DC

136 Perceived coercion among individuals who drive under the influence of alcohol and drugs: Testing the “rolling consent” approach applied to a nationwide telephone survey
S. Faller1, J. M. Webster2, J. S. Protas1, C. Machado2, D. B. Rumaguin1, P. C. Arruda Vieira Duarte3, R. B. De Boni1, F. Pechansky1, 1Center for Drug and Alcohol Research (CPAD) - Federal University of Rio Grande do Sul (UFRGS), Porto Alegre, Brazil, 2Center on Drug and Alcohol Research, University of Kentucky, Lexington, KY, 3Brazilian National Secretariat for Policies on Drugs, Brasilia, Brazil

137 Poly-drug use and heroin dependence in Malaysia, 1968 to 2010
M. Mazlan1, M. Chawarski2, R. Schottenfeld2, 1Substance Abuse Research Center Muar, Muar, Malaysia, 2Yale School of Medicine, Department of Psychiatry, Yale University, New Haven, CT

138 Temporal changes in initiation of injection use in heroin users in Malaysia, 1968 to 2010
E. Tejani1, M. Chawarski1, M. Mazlan2, R. Schottenfeld1, 1Yale University, New Haven, CT, 2Substance Abuse Center, Muar, Malaysia

139 Drug use in rural China
Q. Deng1, Q. Tang1,2, M. Chawarski3, R. Schottenfeld1, W. Hao1, 1Psychiatry, Mental Health of Central South University, Changsha, China, 2Psychiatry, The fifth People Hospital, Nanning, China, 3Psychiatry, Yale University, New Haven, CT

140 Correlates of poor health among retired NFL players: A national study
A. Ben Abdallah, S. M. Cummings, L. B. Cottler, Psychiatry, Washington University, St. Louis, MO
Differences between NFL players who obtain their opioids from doctors only vs. illicit sources
S. M. Cummings, A. Ben Abdallah, L. B. Cottler, Psychiatry, Washington University School of Medicine, St. Louis, MO

Monitoring prescription drug abuse through community pharmacies: A feasibility study
B. Brands1,2, S. Sanghera1,2, A. Elkader1, J. Rehm1,2, B. Sproule1,2, 1Centre for Addiction and Mental Health, Toronto, ON, Canada, 2University of Toronto, Toronto, ON, Canada

Pathways to prescription opioid addiction
B. Sproule1,2, B. Brands3,2, A. Wills3, G. Staios3, T. Chan1,2, K. DeCaria1, 1Centre for Addiction and Mental Health, Toronto, ON, Canada, 2University of Toronto, Toronto, ON, Canada, 3Health Canada, Ottawa, ON, Canada

Association of risk perception and subjective norm on quantity of opioid pills misused
K. S. Leung, A. Ben Abdallah, K. B. Nickel, C. C. O’Leary, C. W. Striley, L. B. Cottler, Psychiatry, Washington University School of Medicine, St. Louis, MO

Factors associated with substance abuse treatment entry among rural, Appalachian drug users in Kentucky
L. M. Shannon1, J. R. Havens2, 1Sociology, Social Work, and Criminology, Morehead State University, Morehead, KY, 2Behavioral Science, University of Kentucky, Lexington, KY

Work histories and employment needs of drug court clients
M. Webster, M. F. Dickson, N. E. Wasarhaley, P. K. Elliston, M. Staton-Tindall, Center on Drug and Alcohol Research, University of Kentucky, Lexington, KY

An economic and ethnographic investigation of Fresh Start (Detroit)
J. K. Roddy1, P. J. Draus1, M. K. Greenwald2, 1Social Sciences, University of Michigan Dearborn, Dearborn, MI, 2SARD, Wayne State University, Detroit, MI

Retention to treatment in incarcerated amphetamine-dependent men with ADHD
M. Konstenius, N. Jayaram Lindstrom, J. Franck, Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden

Trauma exposure, PTSD, and substance abuse: A case control study of women in prison and in the general population
U. Warda, C. Grella, K. Lovinger, N. Messina, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

Brief trauma and mental health assessments for female offenders in addiction treatment
G. A. Rowan-Szal, G. W. Joe, N. G. Bartholomew, J. Pankow, D. D. Simpson, W. K. Lehman, Institute of Behavioral Research, Texas Christian University, Fort Worth, TX

Childhood abuse and substance misuse among criminal offenders
M. T. Swogger, Psychiatry, University of Rochester Medical Center, Rochester, NY

A measure of therapeutic group process for substance-abusing teens
L. Stein1,2,3, R. Martin2, A. Adolfo-Signore1, D. Rohsenow2, C. Kahler2, P. Monti2, W. Hurlbut3, 1CPRC, University of RI, Kingston, RI, RI, 2Psychology, Brown University, Providence, RI, 3Rhode Island Training School, Cranston, RI

Substance abuse treatment participation questionnaire for incarcerated adolescents
R. A. Martin1, L. Stein1,2, R. Lebeau2, M. Clair2,3, C. Kahler1, D. Rohsenow1, P. Monti1, W. Hurlburt3, 1Center for Alcohol and Addiction Studies, Brown University, Providence, RI, 2University of Rhode Island, Kingston, RI, 3The Rhode Island Training School, Cranston, RI


154 *Sex and racial differences in victims of sexual abuse in a community corrections population*
C. B. Clark, A. Perkins, S. Hardy, N. Katiyar, C. McCullumsmith, M. Islam, K. Cropsey, The University of Alabama at Birmingham, Birmingham, AL

155 *Pathways to treatment: Role of gender and culture*
M. Said1, D. Owens3, C. Arfken2, 1ACCESS, Dearborn, MI, 2Psychiatry and Beh. Neurosciences, Wayne State University, Detroit, MI, 3Southeast Michigan Community Alliance, Taylor, MI

156 *Predicting recidivism for released state prison offenders: Examining drug involvement and residential clustering effects on the likelihood of reincarceration*
G. Stahler1, J. Mennis1, S. Belenko1, W. Welsh1, M. Hiller1, G. Zajac2, 1Temple University, Philadelphia, PA, 2Pennsylvania State University, State College, PA

157 *Which psycho-social changes affect drug use among probationers?*
F. Taxman, S. Ainsworth, A. Wooditch, George Mason University, Fairfax, VA

158 *Longitudinal changes in the social networks of drug-using probationers*
A. G. Rhodes1,2, F. S. Taxman1, H. Liu2, 1Criminology, Law, and Society, George Mason University, Fairfax, VA, 2Epidemiology and Community Health, Virginia Commonwealth University, Richmond, VA

159 *Ensuring quality drug treatment for criminal justice clients: Staff’s attitudes toward mandated clients*
J. Astone-Twerell1, K. Morgen2, D. Preston1, T. Hernitche1, 1Samaritan Village, Inc, Briarwood, NY, 2Centenary College, Hackettstown, NJ

160 *Peer-led integration of Motivational Interviewing into community corrections*
P. Smith2, K. S. Ingersoll1, 1Psychiatry and Neurobehavioral Sciences, University of Virginia, Charlottesville, CA, 2Jefferson Area Community Corrections, Charlottesville, VA

161 *Decreasing stigmatizing attitudes about substance abuse among university undergraduate criminal justice students: Implications for preparing future professionals*
N. A. Roget1, J. A. Hartje1, M. S. Berry1, W. L. Woods1, P. D. Riggs2, 1University of Nevada, Reno, Reno, NV, 2University of Colorado, Aurora, CO

162 *Buprenorphine treatment and gender differences for individuals under criminal justice supervision: A pilot study*
K. Cropsey, P. Lane, A. Perkins, S. Hardy, B. Clark, C. McCullumsmith, University of Alabama at Birmingham, Birmingham, AL

163 *12-month outcomes of a pilot study of extended-release injectable naltrexone for opioid-dependent probationers and parolees*
D. M. Coviello1, M. S. Gordon1, J. W. Cornish1,2, T. Y. Boney1, C. A. Clark1, T. W. Kinlock1,4, R. P. Schwartz5, M. J. Fishman6,6, C. P. O’Brien1,2, 1University of Pennsylvania, Philadelphia, PA, 2Veterans Affairs Medical Center, Philadelphia, PA, 3Friends Research Institute, Baltimore, MD, 4University of Baltimore, Baltimore, MD, 5Mountain Manor Treatment Center, Baltimore, MD, 6Johns Hopkins University, Baltimore, MD

164 *Factors associated with the level of knowledge about methadone treatment in the sentenced population of the Puerto Rican prison system*
S. K. Rivera-Quinones, C. E. Albizu, Graduate School of Public Health, University of Puerto Rico, San Juan, Puerto Rico

165 *What does self-identified drug of choice tell us about criminal offenders?*
Assessment of Japanese stimulant control law offenders using the Addiction Severity Index-Japanese version: Comparison with patients in treatment settings
Y. Ogai1, T. Watanabe2,3, T. Koga3, E. Senoo1, K. Nakamura2, N. Mori2, K. Ikeda1, 1Tokyo Institute of Psychiatry, Tokyo, Japan, 2Hamamatsu University School of Medicine, Hamamatsu, Japan, 3Shizuoka Prison, Shizuoka, Japan

Correlation between antiretroviral therapy initiation during incarceration and enrollment in outpatient HIV care among newly released inmates in Odessa Region, Ukraine
T. K. Kiriazova, O. O. Neduzhko, HIV/AIDS Programs, NGO “Future Without AIDS”, Odessa, Ukraine

A disease risk reduction curriculum for substance-abusing offenders
W. E. Lehman, G. Rowan-Szal, J. Greener, N. Bartholomew, IBR, Texas Christian University, Fort Worth, TX

Rural drug users’ HIV risk and community corrections involvement
C. G. Leukefeld, A. M. Young, A. Jonas, R. Seaver, J. R. Havens, Behavioral Science, University of Kentucky, Lexington, KY

Grant-Writing Workshop
Room 212-213
10:00 AM - 2:00 PM
(Pre-Registration Only)

TOWN HALL MEETING
Atlantic Ballroom
12:00 - 2:00 PM

AN OPEN DISCUSSION OF ISSUES IN ACADEMIA/INDUSTRY/GOVERNMENT RELATIONS SPONSORED BY THE CPDD INDUSTRY RELATIONS COMMITTEE

Chair: Charles W. Gorodetzky

Introduction
Charles W. Gorodetzky, Consultant, Kansas City, MO

Conflict of interest
Eric Strain1, Bob Walsh2, 1Johns Hopkins University, Baltimore, MD, 2National Institute on Drug Abuse, Bethesda, MD

Academia/industry relations, especially in conduct of clinical trials
Sharon Walsh1, Paul Fudala2, 1University of Kentucky, Lexington, KY, 2Reckitt Benckiser Pharmaceuticals, Richmond, VA

Big pharma cutbacks in CNS, in general, and specifically in development of medications for treatment of substance abuse
Phil Skolnick1, Beatriz Rocha2, 1National Institute on Drug Abuse, Bethesda, MD, 2Merck & Co., Inc., Rahway, NJ

BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS
Tuesday, June 21, 2011

Symposium VI

K2/SPICE—SYNTHETIC CANNABINOIDS AS EMERGING DRUGS OF ABUSE

Chairs: William Fantegrossi and Jennifer Wiley

2:00  *Synthetic cannabinoids in K2/Spice and the federal scheduling process*
      Terrence L. Boos, Drug Enforcement Administration, Springfield, VA

2:25  *Developing analytical testing capabilities for K2 / Spice products*
      Cindy Moran, Arkansas State Crime Laboratory, Little Rock, AR

2:50  *Clinical aspects of K2 / Spice in substance-abusing adolescents and young adults*
      Keith R. McCain, Arkansas Poison Control Center, Little Rock, AR

3:15  *In vitro and in vivo pharmacology of K2 / Spice*
      William E. Fantegrossi, Pharmacology & Toxicology, College of Medicine, University of Arkansas for Medical Sciences, Little Rock, AR

3:40  *K2/Spice: Transition from research tools to drugs of abuse*
      Jenny L. Wiley, Research Triangle Institute, International, Research Triangle Park, NC

Oral Communications 10

DEViating FROM THE SCRIPT: PRESCRIPTION DRUG ABUSE

Chairs: Theodore Cicero and Howard Chilcoat

2:00  *Rates of substance use in dental clinic patients*
      M. A. Ilgen\textsuperscript{1,2}, P. Edwards\textsuperscript{3}, A. S. Bohnert\textsuperscript{1,2}, F. Blow\textsuperscript{1,2}, \textsuperscript{1}Psychiatry, University of Michigan, Ann Arbor, MI, \textsuperscript{2}Department of Veterans Affairs Healthcare System, Ann Arbor, MI, \textsuperscript{3}University of Michigan School of Dentistry, University of Michigan, Ann Arbor, MI

2:15  *Diversion and abuse of buprenorphine: Patient survey*
      C. Arfken\textsuperscript{1}, C. Johanson\textsuperscript{1,2}, C. Schuster\textsuperscript{1,2}, \textsuperscript{1}Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI, \textsuperscript{2}CRS Associates, Chicago, IL

2:30  *Individual and network determinants of buprenorphine misuse among rural prescription opioid users*
      J. R. Havens\textsuperscript{1}, M. Lofwall\textsuperscript{1,2}, C. G. Leukefeld\textsuperscript{1}, \textsuperscript{1}Center on Drug and Alcohol Research, University of Kentucky, Lexington, KY, \textsuperscript{2}Psychiatry, University of Kentucky, Lexington, KY

2:45  *Illicit use of buprenorphine among young adults in Ohio*
      R. Daniulaityte, R. Carlson, R. Falck, Community Health, Wright State University, Dayton, OH

3:00  *Changes in problem drug behavior among nonmedical OxyContin users*
      H. Chilcoat, J. M. Downing, P. Coplan, Risk Management and Epidemiology, Purdue Pharma, Stamford, CT

3:15  *Age-related changes in the patterns of diversion of prescription opioids in 18-75 year olds entering drug treatment programs*
      T. Cicero\textsuperscript{1}, H. L. Surratt\textsuperscript{2}, S. P. Kurtz\textsuperscript{2}, M. S. Ellis\textsuperscript{1}, J. A. Inciardi\textsuperscript{2}, \textsuperscript{1}Psychiatry, Washington University, St. Louis, MO, \textsuperscript{2}University of Delaware, Coral Gables, FL
3:30  Correlates of illicit drugs use and nonmedical use of Adderall® in the United States  
L. Chen, S. S. Martins, P. K. Alexandre, Mental Health, Johns Hopkins Bloomberg School of  
Public Health, Baltimore, MD

3:45  Diversion of benzodiazepine through healthcare sources  
G. E. Ibanez, S. P. Kurtz, H. L. Surratt, University of Delaware, Coral Gables, FL

Oral Communications 11

HIV/AIDS: DRUGS AND THE DISEASE

Chairs: Michael L. Dennis and Adam W. Carrico

2:00  Skin and needle hygiene intervention for injection drug users: Preliminary results from a  
randomized controlled Stage I pilot trial  
K. Phillips¹, M. D. Stein², K. F. Corsi³, ¹University of Northern Colorado, Greeley, CO, ²Brown  
University and Butler Hospital, Providence, RI, ³University of Colorado Denver School of  
Medicine, Denver, CO

2:15  Improving HIV/AIDS knowledge among cocaine-dependent outpatients  
E. Herrmann¹, S. Heil¹,², S. Higgins¹,², Y. Washio³, R. Donham², K. Ironside², ¹Psychology,  
University of Vermont, Burlington, VT, ³Psychiatry, University of Vermont, Burlington, VT

2:30  Correlates of HAART use among hospitalized HIV-infected crack cocaine users  
R. K. Doshi¹, N. Vogenthaler¹, S. Lewis², L. Gooden³, A. Rodriguez³, L. Metsch³, C. del Rio¹,  
¹Emory University School of Medicine, Atlanta, GA, ²Barry University, Miami Shores, FL,  
³University of Miami Miller School of Medicine, Miami, FL

2:45  Predictors of injection risk behavior among injection drug users enrolled in the PHARM-Link  
Study: A gender-stratified analysis  
S. Blaney², S. Amesty¹, D. Ompad², N. Crawford³, A. Rivera³, C. Fuller¹, ¹Center for Family  
Medicine, Columbia University, New York, NY, ²Center for Urban Epidemiologic Studies,  
New York Academy of Medicine, New York, NY, ³Department of Epidemiology, Columbia  
University, New York, NY

3:00  Longitudinal HIV risk in youth referred to substance treatment  
C. Thurstone¹,², S. Salomonsen-Sautel², S. Mikulich-Gilbertson², M. McQueen³, T. Crowley²,³,  
S. Young³, R. Corley³, J. Sakai³, A. Hoffenberg², C. Hartman², M. Stallings³, J. K. Hewitt³,  
C. Hopfer²,³, ¹Denver Health and Hospital Authority, Denver, CO, ²Psychiatry, University of  
Colorado, Aurora, CO, ³University of Colorado, Boulder, CO

3:15  Psychological factors are associated with stimulant use in a probability-based sample of urban  
MSM  
A. W. Carrico¹, T. M. Rice², L. M. Pollack¹, J. T. Moskowitz¹, W. J. Woods¹, J. A. Catania³,  
¹University of California, San Francisco, San Francisco, CA, ²University of California,  
Berkeley, Berkeley, CA, ³Oregon State University, Corvallis, OR

3:30  Missed opportunities for hepatitis C virus screening in community-based drug treatment centers  
S. Cohen¹, G. Colfax¹, D. J. Feaster², R. Duan², L. R. Metsch², B. R. Schackman³,  
P. T. Korthuis⁴, J. L. Sorensen¹, K. Wiest⁴, E. Antunez¹, R. Mandler⁵, M. Das¹, ¹San Francisco  
Department of Public Health, San Francisco, CA, ²University of Miami Miller School of  
Medicine, Miami, FL, ³Weill Cornell Medical College, NY, NY, ⁴Oregon Health and Science  
University, Portland, OR, ⁵National Institute of Drug Abuse, National Institute of Health,  
Bethesda, MD, ⁶CODA, Inc., Portland, OR
3:45  Impact of Recovery Management Checkups on HIV-positive substance users over 4 years
M. L. Dennis¹, C. K. Scott², R. R. Funk¹, ¹GAIN Coordinating Center and Lighthouse
Institute, Chestnut Health Systems, Normal, IL, ²Lighthouse Institute, Chestnut Health
Systems, Chicago, IL

Symposium VII

ABUSE LIABILITY AND PRODUCT APPEAL ASSESSMENT OF
TOBACCO

Chairs: Dorothy Hatsukami and Jack Henningfield

2:00  Abuse liability assessment of tobacco products
Lawrence Carter, Psychiatric Research Institute - Center for Addiction Research, University of
Arkansas for Medical Sciences, Little Rock, AR

2:30  Marketing, tobacco product appeal and consumer response assessment
Vaughan Rees, Center for Global Tobacco Control, Harvard School of Public Health,
Boston, MA

3:00  Post-marketing surveillance of tobacco products
Jack Henningfield, Pinney Associates, Bethesda, MD

3:30  Discussant
Edward M. Sellers, DL Global Partners, Toronto, ON, Canada

CPDD BUSINESS MEETING
(Members Only)

Regency 1
4:15 - 5:15 PM

CPDD/INRC – DINNER AND DANCING

Grand Ballroom
7:00 - 10:00 PM

BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS
Wednesday, June 22, 2011

CPDD Travel Awards Breakfast  
Room 212  
(By Invitation Only)  
7:00 - 8:30 AM

INRC Welcome  
Great Hall 1-2  
8:00 - 8:30 AM

John Traynor, University of Michigan, USA, INRC President  
Sari Izenwasser, University of Miami Miller School of Medicine, and  
Ellen Unterwald, Temple University School of Medicine, INRC Program Co-Chairs  
Jean Bidlack, University of Rochester, INRC Treasurer

INRC and CPDD Joint Plenary  
Great Hall 1-2  
8:30 - 9:45 AM

Report from the National Institute on Drug Abuse  
Nora D. Volkow, NIDA, Bethesda, MD

INRC/CPDD Symposium 1  
Regency 1  
10:00 AM - 12:00 NOON

EPIGENETICS OF DRUG ABUSE GENES

Chairs: Li-Na Wei and Hiroshi Ueda

10:00  DNA methylation: A dynamic and stable regulator of memory  
Courtney Miller, The Scripps Research Institute, USA

10:30  The role of chromatin modifying enzymes in the acquisition and extinction of context-drug  
associated memory  
Marcelo Wood, University of California, USA

11:00  Epigenetics of opioid receptor genes – nutrients, drugs and behavior  
Li-Na Wei, University of Minnesota Medical School, USA

11:30  Chromatin plasticity in addicted brain: Prodynorphin upregulation in human alcoholics  
Georgy Bakalkin, Uppsala University, Sweden

Oral Communications 12  
Regency 3  
10:00 AM - 12:00 NOON

PULLING OUT ALL THE STOPS: IMPULSIVITY

Chairs: J. David Jentsch and Porche Henry

10:00  Strength of association between two rodent models of impulsivity and cocaine self-  
administration  
J. B. Richards, A. M. Gancarz, M. A. Kausch, L. J. Beyley, D. R. Lloyd, M. Robble, Research  
Institute on Addictions, State University of New York at Buffalo, Buffalo, NY

10:15  Caffeine-primed reinstatement of cocaine-seeking behavior in rats selected for high and low  
impulsivity  
P. Regier¹, M. Carroll², ¹Graduate Program of Neuroscience, University of Minnesota,  
Minneapolis, MN, ²Department of Psychiatry, University of Minnesota, Minneapolis, MN
10:30 Genetic dissection of inhibitory control abilities in mice
J. Jentsch, R. E. Laughlin, Psychology and Psychiatry & Bio-behavioral Sciences, UCLA, Los Angeles, CA

10:45 Young adults with stimulant abuse: Impulsivity and brain dysfunction
S. Specker1, V. Slaymaker2, A. Person1, K. Lim1, 1University of Minnesota, Minneapolis, MN, 2Hazelden, Center City, MN

11:00 Sex differences in the effects of oral d-amphetamine on impulsivity, mood and performance in normal healthy controls
S. C. Reed, F. R. Levin, S. M. Evans, Psychiatry, Columbia University College of Physicians & Surgeons, New York, NY

11:15 Reliability of the Sexual Discounting Task: HIV risk behavior and the discounting of delayed sexual rewards in cocaine dependence
N. R. Bruner, M. W. Johnson, Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD

11:30 Trauma exposure, distress, and measures of impulsivity in cocaine dependence
P. Henry, M. Z. Mintzer, E. C. Strain, G. E. Bigelow, A. Umbricht, Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD

11:45 Impulsivity, affective state, and cognitive performance in heroin-dependent individuals in Guangdong, China
H. Zeng1, T. Lee2, M. C. Chawarski3, R. Schottenfeld3, X. Y. Wu1, 1School of Medicine, Jinan University, Guangzhou, China, 2Department of Psychology, The University of Hong Kong, Hong Kong, Hong Kong, 3School of Medicine, Yale University, New Haven, CT

Symposium VIII

**THE ROLE OF PARENTAL MENTAL DISORDERS AND PARENTAL REARING BEHAVIOR FOR CANNABIS USE AND CANNABIS USE DISORDERS IN OFFSPRING**

Chairs: Silke Behrendt and Ty A. Ridenour

10:00 Lifetime and regular cannabis use during adolescence: Is parental influence moderated by personality?
Hanneke E. Creemers, Erasmus Medical Center/Sophia Children’s Hospital, Rotterdam, Netherlands

10:30 Associations between cannabis use disorders and major depression in parents and their adopted and biological adolescent offspring
Naomi R. Marmorstein, Rutgers University, Camden, NJ

11:00 To what extent does parental psychopathology predict cannabis use age of onset, rate of progression and disorder?
Ty A. Ridenour, Center for Education & Drug Abuse Research, University of Pittsburgh, Pittsburgh, PA

11:30 The role of parental substance use, anxiety, and affective disorders and rearing style for the risk of cannabis use and cannabis use disorders in offspring
Silke Behrendt, Institute of Clinical Psychology and Psychotherapy, Technical University of Dresden, Dresden, Germany
Oral Communications 13

LIGHTING UP—IMAGING BRAINS

Chairs: Thomas J. Crowley and Francis J. McClernon

10:00  A brain imaging study into nicotine-induced dopamine release in cigarette smokers in treatment with bupropion using [11 C] Raclopride in positron emission tomography
A. M. Weinstein1,2, J. Greif2, N. Freedman1, E. Mishani1, A. Weizman3, R. Ebstein4, R. Chisin1, M. Bocher1, 1Nuclear Medicine, Hadassah Medical Organization, Jerusalem, Israel, 2Lung Institute, Sourasky Medical Center, Tel Aviv, Israel, 3Psychiatry, Geha Hospital, Petach Tikvah, Israel, 4Scheinfeld Center for Genetic Studies in the Social Sciences, Hebrew University, Jerusalem, Israel

10:15  Sex differences in tobacco smoking-induced upregulation of Beta2-nAChRs
I. Esterlis1, S. McKee1, F. Bois1, J. Seibyl2,1, C. Mazure1, S. Krishnan-Sarin1, J. Staley1, M. Picciotto1, S. O’Malley1, K. Cosgrove1, 1Psychiatry, Yale University and VACHS, West Haven, CT, 2Inst for Neurodeg D/O, New Haven, CT

10:30  Smoking stereotypy is associated with decreased caudate activation during behavioral control
F. J. McClernon, R. Kozink, M. Hallyburton, K. McCormick, M. Addicott, B. Froeliger, Psychiatry, Duke Medical Center, Durham, NC

10:45  Functional connectivity of insula cortex in human adolescent smokers and non-smokers
D. G. Ghahremani1, A. Galvan2,3, C. M. Baker1, K. M. McGlennen2, R. A. Poldrack4, E. D. London1,3,5, 1Department of Psychiatry & Biobehavioral Sciences, UCLA, Los Angeles, CA, 2Department of Psychology, UCLA, Los Angeles, CA, 3Brain Research Institute, UCLA, Los Angeles, CA, 4Imaging Research Center, University of Texas, Austin, Austin, TX, 5Molecular and Medical Pharmacology, UCLA, Los Angeles, CA

11:00  Craving and severity of cannabis dependence modulate brain responses to cannabis cues
J. Cousijn1,2, A. E. Goudriaan1, K. R. Ridderinkhof1, D. J. Veltman1, W. van den Brink1, R. W. Wiers2, 1Psychiatry, Academic Medical Center, Amsterdam, Netherlands, 2Psychology, University of Amsterdam, Amsterdam, Netherlands

11:15  Resting state connectivity between the amygdala and posterior cingulate cortex predicts abstinence from cannabis
R. Szucs-Reed1,2, M. Goldman2, Z. Wang2, Y. Li2, R. Ehrman1,2, T. Franklin2, J. Suh1,2, K. Kampman2, R. Carson2, J. Shin2, C. O’Brien2,1, A. Childress2,1, 1Philadelphia VA Med Center, Philadelphia, PA, 2Univ of Pennsylvania, Philadelphia, PA

11:30  Using fMRI to evaluate adolescents’ response to a psychosocial cannabis treatment

11:45  Risky and cautious decision processing: Boys with antisocial substance disorder
T. J. Crowley1, M. S. Dalwani1, S. K. Mikulich-Gilbertson1, Y. P. Du1, K. M. Raymond1, M. T. Banich1,2, 1Univ. of Colo. Denver, Aurora, CO, 2Univ. of Colo. Boulder, Boulder, CO
CPDD/INRC Poster Session III
(Lunch)
Odd-numbered posters manned first hour;
Even-numbered, second hour

Set-up time begins Tuesday 1:00 P.M.
Must be removed by Wednesday 2:00 P.M.

POLICY

1 Neighborhood correlates of illicit cigarette sales in NYC
   D. C. Ompad1,2, S. Blaney1, M. Kusick1, M. Cerdá1,2, D. Vlahov1,2, 1Center for Urban
   Epidemiologic Studies, New York Academy of Medicine, New York, NY, 2Department of
   Epidemiology, Columbia University Mailman School of Public Health, New York, NY

2 Dissolvable tobacco: Poison candy or methadone for smokers?
   R. K. Lanier, C. Wright, Rock Creek Pharmaceuticals, Inc., Gloucester, MA

3 State policy and availability of medications in substance abuse treatment programs
   H. K. Knudsen1, A. J. Abraham2, 1Behavioral Science, University of Kentucky, Lexington, KY,
   2Institute for Behavioral Research, University of Georgia, Athens, GA

4 An economic evaluation of a paperwork burden reduction initiative
   J. Croft1, M. Love1, D. Carise2, D. Festinger1, K. Dugosh1, 1Treatment Research Institute,
   Philadelphia, PA, 2Phoenix House, New York, NY

5 The Reinforcing Therapist Performance (RTP) experiment: Preliminary cost-effectiveness
   findings
   D. S. Shepard2, A. Lwin2, G. Strickler2, C. Atuaka2, B. Garner1, 1Chestnut Health Systems,
   Normal, IL, 2Brandeis University, Waltham, MA

6 The relationship between drug use and the business cycle: Potential implications of the global
   financial crisis
   A. Ritter, J. Chalmers, Drug Policy Modelling Program, NDARC, UNSW, Sydney, NSW,
   Australia

7 Combining remedial and motivational strategies to improve consent recall among research
   participants
   D. S. Festinger1, K. L. Dugosh1, D. B. Marlowe1,2, N. Clements1, 1Law and Ethics, Treatment
   Research Institute, Philadelphia, PA, 2National Association of Drug Court Professionals,
   Alexandria, VA

8 Photovoice as a way to engage and retain older African-American methadone clients
   D. Rosen1, J. R. Cornelius2, S. Goodkind1, L. M. Smith2, 1Social Work, University of
   Pittsburgh, Pittsburgh, PA, 2Psychiatry, University of Pittsburgh, Pittsburgh, PA

9 Patient access to buprenorphine treatment in Appalachia: A geographic assessment using
   SAMHSA’s physician-locator website
   E. W. Gunderson1,2, E. C. Kim1, 1University of Virginia, Charlottesville, VA, 2Columbia
   University, New York, NY

10 Sources of diverted prescription opioids among a diverse sample of abusers in South Florida
    S. P. Kurtz1, H. L. Surratt1, T. J. Cicero2, G. E. Ibanez1, M. A. Levi-Minzi1, 1Center for Drug
    and Alcohol Studies, University of Delaware, Coral Gables, FL, 2Department of Psychiatry,
    Washington University School of Medicine, St. Louis, MO
11 Rank-ordering prescribers by opioid abuse and diversion risk
   P. DuBose2, J. D. Haddox1, A. Bender1, J. Markman4, 1Health Policy, Purdue Pharma L.P.,
   Stamford, CT, 2Principled Strategies, Encinitas, CA, 3Polaris Management Partners, New
   York, NY, 4Wolters Kluwer, Philadelphia, PA

POLYDRUGS II

12 WITHDRAWN

13 Turning points in drug use trajectories: Proposition 36 participants’ perspectives
   C. Teruya, M. Olaer, Y. Hser, UCLA Integrated Substance Abuse Programs, Los Angeles, CA

14 Supporting recovery in the community: Preliminary outcomes of clients participating in the
   Phoenix House Bronx Community Recovery Center
   A. A. Mericle1, J. Feliciano2, D. Carise2,3, 1Treatment Research Institute, Philadelphia, PA,
   2Phoenix House, New York, NY, 3University of Pennsylvania, Philadelphia, PA

15 The relationship between therapist and patient gender/race matching and substance use
   outcomes across two MET trials
   A. A. Forcehimes1, M. Nakazawa1, L. Montgomery2, K. A. Burlew2, A. Kosinski3, P. Kothari4,
   1CASAA, University of New Mexico, Albuquerque, NM, 2U. Cincinnati, Cincinnati, OH,
   3Duke, Durham, NC, 4Synergy, Silver Spring, MD

16 Perceived barriers to substance abuse treatment among Asians and Pacific Islanders
   M. Y. Iguchi1, C. L. Masson3, M. Shopshire1, K. Hoffman2, S. Sen1, N. Hengl1, J. L. Sorensen1,
   D. McCarty2, 1University of California, San Francisco, San Francisco, CA, 2Oregon Health
   Sciences University, Portland, OR, 3University of California, Los Angeles, Los Angeles, CA

17 Predictors of therapist turnover and competence in an evidence-based practice: Findings from a
   large-scale dissemination and implementation initiative
   B. Garner, B. D. Hunter, S. H. Godley, M. D. Godley, Chestnut Health Systems, Normal, IL

18 Using Appreciative Inquiry to identify addiction treatment field best practices and prioritize
   future goals for collaborations with key community stakeholders
   P. K. Horvatich, Department of Psychiatry, Virginia Commonwealth University, Richmond, VA

19 Evidence-based multimedia toolkits improve counselor adherence in group counseling with
   minimal training: Preliminary results
   A. C. Brooks1, G. T. DiGuiseppi1, A. Lauder2, D. Knoblach1, D. Carise3, K. C. Kirby1,4,
   1Treatment Research Institute, Philadelphia, PA, 2National Development and Research
   Institutes, New York, NY, 3Phoenix House, New York, NY, 4University of Pennsylvania School
   of Medicine, Philadelphia, PA

20 Counselor characteristics influence MI skill acquisition following workshop and post-workshop
   training
   K. M. Carpenter1, W. Cheng1, J. L. Smith1, A. Brooks3, P. Amrhein2,4, E. V. Nunes1, 1Columbia
   University, New York, NY, 2Montclair State University, Montclair, NJ, 3Treatment Research
   Institute, Philadelphia, PA

21 Training substance abuse clinicians in MI using teleconferencing supervision
   J. L. Smith1, K. M. Carpenter1, P. Amrhein2, A. C. Brooks3, E. V. Nunes1, 1Division of
   Substance Abuse, New York State Psychiatric Institute, New York, NY, 2Montclair State
   University, Montclair, NJ, 3Treatment Research Institute, Philadelphia, PA

22 Maintaining MI skill proficiency: An enhanced training package for clinical supervisors
   practicing in frontier states
   W. L. Woods1, N. A. Roget1, J. A. Hartje1, K. Speck2, A. H. Skinstad3, 1University of Nevada,
   Reno, Reno, NV, 2University of Nebraska, Lincoln, Lincoln, NE, 3University of Iowa, Iowa
   City, IA
23 Growing motivational interviewing capacity and sustainability from a partnership starter project
K. P. Shuster1, G. G. Soto1, P. K. Horvatich2, 1Prince William County Community Services
Board, Richmond, VA, 2Virginia Commonwealth University, Richmond, VA

24 The Health-Related Quality of Life for Drug Abusers Test: A validation study of the English
version in Australia
R. Sud1, J. Emerson1, E. M. Shafaei1, O. M. Lozano3, C. Zubaran1,2, 1University of Western
Sydney, Sydney, NSW, Australia, 2Department of Psychiatry, Sydney West Area Health
Service, Sydney, NSW, Australia, 3University of Huelva, Huelva, Spain

25 Addiction treatment matching in the 21st century: A new solution to an old problem
A. Jaffe, 1California Treatment Services, Los Angeles, CA, 2Integrated Substance Abuse
Program, UCLA, Los Angeles, CA

26 Findings from a three-year follow-up study of the first substance abuse prevention and treatment
project at an institute of higher education in Israel
E. Lawental, M. Schori, Social Work, Tel-Hai Academic College, Nesher, Israel

27 Substances, academics, and college student goals
D. Morisano1,2, E. Rosenberg1, J. B. Hirsh2, J. B. Peterson2, R. O. Pihl3, 1Psychiatry/Child &
Family Institute, Columbia University College of Physicians & Surgeons/St. Luke’s-Roosevelt
Hospital, New York, NY, 2Psychology, University of Toronto, Toronto, ON, Canada,
3Psychology, McGill University, Montreal, QC, Canada

28 Effectiveness of overdose prevention training: Differences between trained and untrained IDUs
S. Lankenau1, K. Wagner1, E. Iverson2, M. McNeely2, J. Jackson Bloom2, K. Silva1,
A. Kecojevic1, 1Community Health and Prevention, Drexel University, Philadelphia, PA,
2Children’s Hospital Los Angeles, Los Angeles, CA, 3University of California, San Diego, San
Diego, CA

29 Health care utilization and experiences in persons with SUDs: Preliminary findings from the
Health Anonymous Research Evaluation
L. Safford1, J. May2, D. Farrell-Moore2, A. Aggarwal1, A. Dibble1, S. Ondersma3, P. Nora1,
D. Svikis1, 1Institute for Drug and Alcohol Studies, Virginia Commonwealth University,
Richmond, VA, 2Richmond Behavioral Health Authority, Richmond, VA, 3Psychiatry, Wayne
State University, Detroit, MI

30 Implementing drug screening in primary care: Not finding what we are looking for?
R. Saitz1,2, D. Alford1,2, J. Witas1,2, D. Allensworth-Davies2, T. Palfai2, D. M. Cheng2,
J. Bernstein2, J. H. Samet1,2, Boston Medical Center, Boston, MA, 2Boston University,
Boston, MA

31 Are dentists ready to offer screening, brief intervention and referral to treatment for substance
use?
J. McNeely1, S. Wright1, J. Rotrosen1,3, D. Shelley1,2, A. G. Matthews4, M. Buchholz2,
F. Curro2, 1NYU School of Medicine, New York, NY, 2NYU College of Dentistry, New
York, NY, 3VA NY Harbor Healthcare System, New York, NY, 4EMMES Corporation,
Rockville, MD

32 Project Engage: SBIRT with medically hospitalized patients
T. Horton2, G. E. Woody1, A. Pecoraro1, P. A. Wright1, B. Silverman4,5, 1Psychiatry, University
of Pennsylvania, Philadelphia, PA, 2Department of Medicine, Christiana Care Health System
and Wilmington Hospital, Wilmington, DE, 3Delaware Physicians Care, Inc. (DPCI),
Wilmington, DE, 4Brandywine Counseling and Community Services, Wilmington, DE, 5Bryn
Mawr Graduate School of Social Work, Bryn Mawr, PA
33 Baseline differences in residents’ attitudes and behaviors in delivering SBIRT services to at-risk drug and alcohol users
   A. Johnson, J. P. Seale, Family Medicine, Mercer University School of Medicine, Macon, GA

34 Enriching attitudes of psychiatry residents toward people with substance use disorders
   M. Cutler1, J. Peirce1, M. Chisolm1, M. Moon2, K. Neufeld1, 1Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, 2Berman Institute of Bioethics, Johns Hopkins University, Baltimore, MD

35 Defining client outcomes: A study of minority-focused substance abuse treatment staff
   A. Jernstrom, S. E. Larios, J. S. Sorensen, University of California San Francisco, San Francisco, CA

36 Psychometric properties of clinical monitoring items
   T. G. Kolwicz1, A. Camilleri1, J. Cacciola1,2, K. Dugosh1, A. Alterman1,2, 1Treatment Research Institute, Philadelphia, PA, 2University of Pennsylvania, Philadelphia, PA

37 A comparative study of sugar, marijuana, cocaine and alcohol dependence: A construct analysis using item response theory
   M. C. Rosa1,2, N. S. Rocha2, A. C. Araujo1, C. M. Gomes1, S. B. Slavutzky2, F. H. Kessler2, E. F. Ferreira1, F. Pechansky2, 1Federal University of Minas Gerais, Belo Horizonte, Brazil, 2Federal University of Rio Grande do Sul, Porto Alegre, Brazil

38 Secondary data analysis using item response theory to improve measurement of recovery
   L. Cai1, Y. Hser2, 1GSEIS & Psychology, UCLA, Los Angeles, CA, 2Psych & Biobehav Sci-ISAP, UCLA, Los Angeles, CA

39 Properties of DSM disordered gambling criteria in French gamblers
   C. Denis2,1, M. Fatseas1,2, V. Beltran1,3, J. Daulouede2,1, M. Auriacombe1,2,1, 1Addiction Psychiatry (UMSR-CNRS), Universite Victor Segalen Bordeaux 2, Bordeaux, France, 2Addiction Treatment Center, CHCP, CHU, Bordeaux, France, 3Bizia Addiction Treatment Center, Bayonne, France

40 Unemployment, client employment status, and substance abuse treatment outcomes in Nevada
   L. Greenfield1, G. E. Bigelow2, W. C. Bailey3, 1Consultant, State of Nevada, Kensington, MD, 2BPRU, Johns Hopkins Medical Institutions, Baltimore, MD, 3SAPTA, State of Nevada, Carson City, NV

PAIN

41 Enhancement of morphine’s effects on pain-suppressed wheel-running by a FAAH inhibitor
   L. L. Miller, L. A. Dykstra, Psychology, University of North Carolina, Chapel Hill, NC

42 Morphine vaccination and its inhibition of morphine-induced CPP and analgesia in rats
   X. Shen1, T. A. Kosten2, A. Y. Lopez1, P. W. O’Malley1, Y. Wu1, B. M. Kinsey1, F. M. Orson1, 1Departments of Medicine, Immunology, Baylor College of Medicine, Houston, TX, 2Departments of Psychiatry, Baylor College of Medicine, Houston, TX

43 Estrogen attenuates nociceptive responses to carrageenan-induced inflammation in a time-dependent manner
   T. Mathew1,2, K. Y. Shivers1,2, L. C. Abrams1,2, T. Schnieder1,2, N. J. Amador1,2, D. Hunter3, S. Jenab1, V. Quinones-Jenab1, 1Biopsychology and Behavioral Neuroscience, Hunter College, New York, NY, 2CUNY Graduate School and University Center, New York, NY, 3NYSPI at Columbia Medical Center, New York, NY

44 Pain in methadone maintenance patients
   R. M. Seewald1, M. Todman2, E. Loran3, D. Sivesind2, D. Roane1, D. Haller1, R. Cruciani1, 1Beth Israel Medical Center, NY, NY, 2New School for Social Research, NY, NY, 3St Luke’s-Roosevelt Hospital, NY, NY
45 Boredom, pain and illicit drug use in MMT patients
   E. G. Loran¹, M. Todman¹, D. Sivesind¹, R. Cruciani², D. Roane², D. Haller³, E. Lehr¹, R. M. Seewald², ¹The New School for Social Research, NY, NY, ²Beth Israel Medical Center, NY, NY, ³St Luke’s Roosevelt, NY, NY

46 Psychological flexibility predicts opioid misuse risk in low back pain patients receiving opioid therapy
   J. S. Potter¹, M. Eckmann¹, S. Ramamurthy¹, A. Stotts², A. Gutierrez¹, K. Rosen¹, ¹Psychiatry, UT Health Science Center, San Antonio, TX, ²Family Medicine, UT Houston, Houston, TX

47 Adherence to clinical guidelines for opioid therapy for chronic pain in patients with substance use disorder
   B. J. Morasco, J. Duckart, S. K. Dobscha, Mental Health and Clinical Neurosciences Division, Portland VA Medical Center, Portland, OR

48 Sex differences in patients with chronic pain and prescription opioid abuse during buprenorphine/naloxone maintenance
   J. Manubay¹,², S. K. Vosburg¹,², S. D. Comer¹,², J. Jones¹,², Z. Cooper¹,², J. Fogel¹,², M. A. Sullivan¹,², ¹Psychiatry, Columbia University, New York, NY, ²Substance Abuse, NYSPI, New York, NY

49 Prevalence of chronic pain and interest in pain management among patients seeking office-based buprenorphine-naloxone treatment
   D. Barry¹,², J. Savant³, M. Beitel¹,², C. Cutter¹,², B. Moore¹, R. Schottenfeld¹, D. Fiellin¹, ¹Yale University School of Medicine, New Haven, CT, ²APT Foundation Pain Treatment Services, New Haven, CT

50 Chronic pain and office-based buprenorphine-naloxone treatment outcomes
   C. J. Cutter¹,², D. Barry¹,², J. Savant³, M. Beitel¹,², B. Moore¹, L. Sullivan¹, R. Schottenfeld¹, D. Fiellin¹, ¹Yale University School of Medicine, New Haven, CT, ²APT Foundation Pain Treatment Services, New Haven, CT

51 Pain acceptance and substance use severity in addictions treatment patients with pain
   F. Kleinberg²,¹, M. Ilgen²,¹, A. Bohnert²,¹, ¹University of Michigan, Ann Arbor, MI, ²Department of Veterans Affairs Healthcare System, Ann Arbor, MI

52 Associations among pain, substance use and depression in HIV-positive men
   J. A. Stein¹, J. C. Tsao¹, D. G. Ostrow², R. C. Stall³, M. W. Plankey⁴, ¹UCLA, Los Angeles, CA, ²University of Chicago, Chicago, IL, ³University of Pittsburgh, Pittsburgh, PA, ⁴Georgetown University Medical Center, Washington, DC

53 Pain medication use among a university sample from Lebanon: A closer look into sources, reasons, and potential correlates
   D. Eslayed¹, L. Ghandour¹, S. Martins², ¹Epidemiology and Population Health, American University of Beirut, Beirut, Lebanon, ²Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

PHARMACOKINETICS, CHEMISTRY

54 Gender differences in pharmacokinetics of buprenorphine: Involvement of weight and metabolism
   D. E. Moody¹, W. B. Fang¹, J. Morrison¹, E. F. McCance-Katz², ¹Pharmacology and Toxicology, University of Utah, Salt Lake City, UT, ²Psychiatry, University of California San Francisco, San Francisco, CA
Sublingual administration of ALKS 33, a novel opioid receptor antagonist, does not alter buprenorphine pharmacokinetics
R. Turncliff¹, R. Jones², E. Fernandez², A. Manari², J. Ransom³, N. Chiang⁴, E. Ehrich¹,
¹Alkermes, Inc, Waltham, MA, ²University of California, San Francisco, San Francisco, CA,
³Fast-Track Drugs & Biologics, N. Potomac, MD, ⁴National Institute on Drug Abuse,
Bethesda, MD

Effects of alcohol on the pharmacokinetics of Remoxy®, an extended-release formulation of oxycodone, in healthy volunteers
A. de Kater¹, G. L. Schoenhard¹, V. Klutzaritz¹, M. J. Lamson², N. Friedmann¹, ¹Pain
Therapeutics, Inc., San Mateo, CA, ²King Pharmaceuticals Research and Development,
Cary, NC

Accuracy of a method to quantify illicit intake of methamphetamine from urine
L. Li¹, G. P. Galloway¹, D. Verotta², E. Everhart³, M. J. Baggott¹, J. R. Coyle¹, J. C. Lopez¹,
J. Mendelson³, ¹Addiction Pharmacology, California Pacific Medical Center Research
Institute, San Francisco, CA, ²Bioengineering and Therapeutic Sciences and Epidemiology and
Biostatistics, UCSF, San Francisco, CA, ³Langley Porter Psychiatric Institute, UCSF, San
Francisco, CA

Discovery of a novel SSRI scaffold from a lead compound identified by in silico screening
T. L. Nolan¹,², D. J. Lapinsky¹, M. Indarte¹, Y. Liu¹, J. D. Madura², C. K. Surratt¹,
¹Pharmaceutical Sciences, Duquesne University, Pittsburgh, PA, ²Chemistry & Biochemistry,
Duquesne University, Pittsburgh, PA

Preclinical antipsychostimulant and antidepressant properties of a monoamine transporter ligand identified via in silico screening
C. Surratt¹, M. Indarte¹,², Y. Liu¹, J. D. Madura², J. N. Talbot³, ¹Division of Pharmaceutical
Sciences, Mylan School of Pharmacy, Duquesne University, Pittsburgh, PA, ²Department of
Chemistry and Biochemistry, Duquesne University, Pittsburgh, PA, ³Department of
Biomedical and Pharmaceutical Sciences, Raabe School of Pharmacy, Ohio Northern
University, Ada, OH

Synthesis and optimization of selective N-phenylethyl piperazine analogues as sigma-2 receptor antagonists
W. Motel¹, M. Small¹, R. Matsumoto², A. MacKerrell¹, A. Coop¹, ¹Pharmaceutical Sciences,
University of Maryland, Baltimore, Baltimore, MD, ²Pharmacy Department, West Virginia
University, Morgantown, WV

Synthesis of M-100907 a 5-HT2AR antagonist and WAY-163909 a 5-HT2CR agonist analogs
M. Shashack¹, P. Seitz¹, A. McGinnis¹, K. Cunningham¹, S. Gilbertson¹,², ¹Pharmacology and
Toxicology, University of Texas Medical Branch, Galveston, TX, ²Chemistry, University of
Houston, Houston, TX

Identification of volatile components in smokeless tobacco products using headspace solid phase microextraction and gas chromatography/mass spectrometry
P. G. Pande¹, R. Daw¹, A. Cox¹, A. Seidenberg², V. Rees², G. Connolly², B. Thomas¹, ¹RTI
International, RTP, NC, ²Harvard School of Public Health, Boston, MA

Analysis of herbal “Spice” mixtures containing synthetic cannabinoids using solid-phase microextraction and gas chromatography/mass spectrometry
B. F. Thomas, P. G. Pande, R. C. Daw, M. Grabenauer, J. L. Wiley, M. D. Mason, A. O. Cox,
K. H. Davis, Research Triangle Institute, Research Triangle Park, NC
Synthesis and monoamine transporter affinity of 3-aryl-3-arylmethoxytropane derivatives
H. Kaur1, S. Izenwasser2, D. Wade2, A. Housman2, G. Gulasey2, M. L. Trudell1, 1Chemistry, University of New Orleans, New Orleans, LA, 2Psychiatry, University of Miami Miller School of Medicine, Miami, FL

Synthesis and biological evaluation of novel cannabinoid antagonists
A. Verma1, S. Izenwasser2, D. Wade2, C. Booth2, M. L. Trudell2, 1Chemistry, University of New Orleans, New Orleans, LA, 2Psychiatry, University of Miami Miller School of Medicine, Miami, FL

Development of bivalent ligands for the CB1-Orexin 1 receptor heterodimers
Y. Zhang, D. Perrey, B. P. Gilmour, K. Warner, T. Langston, H. A. Navarro, B. F. Thomas, Research Triangle Institute, Research Triangle Park, NC

Development and immunological validation of an oxycodone conjugate vaccine in rats
M. Pravetoni1,2, M. LeNaour4, P. S. Portoghese4,2, M. Raleigh3, T. Harmon1, P. R. Pentel1,2,3, 1Minneapolis Medical Research Foundation, Minneapolis, MN, 2Medicine, University of Minnesota, Minneapolis, MN, 3Pharmacology, University of Minnesota, Minneapolis, MN, 4Medicinal Chemistry, University of Minnesota, Minneapolis, MN

ALCOHOL

The dopamine stabilizer (-)-OSU6162 selectively decreases voluntary ethanol consumption in rats: Implications for a novel treatment of alcohol use disorder
P. Steensland1, I. Fredriksson1, J. Franck1, A. Carlsson2, 1Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden, 2The Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden

Effects of alcohol on serotonin (5-HT3) receptor: The role of histone deacetylases and their inhibitor trichostatin A

Decision-making and impulsivity in PTSD and co-occurring cocaine or alcohol dependence: Preliminary analyses
A. E. Waldrop1,2, B. A. Lasher2, J. Coetzee1, E. Herbst2,1, T. C. Neylan2,1, S. L. Batki2,1, 1University of California, San Francisco, San Francisco, CA, 2San Francisco VAMC, San Francisco, CA

Executive cognitive dysfunction in rats with a history of ethanol dependence
G. Gonzalez-Cuevas, R. Martin-Fardon, F. Weiss, The Scripps Research Institute, La Jolla, CA

Alcohol’s effects on behavioral inhibition, risk-taking, and subjective effects in human moderate to heavy drinkers
R. L. Yankelevitz, S. H. Mitchell, Oregon Health & Science University, Portland, OR

Using fMRI to evaluate change language in emerging adults: A translational perspective
A. D. McEachern1, S. W. Feldstein Ewing1, F. Filbey1,3, A. Sabbineni1, D. Truitt1, H. Mead1, K. Ingersoll2, K. Hutchison1, 1The Mind Research Network, Albuquerque, NM, 2University of Virginia, Charlottesville, VA, 3University of Texas at Dallas, Dallas, TX

BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS
Efficacy of antidepressants in alcohol dependence with and without comorbid depression: A systematic review and meta-analysis

M. Farré1,2,3, D. Martínez-Sanvisens2,4, R. Martínez-Riera2,4, F. Fonseca2,4, P. Rossi2,4, C. Castillo2,4, M. Torrens2,4,5, 1Pharmacology Research Unit. Neuropsychopharmacology Program, Institut de Recerca Hospital del Mar (IMIM) - Parc de Salut Mar, Barcelona, Spain, 2Substance Use Disorders Research Group. Neuropsychopharmacology Program, Institut de Recerca Hospital del Mar (IMIM), Barcelona, Spain, 3Department of Pharmacology, Universitat Autònoma de Barcelona, Barcelona, Spain, 4Institut de Neuropsiquiatria i Addiccions (INAD), Parc de Salut Mar, Barcelona, Spain, 5Department of Psychiatry, Universitat de Barcelona, Barcelona, Spain

Sleep problems and suicide attempts in adults seeking alcohol use disorder treatment in Poland

A. Klimkiewicz1, A. S. Bohnert1,2, K. Brower1, M. Wojnar1,3, K. Conner4, M. A. Ilgen1,2, F. C. Blow1,2, 1Psychiatry, University of Michigan, Ann Arbor, MI, 2Department of Veterans Affairs, Ann Arbor, MI, 3Psychiatry, Medical University of Warsaw, Warsaw, Poland, 4University of Rochester Medical Center, Rochester, NY

Alcohol dependence clinical features and experiences observed soon after onset of drinking: Male-female variations

O. A. Adelaja, J. C. Anthony, Epidemiology, Michigan State University, East Lansing, MI

Male-female variation in early receipt of alcohol treatment services soon after drinking onset

B. Ahmedani1, J. C. Anthony2, 1Center for Health Services Research, Henry Ford Health System, Detroit, MI, 2Epidemiology, Michigan State University, East Lansing, MI

Beliefs significantly associated with the consumption of alcohol in school students in Spain

F. J. Bueno-Cañigral1, C. C. Morales-Manrique2, R. Aleixandre-Benavent2, J. C. Valderrama-Zurián3,1, 1Plan Municipal Drogodependencias (PMD), Ayuntamiento de Valencia, Valencia, Spain, 2Unidad de Información e Investigación Social y Sanitaria (UISYS), Universitat de València, Valencia, Spain, 3IVASPE, Generalitat Valenciana, Valencia, Spain

Beliefs significantly associated with the consumption of alcohol among school students in Spain. Differences by gender

C. C. Morales-Manrique1, F. J. Bueno-Cañigral2, J. C. Valderrama-Zurián3,1, R. Aleixandre-Benavent1, 1Unidad de Información e Investigación Social y Sanitaria (UISYS), Universitat de València, Valencia, Spain, 2Plan Municipal Drogodependencias (PMD) Ayuntamiento de Valencia, Valencia, Spain, 3IVASPE Generalitat Valenciana, Valencia, Spain

Relationship of binge drinking to drug use among nighttime weekend drivers

R. Voas, T. Kelley-Baker, E. Romano, J. Lacey, K. Jones, Pacific Institute for Research and Evaluation, Calverton, MD

Knowledge about legal blood alcohol content limits for drunk driving in a sample of Brazilian drivers

T. V. Conceicao1, R. De Boni1, P. Duarte2, F. Pechansky1, 1Center for Drug & Alcohol Research-UFRGS, Porto Alegre, Brazil, 2Brazilian Secretariat for Drug Policies, Brasilia, Brazil

The geography of drug arrests, violence and alcohol in Boston

R. Lipton1, X. Yang2, 1Department of Emergency Medicine, University of Michigan, Ann Arbor, MI, 2Department of Emergency Medicine, Beth Israel Deaconess Medical Center, Boston, MA

Addressing intimate partner violence perpetration in substance use disorder treatment programs in California

P. Sun1,2, H. R. Valenstein1,2, R. C. Cronkite1,2, C. Timko1,2, 1Center for Health Care Evaluation, VA Palo Alto Health Care System, Palo Alto, CA, 2Stanford University, Stanford, CA
**Wednesday, June 22, 2011**

84 *Vivitrol use in Los Angeles County*
D. A. Crevecoeur-MacPhail, J. Viernes, J. Barger, S. Cousins, W. Sugita, D. De Leon, J. Sorg, K. Bachrach, J. Kirby, C. Loch, S. Parker, M. Palmer, R. Rawson, NPI, UCLA ISAP, Los Angeles, CA, Los Angeles County Public Health, Substance Abuse Prevention and Control, Alhambra, CA, Tarzana Treatment Center, Tarzana, CA, Behavioral Health Services, Gardena, CA, Prototypes, Pomona, CA

85 *Knowledge of informed consent increases proportionately with education*
R. D. VanNess, C. M. Geppert, M. P. Bogenschutz, J. S. Tonigan, B. S. McCrady, K. Bradley, Biomedical Research Institute of New Mexico, Albuquerque, NM, Psychology, University of New Mexico, Albuquerque, NM, Center on Alcoholism, Substance Abuse and Addictions, University of New Mexico, Albuquerque, NM, Psychiatry, University of New Mexico, Albuquerque, NM

86 *The relationship between services delivered and substance use outcomes in New Mexico’s Screening, Brief Intervention, Referral and Treatment Initiative*
J. Gryczynski, S. G. Mitchell, T. Peterson, A. Gonzales, A. Moseley, R. P. Schwartz, Friends Research Institute, Baltimore, MD, Sangre de Cristo Community Health Partnership, Santa Fe, NM

87 *Applying web-based technology to disseminate Motivational Interviewing: A usability study*
M. A. Wilhelm, P. K. Horvatich, J. A. Hartje, Center for the Application of Substance Abuse Technologies, University of Nevada, Reno, NV, Department of Psychiatry, Virginia Commonwealth University, Richmond, VA

88 *Examining FASD Training of Trainers participants’ stigmatizing attitudes toward alcohol use in women of childbearing age*
J. A. Hartje, N. A. Roget, M. S. Berry, A. H. Skinstad, University of Nevada, Reno, NV, University of Iowa, Iowa City, IA

89 *Putting down the bottle: Exploring the adaptability of skills used to decrease problematic drinking among heroin and cocaine users*
M. Scherer, R. C. Trenz, P. Harrell, B. E. Mancha, W. W. Latimer, Mental Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

90 *Stability in pro-abstinence behavior measures: 18-years follow-up after intensive 3-month alcoholism treatment program*
M. Radovanovic, V. Rus, M. Rus Makovec, Alcoholism Treatment Center, University Psychiatric Hospital, Ljubljana, Slovenia, Department of Psychology, University of Ljubljana, Ljubljana, Slovenia

91 *Measuring the measure: Does the VA SUD CoC Performance Measure actually measure continuity of care?*

92 *Alcohol and other drug use across international borders*
P. Insúa, M. Lledó, I. Germán, A. A. Colina, I. A. Colina, C. Olaizola, J. P. Daulouede, Faculté de Psychologie, Université du Pays Basque/ Euskal Herriko Unibertsitatea, Gipuzkoa, France, École de Travail Social, Université du Pays Basque/ Euskal Herriko Unibertsitatea, Gipuzkoa, France, Institut Basque de Criminologie (IVAC) (UPV/EHU), Gipuzkoa, Spain, Centre de soins en addictologie, Bayonne, France
COMORBIDITY

93  Efficacy of antidepressants in cocaine, implications of comorbid depression: Systematic review and meta-analysis
M. Torrens1,2,3, D. Martinez-Sanvisens1,2, R. Martinez-Riera1,2, F. Fonseca1,2, P. Rossi1,2, C. Castillo1,2, M. Farre2,4,5,1Institut de Neuropsiquiatria i Addiccions (INAD), Parc de Salut Mar, Barcelona, Spain, 2Substance Use Disorders Research Group Neuropsychopharmacology Program, Institut de Recerca Hospital del Mar (IMIM), Barcelona, Spain, 3Department of Psychiatry, Universitat Autònoma de Barcelona, Barcelona, Spain, 4Pharmacology Research Unit. Neuropsychopharmacology Program, Institut de Recerca Hospital del Mar (IMIM) - Parc de Salut Mar, Barcelona, Spain, 5Department of Pharmacology, Universitat Autònoma de Barcelona, Barcelona, Spain

94  Length of treatment is associated with decrease in tobacco use in comorbid major depression and alcoholism
I. Salloum1, A. Douaihy2, L. Kirisci3, J. R. Cornelius2, 1Psychiatry, University of Miami Miller School of Medicine, Miami, FL, 2Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, 3Pharmaceutical Sciences, University of Pittsburgh School of Pharmacy, Pittsburgh, PA

95  Does depression interfere with contingency-management treatment for pregnant cigarette smokers?

96  Psychological symptoms and modafinil effects on smoking cessation
C. A. Martin1,3, G. Guenthner1, R. Charnigo2, S. Batten1, J. A. Lile3, T. H. Kelly3,1, 1Psychiatry, University of Kentucky, Lexington, KY, 2College of Public Health, University of Kentucky, Lexington, KY, 3Behavioral Science, University of Kentucky College of Medicine, Lexington, KY

97  Severity of psychiatric disorders in tobacco users
V. Beltran2, A. A. Colina2, C. Maitre1, M. Auriacombe1, J. P. Daulouede1, 1Psychiatrie, Université Victor Segalen Bordeaux 2, Bordeaux, France, 2Centre d’Addictologie, Bayonne, France

98  Tobacco use characteristics and quit attempts among smokers with serious mental illness
N. J. Hickman, J. J. Prochaska, Psychiatry, University of California, San Francisco, San Francisco, CA

99  Nicotine reinforcement before and after 72-h smoking abstinence in smokers with schizophrenia
J. Tidey, S. Colby, Psychiatry & Human Behavior, Brown University, Providence, RI

100  Shorter interpuff interval associated with greater nicotine intake in smokers with and without schizophrenia
J. M. Williams1,2, K. K. Gandhi1,2, S. Kumar1, S. E. Lu2,1, 1Psychiatry, Robert Wood Johnson Medical School, New Brunswick, NJ, 2UMDNJ School of Public Health, Piscataway, NJ

101  The impact of cannabis use on cognitive functioning in patients with schizophrenia
M. Yucel1,2, E. Bora1, D. I. Lubman3, N. Solowij4,2, W. J. Brewer2, S. Cotton2, P. Conus6, M. J. Takagi1,2, A. Fornito1, S. J. Wood1, P. D. McGorry2, C. Pantelis1, 1Melbourne Neuropsychiatry Centre, University of Melbourne, Melbourne, VIC, Australia, 2Orygen Youth Health Research Centre, University of Melbourne, Melbourne, VIC, Australia, 3Turning Point Alcohol and Drug Centre, Monash University, Melbourne, VIC, Australia, 4School of Psychology, University of Wollongong, Sydney, NSW, Australia, 5Schizophrenia Research Institute, Sydney, NSW, Australia, 6Université de Lausanne, Clinique de Cery, Switzerland
An examination of self-stigma in schizophrenic patients with a substance abuse disorder
S. Rodrigues, M. Serper, M. Hobart, A. Lennox, J. Vessella, G. Gonzalez, D. Ziedonis, D. Smelson, Edith Nourse Rogers Memorial Veterans Hospital, Bedford, MA, Psychiatry, University of Massachusetts Medical School, Worcester, MA, Psychology, Hofstra University, Hempstead, NY

Naltrexone effects on cannabis and cocaine use in alcohol-dependent patients with schizophrenia: Preliminary analysis
S. L. Batki, Z. Szombathyne Meszaros, J. Dimmock, R. Ploutz-Snyder, UCSF - SF VAMC, San Francisco, CA, SUNY Upstate, Syracuse, NY, USRA NASA, Houston, TX

Predictors of legal problems among patients with bipolar disorder and alcoholism
E. M. Ramos, A. Douaihy, R. Caceda, J. R. Cornelius, I. M. Salloum, Psychiatry and Behavioral Sciences, University of Miami Miller School of Medicine, Miami, FL, Psychiatry, University of Pittsburgh Medical Center, Pittsburgh, PA

Conjoint development of antisocial behaviors and marijuana use from adolescence into young adulthood
M. J. Worley, S. A. Brown, M. C. Stallings, C. J. Hopfer, J. K. Hewitt, University of California, San Diego, La Jolla, CA, University of Colorado, Denver, CO

Does marijuana use trajectory predict self-reported depressive symptoms among community-based adults followed for 20 years (the CARDIA study)?

Affective instability predicts pathways to alcohol and marijuana use disorders in young adults
L. A. Hulvershorn, P. Finn, Psychiatry, Indiana University School of Medicine, Indianapolis, IN, Psychological and Brain Sciences, Indiana University, Bloomington, IN

Psychomotor agitation in substance dependence
A. M. Leventhal, J. Gelernter, D. Oslin, R. F. Anton, L. A. Farrer, H. R. Kranzler, University of Southern California, Los Angeles, CA, Yale University School of Medicine, New Haven, CT, Philadelphia VAMC and University of Pennsylvania, Philadelphia, PA, Medical University of South Carolina, Charleston, SC, Boston University Schools of Medicine and Public Health, Boston, MA, University of Connecticut Health Center, Farmington, CT

Predicting substance use among children with ADHD: Clinical utility of impairment indices
P. A. Graziano, K. Derefinko, E. Gnagy, B. Molina, W. Pelham, Florida International University, Miami, FL, University of Pittsburgh, Pittsburgh, PA

Attention-deficit/hyperactivity disorder subtypes in cocaine-dependent individuals: Frequency and characteristics
M. Mooney, F. Levin, D. Babb, D. Brooks, A. Mahony, J. Grabowski, Psychiatry, University of Minnesota, Minneapolis, MN, Psychiatry, Columbia University, New York, NY

Adult ADHD diagnosis accuracy in substance use disorder clients
M. Malivert, M. Fatseas, C. Denis, M. Auriacombe, Addiction Psychiatry (UMSR-CNRS), Universite Victor Segalen Bordeaux 2, Bordeaux, France, Addiction Treatment Center, CHCP, CHU, Bordeaux, France

Psychiatric comorbidities as a function of substance type and gender within residential substance use treatment
A. N. Banducci, K. W. Chen, L. Guller, R. J. Macatee, C. W. Lejuez, University of Maryland, College Park, MD
113  Childhood trauma, substance use, and mental disorders patterns among homeless in British Columbia  
C. G. Schuetz, C. Taplin, K. Lee, R. M. Krausz, Psychiatry, University of British Columbia, Vancouver, BC, Canada

114  Screening for co-occurring mental disorders: From research validation to knowledge translation  
B. Rush1, S. Castel2, B. Brands1,3, 1Health Systems Research, Centre for Addiction and Mental Health, Toronto, ON, Canada, 2Dept. of Psychiatry, Sunnybrook Health Sciences Centre, Toronto, ON, Canada, 3Health Canada, Ottawa, ON, Canada

115  Factors associated with mental health clinicians’ referrals to 12-step groups  
H. Matusow1, A. Rosenblum1, C. Fong1, H. Vogel3, S. Magura2, 1NDRI, NY, NY, 2WMU, Kalamazoo, MI, 3DTR, Inc., Brooklyn, NY

116  Factors associated with medication adherence among psychiatric outpatients with substance abuse histories  
S. Magura1, A. Rosenblum2, C. Fong2, 1Western Michigan University, Kalamazoo, MI, 2NDRI, New York, NY

117  Improving attendance to specialized psychiatric services offered in a methadone treatment program  
R. K. Brooner, M. Kidorf, V. King, J. Peirce, Johns Hopkins University, Baltimore, MD

118  Prevalence of mood and substance disorders among patients seeking office-based buprenorphine  
J. Savant2, D. Barry1, C. Cutter1, T. Fazzino2, R. Schottenfeld1, D. Fiellin1, 1Yale University School of Medicine, New Haven, CT, 2APT Foundation Inc, New Haven, CT

119  ADOLESCENTS II  
“This is not who I want to be:” experiences of opioid-dependent youth prior to, and during, combined buprenorphine and behavioral treatment  

120  Treatment outcomes with relapse prevention medications for opioid dependence in youth  
M. Fishman1,2, E. Curran2, S. Shah2, C. Perry-Parrish1,2, 1Johns Hopkins University, Baltimore, MD, 2Mountain Manor Treatment Center, Baltimore, MD

121  Absence of gender differences in treatment with relapse prevention medications for opioid dependence in youth  
E. Curran2, C. Perry-Parish1,2, S. Shah2, M. Fishman1,2, 1Johns Hopkins University, Baltimore, MD, 2Mountain Manor Treatment Center, Baltimore, MD

122  Benefits of treatment during treatment: Estimating concurrent effects  
R. Ramchand1, B. A. Griffin1, D. McCaffrey3, D. Almirall2, A. Morral1, 1RAND, Arlington, VA, 2Institute for Social Research, University of Michigan, Ann Arbor, MI, 3RAND, Pittsburgh, PA

123  Development of a novel high-school-based intervention to motivate a tobacco-free lifestyle  
S. Krishnan-Sarin1, K. M. Cummings2, D. Cavallo1, A. Hyland2, J. Gra2, A. Liss1, G. Kong1, C. Connell1, J. Pflieger1, D. Camenga1, A. Brown2, P. Hage2, M. Travers2, 1Yale University School of Medicine, New Haven, CT, 2Roswell Park Cancer Institute, Rochester, NY
Wednesday, June 22, 2011

124 Smoking, alcohol, drugs and delinquency among high school students in Cape Town, South Africa
   T. Carney1, B. Myers1,4, J. Louw2, C. Lombard3, A. Flisher4, 1Alcohol and Drug Abuse Research Unit, Medical Research Council, Cape Town, South Africa, 2Department of Psychology, University of Cape Town, Cape Town, South Africa, 3Biostatistics Unit, Medical Research Council, Cape Town, South Africa, 4Department of Psychiatry and Mental Health, University of Cape Town, Cape Town, South Africa

125 Tobacco use patterns among adolescents entering substance abuse treatment
   V. H. Coleman-Cowger, Research, Chestnut Health Systems, Normal, IL

126 Tobacco use among African-American youth being treated for behavioral healthcare issues
   A. Breland1, J. R. Koch1, J. Irons2, 1Institute for Drug and Alcohol Studies, Virginia Commonwealth University, Richmond, VA, 2Department of Psychology, James Madison University, Harrisonburg, VA

127 The dark side of sniffing: Paint color affects intoxication experiences among adolescent inhalant users
   M. Takagi1, D. I. Lubman2, M. Yücel1, 1Psychiatry, University of Melbourne, Carlton South, VIC, Australia, 2Turning Point Alcohol and Drug Centre, Fitzroy, VIC, Australia

128 The development of methamphetamine use disorder in a clinically ascertained longitudinal sample
   C. Hartman1, S. Salomonsen-Sautel1, T. Crowley1, R. Corley2, J. Sakai1, A. Hoffenberg1, C. Thurstone3, M. Stallings2, C. Hopfer1, 1University of Colorado Denver, Aurora, CO, 2University of Colorado, Boulder, CO, 3Denver Health Authority, Denver, CO

129 Progression of polysubstance abuse and dependence symptoms in a longitudinal clinical sample
   J. Bricker1, S. Salomonsen-Sautel1, S. Min1, R. Corley2, M. Stallings2, J. Hewitt2, T. Crowley1, C. Hopfer1, 1UC Denver, Aurora, CO, 2Institute for Behavioral Genetics, Boulder, CO

130 Prospective study of ADHD and risk for adolescent and young adult drug abuse
   K. Winters1,2, S. Lee1, G. Realmuto1, G. August1, 1University of Minnesota Medical School, Minneapolis, MN, 2Treatment Research Institute, Philadelphia, PA

131 The role of conduct disorder in initiation of substance use
   C. Hopfer1, S. Salomonsen-Sautel1, S. Min1, S. Mikulich-Gilbertson1, M. McQueen2, T. Crowley1, S. Young2, R. Corley2, J. Sakai1, A. Hoffenberg2, C. Thurstone3, C. Hartman1, J. Hewitt2, M. Stallings2, 1Psychiatry, University of Colorado, Aurora, CO, 2University of Colorado, Boulder, CO, 3Denver Health Authority, Denver, CO

132 Substance-dependent, conduct-disordered adolescents: Severity of diagnosis does not predict future incarceration risk
   A. S. Hoffenberg1, S. Salomonsen-Sautel1, N. Beckman3, R. Corley2, M. Stallings2, T. Crowley1, S. Brown3, C. Hopfer1, 1Psychiatry, University of Colorado, Denver, CO, 2Institute of Behavioral Genetics, Boulder, CO, 3University of California at San Diego, San Diego, CA

133 Drug misuse, violence, and HIV risk among youth in an urban Emergency Department
   L. S. Massey1, L. Whiteside1, M. Newton1, M. Walton2, M. Zimmerman1, F. Blow2,4, B. Booth5, R. Cunningham1, 1Emergency Medicine, University of Michigan, Ann Arbor, MI, 2Psychiatry, University of Michigan, Ann Arbor, MI, 3School of Public Health, University of Michigan, Ann Arbor, MI, 4Department of Veterans Affairs, Ann Arbor, MI, 5Department of Veterans Affairs, Little Rock, AR, 6Psychiatry, University of Arkansas for Medical Sciences, Little Rock, AR
134 Investigating the complex relations between culture and substance use: A preliminary model with high risk adolescents
H. Mead1, S. Feldstein Ewing1, A. McEachern1, E. DeVargas1, A. Ortiz-Briggs1, K. Ingersoll2, A. Bryan1, K. Hutchison1, 1Mind Research Network, Albuquerque, NM, 2University of Virginia, Charlottesville, VA

135 Substance abuse problems among minority teens presenting to a general outpatient psychiatry clinic
L. Herman1,2, D. Haller1,2, M. Acosta1, K. Winters4, R. Stinchfield4, 1St. Luke’s - Roosevelt Hospital, New York, NY, 2Columbia University, New York, NY, 3NDRI, New York, NY, 4University of Minnesota, Minneapolis, MN

136 Seeking online information about drugs/alcohol/tobacco by Jewish and Arab schoolchildren in Israel: Who does, who doesn’t and who wants to?
Y. Neumark, C. Lopez-Quintero, B. Feldman, L. Flum, R. Shtarkshall, Braun School of Public Health, Hebrew University-Hadassah, Jerusalem, Israel

137 Drug use resilience and its determinants among school adolescents in Bogota, Colombia
C. Lopez-Quintero, Y. Neumark, Braun School of Public Health, Hebrew University of Jerusalem, Jerusalem, Israel

138 A latent transition analysis of childhood maltreatment and patterns of adolescent substance use
S. H. Shin, School of Social Work, Boston University, Boston, MA

139 Autonomy and relatedness among substance-using mothers and their children
A. Letcher, N. Slesnick, Human Development and Family Science, The Ohio State University, Columbus, OH

140 Three-month efficacy of a brief intervention for reducing marijuana use and consequences among adolescents presenting to indigent primary care clinics
K. M. Bohnert1,2, M. A. Walton2, K. Barry1,2, S. T. Chermack1,2, R. A. Zucker2, M. A. Zimmerman2, B. M. Booth3,4, F. C. Blow1,2, 1SMITREC, VA Ann Arbor, Ann Arbor, MI, 2Psychiatry, University of Michigan Medical School, Ann Arbor, MI, 3VA Little Rock, Little Rock, AR, 4University of Arkansas for Medical Sciences, Little Rock, AR

OPIOIDS: HUMAN I

141 Impact of inpatient research participation on subsequent heroin use patterns
P. Roux1,2, C. Tindall1, J. Murray1, S. K. Vosburg1, P. Saccone1, M. A. Sullivan1, J. M. Manubay1, Z. D. Cooper1, J. D. Jones1, R. D. Foltin1, S. D. Comer1, 1SURC, Columbia University, New York, NY, 2SE4S, Inserm U912, Marseille, France

142 Repeatability of laboratory stressors in heroin users: Early vs. mid treatment

143 Self-reports of heroin users who continue to use heroin after taking naltrexone for extended-release (Vivitrol®): A pilot study
A. DeFlulio, L. Long, K. Mackowick, A. Umbricht, M. Fingerhood, G. E. Bigelow, K. Silverman, Johns Hopkins University School of Medicine, Baltimore, MD

144 Effects of tizanidine and nifedipine in methadone-maintained humans under a naloxone novel-response discrimination procedure
A. Oliveto, N. Sanders, M. J. Mancino, J. B. Guise, W. K. Bickel, W. B. Gentry, University of Arkansas for Medical Sciences, Little Rock, AR

145 Abuse liability indices across repeated alfentanil exposures in healthy normals
D. A. Tompkins, G. E. Bigelow, M. T. Smith, E. C. Strain, Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD

91
146 Novel opioid receptor antagonist, ALKS 33, co-administered with buprenorphine blocks µ agonist effects
R. Jones1, E. Fernandez1, A. Manari1, R. Turncliff2, J. Ransom3, N. Chiang4, 1University of California, San Francisco, San Francisco, CA, 2Alkermes, Inc., Waltham, MA, 3Fast-Track Drugs & Biologics, N. Potomac, MD, 4National Institute on Drug Abuse, Bethesda, MD

147 Inhibitory control indexes early-in-treatment abstinence among opioid-dependent young adults treated with buprenorphine
G. Gonzalez1, C. Hinchey1, S. Gillespie2, E. Sophis2, D. Smelson1,3, G. DiGirolamo2, 1Psychiatry, University of Massachusetts Medical School, Worcester, MA, 2Psychology, College of the Holy Cross, Worcester, MA, 3VA National Center for Homelessness Among Veterans, Edith Nourse Rogers Memorial VA, Bedford, MA

148 Patterns of memory impairments in a sample of active heroin users in Penang, Malaysia
S. Azimi Alamdari1, B. Vicknasingam1, M. C. Chawarski2, 1Centre for Drug Research, University Sains Malaysia, Minden, Malaysia, 2Psychiatry, Yale University, New Haven, CT

149 Breakdowns in conscious and unconscious control in opiate addiction
G. DiGirolamo1, N. Patel1, C. T. Hinchey2, G. Gonzalez1, 1Psychology, College of the Holy Cross, Worcester, MA, 2Psychiatry, University of Massachusetts, Medical School, Worcester, MA

150 Impaired sleep functioning in prescription opioid-dependent individuals
E. E. Hartwell, S. E. Back, K. T. Brady, Psychiatry & Behavioral Sciences, MUSC, Charleston, SC

151 Subjective sleep quality in opioid-dependent subjects in methadone and buprenorphine maintenance treatment
X. Balducci2,1, A. Mathillon1, C. Denis2,1, M. Fatseas1,2, V. Beltran1,3, J. Daulouede3,2,1, M. Auriacombe1,2,3, 1Addiction Psychiatry (UMSR-CNRS), Universite Victor Segalen Bordeaux 2, Bordeaux, France, 2Addiction Treatment Center, CHCP, CHU, Bordeaux, France, 3Bizia Addiction Treatment Center, Bayonne, France

152 Gender and race differences in pre-admission EKG findings at a methadone clinic
D. Antoine, E. Strain, A. Umbricht, Behavioral Pharmacological Research Unit, Johns Hopkins School of Medicine, Baltimore, MD

153 Methadone dose and the QTc interval: Little clinical relevance big unknowns
G. Bart1, B. A. Bart1, R. Karim1, Z. Wyman2, 1Medicine, Hennepin County Medical Center, Minneapolis, MN, 2College of Pharmacy, University of Minnesota, Minneapolis, MN

154 Risk of death during and after opiate substitution therapy in primary care
M. Hickman1, R. Cornish1, P. Vickerman1, J. Strang2, 1School of Social and Community Medicine, University of Bristol, Bristol, United Kingdom, 2National Addiction Centre, Institute of Psychiatry, London, United Kingdom

155 Clinical correlates of spontaneous withdrawal from prescription opioids
S. Babalonis1, S. L. Walsh1,2,3, P. A. Nuzzo1, M. R. Lofwall1,2,3, 1Behavioral Science, University of Kentucky (UK), Lexington, KY, 2Center on Drug and Alcohol Research, UK, Lexington, KY, 3Psychiatry, UK, Lexington, KY

156 Positive affect in treatment onset can have negative impact on later outcomes after residential heroin detoxification program

157 Can we predict a patient’s success with rapid naltrexone induction?
S. Mogali, N. Khan, M. Sullivan, E. Nunes, A. Bisaga, Substance Abuse, New York State Psychiatric Institute, New York, NY
Final outcomes from an acceptance-based intervention to improve methadone detoxification success rates
A. Stotts¹, C. Green¹, T. Northrup¹, J. Schmitz¹, F. G. Moeller¹, J. Grabowski², ¹University of Texas Medical School at Houston, Houston, TX, ²University of Minnesota, Minneapolis, MN

A novel buprenorphine maintenance treatment program in a community-based recovery center in Baltimore City: Initial treatment outcomes
D. Agus³¹, A. M. Daniels¹³, E. Salisbury¹², W. W. Davis¹, S. Foerster², J. Stafford², A. Haskel², M. Fingerhood², ¹Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, ²Johns Hopkins Medical Institutions, Baltimore, MD, ³Behavioral Health Leadership Institute, Baltimore, MD

Suicidality and continued opioid misuse in methadone patients: The role of mindfulness and experiential avoidance
K. Rosen¹, A. Gutierrez¹, K. Ramirez², M. Scavone², J. S. Potter¹, ¹Psychiatry, UT Health Science Center, San Antonio, TX, ²Center for Health Care Services, San Antonio, TX

Determinants of health-related quality of life among methadone maintenance subjects in Taiwan
S. Wang¹, L. Lin², P. S. Lin¹, L. W. Hung¹, C. Y. Chen³, K. C. Tseng⁴, Y. L. Chien⁵, J. D. Wang⁶, I. K. Ho¹, ¹Institute of Population Health Sciences, National Health Research Institutes, Miaoli County, Taiwan, ²Department of Psychiatry, En Chu Kong Hospital, Taipei County, Taiwan, ³Institute of Public Health, National Yang-Ming University, Taipei, Taiwan, ⁴Department of Psychiatry, Taiwan Adventist Hospital, Taipei, Taiwan, ⁵Department of Psychology, National Taiwan University Hospital, Taipei, Taiwan, ⁶Department of Public Health, National Cheng-Kung University, Tainan, Taiwan

The effectiveness of psychosocial intervention for heroin dependence in MMT in Shanghai
J. Du, M. Zhao, Shanghai Mental Health Center, Shanghai, China

WITHDRAWN

12-Step group participation in opioid-dependent patients receiving buprenorphine and behavioral treatments
M. P. Hillhouse, J. Fahey, S. Reed, L. MacGraw, E. Nelson, B. Thornton, W. Ling, Integrated Substance Abuse Programs, University of California, Los Angeles, Los Angeles, CA

Spiritual and religious beliefs and behaviors, self-help participation and opioid use
E. Nelson, M. Hillhouse, M. Smith, S. Reed, W. Ling, Integrated Substance Abuse Programs, University of California, Los Angeles, Los Angeles, CA

BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS
INRC POSTERS
CHEMISTRY AND NOVEL LIGANDS

166 Unexpected opioid activity profiles of analogs of the novel peptide kappa opioid receptor ligand CJ-15,208
(1) Dept. of Med. Chem., Univ. of Kansas, Lawrence, KS, (2) Torrey Pines Inst. for Molecular Studies, Port St. Lucie, FL, (3) Dept. of Pharmacol., Creighton Univ. Sch. of Med., Omaha, NE, USA

167 Kinetics of fluorescent opioid ligand binding to the mu opioid receptor
W. Birdsong (1), S. Arttamangkul (1), K. Rice (2), J. Williams (1). (1) Vollum Institute, Oregon Health & Science Univ., Portland, OR, USA, (2) National Institute on Drug Abuse, Bethesda, MD, USA

168 ALKS 33, a novel opioid receptor modulator, attenuates cocaine-induced increases in extracellular DA concentrations and cocaine self-administration in rats
J.I. Cunningham (1), M.S. Todtenkopf (1), R.L. Dean (1), M.R. Azar (2), G.Koob (3), D.R. Deaver (1), D.J. Eyerman (1). (1) Alkermes, Inc., Waltham, MA, (2) Behavioral Pharma, Inc., La Jolla, CA, (3) The Scripps Research Institute, La Jolla, CA, USA

169 Oral activity of cyclic tetrapeptide JVA-2802: Short-acting KOR antagonism and prevention of stress-induced reinstatement of cocaine-CPP
S.O. Eans (1), M.L. Ganno (1), J.V. Aldrich (2), J.P. McLaughlin (1). (1) Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL; (2) Dept. of Med. Chem., Univ. of Kansas, Lawrence, KS, USA

170 Exploring bifunctional activity of 3-substituted piperidin-4-yl-1,3-dihydroindol-2-one class of NOP ligands at the mu-opioid receptor (MOP)
V. Journigan (1), W. Polgar (2), L. Toll (2), N. T. Zaveri (1). (1) Astreaa Therapeutics, LLC, Mountain View, CA; (2) SRI International, Menlo Park, CA, USA

171 Fluorescent opioid peptides from a cyclic peptide combinatorial library
Y. Li, M. Cazares, J. Thompson, J. Misler, R. Houghten, C. Dooley. Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL, USA

172 Endorphin peptide and glycopeptide analogues with helix address domains provide potent anti-nociception in mice
173 *Kappa opioid tetrapeptides from expanded deconvolution of a positional scanning library*  
J. Misler, M. Cazares, T. LaVoi, T. Gibbins, A. Morales, L. Maida, M. Giulianotti, C. Dooley. Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL, USA

174 *Oral availability of CJ-15,208, an opioid mixed agonist/antagonist analgesic with fewer liabilities in vivo*  
N.C. Ross (1), S. Kulkarni (2), J. V. Aldrich (2) J. P. McLaughlin (1). (1) TPIMS, Port St. Lucie, FL, (2) Dept. of Med. Chem., Univ. of Kansas, Lawrence, KS, USA

175 *Novel peptide and non-peptide opioid agonists lacking a positively charged nitrogen*  
P.W. Schiller, G. Weltrowska, I. Berezowska, T.M.-D. Nguyen, B.C. Wilkes, C. Lemieux, N.N. Chung. Lab. of Chemical Biology and Peptide Research, Clinical Research Institute of Montreal, Montreal, Que., Canada

176 *Lead optimization studies of N-(2-[1,1′-biphenyl]-4-ylethyl)-8-CAC*  
M.A. VanAlstine (1), M.P. Wentland (1), D.J. Cohen (2), J.M. Bidlack (2). (1) Dept. of Chemistry and Chemical Biology, Rensselaer Polytechnic Institute, Troy, NY, (2) Dept. of Pharmacology and Physiology, University of Rochester, Rochester, NY, USA

177 *Novel analogs of endomorphins provide antinociception without spatial and recognition memory deficits produced by morphine*  
J.N. Jernberg (1), X. Zhang (2), J.E. Zadina (1,2,3,4). (1) Graduate Neuroscience Program, Dept. of (2) Medicine & (3) Pharmacology, Tulane Univ. Sch. of Med., (4) SE LA Veterans HCS, New Orleans, LA, USA

PEPTIDE REGULATION

178 *Prodynorphin gene expression in rats treated with ethanol and growth hormone*  

179 *Effects on proopiomelanocortin (POMC) expression and conditioned place aversion during protracted spontaneous withdrawal from chronic intermittent escalating-dose heroin in POMC-EGFP promoter transgenic mice*  
K. Niikura, Y. Zhou, A. Ho, M. J. Kreek. Lab. of Biology of Addictive Diseases, Rockefeller Univ., New York, NY, USA

180 *Differences in opioid peptide levels in Wistar rats from five different suppliers*  
S. Palm, E. Roman, I. Nylander. Dept. Pharmaceutical Biosciences, Uppsala University, Uppsala, Sweden
Pathogenic activities of dynorphin A mutants that cause human neurodegenerative disorder spinocerebellar ataxia type 23: Induction of nociceptive behaviors in mice through non-opioid mechanism


The effect of mastitis and milk congestion on the levels of beta-casomorphin-8 in milk and plasma samples from puerperal women

A. Carlsson (1), L. Righard (2), F. Nyberg (1). (1) Dept. of Pharmaceutical Biosciences, Uppsala Univ., Uppsala, (2) Dept. of Pediatrics, Univ. Hospital, Malmö, Lund University, Lund, Sweden

Microdialysis-mass spectrometry quantification of vasopressin in the hypothalamus and amygdala of freely moving rats

B. Reed (1,2), B.T. Chait (2), M.J. Kreek (1). (1) Lab. of Biology of Addictive Diseases, (2) Lab. of Mass Spectrometry and Gaseous Ion Chemistry, Rockefeller Univ., New York, NY, USA

Regional mRNA expression of the endogenous opioid and dopaminergic systems in brains of C57BL/6J and 129P3/J mice: Strain and heroin effects

S.D. Schlussman, J. Cassin, Y. Zhang, O. Levran, A. Ho, M.J. Kreek. Lab. of Biology of Addictive Diseases, Rockefeller Univ., New York, NY, USA

Dynorphin gene expression in the amygdala after stress exposure

J.T. Silveira, S. Gouty, G. Bull, B.M. Cox. Dept. of Pharmacology, Uniformed Services Univ., Bethesda MD, USA

Regulation of prodynorphin expression in human brain: Transcription factors targeting SNPS associated with alcohol dependence


Dynorphin mutations cause human neurodegenerative disorder spinocerebellar ataxia type 23


Duration of withdrawal from chronic escalating-dose binge cocaine: Effects on cocaine-induced conditioned place preference and expression of selective components of the opioid system

Y. Zhang, S.D. Schlussman, E.R. Butelman, A. Ho, M.J. Kreek. Lab. of Biology of Addictive Diseases, Rockefeller Univ., New York, NY, USA
189 Chronic voluntary alcohol drinking enhances proopiomelanocotin (POMC) gene expression in nucleus accumbens and hypothalamus of alcohol-prefering rats
Y. Zhou (1), G. Columbo (2), K Niikura (1), M.A.M. Carai (2), A. Ho (1), G.L. Gessa (2), M.J. Kreek (1). (1) Lab of Biology of Addictive Diseases, Rockefeller Univ., New York, USA, (2) CNR Neuroscience Institute, Monseratto, Italy

190 Streptozotocin-induced type 1 diabetes impairs learning abilities in Barnes Maze and alters growth hormone receptor but not prodynorphin mRNA expression in the prefrontal cortex of male mice

TOLERANCE, DEPENDENCE, WITHDRAWAL
191 L-Theanine suppresses abstinence signs in morphine-dependent rhesus monkeys and has anxiolytic-like activity in the mouse elevated plus maze
M.D. Aceto, L.S. Harris, L.D. Hughes, I.D. Premaratne, L.E. Wise, A.H. Lichtman. Dept. of Pharmacology, School of Medicine, Virginia Commonwealth Univ., Richmond, VA, USA

192 Down-regulation of beta-arrestin2 contributes to morphine tolerance in the gastrointestinal tract
H. I. Akbarali, M. Kang, H. Maguma, T.H. Smith, G.R. Ross, W.L. Dewey. Dept. of Pharmacology and Toxicology, Virginia Commonwealth Univ., Richmond, VA, USA

193 Acute tolerance to etorphine and morphine dependence in MOPr phosphorylation-deficient mice
E. Barbier, J.B. Wang. Dept. of Pharmaceutical Sciences, Univ. of Maryland Sch. of Pharmacy, Baltimore, MD, USA

194 Analgesic tolerance to high efficacy agonists but not to morphine is reversed in phosphorylation-deficient S375A mu-opiod receptor knockin mice
G. Grecksch (1), A.-K. Imhof (2), C. Pierstorff (1), S. Just (2), C. Doll (2), A. Lupp (2), A. Becker (1), T. Koch (1), R. Stumm (2), V. Höllt (1), S. Schulz (2). (1) Institute of Pharmacology and Toxicology, University Hospital, Otto-von-Guericke-Univ. Magdeburg, (2) Institute of Pharmacology and Toxicology, University Hospital, Friedrich Schiller Univ., Jena, Germany

195 Morphine tolerance, desensitization and recovery in locus coeruleus neurons from morphine-treated rats
E. Levitt, J. Williams. Vollum Institute, Oregon Health and Science Univ., Portland, OR, USA
196 *Differential role for beta-arrestin2 in the development of antinociceptive tolerance and physical dependence in response to distinct opioid analgesics*  
K. M. Raehal, L.M. Bohn. Dept. of Molecular Therapeutics and Neuroscience, Scripps Research Institute, Jupiter, FL, USA

**ADDICTION**

197 *Clinically insignificant QTc changes among former opiate addicts during first years of Methadone Maintenance Treatment*  
E. Peles (1), S. Linzy (2) M.J. Kreek (3), M. Adelson (1,2,3). (1) Dr. Miriam and Sheldon G. Adelson Clinics for Drug Abuse Treatment and Research, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, (2) Las Vegas, NV, USA, (3) Rockefeller Univ., New York, NY, USA

198 *Buprenorphine/naltrexone by iontophoresis: A transdermal approach to drug abuse treatment*  
A. Taverner, S. Cordery, R.H. Guy, M.B. Delgado-Charro, C.P. Bailey, S.M. Husbands. Dept. of Pharmacy and Pharmacology, Univ. of Bath, Bath, UK

199 *Non-medical use of prescription narcotics in the sequence of adolescent drug-use initiation and epidemiology of narcotic use by Indiana adolescents*  
A. YoussefAgha, W. Jayawardene, M. Torabi. Dept. of Applied Health Science, Indiana Univ., Bloomington, IN, USA

200 *Hypothalamic KOP-r and MOP-r expression in Fischer and Lewis rats after dose escalation preference paradigm of heroin self-administration*  
R. Picetti, A. Ho, M.J. Kreek. Rockefeller University, New York, NY, USA

**OPIOIDS AND IMMUNE FUNCTION**

201 *Opioid and alcohol pharmacodynamics: Contributions of innate immune signaling to drug response*  

202 *Regulation of Tat-mediated neurotoxicity and glial inflammatory signaling by CCR5 and the mu-opioid receptor*  
203 Variants of mu opioid receptor influence HIV viral load change in individuals before initiating HAART

204 Variants of kappa opioid receptor influence viral load of HIV-positive females on HAART

205 Opioid and gp120 interactive neuropathogenesis in HIV-1
K.L. Samano (1), P.E. Knapp (2), K.F. Hauser (1). (1) Depts. of Pharmacology and Toxicology, (2) Anatomy and Neurobiology, Virginia Commonwealth Univ., Richmond, VA, USA

206 Expression of OPRK1, PDYN and CXCR4 in the caudate in postmortem brain of HIV-infected and HIV-negative subjects
V. Yuferov (1), A. Ho (1), S. Morgello (2), M.J. Kreek (1). (1) Lab. of Addictive Diseases, Rockefeller Univ., (2) Pathology, Mount Sinai Medical Center, New York, NY, USA

207 Chronic morphine tolerance upregulated spinal proinflammatory cytokines which are revised by HSV vector expressing interleukin 4 in rats
X. Zheng (1, 2), J. Sun (1), S. Liu (1, 2), M. Mata (1), D. Fink (1), S. Hao (1, 2). (1) Dept. of Neurology, Univ. Michigan, Ann Arbor, MI, (2) Dept. of Anesthesiology, Univ. Miami Miller Medical School, Miami, FL, USA

OPIOID RECEPTOR PHYSIOLOGY

208 Opioid-sensitive GABA inputs from RMTγ neurons synapse on midbrain dopamine neurons
A. Matsui, J. T. Williams. Vollum Institute, Oregon Health and Science Univ., Portland, OR, USA

209 (+)-5a Compound, but not nociceptin, excited projection neurons in rat periaqueductal gray slices
L.-W. Tung (1), L.-C. Chiu (1, 2). (1) Grad. Inst. and (2) Dept. Pharmacology, Coll. Medicine, National Taiwan Univ., Taiwan
RECEPTOR PHOSPHORYLATION, DESENSITIZATION, TRAFFICKING AND DOWNREGULATION

210 Differential desensitization of pre- and postsynaptic mu opioid receptors regulating POMC neurons
R.L. Pennock, S.T. Hengtes. Dept. of Biomedical Sciences, Colorado State University, Fort Collins, CO, USA

211 Prolonged stimulation of μ-opioid receptors in locus coeruleus neurons induces β-arrestin-2-dependent heterologous desensitization of α₁-adrenoceptors

212 Agonist-selective patterns of mu-opioid receptor phosphorylation revealed by phosphosite-specific antibodies
C. Doll (1), J. Konietzko (2), F. Pöll (1), T. Koch (2), V. Höltl (2), S. Schulz (1). (1) Institute of Pharmacology and Toxicology, Univ. Hospital, Friedrich Schiller Univ. Jena, (2) Institute of Pharmacology and Toxicology, Univ. Hospital, Otto-von-Guericke-Univ., Magdeburg, Germany

213 Interactions of gonadal steroids and acute stress on levels of phosphorylated mu opioid receptors in the rat hippocampus

214 Mu-opioid receptor desensitization in the ventral tegmental area
J. D. Lowe, C. P. Bailey. Univ. of Bath, Dept. of Pharmacy & Pharmacology, Bath, UK

215 Morphine-induced mu-opioid receptor mediated desensitization of GIRK conductance in locus coeruleus neurons of RMOR mice
A. Madhavan, J.L. Whistler. Ernest Gallo Clinic and Research Center, UCSF, Emeryville, CA, USA

216 Mu and delta opioid receptor heteromerization: The importance of being trafficked
L. Milan-Lobo, J. Enquist, J.L. Whistler. Ernest Gallo Clinic and Research Center, Dept. of Neurology, Univ. of California San Francisco, Emeryville, CA, USA

217 Correlating MOR ligand induced receptor internalization with acute antinociceptive tolerance
C. Dooley, J. Misler, L. Li, K. Reilley, S. Eans, J. McLaughlin. Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL, USA

BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS
**INRC/CPDD Symposium 2**

**HUMAN BRAIN IMAGING OF OPIOID RECEPTORS**

Chairs: Woody Lin and Steve Grant

- **2:00** *Imaging opioid effects on brain systems*
  - Lino Becerra, McLean Hospital, USA

- **2:30** *Mu-opioid receptors and cocaine addiction*
  - David Gorelick, NIDA IRP, USA

- **3:00** *Development and clinical use of a PET radioligand for the kappa receptor*
  - Diana Martinez, Columbia University, USA

- **3:30** *Endogenous opioid system modulation of motivation circuitry*
  - Jon-Kar Zubieta, University of Michigan, USA

**Oral Communications 14**

**HIGH TECH TREATMENT**

Chairs: Alan J. Budney and Steven J. Ondersma

- **2:00** *Telemedicine-based therapy for rural offenders with a history of hazardous drinking*
  - M. Staton-Tindall, C. Leukefeld, M. Webster, R. Freeman, University of Kentucky, Lexington, KY

- **2:15** *Computer-assisted delivery of behavioral treatment for cannabis use disorders: Preliminary results from a controlled trial and implications for dissemination*
  - A. J. Budney¹, C. Stanger¹, P. Costello¹, S. Fearer¹, D. D. Walker², W. K. Bickel¹, ¹University of Arkansas for Medical Sciences, Little Rock, AR, ²University of Washington, Seattle, WA

- **2:30** *Computer-delivered psychosocial treatment for offenders with substance use disorders*
  - S. Sacks¹, L. Marsch², M. Chaple¹, ¹Center for the Integration of Research & Practice, National Development & Research Institutes, New York, NY, ²Center for Technology & Health, National Development & Research Institutes, New York, NY

- **2:45** *A randomized clinical trial of a computer-delivered brief intervention for post-partum drug, alcohol, and tobacco use: Three-month outcomes*
  - S. J. Ondersma¹, D. S. Sviks², J. R. Beatty¹, N. Lockhart¹, ¹Wayne State University, Detroit, MI, ²Virginia Commonwealth University, Richmond, VA

- **3:00** *Impulsivity, biofeedback, and substance abuse treatment*
  - D. C. Lott¹², A. Yang³, ¹Linden Oaks Hospital, Naperville, IL, ²Psychiatry, University of Illinois at Chicago, Chicago, IL, ³Psychiatry and Behavioral Neuroscience, University of Chicago, Chicago, IL

- **3:15** *Is virtual reality the best approach for cue exposure treatment?*
  - O. García-Rodríguez¹, I. Pericot-Valverde³, M. Ferrer-García², R. Secades-Villa¹, J. Gutiérrez-Maldonado², ¹Psychology, University of Oviedo, Oviedo, Spain, ²Personality, assessment and psychological treatments, University of Barcelona, Barcelona, Spain

- **3:30** *Ecological Momentary Assessment of self-identified reasons for specific instances of drug use among participants with and without hepatitis C*
3:45 Practicing relapse prevention in artificial reality environments: Using computer simulations as an adjunct for treatment in veterans with alcohol use disorder
M. Verduin¹, S. LaRowe²,³, R. Joyce¹, H. Myrick²,³, C. Bowers¹, J. Cannon-Bowers¹,
¹University of Central Florida, Orlando, FL, ²Charleston VAMC, Charleston, SC, ³Medical University of South Carolina, Charleston, SC

Oral Communications 15
Rave Reviews: Club Drugs and Hallucinogens

Chairs: Roland R. Griffiths and Jillian H. Broadbear

2:00 In vivo neurochemistry of designer methcathinone analogs abused by humans
M. H. Baumann¹, M. A. Ayestas¹, R. B. Rothman¹, N. V. Cozzi², ¹Translational Pharmacology Sect., IRP, NIDA, NIH, Baltimore, MD, ²Dept. of Pharmacology, University of Wisconsin School of Med. & Public Health, Madison, WI

2:15 Effect of rat strain and ambient temperature on the hypothermic and locomotor stimulant properties of 4-methylmethcathinone
M. Wright¹, D. Angrish², S. Aarde¹, K. Creehan¹, T. J. Dickerson², M. A. Taffe¹, ¹CNAD, The Scripps Research Institute, La Jolla, CA, ²Department of Chemistry, The Scripps Research Institute, La Jolla, CA

2:30 How does exposure to a ‘binge’ dose of MDMA affect behavior of rats trained in a three-way drug discrimination?
J. H. Broadbear, V. Smithies, School of Psychology and Psychiatry, Monash University, Clayton, VIC, Australia

2:45 Human psychopharmacology and dose-effects of salvinorin A, a kappa-opioid agonist hallucinogen present in the plant Salvia divinorum
M. W. Johnson¹, K. A. MacLean¹, C. R. Reissig¹, T. E. Prisinzano², R. R. Griffiths¹, ¹Johns Hopkins University School of Medicine, Baltimore, MD, ²The University of Kansas, Lawrence, KS

3:00 Piperazine containing party pills—effect of an acute dose of trifluoromethylphenylpiperazine on executive functioning using the Stroop paradigm
L. E. Curley¹², R. R. Kydd¹², I. J. Kirk⁴², B. R. Russell¹², ¹School of Pharmacy, The University of Auckland, Auckland, New Zealand, ²Centre for Brain Research, The University of Auckland, Auckland, New Zealand, ³Department of Psychological Medicine, The University of Auckland, Auckland, New Zealand, ⁴Department of Psychology, The University of Auckland, Auckland, New Zealand

3:15 Mephedrone, patterns of use, effects, risk profile and abuse liability
A. R. Winstock¹, J. Marsden², L. Mitcheson¹, ¹Addiction, South London and Maudsley NHS Trust and KCL, London, United Kingdom, ²National Addiction Centre, Kings College London, London, United Kingdom

3:30 Pharmacokinetics of oral 3,4-methylenedioxyamphetamine in humans
M. J. Baggott¹, L. Li¹, G. P. Galloway¹, M. A. Huestis¹, K. Scheidweiler², A. Barnes², J. Mendelson¹, ¹Addiction Pharmacology, California Pacific Medical Center Research Institute, San Francisco, CA, ²Chemistry and Drug Metabolism, Intramural Research Program, NIDA, Baltimore, MD
Wednesday, June 22, 2011

3:45  *Psilocybin dose-effects: Ascending dose sequence associated with greater persisting positive effects at higher doses*
  R. R. Griffiths, M. W. Johnson, Psychiatry and Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD

**Symposium IX**

**NUTRITION AND ADDICTION: FOOD FOR THOUGHT**

Chairs: Rao Rapaka and David Shurtleff

2:00  *Dopamine receptors in addiction-like reward dysfunction and compulsive eating in obese rats*
  Paul Kenny, Laboratory of Behavioral and Molecular Neuroscience, The Scripps Research Institute, Jupiter, FL

2:30  *Iron and the dopaminergic system*
  James R. Connor, College of Medicine, Penn State Milton S. Hershey Medical Center, Hershey, PA

3:00  *Neurochemistry of drug action: Insights from proton magnetic resonance spectroscopic imaging and their relevance to addiction*
  Perry Renshaw, Brain Institute of the University of Utah, Salt Lake City, UT

3:30  *Parameters regarding neuropsychiatric nutritional requirements for intake of omega-3 highly unsaturated fatty acids*
  Joseph Hibbeln, LMBB, National Institutes Alcohol Abuse and Alcoholism, NIH, Bethesda, MD

**INRC/CPDD Symposium 3**

**NEW PERSPECTIVES ON BUPRENORPHINE**

Chairs: Sandra D. Comer and John Traynor

4:15  *The unique pharmacology of buprenorphine*
  John Traynor, University of Michigan, USA

4:45  *New ligands from an old friend*
  Stephen Husbands, Bath, United Kingdom

5:15  *Buprenorphine: A novel receptor target and mechanism of action*
  Gavril Pasternak, Memorial Sloan Kettering Cancer Center, USA

5:45  *Abuse liability of buprenorphine in humans under various states of opioid physical dependence*
  Sandra Comer, Columbia University, USA

**Oral Communications 16**

**CRAVING ATTENTION: MALES VS. FEMALES**

Chairs: Wendy J. Lynch and Carmela M. Reichel

4:15  *Sex differences in cocaine reinforcement and reinstatement vary with stage of addiction*
  S. E. Doyle, C. Ramoa, W. J. Lynch, Psychiatry & Neurobehavioral Sciences, University of Virginia, Charlottesville, VA
Wednesday, June 22, 2011

4:30  *Sex differences in orexin mediation of locomotion and cocaine-seeking in rats*
  L. Zhou, R. E. See, Neurosciences, Medical University of South Carolina, Charleston, SC

4:45  *Methamphetamine self-administration in female rats*
  C. M. Reichel, M. Van Rooljen, S. M. Ghee, C. Chan, R. E. See, Neurosciences, Medical University of South Carolina, Charleston, SC

5:00  *Sex differences in brain activity following corticotropin-releasing hormone in cocaine-dependent men and women*
  M. Moran-Santa Maria¹, K. Johnson², C. Reed¹, C. McWhite¹, K. Brady¹, ¹Psychiatry and Behavioral Neurosciences, Medical University of South Carolina, Charleston, SC, ²Department of Anesthesia, Stanford University, Stanford, CA

5:15  *Gender differences in neural activity during drug craving and gambling urges: An fMRI study*
  H. Kober¹, C. Lacadie², M. N. Potenza¹³, ¹Psychiatry, Yale University, New Haven, CT, ²Diagnostic Radiology, Yale University, New Haven, CT, ³Neurobiology, Yale University, New Haven, CT

5:30  *The role of dopamine vs. glutamate signaling in the nucleus accumbens on motivation for cocaine: Effects of sex and stage of addiction*
  W. J. Lynch, S. E. Doyle, C. King, C. Ramoa, University of Virginia, Charlottesville, VA

5:45  *Menstrual phase differences in subjective-effects of nicotine response*
  A. Allen, M. al’Absi, D. K. Hatsukami, S. S. Allen, Family Medicine & Community Health, University of Minnesota, Minneapolis, MN

6:00  *Reinstatement of methamphetamine seeking in male and female rats treated with modafinil and allopregnanolone*
  N. Holtz¹, M. Carroll¹, A. Lozama², T. Prisinzano², ¹Psychiatry, University of Minnesota, Minneapolis, MN, ²Medicinal Chemistry, University of Kansas, Lawrence, KS

Symposium X  
Diplomat 1-2  
4:15 - 6:15 PM

CPDD INTERNATIONAL COMMITTEE SYMPOSIUM  
VOLATILE SUBSTANCE MISUSE: A GLOBAL CALL FOR ACTION

Chairs: Flavio Pechansky and Colleen A. Dell

4:15  *Phenomenology, natural history and sociocultural aspects of inhalant use and intoxication*
  Matthew O. Howard, University of North Carolina School of Social Work, Chapel Hill, NC

4:45  *Achievements and challenges in understanding the neuropharmacology of inhalant misuse*
  Silvia Cruz¹, Scott Bowen², ¹Cinvestav, Granjas Coapa, Mexico, ²Wayne State University, Detroit, MI

5:15  *Therapeutic interventions for volatile substance misuse*
  Sarah MacLean, Turning Point Alcohol and Drug Centre, University of Melbourne, Fitzroy, VIC, Australia

5:45  *Discussant*
  Robert Balster, Institute for Drug and Alcohol Studies, Virginia Commonwealth University, Richmond, VA
Oral Communications 17

TEEN SCENE: ADOLESCENT DRUG ABUSE

Chairs: C. Debra M. Furr-Holden and Lisa A. Marsch

4:15 Risk-taking: Influence of tobacco use and peers
E. Cavalca1, T. Liss1, C. Lejuez2, E. Reynolds2, C. DeLottinville1, G. Kong1, S. Krishnan-Sarin1, 1Yale University School of Medicine, New Haven, CT, 2Psychology, University of Maryland, Baltimore, MD

4:30 Comparison of DSM-IV and proposed DSM-5 substance use disorder criteria in US adolescents
B. G. Case1,2,3, J. He3, K. R. Merikangas3, 1Statistics and Services Research, Nathan Kline Institute, Orangeburg, NY, 2Child and Adolescent Psychiatry, New York University School of Medicine, New York, NY, 3Developmental Genetic Epidemiology, National Institute of Mental Health, Bethesda, MD

4:45 Characteristics associated with diversion of scheduled prescription medications among young adolescents
S. E. McCabe, B. T. West, C. J. Teter, J. A. Cranford, P. Ross-Durow, A. M. Young, C. J. Boyd, Institute for Research on Women and Gender, University of Michigan, Ann Arbor, MI

5:00 Are adolescent addictive behaviors associated with adolescent pregnancy?
G. P. Lee1, C. L. Storr2,1, N. S. Ialongo1, S. S. Martins1, 1Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, 2University of Maryland, Baltimore, MD

5:15 The growth of neighborhood disorder and marijuana use among urban adolescents transitioning into young adulthood: Making a case for policy and environmental interventions
C. M. Furr-Holden1, M. H. Lee1, A. J. Milam1, R. M. Johnson2, N. S. Ialongo1, 1Mental Health, Johns Hopkins University, Baltimore, MD, 2Community Health Sciences, Boston University, Boston, MA

5:30 A randomized, controlled trial of buprenorphine dosing regimens for opioid-dependent youth
L. A. Marsch1, S. Moore1, R. Solhkhahi2, 1Center for Technology and Health, National Development and Research Institutes, New York, NY, 2Maimonides Medical Center, New York, NY

5:45 Sequenced vs. integrated treatment for co-occurring depression and substance use disorders in adolescents
H. B. Waldron, P. Rhode, C. W. Turner, J. L. Brody, J. Jorgensen, Oregon Research Institute, Eugene, OR

6:00 The relative risks of osmotic-release methylphenidate treatment for adolescent substance abusers
T. Winhusen1, D. Lewis1, P. Riggs2, R. Davies2, L. Adler3, S. Sonne4, E. Somoza1, 1University of Cincinnati, Cincinnati, OH, 2University of Colorado, Denver, CO, 3VA NY Harbor Healthcare System, New York, NY, 4University of South Carolina, Charleston, SC

BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS
Workshop IX  Regency 1  8:00 - 10:00 PM
GETTING SMART ABOUT DEVELOPING INDIVIDUALIZED SEQUENCES OF HEALTH INTERVENTIONS

Chairs: Susan A. Murphy and Daniel Almirall

Developing dynamic, sequential treatments that optimize substance use outcomes: SMART experimental design principles
  Daniel Almirall, Institute for Social Research, University of Michigan, Ann Arbor, MI

Using SMART design technology to develop an adaptive reinforcement-based treatment strategy for pregnant drug abusers
  Hendree Jones, Substance Abuse Treatment Evaluations and Interventions Program, RTI International, Research Triangle Park, NC

Adaptive approach to naltrexone treatment for alcoholism
  David W. Oslin¹, Kevin G. Lynch², ¹Philadelphia Veterans Affairs Medical Center and ²Psychiatry, University of Pennsylvania Medical Center, Philadelphia, PA

Workshop X  Regency 3  8:00 - 10:00 PM
NIDA RESEARCH RESOURCES – AN UPDATE ON THE NIDA DRUG SUPPLY AND ANALYTICAL SERVICES PROGRAM

Chairs: Hari H. Singh and Rao Rapaka

An update on NIDA drug supply program
  F. Ivy Carroll, RTI International, Research Triangle Park, NC

Procedure for acquisition of inventoried drugs and other chemical substances, their storage and distribution under controlled environment
  Kenneth H. Davis, Jr., RTI International, Research Triangle Park, NC

Procedures for analysis of drugs of abuse in experimental biological samples
  David E. Moody, University of Utah, Lake City, UT

Procedure for X-Ray crystallography of chemical compounds and biological substances
  Jeffrey R. Deschamps, Laboratory of Structural Biology, Naval Research Laboratory, U.S. Department of Navy, Washington, DC

Workshop XI  Diplomat 5  8:00 - 10:00 PM
WHAT’S NEW AT NIDA AND NIH: PEER REVIEW AND OTHER POLICIES THAT AFFECT APPLICANTS

Chairs: Meena Hiremath, Teri Levitin and Mark Swieter
Wednesday, June 22, 2011

Workshop XII
Diplomat 4
8:00 - 10:00 PM

A SYSTEMATIC APPROACH TO SELECTION AND MEASUREMENT IN CLINICAL TRIALS RESEARCH

Considerations in defining a drug use primary outcome measure
George Bigelow, Johns Hopkins University School of Medicine, Baltimore, MD

State of the science on measuring drug use: Biological measures
Kenzie Preston, NIDA, Baltimore, MD

State of the science on measuring drug use: Self report
Kathleen Carroll, Yale School of Medicine, West Haven, CT

Beyond drug use: A systematic consideration of other outcomes in evaluations of treatments for substance use disorders
Stephen T. Tiffany, University at Buffalo, SUNY, Buffalo, NY

Discussant
Dennis M. Donovan, University of Washington School of Medicine, Seattle, WA

Workshop XIII
Diplomat 1-2
8:00 - 10:00 PM

WHEN CLINICAL ADVERSE EVENTS SIGNAL DRUG ABUSE POTENTIAL

Chairs: Edward M. Sellers and Kerri A. Schoedel

Collecting abuse-related information in clinical trials: Weighing the use of structured and unstructured scales
Kathleen T. Brady, Clinical Neurosciences Division, Medical University of South Carolina, Charleston, SC

To like or not to like: What patterns of adverse events are indicative of abuse potential?
Sian Ratcliffe, Clinical Development and Medical Affairs, Pfizer Ltd, Sandwich, United Kingdom

Clinical common sense meets MedDRA: The Investigator’s perspective
Myroslava K. Romach, Kendle Early Stage, Toronto, ON, Canada

FDA guidance on abuse potential-related adverse events assessment
Michael Klein, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, MD

Discussant
Robert S. Mansbach, San Diego, CA

Film Night
Regency 2
7:00 - 10:00 PM

AMERICAN METH (Documentary, 2007)
Directed by Justin Hunt, Narrated by Val Kilmer

Starring James Woods and James Garner
CPDD/INRC Poster Session IV

Great Hall 3-6
7:30 - 9:30 AM

Odd-numbered posters manned first hour;
Even-numbered, second hour

Set-up time begins Wednesday 3:00 P.M.
Must be removed by Thursday 1:00 P.M.

PERINATAL

1. The effect of prenatal cocaine exposure and sex/gender on anthropometric growth through ages 16-17 years
   S. E. Messiah\textsuperscript{1,2}, K. L. Arheart\textsuperscript{2,3}, D. C. Vidot\textsuperscript{1}, M. K. Glavach\textsuperscript{1}, V. H. Accornero\textsuperscript{1}, L. Xue\textsuperscript{1}, S. L. Lipshultz\textsuperscript{1}, T. L. Miller\textsuperscript{1}, E. S. Bandstra\textsuperscript{1}, \textsuperscript{1}Pediatrics, University of Miami Miller School of Medicine, Miami, FL, \textsuperscript{2}Epidemiology and Public Health, University of Miami Miller School of Medicine, Miami, FL

2. Executive function at 12 years in prenatally cocaine-exposed children
   S. Minnes\textsuperscript{1}, M. Min\textsuperscript{1}, L. T. Singer\textsuperscript{2}, E. J. Short\textsuperscript{3}, A. Aguirre\textsuperscript{3}, \textsuperscript{1}Mandel School of Applied Social Sciences, Case Western Reserve University, Cleveland, OH, \textsuperscript{2}School of Medicine, Case Western Reserve University, Cleveland, OH, \textsuperscript{3}Psychology, Case Western Reserve University, Cleveland, OH

3. Perinatal smoking and mood and anxiety disorders
   A. Forray, N. Gotman, H. Howell, B. J. Rounsaville, K. A. Yonkers, Yale School of Medicine, New Haven, CT

4. Prenatal tobacco use and mental health conditions in women at risk for other substance use
   A. Sepulveda, D. Terrell, L. Keyser-Marcus, D. Svikis, Institute for Drug and Alcohol Studies, Virginia Commonwealth University, Richmond, VA

5. Effects of anxiety and depression on treatment of opioid dependence during pregnancy
   M. M. Benningfield\textsuperscript{1}, M. S. Dietrich\textsuperscript{1}, H. E. Jones\textsuperscript{2}, K. Kaltenbach\textsuperscript{3}, S. H. Heil\textsuperscript{4}, S. M. Stine\textsuperscript{5}, M. G. Coyle\textsuperscript{6}, A. M. Arria\textsuperscript{7}, P. Selby\textsuperscript{8}, A. Baewart\textsuperscript{9}, P. R. Martin\textsuperscript{1}, \textsuperscript{1}Vanderbilt University, Nashville, TN, \textsuperscript{2}Johns Hopkins University, Baltimore, MD, \textsuperscript{3}Thomas Jefferson University, Philadelphia, PA, \textsuperscript{4}University of Vermont, Burlington, VT, \textsuperscript{5}Wayne State University, Detroit, MI, \textsuperscript{6}Brown University, Providence, RI, \textsuperscript{7}University of Maryland, College Park, MD, \textsuperscript{8}University of Toronto, Toronto, ON, Canada, \textsuperscript{9}Medical University of Vienna, Vienna, Austria

6. Feto-maternal outcome of pregnancy in women maintained on methadone but using illicit substances
   J. L. Igboekwu, Forensic Psychiatry, Ravenswood Low Secure Hospital, Fareham, United Kingdom

7. Infant pupil diameter in response to opioid administration
   S. H. Heil\textsuperscript{1,2}, D. Gaalema\textsuperscript{1}, S. T. Higgins\textsuperscript{1,2}, S. C. Sigmon\textsuperscript{1,2}, A. Johnston\textsuperscript{1}, \textsuperscript{1}Psychiatry, University of Vermont, Burlington, VT, \textsuperscript{2}Psychology, University of Vermont, Burlington, VT, \textsuperscript{3}Pediatrics, University of Vermont, Burlington, VT

8. Differences in the profile of neonatal abstinence syndrome signs in methadone- vs. buprenorphine-exposed infants
   D. Gaalema\textsuperscript{1}, S. Heil\textsuperscript{1}, T. Scott\textsuperscript{1}, M. Coyle\textsuperscript{2}, K. Kaltenbach\textsuperscript{3}, H. Jones\textsuperscript{4}, P. Martin\textsuperscript{5}, S. Stine\textsuperscript{6}, A. Arria\textsuperscript{7}, \textsuperscript{1}U of Vermont, Burlington, VT, \textsuperscript{2}Brown U, Providence, RI, \textsuperscript{3}Thomas Jefferson U, Philadelphia, PA, \textsuperscript{4}Johns Hopkins U, Baltimore, MD, \textsuperscript{5}Vanderbilt U, Nashville, TN, \textsuperscript{6}Wayne State U, Detroit, MI
9 Absence of sex differences related to the neonatal abstinence syndrome among infants born to women in opioid agonist treatment
A. Unger1, R. Jagsch2, A. Bäwert1, B. Winklbaur1, P. R. Martin3, M. Coyle4, K. Kaltenbach5, S. Heil6, S. Stine7, G. Fischer1, 1Psychiatry, Medical University of Vienna, Vienna, Austria, 2Psychology, University of Vienna, Vienna, Austria, 3Psychiatry, Vanderbilt University School of Medicine, Nashville, TN, 4Center for Young Adult Health and Development, University of Maryland, Maryland, MD, 5Pediatrics, Thomas Jefferson University, Philadelphia, PA, 6Psychiatry, University of Vermont, Burlington, VT, 7Psychiatry, Wayne State University, Detroit, MI

10 Comparison of maternal and neonatal outcome parameters in pregnant opioid-maintained women in a RCT vs. in standardized routine care
V. Metz1, K. Graf-Rohrmeister1, R. Jagsch2, N. Ebner1, J. Würzl1, A. Pribasnig1, C. Aschauer1, G. Fischer1, 1Medical University of Vienna, Vienna, Austria, 2Faculty of Psychology, Vienna University, Vienna, Austria

11 Evidence-based research in pregnant opioid-dependent women: A comparison of two European samples
B. Winklbaur1, K. Graf-Rohrmeister2, R. Jagsch3, A. Baewert1, A. Unger1, V. Metz1, K. Thau1, G. Fischer1, 1Department of Psychiatry & Psychotherapy, Medical University Vienna, Vienna, Austria, 2Department of Neonatology, Medical University Vienna, Vienna, Austria, 3Faculty of Psychology, University of Vienna, Vienna, Austria

12 Effect of cocaine on treatment outcomes in opioid-using pregnant women
S. M. Stine1, P. Thakur1, H. Jones2, G. Fisher3, K. Kaltenbach4, S. Heil5, P. Martin6, M. Coyle7, P. Selby1, 1Psychiatry and Behavioral Neurosciences, Wayne State University, Detroit, MI, 2John’s Hopkins University, Baltimore, MD, 3University of Vienna, Vienna, Austria, 4Thomas Jefferson University, Philadelphia, PA, 5University of Vermont, Burlington, VT, 6Vanderbilt University, Nashville, TN, 7Brown University, Rhode Island, RI

13 Comparison of buprenorphine and methadone treatment among Medicaid enrollees
A. Schuster1,2, K. Stoller3, P. Fagan1,3, 1Johns Hopkins Healthcare LLC, Glen Burnie, MD, 2Health Policy and Management, Johns Hopkins University SPH, Baltimore, MD, 3Department of Psychiatry and Behavioral Sciences, Johns Hopkins University SOM, Baltimore, MD

REWARD AND PUNISHMENT

14 Does tolerance develop to the analgesic, rewarding and pro-emetic effects of oxycodone?
V. Batra, L. M. Schrott, Pharmacology, Toxicology and Neuroscience, Louisiana Health Sciences Center-Shreveport, Shreveport, LA

15 Cholinergic modulation of reinforcement effects in a reinstatement model of drug relapse using sucrose reward
J. A. Pipkin, V. Greenfield, J. Valentine, A. Butt, Psychology, California State University, San Bernardino, San Bernardino, CA

16 Gestational intravenous nicotine increases motivation for sucrose reward in adult rat offspring
R. T. Lacy, L. L. Hord, A. J. Morgan, S. B. Harrod, Psychology, University of South Carolina, Columbia, SC

17 Are Oreo cookies addictive?
F. Leri, A. M. Levy, University of Guelph, Guelph, ON, Canada

18 Individual differences in response to novelty associates with binge-like palatable food intake
N. C. Anastasio1,2, S. J. Stutz1,2, R. G. Fox1,2, J. D. Hommel1,2, K. A. Cunningham1,2, 1Ctr Addiction Research, UTMB, Galveston, TX, 2Pharm & Tox, UTMB, Galveston, TX
Orx/Hcrt neurons, within different subregions of the hypothalamus, are differentially recruited by cues conditioned to cocaine vs. natural reward
R. Martin-Fardon, F. Weiss, Mol and Integrative Neuroscience, The Scripps Research Inst, La Jolla, CA

The effect of the CB1 neutral antagonist PIMSR1 on appetitive disorders
H. H. Seltzman1, P. H. Reggio2, E. L. Gardner3, L. Chun3, Z. X. Xi3, G. H. Bi3, F. Navas, III1, J. A. Marusich1, J. L. Wiley1, 1Research Triangle Institute, Research Triangle Park, NC, 2University of North Carolina, Greensboro, NC, 3National Institute on Drug Abuse, Baltimore, MD

A comparison of the rewarding valences of stimulant treatments in adult and adolescent mice
E. B. Bisen-Hersh1,2, A. M. Myers1, E. A. Walker1,3, 1Neuroscience Program, Temple University, Philadelphia, PA, 2Psychology, Temple University, Philadelphia, PA, 3Pharmaceutical Sciences, Temple University, Philadelphia, PA

Novelty-seeking correlates with a stronger response of adolescent mice to the rewarding properties of cocaine in the conditioned place preference procedure
M. M. Rodriguez-Arias, R. Muñoz, M. A. Aguilar, J. Miñarro, Psychobiology, School of Psychology, Valencia, Spain

Effects of punishment on seeking and consumption of cocaine and water reinforcers
M. A. Kausch, A. M. Gancarz, L. J. Belay, D. R. Lloyd, M. A. Robble, J. B. Richards, Research Institute on Addictions, State University of New York at Buffalo, Buffalo, NY

Punishment of cocaine choice: Effects of delaying punishment
W. L. Woolverton1, K. Freeman1, J. Myerson2, L. Green2, 1Psychiatry, Univ of Mississippi Medical Ctr, Jackson, MS, 2Psychology, Washington University, St. Louis, MO

Exposure to alcohol during adolescence or adulthood alters the rewarding effects of cocaine in adult rats
M. Hutchison, A. L. Riley, Psychology, American University, Washington, DC

STIMULANTS: ANIMAL II

Activation of the corticotropin-releasing factor system in the amygdala is responsible for the reinstatement of methamphetamine-seeking behavior induced by footshock stress
Y. Nawata, K. Kitaichi, T. Yamamoto, Department of Pharmacology, Faculty of Pharmaceutical Science, Nagasaki International University, 2825-7 Huis Ten Bosch Sasebo, Japan

Escalating vs. binge methamphetamine exposure reveals vulnerability of dopamine regulation in ventral tegmental area
C. Keller, M. F. Salvatore, S. Spann, G. F. Guerin, N. E. Goeders, Pharmacology, Toxicology & Neuroscience, LSU Health Sciences Center-Shreveport, Shreveport, LA

Escalation and reinstatement of stimulant seeking in adolescent and adult rats
M. E. Carroll, N. A. Holtz, J. J. Anker, Psychiatry, University of Minnesota, Minneapolis, MN

Stimulus control of escalated cocaine intake and escalation under short access sessions
J. Beckmann, C. Gipson, M. Bardo, University of Kentucky, Lexington, KY

Spiking brain cocaine levels and the implications for a model of addiction
C. Dobrin, B. A. Zimmer, D. C. Roberts, Physiology and Pharmacology, Wake Forest University School of Medicine, Winston Salem, NC

Relationship between impulsivity and amphetamine conditioned place preference
J. R. Yates, M. T. Bardo, Psychology, University of Kentucky, Lexington, KY
32 Identifying traits that track with an increased risk for addiction vulnerability
R. G. Fox1,2, N. C. Anastasio1,2, S. J. Stutz1,2, F. G. Moeller1, R. B. Emeson1,
K. A. Cunningham1,2, 1Ctr Addiction Research, UTMB, Galveston, TX, 2Pharm & Tox, UTMB,
Galveston, TX. 3Psych & Behav Sci, UTHSC, Houston, TX, 4Ctr Molec Neurosci, Vanderbilt,
Nashville, TN

33 Prenatal stress and genetic background interact to determine cocaine-seeking behavior in mice
T. E. Kippin1,2, J. C. Campbell1, K. K. Szumlinski1,2, C. P. Knight1, K. Ploense1, N. Woodward1,
1Psychology, University of California at Santa Barbara, Santa Barbara, CA, 2Neuroscience
Research Institute, University of California, Santa Barbara, CA

34 Effect of single-prolonged stress, a model of PTSD, on anxiety and cocaine-induced behaviors
N. Enman, E. M. Unterwald, Pharmacology & Center for Substance Abuse Research, Temple
University School of Medicine, Philadelphia, PA

35 Effects of cross-drug preexposure on cocaine- and vanoxerine-induced conditioned taste
aversions
K. M. Serafine1, K. C. Rice2, A. L. Riley1, 1Psychology- Psychopharmacology Laboratory,
American University, Washington, DC, 2Chemical Biology Research Branch, National
Institute on Drug Abuse and National Institute on Alcohol Abuse and Alcoholism,
Bethesda, MD

36 Accumbens dopamine bi-directionally regulates methamphetamine-seeking in mice
K. D. Lominac, K. K. Szumlinski, Psychology, University of California, Santa Barbara, Santa
Barbara, CA

37 Social interaction- vs. cocaine conditioned place preference is associated with a differential
activation of nucleus accumbens shell cholinergic interneurons
G. Zernig, M. Fritz, S. Klement, R. El Rawas, A. Saria, Experimental Psychiatry Unit, General
Psychiatry and Social Psychiatry, Medical University Innsbruck, Innsbruck, Austria

38 Accumbens histone deacetylases actively regulate cocaine-seeking in cocaine-experienced mice
B. W. Miller1, T. E. Kippin1, E. J. Nestler2, K. K. Szumlinski1, 1Psychology, University of
California, Santa Barbara, Santa Barbara, CA, 2Mount Sinai School of Medicine, New
York, NY

39 Profile of glutamate anomalies observed within the accumbens core during short-term
withdrawal from excessive cocaine intake
S. M. Webb, B. W. Miller, A. D. Sacramento, A. Haider, K. D. Lominac, T. E. Kippin, O. Ben-
Shahar, K. K. Szumlinski, Psychology, University of California, Santa Barbara, Santa
Barbara, CA

40 LY379268, a selective group II metabotropic glutamate receptor agonist, dose dependently
decreases methamphetamine self-administration in rats
J. T. Crawford, D. C. Roberts, T. J. Beveridge, Physiology and Pharmacology, Wake Forest
University Health Sciences, Winston Salem, NC

41 Manipulations of ventral prefrontal cortex Group1 mGluRs do not affect incubation of cue-
induced reinstatement of cocaine-seeking behavior
O. Ben-Shahar, A. Sacramento, A. Caruana, S. Webb, E. Gordon, K. Ploense, N. Rudy,
T. E. Kippin, K. K. Szumlinski, Psychology, UCSB, Santa Barbara, CA

42 Contribution of corticosterone and neurosteroids to the efficacy of metyrapone in reducing
cocaine-related behaviors
C. D. Schmoutz, G. F. Guerin, N. E. Goeders, LSU Health Sciences Center, Shreveport, LA
43 Determining efficacious doses of metyrapone and oxazepam combinations to treat methamphetamine cue-reactivity in rats
E. M. Cornett, G. F. Guerin, N. E. Goeders, Pharmacology, Toxicology and Neuroscience, Louisiana State University Health Sciences Center, Shreveport, LA

44 Inhibiting glycine transporter-1 during extinction training attenuates reacquisition of cocaine self-administration in squirrel monkeys and rats
C. Achat-Mendes1, B. A. Nic Dhonnchadha2, L. Hede-Brierley2, J. Whaley2, D. M. Platt1, K. M. Kantak2, R. D. Spealman1, 1Harvard Medical School/NEPRC, Southborough, MA, 2Boston University, Boston, MA

45 Preclinical evaluation of GZ-793A as a pharmacotherapy for methamphetamine abuse

46 PPARα as a therapeutic target in drug abuse
W. R. Miller1,2, S. Stutz3, R. Fox3, K. Cunningham3, K. Dineley2, 1Neuroscience, University of Texas Medical Branch, Galveston, TX, 2Neurology, University of Texas Medical Branch, Galveston, TX, 3Center for Addiction Research, Pharmacology and Toxicology, University of Texas Medical Branch, Galveston, TX

47 Cocaine self-administration modifies hippocampal neuron morphology in Lewis rats
E. Ambrosio1, M. Miguëns1, A. Kastanauskaitė1, S. M. Coria1, I. Ballestros-Yañez2, J. De Felipe3, 1Psychobiology, UNED, Madrid, Spain, 2Inorganic, Organic and Biochemistry, Castilla La Mancha University, Ciudad Real, Spain, 3Cajal Institute and Cortical Circuits Laboratory, Superior Council of Scientific Research, and Polytechnical University, Madrid, Spain

48 Methamphetamine-induced cerebral blood flow changes and its implications as a risk for Parkinson's disease
S. M. Kousik1, T. C. Napier1,2, P. M. Carvey1, 1Pharmacology, Rush University, Chicago, IL, 2Center for Compulsive Behavior and Addiction, Chicago, IL

49 Repeated administration of a mutant cocaine esterase: Effects on plasma cocaine levels, cocaine-induced cardiovascular activity, and immune responses in rhesus monkeys
G. T. Collins1, R. L. Brim1, D. Narasimhan1, K. R. Noon1, N. W. Lukacs2, R. K. Sunahara1, J. H. Woods1, M. C. Ko1, 1Pharmacology, University of Michigan Medical School, Ann Arbor, MI, 2Pathology, University of Michigan Medical School, Ann Arbor, MI

IMAGING

50 Orbital frontal cortex activity predicts executive cognitive functioning in early adolescents
Z. Zhai1, S. Pajtek2, E. C. Long2, B. Luna2, T. A. Ridenour1, D. B. Clark2, 1University of Pittsburgh, Pittsburgh, PA, 2Western Psychiatric Institute and Clinic, Pittsburgh, PA

51 “Unseen” vulnerability: Cocaine relapse is associated with limbic activation to drug cues presented outside awareness
A. R. Childress1,2, J. J. Suh1,2, R. N. Ehrman1,2, Y. Li1, Z. Wang1, A. V. Hole1,2, R. Fabianski1, D. Willard1, T. Franklin1, M. Goldman1, R. Szuces-Reed1,2, J. Magland1, C. Tjoa1, C. P. O’Brien1,2, 1Univ. of Pennsylvania School of Medicine, Philadelphia, PA, 2VA VISN 4 MIRECC, Philadelphia, PA

52 Can an acute dose of baclofen reduce the risk of relapse in cue-vulnerable smokers?
53 Characterizing brain substrates of affect dysregulation in cocaine dependence
J. Suh1,2, R. Ehrman1,2, Y. Li1, Z. Wang1, D. Willard1, R. Fabianski1, R. Carson1, R. Hazan1, J. Shin1, R. Szucs-Reed1,2, M. Goldman1, T. Franklin1, C. P. O'Brien1,2, A. R. Childress1,2, 1Dept of Psychiatry, U of Pennsylvania, Philadelphia, PA, 2MIRECC, VAMC, Philadelphia, PA

54 Feeling left out? Predicting the behavioral and brain response to social stress
C. A. Hanlon1,2, A. Lack2, L. J. Porrino2, 1Medical University of South Carolina, Charleston, SC, 2Wake Forest University School of Medicine, Winston-Salem, NC

55 N-acetylcysteine changes glutamate levels in cocaine-dependent subjects: An open label magnetic resonance spectroscopy study
L. Schmaal, A. E. Goudriaan, W. Van den Brink, Academic Medical Center, Amsterdam, Netherlands

56 DCM of working memory system in cocaine dependence
L. Ma1, J. L. Steinberg1, K. M. Hasan2, P. A. Narayana2, L. A. Kramer2, F. G. Moeller1, 1Department of Psychiatry and Behavioral Sciences, University of Texas Health Science Center, Houston, TX, 2Department of Diagnostic and Interventional Imaging, University of Texas Health Science Center, Houston, TX

57 In vivo evidence for lower striatal vesicular monoamine transporter in cocaine abusers
R. Narendran1, D. Martinez2, B. Lopresti1, N. S. Mason1, P. Keating1, M. Himes1, C. Mathis1, W. G. Frankle1, 1Radiology, University of Pittsburgh, Pittsburgh, PA, 2Psychiatry, Columbia University Medical Center, New York, NY

58 PET imaging of dopamine transmission in cocaine dependence predicts response to treatment
D. Martinez, K. Carpenter, F. Liu, M. Slifstein, A. Broft, A. Calvo-Friedman, H. Kleber, E. Nunes, Columbia University/NYSPI, New York, NY

59 Functional neuroimaging of the subjective effects of intranasal d-amphetamine
T. H. Kelly1, C. S. Kluemper1, C. E. Emurian1, C. R. Corbly1, C. R. Martin1, J. E. Joseph2, J. A. Lile1, 1University of Kentucky, Lexington, KY, 2Medical University of South Carolina, Charleston, SC

60 Amphetamine-opioid interactions in the human brain reward system—a PET study using [11C]carfentanil
J. Guterstam, N. Jayaram-Lindström, S. Cervenka, L. Farde, C. Hallin, J. Franck, Karolinska Institutet, Stockholm, Sweden

61 Neural correlates of reward processing in methamphetamine use
G. Tau1,2, T. Pampanini1,2, T. Torres-Sanchez1,2, P. Wang1,2, B. Graniello1,2, F. Tian1,2, B. Gunter1,2, F. Garcia1,2, Z. Wang1,2, D. Martinez2, B. S. Peterson1,2, 1Child and Adolescent Psychiatry, Columbia University / New York State Psychiatric Institute, New York, NY, 2Psychiatry, Columbia University / New York State Psychiatric Institute, New York, NY

62 Altered brain high energy phosphate levels in methamphetamine-dependent women
Y. H. Sung1, D. A. Yurgelun-Todd1,3,4, X. Shi2, D. G. Kondo1, K. J. Lundberg1, E. C. McGlade1, R. E. Harrell1, T. L. Hellem1, R. S. Huber1, K. K. Delmastro1, S. E. Kim2, E. K. Jeong2, P. F. Renshaw1,3,4, 1Dept. of Psychiatry, Brain Institute, Salt Lake City, UT, 2Depat. of Radiology, UCAIR, Salt Lake City, UT, 3VISN 19 MIRECC, Salt Lake City, UT, 4USTAR, Salt Lake City, UT
Differential neuroanatomical correlates of adolescent and adult methamphetamine abuse

I. Lyoo, S. J. Yoon, T. S. Kim, J. Hwang, J. E. Kim, S. J. Bae, D. J. Kim, P. F. Renshaw

Investigating changes in fractional anisotropy in white matter of methamphetamine users using diffusion tensor imaging


The effect of methamphetamine on grey matter structure in the human brain using voxel-based morphometry


Differentiating the association between cigarette smoking and methamphetamine use on gray matter abnormalities seen in methamphetamine abusers


Reduced hippocampal volumes in regular cannabis users

V. Lorenzetti, N. Solowij, A. Fornito, D. Lubman, M. Takagi, C. Pantelis, M. Seal

Unexpected changes in striatal activation with treatment during the guess/reward fMRI task in comorbid MDD-CUD youth

J. R. Cornelius, H. Aizenstein, T. Chung, A. Douaihy, I. Salloum, D. Daley

Brain activity related to decision-making among adolescents in substance abuse treatment


Neuroimaging heavy cannabis users vs. sporadic and non-users: Working memory and decision-making

A. E. Goudriaan, J. Cousijn, L. Porrino, W. van den Brink, D. J. Veltman, R. W. Wiers

Nicotine effects on default mode and extra-striate resting state networks

J. Tanabe, E. Nyberg, L. Martin, D. Cordes, E. Kronberg, J. Tregellas
72 Functional MRI-based support vector machine classification of tobacco smokers’ nicotine craving: Possible use in real-time neurofeedback
Y. S. Shah¹, S. J. Peltier¹, L. Hernandez-Garcia¹, D. C. Noll¹, K. L. Phan¹, J. K. Zubieta¹, M. K. Greenwald², ¹University of Michigan, Ann Arbor, MI, ²Wayne State University, Detroit, MI

73 Anterior cingulate proton spectroscopy glutamate levels differ as a function of smoking cessation outcome
Y. Mashhoon¹, A. C. Janes¹, J. E. Jensen¹, A. P. Prescott¹, G. Pachas², P. F. Renshaw¹, M. Fava², A. E. Evins², M. J. Kaufman¹, ¹Neuroimaging Center, McLean Hospital | Harvard Medical School, Belmont, MA, ²Massachusetts General Hospital | Harvard Medical School, Boston, MA

74 The effects of nicotine and non-nicotine components of cigarette smoking on cerebral blood flow
M. Addicott¹, R. Kozink¹, T. Harshbarger², B. Froeliger¹, D. Ban¹, J. Rose¹, F. J. McClernon¹, ¹Psychiatry, Duke Medical Center, Durham, NC, ²Radiology, Duke Medical Center, Durham, NC

GENETICS
75 Cocaine-induced changes in prefrontal cortex glutamate receptor expression depend upon Homer1 and Homer2 proteins
A. W. Ary, B. W. Miller, C. L. McKenna, L. M. Smith, K. K. Szumlinski, Psychology, University of California, Santa Barbara, Santa Barbara, CA

76 Sway: A new genetic model for diminished cocaine-reinforced behavior
K. Grasing¹, S. He¹, Y. Yang¹, E. Bryda², ¹Substance Abuse Research Laboratory, VA Medical Center, Kansas City, MO, ²Veterinary Medicine, University of Missouri, Columbia, MO

77 Dopamine transporter, substance abuse, and sex differences in novelty-seeking
R. Ashare¹, C. Hodgkinson², M. Enoch², D. Goldman², R. Sinha¹, ¹Yale University, New Haven, CT, ²LNG at NIAAA, Bethesda, MD

78 Compulsive drug-taking behavior: Interaction of specific genetic variants with response to cocaine vaccine on treatment effectiveness in cocaine dependence
J. A. Lindsay, D. Nielsen, T. R. Kosten, Baylor College of Medicine, Houston, TX

79 Preliminary pharmacogenetic study of treatment for methamphetamine dependence
K. G. Heinzerling, J. McCracken, L. Ray, A. Swanson, S. Shoptaw, UCLA, Los Angeles, CA

80 Genome-wide association study of addiction to smoking and other substances of abuse
M. D. Li¹, S. G. Yi¹, J. Z. Ma², ¹Psychiatry and Neurobehavioral Sciences, University of Virginia, Charlottesville, VA, ²Public Health Sciences, University of Virginia, Charlottesville, VA

81 ANKK1 polymorphisms may influence beta2-nicotinic acetylcholine receptor availability in nonsmokers
K. Cosgrove¹, B. Yang¹, I. Esterlis¹, D. Lee¹, R. Gadsden¹, S. Helmbrecht¹, F. Bois¹, J. Seibyl², G. Tamagnan², J. Staley¹, J. Geiernter¹, ¹Psychiatry, Yale University School of Medicine, New Haven, CT, ²Institute for Neurodegenerative Disorders, New Haven, CT

82 Learning and memory differences in the dopamine receptor D2 Taq1A & C957T gene SNP among HIV-positive alcohol abusers
P. Khatakar¹, V. Bryant¹, M. José-Miguez Perez¹, R. Malow¹, B. Lerner¹, J. Dévieux¹, R. Rosenberg¹, N. Gandhi², M. Nair², ¹Stempel College of Social Work and Public Health, Florida International University, North Miami, FL, ²Immunology, Institute of Neuro-Immune Pharmacology, Florida International University, Miami, FL
83 Comparative gene expression profiling analysis of lymphoblastoid cells in heroin addicts
C. Chen¹, D. Liao², M. Cheng³, S. Hsu¹, C. Lai², H. Tsai¹, ¹National Health Research Institutes, Zhunan, Taiwan, ²Bali Psychiatric Center, Taipei, Taiwan, ³Yuli Mental Health Research Center, Hualien, Taiwan

84 GABRA2 and parental control in relation to adolescent substance use: The TRAILS study
H. E. Creemers¹,², R. Veenstra³, D. Dick², J. Meyers², F. van Oort², W. Vollebergh³, J. Ormel³, F. Verhulst², A. Huizink¹, ¹University of Amsterdam, Amsterdam, Netherlands, ²Erasmus Medical Center, Rotterdam, Netherlands, ³Groningen University, Groningen, Netherlands, ⁴Virginia Commonwealth University, Richmond, VA, ⁵Utrecht University, Utrecht, Netherlands

85 Genetic and environmental contributions to cannabis withdrawal and abuse/dependence in a national adult twin sample
N. O. Nat¹, A. Agrawal², H. E. Creemers¹, A. C. Huizink¹, N. G. Martin³, M. T. Lynskey², ¹University of Amsterdam, Amsterdam, Netherlands, ²Washington University School of Medicine, Saint Louis, MO, ³Queensland Institute of Medical Research, Herston, QLD, Australia

86 A low-density gene array association study implicates different pathways in primary affective disorders vs. those comorbid with substance dependence
D. Cui¹, H. Kranzler³, H. Zhang², L. Price², L. Carpenter³, A. Tyrka³, J. Gelernter³, ¹Shanghai Mental Health Center, Shanghai Jiao Tong University, School of Medicine, Shanghai, China, ²Psychiatry, Yale University, New Haven, CT, ³Psychiatry, University of Pennsylvania, Philadelphia, PA, ⁴Psychiatry, Brown University, Providence, RI

CANNABINOIDS

87 Discriminative properties and cytotoxicities of cannabinoid receptor agonist CP 55,490
M. Funada, K. Tomyama, K. Wada, Drug Dependence Research, NIMH, NCNP, Kodaira, Japan

88 Recipe for THC-like abuse: JWH indole-derived cannabinoids and K2/Spice
J. A. Marusich¹, J. Huffman², J. Wiley¹, ¹RTI, International, Research Triangle Pk, NC, ²Clemson University, Clemson, SC

89 The relationship between objective and subjective effects measures used in abuse liability testing: An exploratory analysis using opioid agonists
M. J. Shram¹, K. A. Schoedel¹, B. Chakraborty¹, B. Setnik², V. Goli², M. K. Romach¹, ¹Kendle Early Stage, Toronto, ON, Canada, ²King Pharmaceuticals, Raleigh, NC, ³Departments of Anesthesiology, Psychiatry and Behavioral Sciences, Duke University, Durham, NC, ⁴Department of Psychiatry, University of Toronto, Toronto, ON, Canada

90 Marijuana self-administration in high- and low-impulsive sensation seekers using a modified progressive-ratio procedure

91 Childhood ADHD and adult marijuana use
K. J. Derefinko¹, M. MacLean¹, P. A. Graziano¹, B. S. Molina², E. Gnagy¹, W. E. Pelham¹, ¹Florida International University, Miami, FL, ²University of Pittsburgh, Pittsburgh, PA, ³Buffalo State College, Buffalo, NY

92 Vulnerability for SUD, drug use and risk for violent behavior
M. D. Reynolds, R. E. Tarter, L. Kirisci, CEDAR, School of Pharmacy, University of Pittsburgh, Pittsburgh, PA
93 Acute stress response in marijuana smokers with and without past trauma exposure

G. Bedi1,2, Z. D. Cooper1,2, M. Haney1,2, 1Columbia University, New York, NY, 2NYSPI, New York, NY

94 Effect of stress on attentional bias and cognition in marijuana-dependent individuals

K. L. Price, N. A. Baker, K. S. Nicholas, K. S. Allenby, C. B. McWhite, K. S. Fischer, K. T. Brady, Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina, Charleston, SC

95 Verbal and visual learning and memory in short- and long-term heavy cannabis users

N. Solowij2, M. Takagi1,3, M. L. Seal4, V. Lorenzetti1, I. H. Harding1, D. I. Lubman5, M. Yücel1,3, 1Psychiatry, University of Melbourne, Carlton South, VIC, Australia, 2Psychology, University of Wollongong, Wollongong, VIC, Australia, 3Orygen Youth Health Research Centre, Melbourne, VIC, Australia, 4Murdoch Children’s Research Institute, Melbourne, VIC, Australia, 5Turning Point Alcohol and Drug Centre, Melbourne, VIC, Australia

96 Oral THC does not block the discriminative stimulus effects of marijuana in cannabis-dependent individuals

L. H. Lundahl, C. L. Steinmiller, M. K. Greenwald, C. E. Johanson, Psychiatry and Behavioral Neuroscience, Wayne State University School of Medicine, Detroit, MI

97 Dose effects of oral THC in heavy cannabis users

R. Vandrey, M. L. Stitzer, Johns Hopkins University, Baltimore, MD

98 Cannabis withdrawal syndrome in DSM-V

D. Gorelick1, K. H. Levin1, M. L. Copersino2, S. J. Heishman1, F. Liu1, D. L. Boggs3, D. L. Kelly3, 1IRP, NIH/NIDA, Baltimore, MD, 2McLean Hospital/Harvard Medical School, Belmont, MA, 3MPRC, Univ. of Maryland, Baltimore, MD

99 A disability-adjusted cannabis withdrawal scale reveals withdrawal symptoms associated with relapse

D. Allsop1, M. M. Norberg1, A. J. Budney2, J. Copeland1, 1Medicine, University of New South Wales, Sydney, NSW, Australia, 2Psychiatry, University of Arkansas for Medical Sciences, Little Rock, AR

100 Effect of tobacco cigarette smoking on marijuana withdrawal and relapse


101 Impact of cigarette use on treatment outcome in blunt smokers and other cannabis users in a cannabis-dependent sample

D. J. Brooks1, J. J. Mariani2,1, F. R. Levin2,1, 1Substance Abuse, NYSPI, New York, NY, 2Psychiatry, Columbia University, New York, NY

102 Cognitive behavioral therapy and the nicotine transdermal patch for dual nicotine and cannabis dependence: A pilot study

K. P. Hill, L. Toto, S. F. Greenfield, G. Trksak, J. M. Rodolico, S. E. Lukas, Alcohol and Drug Abuse Treatment Program, McLean Hospital, Belmont, MA

103 Motivational enhancement and mindfulness meditation for young adult female marijuana users

M. A. de Dios1,2, D. Herman1,2, C. Hagerty2, B. J. Anderson2, W. Britton1,2, M. Stein2,3, 1Psychiatry and Human Behavior, Alpert Medical School of Brown University, Providence, RI, 2General Medicine Research Unit, Butler Hospital, Providence, RI, 3Medicine, Alpert Medical School, Providence, RI

104 Marijuana purchasing behavior among young-adult marijuana users

R. Collins, P. C. Vincent, C. Vetter, M. Lambiase, M. Insana, D. Saltino, Community Health and Health Behavior, University at Buffalo, Buffalo, NY
105 Marijuana users' social networks, marijuana use, and problems
P. C. Vincent, R. L. Collins, S. Wilson, J. Smith, M. Insana,
1Health Behavior/SPHHP, University at Buffalo, SUNY, Buffalo, NY,
2Research Institute on Addictions, Buffalo, NY

106 Randomized controlled trial of a web-based intervention for cannabis use
S. Rooke, J. Copeland, M. Norberg, J. McCambridge,
1National Cannabis Prevention and Information Centre, University of New South Wales, Randwick, NSW, Australia,
2University of London, London, United Kingdom

107 Randomized controlled trial of a brief cannabis intervention delivered by telephone
P. J. Gates, J. Copeland, M. Norberg, E. DiGiusto,
1National Cannabis Prevention and Information Centre, Sydney, NSW, Australia,
2National Drug and Alcohol Research Centre, Sydney, NSW, Australia

108 A pilot study of postal treatment for cannabis dependence
J. Copeland, T. E. Wright, M. M. Norberg, K. Hickey,
1National Cannabis Prevention and Information Centre, University of New South Wales, Randwick, NSW, Australia,
2National Drug and Alcohol Research Centre, University of New South Wales, Randwick, NSW, Australia

109 Towards defining primary outcomes in treatment studies for cannabis use disorders: Results from confirmatory factor analysis of outcomes from three randomized controlled trials
E. N. Peters, C. Nich, K. M. Carroll, Psychiatry, Yale University School of Medicine, New Haven, CT

110 Associations of women’s coping resources with lifetime marijuana use and alcohol abuse across racial ethnic groups: Results from a national survey
S. Balan, G. Widner, R. K. Price, Washington University in St. Louis School of Medicine, St. Louis, MO

SEDATIVE-HYPNOTICS, INHALANTS

111 The neuropharmacological and toxicological effects of inhaling a local Egyptian glue
A. A. Elkoussi, M. A. Elshahed, M. S. Abdelrahman, Pharmacology, Assiut College of Medicine, Assiut, Egypt

112 Discriminative stimulus effects of propofol
M. J. Forster, M. B. Gatch, Pharmacology & Neuroscience, UNT Health Science Center, Fort Worth, TX

113 Individual differences in the likelihood of rebound insomnia
S. Randall, T. Roehrs, E. Harris, R. Maan, T. Roth,
1Henry Ford Health System, Detroit, MI,
2Psychiatry & Behavioral Neuroscience, Wayne State University School of Medicine, Detroit, MI

114 Acute tolerance to chlordiazepoxide qualitatively changes the interaction between flumazenil and pregnanolone in rhesus monkeys discriminating midazolam
L. R. Gerak, C. P. France, Pharmacology, University of Texas Health Science Center at San Antonio, San Antonio, TX,
2Psychiatry, University of Texas Health Science Center at San Antonio, San Antonio, TX

115 Psychiatrist decision-making towards prescribing benzodiazepines: The dilemma with substance abusers
C. Marienfeld, E. Tek, E. Diaz, R. Schottenfeld, Psychiatry, Yale University, New Haven, CT

116 Benzodiazepine use in methadone maintenance treatment patients
A. K. Mamczur, J. J. Mariani, R. Brady, E. V. Nunes, F. R. Levin,
1Psychiatry/Division on Substance Abuse, Columbia University/New York State Psychiatric Institute, New York, NY,
2Narco Freedom, Inc., New York, NY
CLUB DRUGS, HALLUCINOGENS

117 Increase of brain activity and change in REM sleep induced by ketamine: Possible relationship to its psychotomimetic effect
K. Takeda1, M. Narita1, K. Yoshizawa1, M. Rahmadi1, S. Hiyayama1,2, H. Nagase2, N. Kuzumaki1, T. Suzuki1, 1Toxicology, Hoshi Univ. Sch. Pharm. Pharmaceut. Sci., Tokyo, Japan, 2Medicinal Chemistry, Sch. Pharm. Kitasato Univ., Tokyo, Japan

118 Evidence for molecular changes in the circadian system following MDMA treatment
R. P. Ogeil1, D. J. Kennaway2, M. D. Salkeld2, S. M. Rajaratnam1, J. H. Broadbear1, 1School of Psychology and Psychiatry, Monash University, Clayton, VIC, Australia, 2Discipline of Obstetrics & Gynecology, University of Adelaide, Adelaide, SA, Australia

119 Does sex, age and drug history affect behavioral responses to low-dose MDMA and amphetamine in a sensitization paradigm?
J. D’Souza, J. H. Broadbear, School of Psychology and Psychiatry, Monash University, Clayton, VIC, Australia

120 MDMA (ecstasy) impairs short-term memory recognition in rats
S. A. Perrine1, A. N. Prussack1, A. L. Eagle1, D. M. Thomas3,4, M. P. Galloway1,2, 1Psychiatry and Behavioral Neurosciences, Wayne State University School of Medicine, Detroit, MI, 2Anesthesiology, Wayne State University School of Medicine, Detroit, MI, 3Pharmaceutical Science, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, MI, 4Research Services, John D. Dingell VA Medical Center, Detroit, MI

121 Human MDMA (Ecstasy) users have altered brain activation during semantic encoding
T. J. Watkins1,2, V. Raj1,2, D. R. Di Iorio1,2, M. Dietrich1, S. Park1, J. U. Blackford1, R. Cowan1,2, 1Psychiatric Neuroimaging Program, Vanderbilt University, Nashville, TN, 2Vanderbilt Addiction Center, Vanderbilt University, Nashville, TN, 3Psychology, Vanderbilt University, Nashville, TN

122 Determining the effects of an acute dose of trifluromethylphenylpiperazine on the human reward pathway using a gambling task
B. R. Russell1,2, R. R. Kydd3,2, I. J. Kirk4,2, L. E. Curley1,2, 1School of Pharmacy, The University of Auckland, Auckland, New Zealand, 2Centre for Brain Research, The University of Auckland, Auckland, New Zealand, 3Department of Psychological Medicine, The University of Auckland, Auckland, New Zealand, 4Department of Psychology, The University of Auckland, Auckland, New Zealand

123 MDMA (Ecstasy) use is associated with increased amygdalar and hippocampal activation during novelty detection
P. Mortensen, M. Benningfield, J. U. Blackford, T. J. Watkins, C. R. Di Iorio, R. Cowan, Vanderbilt University, Nashville, TN

124 MDMA (Ecstasy) use is associated with lasting increases in cortical 5-HT2A receptors
C. R. Di Iorio, R. M. Kessler, M. S. Dietrich, A. Cao, T. J. Watkins, J. U. Blackford, B. P. Rogers, R. Cowan, Vanderbilt University, Nashville, TN

125 Australia drug market in 2010
L. Burns, N. Sindicich, National Drug and Alcohol Research Centre, New South Wales, NSW, Australia

126 Web-based survey of psilocybin-occasioned mystical experience
K. A. MacLean, J. M. Leoutsakos, M. W. Johnson, R. R. Griffiths, Psychiatry and Behavioral Sciences, Johns Hopkins University, Baltimore, MD
THEORETICAL, COMMENTARY

127 Confidentiality and integration of substance use disorders treatment with medical care
J. L. Sorensen1,2, J. Manuel1,2, S. Larios1,2, H. Newville1,2, Psychiatry, University of California,
San Francisco, San Francisco, CA, 1San Francisco General Hospital, San Francisco, CA

128 Recommendations on national drugged driving policies submitted to the Office of National Drug
Control Policy
R. L. DuPont1, B. K. Logan2, S. K. Talpins3,1, R. B. Voas4, 1Institute for Behavior and Health,
Inc., Rockville, MD, 2Center for Studies of Law in Action, Indiana University,
Bloomington, IN, 3National Partnership on Alcohol Misuse and Crime, Washington, DC,
4Pacific Institute for Research and Evaluation, Calverton, MD

129 Addressing global drug policy
C. B. McCoy, J. Shultz, Epidemiology & Public Health, University of Miami, Miami, FL

130 Update on formulations to deter tampering
E. M. Sellers1,2, M. K. Romach1, K. A. Schoedel1, 1Kendle Early Stage - Toronto, Toronto, ON,
Canada, 2DL Global Partners Inc, Toronto, ON, Canada

131 The role of tamper testing in the assessment of abuse potential
R. Fant1, E. J. Cone2, J. E. Henningfield1, 1Clinical Pharmacology, Pinney Associates,
Bethesda, MD, 2ConeChem Research, Severna Park, MD

132 Risk Evaluation and Mitigation Strategies: New challenges and opportunities for drug abuse
investigators
S. H. Schnoll, R. V. Fant, M. D. Ertischek, J. E. Henningfield, Risk Management Services,
Pinney Associates, Bethesda, MD

133 Tobacco product dependence liability assessment to support the WHO Framework Convention
on Tobacco Control
J. Henningfield1,2, N. Gray1, G. Zaatari1,2, D. Bettcher4, 1Study Group on Tobacco Product
Regulation, WHO, Geneva, Switzerland, 2Johns Hopkins University, Baltimore, MD,
3American University of Beirut, Beirut, Lebanon, 4WHO Tob Free Initiative, Geneva,
Switzerland

134 Design considerations for interactive video interventions on mobile devices
I. D. Aronson, NDRI, New York, NY

135 Fielding respondent-driven sampling to study veteran reintegration, mental health and substance
abuse in the inner city
A. S. Bennett, A. Golub, National Development and Research Institutes, Inc., New York, NY

136 Drug use history among patients in substitution therapy in Bucharest, Romania
A. O. Abagiu1,2, I. C. Fierbinteanu2, I. G. Stoica2, F. Georgescu2, F. Gheorghe2, S. C. Popa2,
E. Cojocaru2, V. Leoveanu1, A. Koulousas2, R. Ianos-Rancovici2, E. M. Paris3, M. Georgescu2,
1National Institute for Infectious Diseases Prof. Dr Matei Bals, Bucharest, Romania,
2Romanian Association Against AIDS, Bucharest, Romania

137 Adapting standardized research instruments to match a rural Native American community’s
experience: Building the base
B. Greenfield1, D. Lupee2, Y. Yamutewa2, E. Homer2, R. Chavez1, R. Currier3,2, K. Venner1,
1University of New Mexico Center on Alcoholism, Substance Abuse, and Addictions,
Albuquerque, NM, 2Pueblo of Zuni MICRA Project, Zuni, NM, 3Zuni Recovery Center,
Zuni, NM
Models of interorganizational change for implementing EBPs in correction-provider networks
M. S. Shafer1, D. Duffee1, L. Stein1, W. Lehman2, P. Friedman3, M. Prendergrast4, P. Noble-Desy5, 1Arizona State University, Phoenix, AZ, 2Texas Christian University, Ft. Worth, TX, 3Brown University, Providence, RI, 4University of Rhode Island, Providence, RI, 5Washington State Department of Corrections, Tumwater, WA, 6University of California, Los Angeles, Los Angeles, CA

Prevalence, frequency, correlates and outcomes of benzodiazepine use among patients in methadone maintenance treatment
M. Vazirian, A. Khazaeli, M. Chawarski, R. Schottenfeld, Psychiatry, Yale University, New Haven, CT

Entry into methadone treatment via interim maintenance: 12-month outcomes
R. P. Schwartz1,2, J. H. Jaffe2, S. M. Kelly1, D. Gandhi2, K. E. O’Grady3, 1Friends Research Institute, Baltimore, MD, 2U of MD, Balto, MD, 3U of MD, College Park, MD

Characteristics of newly admitted methadone vs. buprenorphine patients
S. G. Mitchell1, S. M. Kelly1, J. Gryczynski1, C. P. Myers2, K. E. O’Grady3, Y. K. Olsen4, R. P. Schwartz1, J. H. Jaffe1, 1Friends Research Institute, Baltimore, MD, 2Patrick Myers Assoc., Baltimore, MD, 3U of MD, College Park, MD, 4BSAS, Baltimore, MD

Variations in outcomes and patient characteristics associated with methadone and buprenorphine dose
L. Mooney, M. Hillhouse, C. Thomas, A. Hasson, W. Ling, UCLA, Los Angeles, CA

Treatment completion in opioid-dependent pregnant patients randomized to agonist treatment: The role of intravenous drug use

Buprenorphine induction outcomes for heroin and prescription opioid users
S. Nielsen, M. Hillhouse, J. Fahey, W. Ling, Integrated Substance Abuse Programs, UCLA, Los Angeles, CA

An analysis of counseling sessions attended by opioid-dependent participants in a multicenter trial of buprenorphine/naloxone
F. J. Vocci1, K. O’Grady2, P. Casadonte3, W. Ling4, P. Fudala5, R. Walsh6, 1Friends Research Institute, Baltimore, MD, 2University of Maryland, College Park, College Park, MD, 3New York University, New York, NY, 4UCLA, Los Angeles, CA, 5Reckitt-Benckiser Pharmaceuticals, Inc, Richmond, VA, 6NIDA, Rockville, MD

Employment-based reinforcement of adherence to depot naltrexone treatment in unemployed opiate-dependent adults: 12-month follow-up
M. Koffarnus, J. J. Everly, A. DeFulio, A. Umbricht, M. Fingerhood, G. E. Bigelow, K. Silverman, Psychiatry, Johns Hopkins University School of Medicine, Baltimore, MD

Employment-based reinforcement of adherence to oral naltrexone treatment within unemployed injection drug users: 12-month follow-up
K. Dunn, A. DeFulio, J. Everly, W. Donlin, A. Umbricht, M. Fingerhood, G. Bigelow, K. Silverman, Johns Hopkins University, Baltimore, MD
148 Contingency management at a MMT clinic in Shanghai, China
H. Zhang1,2, H. Jiang1, J. Du1, A. Dong1, J. Wang1, M. Chawarski2, R. Schottenfeld2, M. Zhao3, Y. Hser4, 1Shanghai Yangpu District Mental Health Center, Shanghai, China, 2Psychiatry, Yale University, New Haven, CT, 3Shanghai Mental Health Center, SJTU, Shanghai, China, 4UCLA ISAP, Los Angeles, CA

149 The feasibility of providing educational counseling for heroin abusers participating in needle-syringe exchange programs in Penang, Malaysia
Z. Shamandi1, B. Vicknasingam1, M. Chawarski2, 1Centre for Drug Research, Universiti Sains Malaysia, Minden, Malaysia, 2School of Medicine, Yale University, New Haven, CT

150 Comprehension testing of the medication guide for oxycontin
L. Sandstrom1, P. M. Coplan1, L. A. Morris2, 1Risk Management & Epidemiology, Purdue Pharma L.P., Stamford, CT, 2Louis A. Morris & Assoc, Dix Hills, NY

151 Provider acceptability of automated ancillary services for buprenorphine treatment
B. A. Moore1,2, T. Fazzino2, E. Necrason3, B. J. Rounsaville1, L. E. Sullivan1, D. A. Fiellin1, 1Yale University, New Haven, CT, 2APT Foundation, New Haven, CT, 3U. of Hartford, West Hartford, CT

152 Utilization of an automated therapeutic telephone system in primary care buprenorphine
T. Fazzino2, B. A. Moore1,2, 1Psychiatry, Yale University, New Haven, CT, 2APT Foundation, New Haven, CT

153 Expanding the continuum of care in opioid agonist treatment using web-based videoconferencing
V. L. King, M. Kidorf, J. Peirce, R. Brooner, Psychiatry, Johns Hopkins SOM, Baltimore, MD

154 Developing a computerized sexual risk assessment and feedback tool for use in substance abuse treatment
D. A. Calsyn, B. Hartzler, E. A. Wells, K. M. Peavy, Alcohol & Drug Abuse Institute/Psychiatry & Behavioral Sciences, University of Washington, Seattle, WA

OPIOIDS: ANIMAL

155 Spontaneous withdrawal in opiate-dependent Fischer 344, Lewis and Sprague-Dawley rats
J. L. Cobuzzi, A. L. Riley, Psychology, American University, Washington, DC

156 Effects of voluntary exercise on two models of morphine withdrawal
R. E. Balter1, L. A. Dykstra1,2, 1Curriculum in Neurobiology, University of North Carolina-Chapel Hill, Chapel Hill, NC, 2Psychology, University of North Carolina, Chapel Hill, Chapel Hill, NC

157 Chronic morphine treatment influences mu-opioid receptor agonist effects on intracranial self-stimulation
A. Altarifi, S. S. Negus, Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA

158 Identification of a novel allosteric modulator of opioid receptors: SoRI-25825
S. C. Wilson1, C. M. Dersch1, S. K. Saini2, S. Ananthan2, R. B. Rothman1, 1Translational Pharmacology Research Section, IRP, NIDA, NIH, Baltimore, MD, 2Organic Chemistry Department, Southern Research Institute, Birmingham, AL

159 Sigma-1 receptor function is critical for both the discriminative stimulus and aversive effects of the kappa-opioid receptor agonist U-50,488H

160 Naloxone-induced taste aversions in opiate-naïve F344 and LEW rat strains
A. Desko, J. L. Cobuzzi, A. L. Riley, Psychology, American University, Washington, DC
The atypical antidepressant mirtazapine attenuates the expression of morphine-induced place preference
S. M. Graves, J. R. Riddle, T. C. Napier, Pharmacology; Center for Compulsive Behaviors and Addictions, Rush University Medical Center, Chicago, IL

Dose preference and dose escalation of heroin in extended-access self-administration in Fischer and Lewis rats
R. Picetti, A. Ho, M. J. Kreek, The Rockefeller University, New York, NY

Regional differences in the role of the VTA on heroin-induced conditioned immunomodulation
L. W. Hutson, J. L. Szczytkowski, T. B. Saurer, D. T. Lysle, Psychology, University of North Carolina, Chapel Hill, NC
INRC POSTERS

OPIOID PHARMACOLOGY

164  In vivo modulation of the behavioral effects of the kappa-opioid hallucinogen salvinorin A by P-glycoprotein ligands
E.R. Butelman (1), S. Rus (1), K. Lovell (2), T.E. Prisinzano (2), M.J. Kreek (1). (1) The Rockefeller Univ., New York, NY, (2) Dept. of Medicinal Chemistry, Univ. of Kansas, Lawrence, KS, USA

165  Role of dynorphin/kappa opioid receptor in forced swim test behavior in rats
N.Z. Fang, Y. Zhou, S. Chen, B. Mayer-Blackwell, B. Reed, M.J. Kreek. Lab. of the Biology of Addictive Diseases, Rockefeller Univ., New York, NY, USA

166  Differential KOR agonist-induced activation of ERK1/2 MAP kinase mediates paradoxical potentiation of cocaine-conditioned place preference
J.P. McLaughlin (1,2), M.R. Hoot (2), K. Rasakham (1,3). (1) Northeastern Univ., Dept. of Psychology, Boston, MA, (2) Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL, (3) Temple Univ. School of Medicine, Dept. of Pharmacology, Philadelphia, PA, USA

167  Pharmacological profile of delta and kappa opioid receptor subtypes in spinal cord
R.M. van Rijn, D.I. Brissett, J.L. Whistler. Ernest Gallo Clinic and Research Center, Dept. of Neurology, Univ. of California San Francisco, CA, USA

168  Morphine-induced motor stimulation after repeated administration: Age-related differences in mice
W. Koek. Dept. of Psychiatry and Pharmacology, Univ. of Texas Health Science Center at San Antonio, TX, USA

169  Pharmacokinetic interaction and safety of naltrexone hydrochloride co-administered with oral opioids

170  The kinetics of priming-induced functional competence of delta opioid receptors
L. Scarlota, M. Rowan, K. Berg, W. Clarke. Dept. of Pharm., Univ. of Texas Health Sci. Center, San Antonio, TX, USA

171  Orphanin FQ/Nociceptin activates Oct-2 in SH-SY5Y human neuroblastoma cells
C.L. Donica (1), K.M. Standifer (2). (1) OK Center for Neuroscience, (2) Dept of Pharmaceutical Sciences, OUHSC, Oklahoma City, OK, USA
172 The novel opioid antagonist, ALKS 37, reduces morphine-induced slowing of gastrointestinal transit in rodents and hydrocodone-induced slowing in dogs

173 Suppression of malignancy of gefitinib-resistant human non-small-cell lung cancer (NSCLC) cells by activation of δ-opioidergic system

174 Detection of nor-BNI in mouse brain weeks after administration using LC-MS/MS
K.A. Patkar, M.L. Ganno, H.D. Singh, N.C. Ross, J.P. McLaughlin. Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL, USA

175 Using the transitive inference task to study the relational memory deficits associated with withdrawal from chronic nicotine in the C57BL/6 mouse

176 Social influences on morphine sensitivity in adolescent rodents
S. Eitan, S.R. Hofford, S.L. Cole, D.J. Evert, P.J. Wellman. Behavioral and Cellular Neuroscience Program, Dept. of Psychology, Texas A&M University, College Station, TX, USA

177 Effects of morphine on acetic acid-induced suppression of appetitive and reward-related behaviors in mice
H. Neelakantan, S.J. Ward, E.A. Walker. Dept. of Pharmaceutical Sciences, Temple Univ. School of Pharmacy, Philadelphia, PA, USA

178 Enkephalinergic system is involved in cocaine-induced behavioral sensitization and the associated increase in AMPA receptor surface expression in nucleus accumbens and caudate putamen
B. Mongi Bragato (1), M. A. Assis (1), M. Bartos (1), A. Zimmer (3), L. M. Cancela (1). (1) IFEC-CONICET, Dept. de Farmacología, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba, Córdoba. Argentina, (2) Institute of Molecular Psychiatry, Univ. of Bonn, Bonn, Germany
Modulation of behavioral responses to stress by opioid receptor systems

Repeated morphine administration alters contextual learning, synaptic plasticity, and requires phosphorylation of gluR1-containing AMPA receptors in the hippocampus
G.S. Portugal, Y. Xia, J. Liu, J.A. Morón Concepcion. Dept. of Anesthesiology, College of Physicians and Surgeons, Columbia Univ. Medical Center, New York, NY, USA

The impact of long-term GHB treatment on spatial learning in male rats

The superoxide-generating enzyme NADPH oxidase is required for the normal expression of opioid addictive behaviors
M. A. Beckerman (1), M. J. Glass (1,2). (1) Dept. of Neurology and Neuroscience, and (2) Graduate Program in Neuroscience, Weill Cornell Medical College, New York, NY, USA

Modulation of full-length mu opioid receptor (MOR-1) expression and function by truncated proteins with single transmembrane domain of the mu opioid receptor gene, OPRM1

OPRM1 A118G SNP reduces MOPR expression in some, but not all, brain regions in a mouse model
Y-J. Wang (1), P. Huang (1), A. Ung (1), J. Blendy (2), L-Y. Liu-Chen (1). (1) Dept. Pharmacol., Temple Univ. School of Medicine, (2) Dept. Pharmacol., Univ of Pennsylvania, Philadelphia, PA, USA

Selective interaction of G-protein coupled receptors with isoforms of ADP-ribosylation factor (ARF)
T. Koch, M. Rankovic, J. Konietzko, E. Kahl, V. Höllt. Dept. of Pharmacology and Toxicology, Otto-von-Guericke-Univ., Magdeburg, Germany

Role of Galpha, protein in opioid agonist-dependent signaling and behavior
J. Lamberts (1), E. Jutkiewicz (1,2), J. Traynor (1,2). (1) Dept. of Pharmacology and (2) Substance Abuse Research Center, Univ. of Michigan, Ann Arbor, MI, USA
187  *DOR-KOR heteromer signaling in peripheral sensory neurons*
B.A. McGuire, W.P. Clarke, K.A. Berg. Department of Pharmacology, University of Texas Health Science Center, San Antonio, TX, USA

188  *Both JNK and β-arrestin 2 play a role in ligand dependent signaling of the mu opioid receptor*
N. Mittal (1,2), M. Tan (1), O. Egbuta (1), N. Desai (1), C. Crawford (2), T. Xie (1), C. Evans (1), W. Walwyn (1). (1) Dept. Psychiatry & Biobehavioral Sciences, Stefan Hatos Ctr Neuropharmacol., Semel Institute, UCLA, CA, (2) Dept of Psychology, California State Univ., San Bernardino, CA, USA

189  *Mu- and delta-opioid receptor agonists mediate up-regulation of RGS19 protein in SH-SY5Y cells*
Q. Wang, J.R. Traynor. Dept. of Pharmacology and Substance Abuse Research Center, Univ. of Michigan, Ann Arbor, MI, USA

**GENETICS**

190  *Csnk1e is a genetic regulator of sensitivity to psychostimulants and opioids*
C.D. Bryant (1), L. Zhou (3,4), C. Olker (3,4), M.H. Vitaterna (3,4), F.W. Turek (3,4), A.A. Palmer (1,2). (1) Dept. of Human Genetics, (2) Dept. of Psychiatry and Behavioral Neuroscience, Univ. of Chicago, Chicago, IL, (3) Center for Sleep and Circadian Biology, (4) Dept. of Neurobiology and Physiology, Northwestern Univ., Evanston, IL, USA

191  *Effects of A118G polymorphism and personality factors on HPA-axis response to metyrapone in normal volunteers*
E. Ducat, B. Ray, M. Randesi, A. Ho, M.J. Kreek. Lab. of Biology of Addictive Disease, Rockefeller Univ., New York, NY, USA

192  *Pharmacogenetics of methadone dose requirement in opioid addiction treatment*
O. Levran (1), E. Peles (2), S. Hamon (1), M. Randesi (1), M. Adelson (2), M.J. Kreek(1). (1) Lab. of Biology of Addictive Diseases, Rockefeller Univ., New York, NY, USA, (2) Dr. Miriam and Sheldon G. Adelson Clinic for Drug Abuse, Treatment and Research, Elias Sourasky Medical Center, Tel Aviv, Israel

193  *A naturally occurring genetic model of human mu-opioid receptor genetic variation*
E.J. Vallender, Z. Xie, D.M. Platt, G.M. Miller. Div. of Neuroscience, New England Primate Research Center, Harvard Medical School, Southborough, MA, USA

194  *Epigenetic mechanism of prodynorphin upregulation in the brain of human alcoholics: Dependence on promoter methylation and USF2 transcription factor*
PAIN AND ANALGESIA

195 Using an operant orofacial assay to measure the analgesic effects of morphine and the hyperalgesic effects of withdrawal
E.M. Anderson (2), R.M. Caudle (1,2). (1) Dept. of Oral Surgery, (2) Dept. of Neuroscience, Univ. of Florida, College of Medicine, Gainesville, FL, USA

196 Activation of spinal mu and delta opioid receptors potently inhibits substance P release induced by peripheral noxious stimuli
H. Beaudry, D. Dubois, L. Gendron. Université de Sherbrooke, Québec, Canada

197 Interactions between cortical cannabinoid and opioid receptors during neuropathic pain
I. Bushlin, A. Gupta, L.K. Miller, S.D. Stockton Jr., L.A. Devi. Dept. of Pharmacology and Systems Therapeutics, Mount Sinai School of Medicine, New York, NY, USA

198 Morphine-induced hyperalgesia is associated with AMPAR trafficking in the dorsal horn of the spinal cord

199 Antinociceptive effects of NOP receptor agonists, nociceptin, Ro 64-6198 and (+)-5a compound, given by intra-periaqueductal gray injection
L.-C. Chiou (1,2,3,4), H.-J. Lee (1,3), Y.-Y. Liao (2). (1) Dept. Pharmacology, Coll. Medicine, (2) Grad. Inst. Pharmacology, (3) Zoology, National Taiwan Univ., Taipei, Taiwan

200 Antinociception of perineurally applied drugs via modulation of tight junction proteins in the perineurium

201 Analysis of antinociceptive efficacy following microinjection of mu-opioid receptor agonists into the periaqueductal gray of the rat

202 Pharmacological functional magnetic resonance imaging analysis for pain research with understanding the mechanisms within the brain that provoke pain
Opioid withdrawal-induced hyperalgesia is mediated in the peripheral nervous system via Transient Receptor Potential Vanilloid 1 (TRPV1)
J.A. Jira (1), V. Spahn (2), O. Fischer (2), C. Zöllner (1). (1) Univ. Hospital Hamburg Eppendorf, Center for Anaesthesiology and Intensive Care Medicine, Hamburg, (2) Charité Berlin, CBF, Dept. of Anesthesiology and Operative Intensive Care Medicine, Berlin, Germany

Remifentanil exposure produces prolonged hyperalgesia under certain pain conditions but not morphine tolerance in rats
E.M. Jutkiewicz, Y.Sun, J.S. Schimmel, J.R. Traynor. Dept. of Pharmacology and Substance Abuse Research Center, Univ. of Michigan Medical School, Ann Arbor, MI, USA

Nicotine prevents neuropathic pain following peripheral nerve injury through the suppression of neuroinflammation.
S. Kishioka, N. Kiguchi, Y. Kobayashi, S. Tominaga, J. Nakamura, T. Maeda, Dept. of Pharmacology, Wakayama Medical Univ., Wakayama City, Japan

Stimulation of the brain reward system attenuates the analgesic effects of the NMDA antagonist LY235959
C.M. Knapp (1), L. Tozier (1,2), S. Tapan (1), C. Kornetsky (1,2). (1) Division of Psychiatry, (2) Dept of Pharmacology, Boston Univ. School of Medicine, Boston MA, USA

µ-Opioid control of P2X3 receptors in DRG sensory neurons of rat is crucially dependent on the experimental in vitro conditions

Truncated MOR-1 splice variants: Targets for potent opioid analgesics lacking side-effects
S. Majumdar (1), S.G. Grinnell (1), V. Le Rouzic (1), M. Burgman (1), L. Polikar (1), M. Ansonoff (2), Y. Xiang Pan (1), J. E. Pintar (2), G. W. Pasternak (1). (1) Lab. of Molecular Pharmacology and Chemistry, Memorial Sloan-Kettering Cancer Center, New York, NY, (2) Dept. of Cell Biology and Neuroscience, Univ. of Medicine and Dentistry of New Jersey, Piscataway, NJ, USA

Morphine resistance and its underlying mechanisms in an experimental mouse model of fibromyalgia
T. Mukae, M. Nishiyori, K. Araki, H. Ueda. Div. of Molecular Pharmacology and Neuroscience, Nagasaki Univ. Graduate School of Biomedical Sciences, Nagasaki, Japan
210 **HDAC inhibitors recover the epigenetically silenced mu-opioid receptor expression in neuropathic pain model**  
H. Ueda, H. Uchida, K. Araki. Div. of Molecular Pharmacology and Neuroscience, Nagasaki Univ. Graduate School of Biomedical Sciences, Nagasaki, Japan

211 **Involvement of long-chain fatty acid receptors, GPR40 and GPR120, in the induction of antinociception of docosahexaenoic acid**  
K. Nakamoto (1), T. Nishinaka (1), K. Matsumoto (1), M. Mankura (2), S. Tokuyama (1).  
(1) Dept. of Clinical Pharmacy, School of Pharmaceutical Sciences, Kobe Gakuin Univ., Japan, (2) Ikeda Tohka Industries Co., Ltd., Japan

212 **Different μ-opioid receptor activation profiles of oxycodone and morphine at specific brain regions in mouse femur bone cancer pain model**  
(1) Pain & Neurology, Discovery Research Lab., SHIONOGI Co., Ltd., Shiga, (2)Dept. of Toxicology, Hoshi Univ. School of Pharmacy and Pharmaceutical Sciences, Tokyo, Japan

213 **Possible change in microRNAs associated with mesolimbic motivation/valuation circuitry under neuropathic pain**  

214 **Effects of dextromethorphan/morphine on treatment of neuropathic pain in mice**  
P.-L. Tao (1,2), P.-H. Lee (2), E. Y.-K. Huang (2).  

215 **Sleep disturbances in a neuropathic pain-like condition are associated with altered GABAergic transmission in the cingulate cortex**  

216 **Investigation on DNA methylation status of opioid peptides promoters in PBMCs of subjects with bipolar disorder**  
(1) Dept. of Pharmacology, Univ. of Bologna, Bologna, (2) Dept. of Psychiatry, (3) Dept. of Neurological Sciences, Univ. of Milan, Milano, (4) Dept. of Biomedical Sciences, Univ. of Teramo, Teramo, Italy

217 **Opioids block the effects of the HIV entry inhibitors maraviroc and AMD-3100 in CNS glia**  
N. El-Hage, S.M. Dever, T. Ahmed, Y. Zhang, K.F. Hauser, Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA, USA
INRC Symposium 4
Therapeutic Potential of Nociceptin Receptor Ligands
Chairs: Claes Wahlestedt and Lawrence Toll

9:30  To mix or not to mix: Modulation of opioid activity by nociceptin receptor ligands
      Nurulain Zaveri, Astraea Therapeutics, USA

10:00  Therapeutic potential of NOP ligands as spinal analgesics
       Holden Ko, University of Michigan, USA

10:30  The nociceptin/orphanin FQ system as a treatment target for addiction
       Roberto Ciccocioppo, University of Camerino, Italy

11:00  Discovery and development of nociceptin receptor agonists in alcohol dependence
       Shaun Brothers, University of Miami Miller School of Medicine, USA

Symposium XI
Rethinking the Effects of Methamphetamine
Chairs: Hedy Kober and Matthew G. Kirkpatrick

9:30  Cognitive regulation of craving in methamphetamine users
      Hedy Kober, Yale University, New Haven, CT

9:55  Top down control and aggression in methamphetamine users
      Edythe London, University of California, Los Angeles, Los Angeles, CA

10:20  Acute cognitive effects of methamphetamine in humans
       Matthew Kirkpatrick, Psychiatry, University of Chicago, Chicago, IL

10:45  Mechanism of methamphetamine action and behavior: Are we looking at the correct behaviors?
       John Mendelson, California Pacific Medical Center Research Institute, St. Luke’s Hospital,
       San Francisco, CA

11:10  Discussant
       Carl L. Hart, Columbia University, New York, NY

Oral Communications 18
Environment and Behavior: Taking Drugs in Context
Chairs: Mark A. Smith and Michelle Baladi

9:30  Eating a high fat chow differentially affects sensitivity of adolescent male and female rats to
      cocaine-induced locomotor activity
      M. Baladi1, C. P. France1,2, 1Pharmacology, University of Texas Health Science Center, San
      Antonio, TX, 2Psychiatry, University of Texas Health Science Center, San Antonio, TX

9:45  Time of day influences voluntary intake and behavioral response to drug and food reward
      D. R. Keith, C. L. Hart, R. Silver, Columbia University, New York, NY

10:00  Aerobic exercise decreases the acquisition of cocaine self-administration
       M. A. Smith, E. G. Pitts, Psychology, Davidson College, Davidson, NC
Thursday, June 23, 2011

10:15  Exercise as a novel approach to methamphetamine treatment
       J. Chudzynski¹, R. Rawson¹, J. Penate¹, B. Dolezal², D. Dickerson¹, C. Cooper¹, L. Mooney¹,
       ¹Integrated Substance Abuse Programs, UCLA, Los Angeles, CA, ²Exercise Physiology
       Research Laboratory, UCLA, Los Angeles, CA

Symposium XII

SOCIAL ENVIRONMENT AND DRUG-SEEKING:
NEUROBIOLOGICAL FACTORS

Chairs: Linda Dykstra and Mark A. Smith

10:45  Social context attenuates brain and HPA axis activation that occurs in response to drug and
drug cues
       Janet Neisewander, Arizona State University, Tempe, AZ
11:05  Neurocircuitry of social stress and cocaine self-administration
       Klaus Miczek, Tufts University, Medford, MD
11:25  Molecular mechanisms of environmental enrichment
       Tom Green, University of Texas Medical Branch, Galveston, TX

Symposium XIII

NEUROCOGNITIVE DYSFUNCTION IN ADDICTION:
MECHANISMS AND INTERVENTIONS

Chairs: Warren K. Bickel and Will M. Aklin

9:30   Modeling executive function in reinforcement learning: Implications of situation representations
       for addiction and treatment
       A. David Redish, University of Minnesota, Minneapolis, MN
9:50   Targeting memory processes in addiction: Effects of beta-blockers on cravings in response to
       drug-cued memories
       Efrat Aharonovich, Columbia University, New York, NY
10:10  Executive function therapy for addiction
       Warren Bickel, University of Arkansas for Medical Sciences, Little Rock, AR

Symposium XIV

BRAIN IMAGING AS A TOOL FOR TREATMENT DEVELOPMENT IN
STIMULANT ABUSE

Chair: F. Gerard Moeller

10:45  PharmacoMRI as a tool for medication development in cocaine dependence
       F. Gerard Moeller, University of Texas Health Science Center at Houston, Houston, TX
11:05  White matter damage in experimental cocaine abuse: DTI studies
       Ponnada A. Narayana, University of Texas Health Science Center at Houston, Houston, TX
Nonhuman primate proton MRS studies of chronic cocaine’s effects: A model to study novel treatments for cocaine-induced glutamatergic abnormalities
Marc J. Kaufman, Brain Imaging Center, McLean Hospital/Harvard Medical School, Belmont, MD

BRUNCH WITH CHAMPIONS
(Pre-Registrants Only)
Room 312
11:30 AM - 1:00 PM

INRC Lunch Break
(Lunch on your own)
11:30 AM - 1:00 PM

INRC Symposium 5
Diplomat 1-2
1:00 - 3:00 PM

SEX DIFFERENCES IN PAIN AND OPIOID ANALGESIA
Chairs: Vishnudutt Purohit and Cora Lee Wetherington

1:00 Gender differences in pain
Linda LeResche, University of Washington, USA

1:30 Opioid analgesia and sex differences: An overview
Elise Y. Sarton, University Medical Center, The Netherlands, Leiden, United Kingdom

2:00 Impact of age and sex in the antihyperalgesic actions of morphine: Role of periaqueductal gray
Anne Z. Murphy, Georgia State University, USA

2:30 The importance of sex in pain: Sexual dimorphic expression in spinal cord of mu-opioid and kappa-opioid receptor heterodimers
Alan Gintzler, State University of New York Downstate Medical Center, USA

Oral Communications 19
Regency 3
1:00 - 3:00 PM

NICOTINE IN NON-HUMANS
Chairs: Dustin J. Stairs and Natalie A. Peartree

1:00 Behavioral, biochemical, and molecular indices of nicotine withdrawal: Differential impact of sex on stress-related markers
O. V. Torres, L. A. Natividad, A. K. Muñiz, L. E. O’Dell, Psychology, University of Texas at El Paso, El Paso, TX

1:15 β-Carbolines found in cigarette smoke suppress monoamine metabolism in mouse brain
G. F. Marrone¹, S. J. Heishman¹, R. B. Rothman¹, S. F. Ali², M. H. Baumann¹, ¹Translational Pharmacology Sect., IRP, NIDA, NIH, Baltimore, MD, ²Dept. of Neurochemistry, NCTR, FDA, Jefferson, AR

1:30 Nicotinic α4β2 receptors and the discriminative stimulus effects of nicotinic receptor agonists in rhesus monkeys
C. S. Cunningham, L. R. McMahon, Pharmacology, UTHSCSA, San Antonio, TX
Effects of environmental enrichment on the locomotor stimulant effects of repeated nicotine pretreatment and the relationship with brain nicotinic acetylcholine receptor densities in rats
D. J. Stairs¹, C. S. Bockman², L. A. Hasselquist¹, T. Hickle¹, ¹Department of Psychology, Creighton University, Omaha, NE, ²Department of Pharmacology, Creighton University, Omaha, NE

Caffeine and its interaction with nicotine-associated cues in the persistence and reinstatement of nicotine-seeking behavior in rats
X. Liu, Psychiatry and Human Behavior, University of Mississippi Medical Center, Jackson, MS

The influence of social interactions and nicotine on corticosterone and behavioral responses in female and male adolescent rats
N. A. Peartree¹, N. S. Pentkowski¹,², M. R. Painter¹, T. H. Cheung², K. J. Thiel¹, J. L. Neisewander², ¹School of Life Sciences, Arizona State University, Scottsdale, AZ, ²Psychology, Arizona State University, Tempe, AZ

Calcium signaling underlying nicotine’s suppressive effect on TLR3 and TLR4 pathways
W. Y. Cui¹, J. Wang², R. Polanowska-Grabow³, J. Saucerman³, J. Gu⁴, S. Chang⁴, M. D. Li², ¹Life Science, Peking University, Beijing, China, ²Psychiatry and Neurobehavioral Sciences, University of Virginia, Charlottesville, VA, ³Biomedical Engineering, University of Virginia, Charlottesville, VA, ⁴NeuroImmune Pharmacology, Seton Hall University, South Orange, NJ

Nicotine inhibits estrogen signaling and increases post-ischemic hippocampal damage in female rats
A. P. Raval, Neurology, University of Miami, Miami, FL

Oral Communications 20

IMMUNE FUNCTION: FIGHTING OFF DRUGS

HIV-1 gp120 induces the expression of the transcription factor NF-E2-related factor 2 in astrocytes
V. B. Pichili, T. Samikkannu, N. Gandhi, Z. M. Saiyed, M. Agudelo, P. Khattavkar, A. Yndart, M. P. Nair, Department of Immunology, Institute of NeuroImmune Pharmacology, Florida International University, Miami, FL

HIV-1 Tat protein expression in mouse brain impairs learning and memory performance but potentiates the behavioral psychostimulant effects of cocaine
J. P. McLaughlin, S. M. Gomes, E. I. Sypek, C. F. Shay, A. N. Carey, Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL

The impact of methamphetamine use on outcomes in herpes simplex virus type 2 disease and immune response
F. D. Valencia, G. N. Milligan, K. A. Cunningham, N. Bourne, University of Texas Medical Branch, Galveston, TX

Cannabinoids inhibit T-cells in an in vitro assay for graft rejection, the mixed lymphocyte reaction
R. R. Hartzell¹,², J. J. Meissler¹,², M. W. Adler¹, T. K. Eisenstein¹,², ¹Center for Substance Abuse Research, Temple University, Philadelphia, PA, ²Microbiology and Immunology, Temple University, Philadelphia, PA
Oral Communications 21

COMING TO TERMS WITH DRUG ABUSE: CRIMINAL JUSTICE

Chairs: Gerald Stahler and Catina C. O’Leary

2:00  Enhancing substance abuse treatment for women in drug court
      N. P. Messina, UCLA Integrated Substance Abuse Programs, Los Angeles, CA

2:15  Four- and eight-month outcomes from a randomized peer-partnered case management intervention among community-recruited female offenders
      C. C. O’Leary, S. E. Bradford, C. L. Striley, L. B. Cottler, Psychiatry, Washington University School of Medicine, Saint Louis, MO

2:30  Level of crime predicts differential mortality risk prior to opioid maintenance treatment
      T. Clausen, A. Bukten, Norwegian Centre for Addiction Research, University of Oslo, Oslo, Norway

2:45  The prevalence of HIV risk behaviors among felony drug court clients
      K. L. Dugosh¹, D. S. Festinger¹,³, D. S. Metzger¹,³, D. B. Marlowe¹,²,³, ¹Treatment Research Institute, Philadelphia, PA, ²National Association of Drug Court Professionals, Alexandria, VA, ³Department of Psychiatry, University of Pennsylvania, Philadelphia, PA

CPDD SWEEPSTAKES DRAWING

YOU MUST BE SEATED IN ONE OF THE AFTERNOON SESSIONS IN ORDER TO HAVE YOUR BADGE COLLECTED

END OF CPDD PROGRAM

HAVE A SAFE TRIP HOME!

SEE YOU IN LA QUINTA, CALIFORNIA, JUNE 9-15, 2012

INRC Program Continues....
INRC ORAL SESSION

Chair: Craig Stevens, Ph.D., Oklahoma State Univ College of Osteopathic Med, USA

3:15-3:30  Regulation of opioid dependence by let-7 microRNAs
Y. He and Z. Wang, Dept. of Biopharmaceutical Sciences, Cancer Center, & Program for Collaborative Research in the Pharmaceutical Sciences, Univ. of Illinois, Chicago, IL, USA

3:30-3:45  Mu opioid receptor biased ligands: Delivering powerful analgesia and minimizing side effects
S.M. DeWire, D. Yamashita, C.J. LaBuda, M.W. Lark, and J.D. Violin, Trevena Inc., King of Prussia, PA, USA

3:45-4:00  Deciphering mu-opioid receptor phosphorylation & dephosphorylation
C. Doll, F. Pöll, S. Schulz, Institute of Pharmacology and Toxicology, Univ. Hospital, Friedrich Schiller Univ. Jena, Germany

4:00-4:15  Differential binding of non-visual arrestins to the intracellular domains of the mu-opioid receptor
K. Saxena, Y.-J. Chen, I. Rodriguez-Martin, V. Gurevich, J. Benovic, G. Henderson, E. Kelly, School of Physiology and Pharmacology, Univ. of Bristol, Bristol, UK, Dept. of Pharmacology, Vanderbilt Univ. School of Medicine, Nashville, TN, Dept. of Biochemistry and Molecular Biology, Thomas Jefferson Univ., Philadelphia, PA, USA

4:15-4:30  Bivalent ligand MDAN-21 blocks receptor endocytosis by bridging mu-delta opioid heteromers
A.S. Yekkirala (1,2), A.E. Kalyuzhny (3), P.S. Portoghese (1,2,3), (1) Dept. of Medicinal Chemistry, College of Pharmacy, (2) Dept. of Pharmacology, (3) Dept. of Neuroscience, Medical School., Univ. of Minnesota, Minneapolis, MN, USA

4:30-4:45  Changes in ligand-biased signaling are associated with opioid tolerance
E.N. Bobeck (1), T.A. Macey (2), K.L. Suchland (1), M.M. Morgan (1), S.L. Ingram (1), (1) Dept. of Psychology, WSU Vancouver, Vancouver, WA, (2) VA Hospital, Oregon Health and Science Univ., Portland OR, USA

4:45-5:00  RGS9 knockout enhances MOR-mediated inhibition of adenylyl cyclase in a CNS region-dependent manner
D.E. Selley (1), V. Zachariou (3), M.P. Cassidy (1), C.K. Chen (2), E.J. Nestler (4) and L.J. Sim-Selley(1), (1) Dept. of Pharmacology & Toxicology and (2) Biochemistry and Molecular Biology, Virginia Commonwealth Univ., Richmond, VA, USA, (3) Dept. of
Pharmacology, Univ. of Crete, Faculty of Medicine, Heraklion, Crete, Greece, (4) Fishberg Dept. of Neuroscience, Mount Sinai School of Medicine, New York, NY, USA

5:00-5:15  *Mouse strain-specific analgesic responses in MOR-1 and DOR-1 KO mice*

**INRC BUSINESS MEETING**

Diplomat 1
5:15 PM – 6:30 PM

**INRC DATA BLITZ**

Diplomat 1
8:00 PM – 10:00 PM

*BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS*
BREAKFAST
Great Hall 2
7:30 AM – 8:30 AM

PLENARY SESSION
Great Hall 2
8:30 AM – 9:30 AM

*Transcriptional and Epigenetic Mechanisms of Drug Addiction*
Eric Nestler, Director, Brain Institute; Mount Sinai School of Medicine, New York, NY USA

INRC Symposium 6
Great Hall 2
9:45 AM-11:50 AM

**GENETIC MOUSE MODELS FOR THE OPIOID SYSTEM**
Chair: Brigitte Kieffer, Institut de Génétique et de Biologie Moléculaire et Cellulaire Parc d'innovation, France

9:45-10:10  *Functional characterization of the OPRM1 A112G SNP in mice*
Julie Blendy, University of Pennsylvania, USA

10:10-10:35  *The role of OPRM1 variation for alcohol reward examined using a reverse translational approach*
Markus Heilig, NIAAA, USA

10:35-11:00  *Direct visualization of delta opioid receptor internalization under physiological conditions*
Dominique Massotte/Brigitte Kieffer, Institut de Génétique et de Biologie Moléculaire et Cellulaire, France

11:00-11:25  *Opioids induced cellular and behavioral changes in MOPr phosphorylation-deficient (PD) mice*
Jia Bei Wang, University of Maryland, USA

11:25-11:50  *Dynorphins regulate the intensity of fear memory: From mice to men*
Andreas Zimmer, University of Bonn, Germany

LUNCH BREAK (Lunch on your own) 11:50 AM – 1:15 PM

INRC Symposium 7
Great Hall 2
1:15 PM – 3:15 PM

**DELTA OPIOID RECEPTORS – NOVEL COMPOUNDS AND USES**
Chair: Ellen Unterwald, Temple University School of Medicine, USA

1:15-1:40  *Dual efficacy of DOR subtype selective ligands for ethanol consumption and its side effects of withdrawal-induced anxiety and hyperalgesia*
Jennifer Whistler and Richard van Rijn, Ernest Gallo Clinic and Research Center, University of California San Francisco, USA
1:40-2:05 Inhibition of human multiple myeloma cell proliferation by naltrindole
Richard D. Howells, UMDNJ-NJ Medical School, USA

2:05-2:30 Delta agonist glycopeptides: CNS active drugs from endogenous neuropeptides
Robin Polt, University of Arizona, USA

2:30-2:55 Delta opioid receptor agonists in Parkinson’s disease: A reappraisal
Michele Morari, University of Ferrara, Italy

Hot topic
2:55-3:10 Identity of dorsal root ganglion and spinal neurons mediating delta opioid receptor analgesia
G. Scherrer (1), B.L. Kieffer (2), A.I. Basbaum (3), A.B. MacDermott (1), (1) Columbia University, USA, (2) IGBMC, France, (3) UCSF, USA

INRC Symposium 8
Great Hall 2
3:30 PM – 5:35 PM

NOVEL THERAPEUTIC APPLICATIONS OF KAPPA OPIOID RECEPTOR LIGANDS

Chairs: Ivy Carroll, Research Triangle Institute
Bill Carlezon, McLean Hospital, USA

3:30-3:55 Natural product-derived KOP ligands as novel treatments for drug abuse
Thomas E. Prisinzano, University of Kansas, USA

3:55-4:20 High throughput in vivo screening for the identification of novel analgesics
Richard Houghten, Torrey Pines Institute for Molecular Studies, USA

4:20-4:45 Kappa opioid receptor ligands and development of antipruritic agents
Alan Cowan, Temple University School of Medicine, USA

4:45-5:10 Disruption of kappa opioid receptor function attenuates behavioral effects of stress in rodents
Bill Carlezon, McLean Hospital, USA

5:10-5:35 Discovery and development of selective kappa opioid receptor antagonists
Ivy Carroll, RTI, USA

INRC BANQUET
CATALINA YACHT
7:00 PM – 10:00 PM
BREAKFAST  Great Hall 2  7:30 AM – 8:00 AM

FOUNDERS LECTURE  Great Hall 2  8:00 AM – 9:00 AM

Dynorphins and the Kappa Opioid Receptor System – Past and Future
Charles Chavkin, Allan and Phyllis Treuer Endowed Chair of Pain Research and Professor, Department of Pharmacology, University of Washington, Seattle, WA, USA

INRC Symposium 9  Great Hall 2  9:15 AM – 11:15 AM

MOR REGULATORY PROTEINS

Chair:  Laura Bohn, The Scripps Research Institute, USA

9:15-9:40  RGS9-2 actions in the nucleus accumbens modulate opiate addiction and analgesia
           Vanna Zachariou, University of Crete, Greece

9:40-10:05  In vivo evidence for the role of PKC and other intracellular molecules in opioid tolerance
           William L. Dewey, Virginia Commonwealth University, USA

10:05-10:30  CaMKII in opioid tolerance and opioid-induced hyperalgesia
             Zaijie Jim Wang, University of Illinois, USA

10:30-10:55  Mu opioid regulation by beta-arrestins and implications for drug development
             Laura M. Bohn, The Scripps Research Institute, USA

Hot Topic
10:55-11:10  Desensitization and trafficking of mu-opioid receptors in locus coeruleus neurons: Modulation by kinases
             S. Arttamangkul, H.W. Lu, J.T. Williams, Vollum Institute, Oregon Health & Science University, Portland, Oregon, USA

INRC Symposium 10  Great Hall 2  11:30 AM – 1:40 PM

YOUNG INVESTIGATOR SYMPOSIUM: OPIOID MODULATION OF NEURAL CIRCUITS

Chair:  Michael Bruchas, Washington University School of Medicine, USA

11:30-11:35  Introduction
             Michael Bruchas, Washington University School of Medicine, USA
**Saturday, June 25, 2011**

<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
<th>Speaker</th>
<th>Institution/Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:35-12:00</td>
<td>Stress regulation of kappa opioid receptor signaling in the extended amygdala</td>
<td>Thomas Kash, University of North Carolina School of Medicine, USA</td>
<td></td>
</tr>
<tr>
<td>12:00-12:25</td>
<td>Opioid enhancement of GABA&lt;sub&gt;4&lt;/sub&gt; receptor function in VTA dopamine neurons: A novel non-G protein mediated signaling mechanism induced by stress</td>
<td>Elyssa B. Margolis, Ernest Gallo Clinic &amp; Research Center, UCSF, USA</td>
<td></td>
</tr>
<tr>
<td>12:25-12:50</td>
<td>Dopamine-mediated synaptic transmission in the VTA</td>
<td>Christopher Ford, Case Western Reserve University, USA</td>
<td></td>
</tr>
<tr>
<td>12:50-1:15</td>
<td>Context-dependent sensitization to morphine alters hippocampal neuroplasticity</td>
<td>Jose Moron-Concepcion, Columbia University Medical Center, USA</td>
<td></td>
</tr>
<tr>
<td>1:15-1:40</td>
<td>Drug-induced GABA transporter currents enhance GABA release and produce opioid withdrawal behaviours</td>
<td>Elena Bagley, The University of Sydney, Australia</td>
<td></td>
</tr>
</tbody>
</table>

END OF INRC
SEE YOU NEXT YEAR!

*BADGES MUST BE WORN FOR ALL SESSIONS AND SOCIAL EVENTS*
<table>
<thead>
<tr>
<th>Author Name</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aarde, S.</td>
<td>102</td>
</tr>
<tr>
<td>Aarde, S.M.</td>
<td>64</td>
</tr>
<tr>
<td>Abagiu, A.O.</td>
<td>120</td>
</tr>
<tr>
<td>Abdelrahman, M.S.</td>
<td>118</td>
</tr>
<tr>
<td>Abharian, P.</td>
<td>92</td>
</tr>
<tr>
<td>Abraham, A.J.</td>
<td>78</td>
</tr>
<tr>
<td>Abrams, L.C.</td>
<td>81</td>
</tr>
<tr>
<td>Accornero, V.H.</td>
<td>66, 108</td>
</tr>
<tr>
<td>Achat-Mendes, C.</td>
<td>112</td>
</tr>
<tr>
<td>Acosta, M.</td>
<td>91</td>
</tr>
<tr>
<td>Acquavita, S.P.</td>
<td>24</td>
</tr>
<tr>
<td>Acri, J.</td>
<td>30</td>
</tr>
<tr>
<td>Adams, S.</td>
<td>29</td>
</tr>
<tr>
<td>Addicott, M.</td>
<td>77, 115</td>
</tr>
<tr>
<td>Adelaja, O.A.</td>
<td>85</td>
</tr>
<tr>
<td>Adkins, R.E.</td>
<td>57</td>
</tr>
<tr>
<td>Adler, L.</td>
<td>105</td>
</tr>
<tr>
<td>Adler, M.W.</td>
<td>29, 134</td>
</tr>
<tr>
<td>Adolfo-Signore, A.</td>
<td>69</td>
</tr>
<tr>
<td>Agarrov, A.</td>
<td>62</td>
</tr>
<tr>
<td>Agnelli, R.</td>
<td>58</td>
</tr>
<tr>
<td>Agrawal, A.</td>
<td>80, 116</td>
</tr>
<tr>
<td>Agudelo, M.</td>
<td>67, 84, 134</td>
</tr>
<tr>
<td>Aguilar, M.A.</td>
<td>64, 110</td>
</tr>
<tr>
<td>Aguirre, A.</td>
<td>108</td>
</tr>
<tr>
<td>Agus, D.</td>
<td>93</td>
</tr>
<tr>
<td>Aharonovich, E.</td>
<td>132</td>
</tr>
<tr>
<td>Ahmedani, B.</td>
<td>85</td>
</tr>
<tr>
<td>Aiello, J.</td>
<td>10</td>
</tr>
<tr>
<td>Ainsworth, S.</td>
<td>70</td>
</tr>
<tr>
<td>Aizenstein, H.</td>
<td>114</td>
</tr>
<tr>
<td>Aklin, W.M.</td>
<td>132</td>
</tr>
<tr>
<td>alAbsi, M.</td>
<td>104</td>
</tr>
<tr>
<td>Alam-Mehrjerdi, Z.</td>
<td>92</td>
</tr>
<tr>
<td>Albizu, C.E.</td>
<td>70</td>
</tr>
<tr>
<td>Aleixandre-Benavent, R.</td>
<td>85</td>
</tr>
<tr>
<td>Alessi, S.M.</td>
<td>21</td>
</tr>
<tr>
<td>Alexandre, P.K.</td>
<td>73</td>
</tr>
<tr>
<td>Alford, D.</td>
<td>80</td>
</tr>
<tr>
<td>Ali, S.F.</td>
<td>133</td>
</tr>
<tr>
<td>Allen, A.</td>
<td>104</td>
</tr>
<tr>
<td>Allen, S.S.</td>
<td>104</td>
</tr>
<tr>
<td>Allenby, K.S.</td>
<td>117</td>
</tr>
<tr>
<td>Allensworth-Davies, D.</td>
<td>80</td>
</tr>
<tr>
<td>Allsop, D.</td>
<td>117</td>
</tr>
<tr>
<td>Almirall, D.</td>
<td>89, 106</td>
</tr>
<tr>
<td>Altarifi, A.</td>
<td>122</td>
</tr>
<tr>
<td>Alterman, A.</td>
<td>81</td>
</tr>
<tr>
<td>Alvers, K.M.</td>
<td>64, 112</td>
</tr>
<tr>
<td>Amador, N.J.</td>
<td>81</td>
</tr>
<tr>
<td>Ambrosio, E.</td>
<td>23, 112</td>
</tr>
<tr>
<td>Amesty, S.</td>
<td>67, 73</td>
</tr>
<tr>
<td>Ang, A.</td>
<td>60</td>
</tr>
<tr>
<td>Angrish, D.</td>
<td>102</td>
</tr>
<tr>
<td>Anker, J.J.</td>
<td>26, 63, 110</td>
</tr>
<tr>
<td>Anselmi, C.</td>
<td>28</td>
</tr>
<tr>
<td>Anthony, J.C.</td>
<td>21, 22, 66, 68, 85</td>
</tr>
<tr>
<td>Antoine, D.</td>
<td>92</td>
</tr>
<tr>
<td>Anton, R.F.</td>
<td>88</td>
</tr>
<tr>
<td>Antunez, E.</td>
<td>73</td>
</tr>
<tr>
<td>Apelt, S.M.</td>
<td>9</td>
</tr>
<tr>
<td>Arangua, L.E.</td>
<td>22</td>
</tr>
<tr>
<td>Arasteh, K.</td>
<td>10</td>
</tr>
<tr>
<td>Araujo, A.C.</td>
<td>81</td>
</tr>
<tr>
<td>Arcari, C.</td>
<td>22</td>
</tr>
<tr>
<td>Arcidiacono, S.</td>
<td>18</td>
</tr>
<tr>
<td>Arenander, J.</td>
<td>58</td>
</tr>
<tr>
<td>Arfken, C.L.</td>
<td>15, 21, 67, 70, 72</td>
</tr>
<tr>
<td>Arheart, K.L.</td>
<td>108</td>
</tr>
<tr>
<td>Aronson, I.D.</td>
<td>120</td>
</tr>
<tr>
<td>Arora, S.</td>
<td>23</td>
</tr>
<tr>
<td>Arria, A.M.</td>
<td>108</td>
</tr>
<tr>
<td>Arruda Vieira Duarte, P.C.</td>
<td>68</td>
</tr>
<tr>
<td>Ary, A.W.</td>
<td>26, 115</td>
</tr>
<tr>
<td>Aschauer, C.</td>
<td>109</td>
</tr>
<tr>
<td>Ashare, R.</td>
<td>115</td>
</tr>
<tr>
<td>Ashworth, J.B.</td>
<td>13</td>
</tr>
<tr>
<td>Astemborski, J.</td>
<td>67</td>
</tr>
<tr>
<td>Astone-Twerell, J.</td>
<td>70</td>
</tr>
<tr>
<td>Ator, N.A.</td>
<td>26</td>
</tr>
<tr>
<td>Attuaka, C.</td>
<td>78</td>
</tr>
<tr>
<td>August, G.</td>
<td>90</td>
</tr>
<tr>
<td>Auriacombe, M.</td>
<td>18, 81, 87, 88, 92</td>
</tr>
<tr>
<td>Ayestas, M.A.</td>
<td>63, 102</td>
</tr>
<tr>
<td>Azimi Alamdari, S.</td>
<td>92</td>
</tr>
<tr>
<td>Aziziyeh, A.</td>
<td>27</td>
</tr>
<tr>
<td>Babalonis, S.</td>
<td>92</td>
</tr>
<tr>
<td>Babb, D.</td>
<td>88</td>
</tr>
<tr>
<td>Babuscio, T.</td>
<td>12, 24</td>
</tr>
<tr>
<td>Bachrach, K.</td>
<td>86</td>
</tr>
<tr>
<td>Back, S.E.</td>
<td>13, 22, 92</td>
</tr>
<tr>
<td>Badger, G.J.</td>
<td>17, 24, 87</td>
</tr>
<tr>
<td>Baer, S.J.</td>
<td>114</td>
</tr>
<tr>
<td>Baevert, A.</td>
<td>108, 109</td>
</tr>
<tr>
<td>Baggott, M.J.</td>
<td>16, 59, 83, 102</td>
</tr>
<tr>
<td>Bailey, G.</td>
<td>56</td>
</tr>
<tr>
<td>Bailey, W.C.</td>
<td>81</td>
</tr>
<tr>
<td>Bakalkin, G.</td>
<td>75</td>
</tr>
<tr>
<td>Baker, A.K.</td>
<td>24</td>
</tr>
<tr>
<td>Baker, C.M.</td>
<td>77</td>
</tr>
<tr>
<td>Baker, N.A.</td>
<td>117</td>
</tr>
<tr>
<td>Baladi, M.</td>
<td>131</td>
</tr>
<tr>
<td>Balan, S.</td>
<td>6, 118</td>
</tr>
<tr>
<td>Balducci, X.</td>
<td>92</td>
</tr>
<tr>
<td>Balester Mouret, S.</td>
<td>22</td>
</tr>
<tr>
<td>Ballard, M.E.</td>
<td>6</td>
</tr>
<tr>
<td>Ballesteros-Yañez, I.</td>
<td>112</td>
</tr>
<tr>
<td>Ballis, M.</td>
<td>18</td>
</tr>
<tr>
<td>Balster, R.L.</td>
<td>2, 26, 104</td>
</tr>
<tr>
<td>Balter, R.E.</td>
<td>122</td>
</tr>
<tr>
<td>Ban, D.</td>
<td>115</td>
</tr>
<tr>
<td>Bandstra, E.S.</td>
<td>5, 66, 108</td>
</tr>
<tr>
<td>Banducci, A.N.</td>
<td>88</td>
</tr>
<tr>
<td>Banich, M.T.</td>
<td>11, 77</td>
</tr>
<tr>
<td>Bantchevska, D.</td>
<td>65</td>
</tr>
<tr>
<td>Bardo, M.T.</td>
<td>64, 110, 112</td>
</tr>
<tr>
<td>Barger, J.</td>
<td>86</td>
</tr>
<tr>
<td>Barnes, A.</td>
<td>102</td>
</tr>
<tr>
<td>Barnes, K.</td>
<td>16</td>
</tr>
<tr>
<td>Baron, M.</td>
<td>57</td>
</tr>
<tr>
<td>Barondess, D.A.</td>
<td>21</td>
</tr>
<tr>
<td>Barry, D.</td>
<td>82, 89</td>
</tr>
<tr>
<td>Barry, K.</td>
<td>91</td>
</tr>
<tr>
<td>Bart, B.A.</td>
<td>92</td>
</tr>
<tr>
<td>Bart, G.</td>
<td>92</td>
</tr>
<tr>
<td>Barth, K.</td>
<td>16</td>
</tr>
<tr>
<td>Bartholomew, N.G.</td>
<td>69, 71</td>
</tr>
<tr>
<td>Barthwell, A.</td>
<td>8</td>
</tr>
<tr>
<td>Bass, A.</td>
<td>13</td>
</tr>
<tr>
<td>Bass, C.E.</td>
<td>62</td>
</tr>
<tr>
<td>Basso-Musso, L.</td>
<td>27</td>
</tr>
<tr>
<td>Bastle, R.M.</td>
<td>63</td>
</tr>
<tr>
<td>Author</td>
<td>Pages</td>
</tr>
<tr>
<td>--------</td>
<td>-------</td>
</tr>
<tr>
<td>Bastos, T.M.</td>
<td>11</td>
</tr>
<tr>
<td>Basu, A.</td>
<td>6</td>
</tr>
<tr>
<td>Batel, P.</td>
<td>22</td>
</tr>
<tr>
<td>Batki, S.L.</td>
<td>84, 88</td>
</tr>
<tr>
<td>Batra, V.</td>
<td>109</td>
</tr>
<tr>
<td>Batten, S.</td>
<td>87</td>
</tr>
<tr>
<td>Baumann, M.H.</td>
<td>63, 102, 133</td>
</tr>
<tr>
<td>Bäwert, A.</td>
<td>109</td>
</tr>
<tr>
<td>Beadnell, B.</td>
<td>10</td>
</tr>
<tr>
<td>Beardsley, P.M.</td>
<td>63</td>
</tr>
<tr>
<td>Beatty, G.</td>
<td>58</td>
</tr>
<tr>
<td>Beatty, J.R.</td>
<td>101</td>
</tr>
<tr>
<td>Becerra, L.</td>
<td>101</td>
</tr>
<tr>
<td>Becker, K.</td>
<td>10</td>
</tr>
<tr>
<td>Beckman, N.</td>
<td>90</td>
</tr>
<tr>
<td>Beckmann, J.</td>
<td>110, 112</td>
</tr>
<tr>
<td>Bedi, G.</td>
<td>117</td>
</tr>
<tr>
<td>Behrendt, S.</td>
<td>76</td>
</tr>
<tr>
<td>Behrens, A.</td>
<td>18</td>
</tr>
<tr>
<td>Beitel, M.</td>
<td>82</td>
</tr>
<tr>
<td>Beltran, V.</td>
<td>81, 87, 92</td>
</tr>
<tr>
<td>Ben Abdallah, A.</td>
<td>14, 20, 56, 68, 69</td>
</tr>
<tr>
<td>Benamar, K.</td>
<td>29</td>
</tr>
<tr>
<td>Benbenishty, R.</td>
<td>27</td>
</tr>
<tr>
<td>Benchaar, M.</td>
<td>22</td>
</tr>
<tr>
<td>Bender, A.</td>
<td>79</td>
</tr>
<tr>
<td>Benishek, L.A.</td>
<td>12</td>
</tr>
<tr>
<td>Bennett, A.S.</td>
<td>120</td>
</tr>
<tr>
<td>Bennett, R.</td>
<td>15, 59</td>
</tr>
<tr>
<td>Benningfield, M.M.</td>
<td>108, 119</td>
</tr>
<tr>
<td>Benowitz, N.L.</td>
<td>61</td>
</tr>
<tr>
<td>Ben-Shahar, O.</td>
<td>111</td>
</tr>
<tr>
<td>Benzano, D.</td>
<td>68</td>
</tr>
<tr>
<td>Berger, A.</td>
<td>25</td>
</tr>
<tr>
<td>Berkel, L.A.</td>
<td>22</td>
</tr>
<tr>
<td>Berning, A.</td>
<td>68</td>
</tr>
<tr>
<td>Bernstein, L.M.</td>
<td>87</td>
</tr>
<tr>
<td>Bernstein, J.</td>
<td>80</td>
</tr>
<tr>
<td>Berry, M.S.</td>
<td>70, 86</td>
</tr>
<tr>
<td>Berry, S.</td>
<td>10</td>
</tr>
<tr>
<td>Bettcher, D.</td>
<td>120</td>
</tr>
<tr>
<td>Beveridge, T.J.</td>
<td>111</td>
</tr>
<tr>
<td>Beyley, L.J.</td>
<td>64, 75, 110</td>
</tr>
<tr>
<td>Bi, G.H.</td>
<td>110</td>
</tr>
<tr>
<td>Bickel, W.K.</td>
<td>17, 21, 91, 101, 114, 132</td>
</tr>
<tr>
<td>Bidwell, L.</td>
<td>65</td>
</tr>
<tr>
<td>Bierut, L.</td>
<td>65</td>
</tr>
<tr>
<td>Bigelow, G.E.</td>
<td>28, 76, 81, 91, 107, 121</td>
</tr>
<tr>
<td>Birchfield, T.R.</td>
<td>7</td>
</tr>
<tr>
<td>Bisaga, A.</td>
<td>27, 92</td>
</tr>
<tr>
<td>Bisen-Hersh, E.B.</td>
<td>110</td>
</tr>
<tr>
<td>Bizon, J.L.</td>
<td>20, 63</td>
</tr>
<tr>
<td>Black, A.C.</td>
<td>65</td>
</tr>
<tr>
<td>Black, R.A.</td>
<td>14, 15</td>
</tr>
<tr>
<td>Blackford, J.U.</td>
<td>119</td>
</tr>
<tr>
<td>Blaine, S.</td>
<td>77</td>
</tr>
<tr>
<td>Blanco, C.</td>
<td>28</td>
</tr>
<tr>
<td>Blaney, S.</td>
<td>67, 73, 78</td>
</tr>
<tr>
<td>Blank, J.C.</td>
<td>18</td>
</tr>
<tr>
<td>Blank, M.D.</td>
<td>61</td>
</tr>
<tr>
<td>Bleich, L.</td>
<td>21</td>
</tr>
<tr>
<td>Blokhina, E.A.</td>
<td>67</td>
</tr>
<tr>
<td>Blough, B.E.</td>
<td>63</td>
</tr>
<tr>
<td>Blow, F.C.</td>
<td>72, 85, 90, 91</td>
</tr>
<tr>
<td>Bobashev, G.</td>
<td>8</td>
</tr>
<tr>
<td>Bocher, M.</td>
<td>77</td>
</tr>
<tr>
<td>Bockman, C.S.</td>
<td>134</td>
</tr>
<tr>
<td>Bodenheimer, H.</td>
<td>9</td>
</tr>
<tr>
<td>Bogenschutz, M.P.</td>
<td>13, 18, 86</td>
</tr>
<tr>
<td>Boggs, D.L.</td>
<td>117</td>
</tr>
<tr>
<td>Bohnert, A.S.</td>
<td>68, 72, 82, 85</td>
</tr>
<tr>
<td>Bohnert, K.M.</td>
<td>91</td>
</tr>
<tr>
<td>Bois, F.</td>
<td>77, 115</td>
</tr>
<tr>
<td>Bolanos, F.</td>
<td>60</td>
</tr>
<tr>
<td>Bolden, M.</td>
<td>21</td>
</tr>
<tr>
<td>Boney, T.Y.</td>
<td>70</td>
</tr>
<tr>
<td>Boos, T.L.</td>
<td>57, 72</td>
</tr>
<tr>
<td>Booth, B.M.</td>
<td>13, 90, 91</td>
</tr>
<tr>
<td>Booth, C.</td>
<td>84</td>
</tr>
<tr>
<td>Booth, R.E.</td>
<td>9, 62</td>
</tr>
<tr>
<td>Bora, E.</td>
<td>87</td>
</tr>
<tr>
<td>Borges, M.D.</td>
<td>11</td>
</tr>
<tr>
<td>Bosc, E.</td>
<td>18</td>
</tr>
<tr>
<td>Bourne, N.</td>
<td>62, 134</td>
</tr>
<tr>
<td>Bowen, S.</td>
<td>7, 104</td>
</tr>
<tr>
<td>Bowers, C.</td>
<td>102</td>
</tr>
<tr>
<td>Boyd, C.J.</td>
<td>105</td>
</tr>
<tr>
<td>Bracken, B.K.</td>
<td>15</td>
</tr>
<tr>
<td>Bradford, S.E.</td>
<td>14, 56, 135</td>
</tr>
<tr>
<td>Bradley, K.</td>
<td>86</td>
</tr>
<tr>
<td>Bradstreet, M.P.</td>
<td>24</td>
</tr>
<tr>
<td>Brady, K.T.</td>
<td>8, 13, 16, 22, 56, 67, 92, 104, 107, 117</td>
</tr>
<tr>
<td>Brady, R.</td>
<td>118</td>
</tr>
<tr>
<td>Brains, B.</td>
<td>27, 69, 89</td>
</tr>
<tr>
<td>Breland, M.</td>
<td>11, 12, 15, 60, 61</td>
</tr>
<tr>
<td>Bremer, N.M.</td>
<td>62</td>
</tr>
<tr>
<td>Brensilver, M.</td>
<td>59</td>
</tr>
<tr>
<td>Bresani, E.</td>
<td>12</td>
</tr>
<tr>
<td>Bressan, R.</td>
<td>28</td>
</tr>
<tr>
<td>Brewer, J.</td>
<td>24</td>
</tr>
<tr>
<td>Brewer, W.J.</td>
<td>87</td>
</tr>
<tr>
<td>Bricker, J.</td>
<td>90</td>
</tr>
<tr>
<td>Bridden, C.</td>
<td>67</td>
</tr>
<tr>
<td>Brigham, G.S.</td>
<td>13</td>
</tr>
<tr>
<td>Brim, R.L.</td>
<td>112</td>
</tr>
<tr>
<td>Britton, W.</td>
<td>117</td>
</tr>
<tr>
<td>Broadbear, J.H.</td>
<td>102, 119</td>
</tr>
<tr>
<td>Brody, J.L.</td>
<td>105</td>
</tr>
<tr>
<td>Broft, A.</td>
<td>113</td>
</tr>
<tr>
<td>Brom, D.</td>
<td>27</td>
</tr>
<tr>
<td>Brooks, A.C.</td>
<td>12, 79</td>
</tr>
<tr>
<td>Brooks, D.</td>
<td>27, 88</td>
</tr>
<tr>
<td>Brooks, D.J.</td>
<td>58, 117</td>
</tr>
<tr>
<td>Brooner, R.K.</td>
<td>10, 27, 89, 122</td>
</tr>
<tr>
<td>Brothers, S.</td>
<td>131</td>
</tr>
<tr>
<td>Brower, K.</td>
<td>85</td>
</tr>
<tr>
<td>Brown, A.</td>
<td>89</td>
</tr>
<tr>
<td>Brown, G.S.</td>
<td>15, 17, 59</td>
</tr>
<tr>
<td>Brown, L.S.</td>
<td>67</td>
</tr>
<tr>
<td>Brown, D.C.</td>
<td>65</td>
</tr>
<tr>
<td>Brown, R.D.</td>
<td>14</td>
</tr>
<tr>
<td>Brown, S.A.</td>
<td>60, 88, 90</td>
</tr>
<tr>
<td>Bruner, N.R.</td>
<td>76</td>
</tr>
<tr>
<td>Bruno, R.</td>
<td>23</td>
</tr>
<tr>
<td>Bruzios, C.</td>
<td>56</td>
</tr>
<tr>
<td>Bryan, A.</td>
<td>91</td>
</tr>
<tr>
<td>Bryant, V.</td>
<td>115</td>
</tr>
<tr>
<td>Bryda, E.</td>
<td>115</td>
</tr>
<tr>
<td>Bucher Bartelson, B.</td>
<td>14</td>
</tr>
<tr>
<td>Buchholtz, C.</td>
<td>14</td>
</tr>
<tr>
<td>Buchholz, M.</td>
<td>80</td>
</tr>
<tr>
<td>Budman, S.H.</td>
<td>14, 15</td>
</tr>
<tr>
<td>Budney, A.J.</td>
<td>30, 65, 101, 114, 117</td>
</tr>
</tbody>
</table>
Budygin, E.A.  58  
Bueno-Cañigral, F.J.  85  
Bukten, A.  135  
Bumaguin, D.B.  68  
Burlew, A.K.  10  
Burlew, K.A.  79  
Burmeister, M.  6  
Burns, L.  23, 119  
Burton, M.  24  
Busse, A.  57  
Butelman, E.  25  
Butler, S.F.  14, 15  
Butt, A.  109  
Byrne, S.  24  
Cacciola, J.  81  
Caceda, R.  88  
Cai, L.  81  
Calderon, S.  31  
Calsyn, D.A.  10, 20, 122  
Calvo-Friedman, A.  113  
Camenga, D.  89  
Camilleri, A.  81  
Campbell, A.  66  
Campbell, J.C.  111  
Campello, G.  57  
Campollo, O.  12, 13  
Campos, M.B.  11  
Canal, C.  62  
Canamar, C.  15  
Cannon-Bowers, J.  102  
Cao, A.  119  
Carbonaro, T.  7, 59  
Cardoso, A.V.  11  
Carey, A.N.  134  
Carise, D.  12, 78, 79  
Carlson, R.G.  13, 72  
Carlsson, A.  84  
Carmody, T.  12  
Carney, T.  90  
Carpenedo, C.M.  12  
Carpenter, K.M.  79, 113  
Carpenter, L.  116  
Carpenter, M.J.  19  
Carpiano, R.M.  22  
Carr, A.E.  18  
Carrico, A.W.  73  
Carroll, F.  2, 106  
Carroll, K.M.  12, 24, 107, 118  
Carroll, M.E.  63, 75, 104, 110  
Carson, R.  77, 112, 113  
Carter, A.E.  13, 17  
Carter, L.  74  
Caruana, A.  111  
Carvey, P.M.  112  
Casadonte, P.  121  
Case, B.G.  105  
Cassar, J.  23  
Cassidy, T.A.  14, 15  
Castagné, V.  64  
Castel, S.  89  
Castillo, C.  60, 85, 87  
Catania, J.A.  73  
Cavalca, E.  105  
Cavallo, D.  20, 89  
Cavazos, P.  65  
Cerdá, M.  78  
Cervenka, S.  113  
Chaisson, C.  67  
Chakraborty, B.  7, 116  
Chalmers, J.  78  
Chan, C.  104  
Chan, T.  69  
Chang, J.  91  
Chang, L.  19, 66  
Chang, S.  134  
Chang, Y.  9, 64  
Chaple, M.  101  
Charles, T.  67  
Charnigo, R.  87  
Chavez, R.  120  
Chawarski, M.C.  68, 76, 92, 121, 122  
Cheetham, S.C.  63  
Chen, C.  65, 116  
Chen, C.Y.  93  
Chen, K.W.  88  
Chen, L.  73  
Chen, N.  13  
Chen, S.  30  
Chen, W.  65  
Cheng, D.M.  67, 80  
Cheng, K.  7  
Cheng, M.  116  
Cheng, W.  27, 79  
Chermack, S.T.  91  
Cheung, T.H.  134  
Chhatre, S.  22  
Chiang, N.  83, 92  
Chien, Y.L.  93  
Chilcoat, H.  14, 72  
Childress, A.R.  2, 77, 112, 113  
Chisin, R.  77  
Chisolm, M.S.  18, 24, 81, 121  
Chitnavis, P.  61  
Cho, D.  57  
Christensen, C.  67  
Christensen, D.R.  17  
Christou, D.  11, 60, 61  
Chudzynski, J.  132  
Chun, L.  110  
Chung, T.  114  
Ciccioccioppo, R.  131  
Cicero, T.J.  67, 72, 78  
Clair, M.  69  
Clark, B.  21, 70  
Clark, C.A.  70  
Clark, C.B.  20, 70  
Clark, D.B.  112  
Claus, E.  11  
Claus, R.E.  57  
Clausen, T.  135  
Clements, N.  78  
Cloak, C.  66  
Coates, S.J.  59  
Cobb, C.O.  61  
Cobuzzi, J.L.  122  
Coetzee, J.  84  
Cohen, J.  61  
Cohen, S.  73  
Cohn, J.  67  
Cojocaru, E.  120  
Colby, S.M.  65, 87  
Coleman, S.  67  
Coleman-Cowger, V.H.  90  
Colfax, G.  73  
Colina, A.A.  86, 87  
Colina, I.A.  86  
Collado-Rodriguez, A.  65  
Collins, G.T.  112
Collins, J.  65
Collins, R.L.  117, 118
Comer, S.D.  13, 23, 28, 82, 91, 103, 117
Compton, R.  68
Conceicao, T.V.  85
Cone, E.J.  120
Connell, C.  89
Conner, K.  85
Connery, H.  14, 56
Connolly, G.N.  20, 83
Connor, J.R.  103
Conti, A.  7
Conus, P.  87
Conway, S.  25
Cook, J.M.  7
Coop, A.  83
Cooper, C.  132
Cooper, Z.D.  28, 82, 91, 117
Copeland, J.  117, 118
Copersino, M.L.  19, 117
Coplan, P.M.  14, 72, 122
Corbly, K.F.  9, 73
Cosgrove, K.  77, 115
Costa, J.P.  11
Costello, P.  101
Cottler, L.B.  14, 15, 20, 22, 56, 65, 68, 69, 135
Cotton, S.  87
Courson, J.A.  26
Courty, P.  57
Cousijn, J.  77, 114
Cousins, S.  86
Coviello, D.M.  70
Cowan, A.  29
Cowan, R.  119
Cox, A.O.  83
Coyle, J.R.  16, 59, 83
Coyle, M.G.  24, 108, 109, 121
Cozzi, N.V.  102
Craige, C.  62
Cranford, J.A.  105
Crawford, C.A.  64
Crawford, J.T.  111
Crawford, N.  73
Creceles, R.E.  56
Crechan, K.  64, 102
Creemers, H.E.  66, 76, 116
Crevecoeur-MacPhail, D.A.  86
Crisafulli, M.  56
Croft, J.  78
Cronkite, R.C.  85
Crooks, P.  112
Cropsey, K.L.  20, 21, 70
Crouch, K.  28
Crowley, T.J.  11, 73, 77, 90
Cruciani, R.  81, 82
Cruz, S.  104
Cruz, V.  68
Cui, D.  116
Cui, W.Y.  134
Cummings, K.M.  89
Cummings, S.M.  15, 68, 69
Cunningham, C.S.  133
Cunningham, J.K.  12, 13
Cunningham, K.A.  17, 26, 61, 62, 83, 109, 111, 112, 134
Cunningham, R.  90
Curley, L.E.  102, 119
Curran, E.  89
Currier, R.  120
Curro, F.  80
Cutler, M.  81
Cutter, C.J.  82, 89
D’Apolito, K.  57
D’Sa, C.  16
D’Souza, J.  119
Dahlgren, M.K.  28
Dahne, J.R.  66
Dakwar, E.  13
Daley, D.  114
Dallery, J.  21
Dalwani, M.S.  77
Damborsky, J.C.  20
Daniels, A.M.  93
Daniulaityte, R.  72
Dantona, R.L.  17
Dart, R.C.  14
Das, M.  73
Daughters, S.B.  19, 60
Daulouede, J.P.  81, 86, 87, 92
David, S.P.  6
Davies, R.  105
Davis, J.  14
Davis, Jr., K.H.  57, 83, 106
Davis, W.W.  93
Daw, R.C.  83
Daza-Losada, M.  64
De Boni, R.B.  68, 85
de Dios, M.A.  117
De Felipe, J.  112
De Graaff, B.  23
de Kater, A.  83
De La Garza, II, R.  15, 16, 17, 27, 59
De Leon, D.  86
de Wit, H.  6
DeBoni, R.  68
DeCaria, K.  69
DeFulio, A.  91, 121
del Rio, C.  73
Deleone, C.  24
Dell, C.A.  104
Delmastro, K.K.  113
DeLottinville, C.  105
Delucchi, K.L.  9
Deng, Q.  68
Denis, C.  18, 81, 88, 92
Denisco, R.  25
Dennis, M.L.  30, 73, 74
Dereffinko, K.J.  88, 116
Dersch, C.M.  122
Des Jarlais, D.C.  9, 10
DeSantis, S.M.  13
Deschamps, J.R.  106
Desko, A.  122
Desrochers, D.C.  9, 10
DeSantis, S.M.  13
Deschamps, J.R.  106
Desko, A.  122
DeVane, L.  16
DeVargas, E.  91
Dévieux, J.  115
Dewey, W.  2
DeWitt, S.  77
<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dhingra, L.</td>
<td>25</td>
</tr>
<tr>
<td>Di Iorio, C.R.</td>
<td>119</td>
</tr>
<tr>
<td>Di Iorio, D.R.</td>
<td>119</td>
</tr>
<tr>
<td>Diaz, E.</td>
<td>118</td>
</tr>
<tr>
<td>Diaz, F.</td>
<td>12, 13</td>
</tr>
<tr>
<td>Dibble, A.</td>
<td>80</td>
</tr>
<tr>
<td>Dick, D.</td>
<td>116</td>
</tr>
<tr>
<td>Dickerson, D.L.</td>
<td>13, 132</td>
</tr>
<tr>
<td>Dickerson, T.J.</td>
<td>102</td>
</tr>
<tr>
<td>Dickey, E.D.</td>
<td>63</td>
</tr>
<tr>
<td>Dickson, M.F.</td>
<td>69</td>
</tr>
<tr>
<td>Dietrich, M.S.</td>
<td>108, 119</td>
</tr>
<tr>
<td>DiGirolamo, G.</td>
<td>92</td>
</tr>
<tr>
<td>Digiusto, E.</td>
<td>118</td>
</tr>
<tr>
<td>DiGiuseppi, G.T.</td>
<td>79</td>
</tr>
<tr>
<td>DiLeone, R.J.</td>
<td>16, 61, 62</td>
</tr>
<tr>
<td>Dillon, P.M.</td>
<td>11, 19, 61</td>
</tr>
<tr>
<td>Dimmock, J.</td>
<td>88</td>
</tr>
<tr>
<td>Dinele, R.</td>
<td>112</td>
</tr>
<tr>
<td>Dinh, A.T.</td>
<td>58</td>
</tr>
<tr>
<td>DiPirro, J.M.</td>
<td>65</td>
</tr>
<tr>
<td>Dobrin, C.</td>
<td>110</td>
</tr>
<tr>
<td>Dobscha, S.K.</td>
<td>82</td>
</tr>
<tr>
<td>Dolezal, B.</td>
<td>132</td>
</tr>
<tr>
<td>Domenech, L.</td>
<td>27</td>
</tr>
<tr>
<td>Dominy, S.</td>
<td>9</td>
</tr>
<tr>
<td>Dong, A.</td>
<td>122</td>
</tr>
<tr>
<td>Donham, R.</td>
<td>73</td>
</tr>
<tr>
<td>Donlin, W.</td>
<td>121</td>
</tr>
<tr>
<td>Donovan, D.M.</td>
<td>13, 18, 107</td>
</tr>
<tr>
<td>Donovan, J.</td>
<td>16</td>
</tr>
<tr>
<td>Doshi, R.K.</td>
<td>73</td>
</tr>
<tr>
<td>Douaihy, A.</td>
<td>87, 88, 114</td>
</tr>
<tr>
<td>Dougherty, W.</td>
<td>57</td>
</tr>
<tr>
<td>Dow-Edwards, D.</td>
<td>5, 18</td>
</tr>
<tr>
<td>Downing, J.M.</td>
<td>14, 72</td>
</tr>
<tr>
<td>Doyle, S.E.</td>
<td>103, 104</td>
</tr>
<tr>
<td>Draper, J.</td>
<td>61</td>
</tr>
<tr>
<td>Draus, P.J.</td>
<td>69</td>
</tr>
<tr>
<td>Drexler, K.</td>
<td>15</td>
</tr>
<tr>
<td>Du, J.</td>
<td>93, 122</td>
</tr>
<tr>
<td>Du, Y.P.</td>
<td>77</td>
</tr>
<tr>
<td>Duan, R.</td>
<td>10, 73</td>
</tr>
<tr>
<td>Duarte, P.</td>
<td>85</td>
</tr>
<tr>
<td>Dubose, B.</td>
<td>66</td>
</tr>
<tr>
<td>DuBose, P.</td>
<td>79</td>
</tr>
<tr>
<td>Duckart, J.</td>
<td>82</td>
</tr>
<tr>
<td>Duffee, D.</td>
<td>121</td>
</tr>
<tr>
<td>Dugosh, K.L.</td>
<td>12, 78, 81, 135</td>
</tr>
<tr>
<td>Duke, A.N.</td>
<td>20, 28</td>
</tr>
<tr>
<td>Dunn, C.</td>
<td>13</td>
</tr>
<tr>
<td>Dunn, K.E.</td>
<td>8, 21, 121</td>
</tr>
<tr>
<td>Dunne, E.</td>
<td>66</td>
</tr>
<tr>
<td>DuPont, R.L.</td>
<td>120</td>
</tr>
<tr>
<td>Durham, T.</td>
<td>10</td>
</tr>
<tr>
<td>Duvall, J.L.</td>
<td>11</td>
</tr>
<tr>
<td>Dvoskin, L.</td>
<td>112</td>
</tr>
<tr>
<td>Dykstra, L.A.</td>
<td>81, 122, 132</td>
</tr>
<tr>
<td>Eaddy, J.L.</td>
<td>13</td>
</tr>
<tr>
<td>Eagle, A.L.</td>
<td>119</td>
</tr>
<tr>
<td>Easterbrook, A.</td>
<td>22</td>
</tr>
<tr>
<td>Eaton, T.A.</td>
<td>14</td>
</tr>
<tr>
<td>Ebner, N.</td>
<td>109</td>
</tr>
<tr>
<td>Ebstein, R.</td>
<td>77</td>
</tr>
<tr>
<td>Eckmann, M.</td>
<td>82</td>
</tr>
<tr>
<td>Edwards, P.</td>
<td>72</td>
</tr>
<tr>
<td>Ehrich, E.</td>
<td>83</td>
</tr>
<tr>
<td>Ehrman, R.N.</td>
<td>77, 112, 113</td>
</tr>
<tr>
<td>Eisenstein, T.K.</td>
<td>26, 134</td>
</tr>
<tr>
<td>Eissenberg, T.</td>
<td>20, 61</td>
</tr>
<tr>
<td>Ekhtiari, H.</td>
<td>92</td>
</tr>
<tr>
<td>El Rawas, R.</td>
<td>111</td>
</tr>
<tr>
<td>Elkader, A.</td>
<td>69</td>
</tr>
<tr>
<td>Elkoussi, A.A.</td>
<td>118</td>
</tr>
<tr>
<td>Ellis, M.S.</td>
<td>72</td>
</tr>
<tr>
<td>Elliston, P.K.</td>
<td>69</td>
</tr>
<tr>
<td>Elsayed, D.</td>
<td>14, 82</td>
</tr>
<tr>
<td>Elshahed, M.A.</td>
<td>118</td>
</tr>
<tr>
<td>Eltareb, M.H.</td>
<td>18</td>
</tr>
<tr>
<td>Elton, A.</td>
<td>19, 114</td>
</tr>
<tr>
<td>Emerson, J.</td>
<td>80</td>
</tr>
<tr>
<td>Emeson, R.B.</td>
<td>111</td>
</tr>
<tr>
<td>Emurian, C.E.</td>
<td>113</td>
</tr>
<tr>
<td>English, J.S.</td>
<td>20</td>
</tr>
<tr>
<td>Enman, N.</td>
<td>111</td>
</tr>
<tr>
<td>Enoch, M.</td>
<td>115</td>
</tr>
<tr>
<td>Epstein, D.H.</td>
<td>91, 101</td>
</tr>
<tr>
<td>Erdem, G.</td>
<td>65</td>
</tr>
<tr>
<td>Erickson, S.</td>
<td>10</td>
</tr>
<tr>
<td>Ernst, T.</td>
<td>19, 66</td>
</tr>
<tr>
<td>Ertischek, M.D.</td>
<td>120</td>
</tr>
<tr>
<td>Eshera, N.</td>
<td>60</td>
</tr>
<tr>
<td>España, R.A.</td>
<td>25</td>
</tr>
<tr>
<td>Esterlis, I.</td>
<td>77, 115</td>
</tr>
<tr>
<td>Evans, E.</td>
<td>12</td>
</tr>
<tr>
<td>Evans, S.M.</td>
<td>76</td>
</tr>
<tr>
<td>Evans-Polce, R.J.</td>
<td>22</td>
</tr>
<tr>
<td>Evatt, D.P.</td>
<td>61</td>
</tr>
<tr>
<td>Everhart, E.</td>
<td>83</td>
</tr>
<tr>
<td>Everly, J.J.</td>
<td>121</td>
</tr>
<tr>
<td>Evins, A.E.</td>
<td>6, 115</td>
</tr>
<tr>
<td>Fabianski, R.</td>
<td>112, 113</td>
</tr>
<tr>
<td>Fadel, J.R.</td>
<td>61</td>
</tr>
<tr>
<td>Fagan, P.</td>
<td>109</td>
</tr>
<tr>
<td>Fahey, J.</td>
<td>93, 121</td>
</tr>
<tr>
<td>Fain, T.</td>
<td>10</td>
</tr>
<tr>
<td>Fairman, B.</td>
<td>22</td>
</tr>
<tr>
<td>Falck, R.</td>
<td>13, 72</td>
</tr>
<tr>
<td>Falcon, R.</td>
<td>68</td>
</tr>
<tr>
<td>Faller, S.</td>
<td>68</td>
</tr>
<tr>
<td>Fan, J.</td>
<td>12</td>
</tr>
<tr>
<td>Fan, W.Y.</td>
<td>29</td>
</tr>
<tr>
<td>Fang, W.B.</td>
<td>82</td>
</tr>
<tr>
<td>Fant, R.V.</td>
<td>120</td>
</tr>
<tr>
<td>Fantegrossi, W.E.</td>
<td>72</td>
</tr>
<tr>
<td>Farde, L.</td>
<td>113</td>
</tr>
<tr>
<td>Farmer, S.L.</td>
<td>24</td>
</tr>
<tr>
<td>Farré, M.</td>
<td>85, 87</td>
</tr>
<tr>
<td>Farrell, E.</td>
<td>22</td>
</tr>
<tr>
<td>Farrell-Moore, D.</td>
<td>80</td>
</tr>
<tr>
<td>Farrer, L.A.</td>
<td>88</td>
</tr>
<tr>
<td>Fatséas, M.</td>
<td>18, 81, 88, 92</td>
</tr>
<tr>
<td>Faulknor, J.</td>
<td>13</td>
</tr>
<tr>
<td>Fava, M.</td>
<td>6, 115</td>
</tr>
<tr>
<td>Fazzino, T.</td>
<td>89, 122</td>
</tr>
<tr>
<td>Fearer, S.</td>
<td>101</td>
</tr>
<tr>
<td>Feaster, D.J.</td>
<td>10, 73</td>
</tr>
<tr>
<td>Feldman, B.</td>
<td>91</td>
</tr>
<tr>
<td>Feldstein Ewing, S.W.</td>
<td>77, 84, 91</td>
</tr>
<tr>
<td>Feliciano, J.</td>
<td>79</td>
</tr>
<tr>
<td>Fenton, M.</td>
<td>28</td>
</tr>
<tr>
<td>Fernández Artamendi, S.</td>
<td>17</td>
</tr>
<tr>
<td>Fernandez, E.</td>
<td>83, 92</td>
</tr>
<tr>
<td>Fernandez, P.</td>
<td>11</td>
</tr>
<tr>
<td>Fernández-Artamendi, S.</td>
<td>17, 65</td>
</tr>
<tr>
<td>Fernández-Hermida, J.R.</td>
<td>17, 65</td>
</tr>
<tr>
<td>Ferrara, J.</td>
<td>9</td>
</tr>
<tr>
<td>Ferreira, E.F.</td>
<td>11, 81</td>
</tr>
</tbody>
</table>
CPDD AUTHOR INDEX

Ferrer-García, M.  101
Festinger, D.S.  78, 135
Fields, S.  65
Fiellin, D.A.  9, 58, 82, 89, 122
Fierbinteanu, I.C.  120
Filbey, F.M.  77, 84
Fingerhood, M.  91, 93, 121
Fink, L.H.  62
Finn, P.  88
Finnegan, L.  24
Filbey, F.M.  77, 84
Fingerhood, M.  91, 93, 121
Fink, L.H.  62
Fiellin, D.A.  9, 58, 82, 89, 122
Fierbinteanu, I.C.  120
Frost, E.B.  29
Friedman, R.  6, 115
Friedman, S.R.  10
Friedmann, N.  83
Friedrich, D.  22
Fries, J.  77
Fritz, M.  111
Froeliger, B.  77, 115
Froimowitz, M.  26
Fudala, P.  121
Fuller, C.  67, 73
Fuller, P.M.  62
Funada, M.  116
Funk, R.R.  74
Furr-Holden, C.M.  105
Gaalema, D.  108
Gadsden, R.  115
Gagne, A.  57
Galanter, M.  131
Galanter, M.  24
Galea, S.  68
Gallo, D.A.  6
Galloway, G.P.  16, 59, 83, 102
Galloway, M.P.  119
Galvan, A.  77
Gancarz, A.M.  64, 75, 110
Gandhi, D.  9, 121
Gandhi, K.K.  61, 87
Gandhi, N.  67, 84, 115, 134
Garavan, H.  29
Garcia, F.  113
Garcia-Estrada, M.  27
Garcia-Fernández, G.  17, 65
Garcia-Rodriguez, O.  17, 65, 101
Gardner, E.L.  26, 110
Garner, B.  78, 79
Gatch, M.B.  7, 59, 118
Gates, P.J.  118
Geffert, L.M.  62
Geisel, K.  66
Gelberg, L.  22
Gelernter, J.  88, 115, 116
Geller, E.B.  29
Gentry, W.B.  91
Georgescu, F.  120
Georgescu, M.  120
Geppert, C.M.  86
Gerak, L.R.  118
Gerbaud, L.  57
Germán, I.  86
Gera, G.  57
Ghahremani, D.G.  77
Ghandour, L.  14, 82
Ghee, S.M.  104
Gheorghe, F.  120
Ghitza, U.  57
Ghozland, S.G.  57
Gibson, K.D.  15
Gilbertson, S.R.  62, 83
Gillespie, S.  92
Gilmour, B.P.  84
Ginsburg, B.C.  5
Gintzler, A.  133
Gipson, C.D.  64, 110
Glaser, P.E.  16, 59
Glasner-Edwards, S.  60
Glavach, M.K.  108
Glavach, M.S.  66
Gnagy, E.  88, 116
Godley, M.D.  79
Godley, S.H.  79
Goeders, N.E.  110, 111, 112
Gold, M.S.  64
Goldman, D.  115
Goldman, M.  77, 112, 113
Goli, V.  13, 116
Golub, A.  12, 120
Gomes, C.M.  11, 81
Gomes, S.M.  134
Gomez, Z.  10
Gonçalves, F.A.  11
Gonçalves, V.M.  68
Gonzales, A.  86
Gonzales, R.M.  19
Gonzalez, G.  56, 88, 92
Gonzalez-Cuevas, G.  84
Gooden, L.  73
Goodkind, S.  78
Goodteacher, E.  57
Gorbach, P.M.  10
Gordon, A.J.  9
Gordon, A.D.  57
<table>
<thead>
<tr>
<th>Author</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gordon, E.</td>
<td>111</td>
</tr>
<tr>
<td>Gordon, M.S.</td>
<td>70</td>
</tr>
<tr>
<td>Gore-Langton, R.</td>
<td>57</td>
</tr>
<tr>
<td>Gorelick, D.</td>
<td>101, 117</td>
</tr>
<tr>
<td>Gorka, S.M.</td>
<td>19</td>
</tr>
<tr>
<td>Gorgetzky, C.W.</td>
<td>71</td>
</tr>
<tr>
<td>Gossage, J.</td>
<td>68</td>
</tr>
<tr>
<td>Gotman, N.</td>
<td>108</td>
</tr>
<tr>
<td>Goudriaan, A.E.</td>
<td>77, 113, 114</td>
</tr>
<tr>
<td>Grabenauer, M.</td>
<td>83</td>
</tr>
<tr>
<td>Grabinski, M.</td>
<td>21</td>
</tr>
<tr>
<td>Grabowski, J.</td>
<td>27, 88, 93</td>
</tr>
<tr>
<td>Grady, J.</td>
<td>22</td>
</tr>
<tr>
<td>Graf, J.</td>
<td>89</td>
</tr>
<tr>
<td>Graf-Rohrmeister, K.</td>
<td>109</td>
</tr>
<tr>
<td>Graniello, B.</td>
<td>113</td>
</tr>
<tr>
<td>Grant, S.</td>
<td>101</td>
</tr>
<tr>
<td>Grasing, K.</td>
<td>115</td>
</tr>
<tr>
<td>Graves, S.M.</td>
<td>123</td>
</tr>
<tr>
<td>Gray, K.M.</td>
<td>19</td>
</tr>
<tr>
<td>Gray, N.</td>
<td>120</td>
</tr>
<tr>
<td>Graziano, P.A.</td>
<td>88, 116</td>
</tr>
<tr>
<td>Greaves-Lord, K.</td>
<td>66</td>
</tr>
<tr>
<td>Green, C.E.</td>
<td>27, 58, 93</td>
</tr>
<tr>
<td>Green, L.</td>
<td>110</td>
</tr>
<tr>
<td>Green, T.A.</td>
<td>61, 62, 132</td>
</tr>
<tr>
<td>Greener, J.</td>
<td>71</td>
</tr>
<tr>
<td>Greenfield, B.</td>
<td>120</td>
</tr>
<tr>
<td>Greenfield, L.</td>
<td>81</td>
</tr>
<tr>
<td>Greenfield, S.F.</td>
<td>56, 117</td>
</tr>
<tr>
<td>Greenfield, V.Y.</td>
<td>64, 109</td>
</tr>
<tr>
<td>Greenwald, M.K.</td>
<td>17, 21, 67, 69, 115, 117</td>
</tr>
<tr>
<td>Greif, J.</td>
<td>77</td>
</tr>
<tr>
<td>Grella, C.</td>
<td>20, 69</td>
</tr>
<tr>
<td>Griffin, B.A.</td>
<td>66, 89</td>
</tr>
<tr>
<td>Griffin, M.</td>
<td>14</td>
</tr>
<tr>
<td>Griffing, S.</td>
<td>12</td>
</tr>
<tr>
<td>Griffiths, R.R.</td>
<td>20, 61, 102, 103, 119</td>
</tr>
<tr>
<td>Grinevich, V.</td>
<td>58</td>
</tr>
<tr>
<td>Gross, R.</td>
<td>15</td>
</tr>
<tr>
<td>Gruber, S.A.</td>
<td>27, 28</td>
</tr>
<tr>
<td>Gruber, V.A.</td>
<td>58</td>
</tr>
<tr>
<td>Gryczynski, J.</td>
<td>86, 121</td>
</tr>
<tr>
<td>Gu, J.</td>
<td>134</td>
</tr>
<tr>
<td>Guarino, H.</td>
<td>89</td>
</tr>
<tr>
<td>Gubrij, Z.</td>
<td>114</td>
</tr>
<tr>
<td>Guenthner, G.</td>
<td>87</td>
</tr>
<tr>
<td>Guerin, G.F.</td>
<td>110, 111, 112</td>
</tr>
<tr>
<td>Guidi, M.</td>
<td>64</td>
</tr>
<tr>
<td>Guise, J.B.</td>
<td>91</td>
</tr>
<tr>
<td>Gulasey, G.</td>
<td>84</td>
</tr>
<tr>
<td>Guller, L.</td>
<td>88</td>
</tr>
<tr>
<td>Gulley, J.M.</td>
<td>19, 63</td>
</tr>
<tr>
<td>Gunderson, E.W.</td>
<td>58, 78</td>
</tr>
<tr>
<td>Gunter, B.</td>
<td>113</td>
</tr>
<tr>
<td>Guptarak, J.</td>
<td>62</td>
</tr>
<tr>
<td>Guterstam, J.</td>
<td>113</td>
</tr>
<tr>
<td>Gutierrez, A.</td>
<td>82, 93</td>
</tr>
<tr>
<td>Gutierrez-Maldonado, J.</td>
<td>101</td>
</tr>
<tr>
<td>Haberman, R.P.</td>
<td>63</td>
</tr>
<tr>
<td>Haddad, S.</td>
<td>6</td>
</tr>
<tr>
<td>Haddock, C.K.</td>
<td>22</td>
</tr>
<tr>
<td>Haddox, J.D.</td>
<td>79</td>
</tr>
<tr>
<td>Hagan, H.</td>
<td>10</td>
</tr>
<tr>
<td>Hage, P.</td>
<td>89</td>
</tr>
<tr>
<td>Hagerty, C.</td>
<td>117</td>
</tr>
<tr>
<td>Haider, A.</td>
<td>111</td>
</tr>
<tr>
<td>Haile, C.N.</td>
<td>15, 16, 27, 59</td>
</tr>
<tr>
<td>Hall, B.</td>
<td>16</td>
</tr>
<tr>
<td>Hall, J.</td>
<td>9</td>
</tr>
<tr>
<td>Hall, S.M.</td>
<td>19, 22</td>
</tr>
<tr>
<td>Halldin, C.</td>
<td>113</td>
</tr>
<tr>
<td>Haller, D.L.</td>
<td>10, 81, 82, 91</td>
</tr>
<tr>
<td>Hallyburton, M.</td>
<td>77</td>
</tr>
<tr>
<td>Hammer, Jr., R.P.</td>
<td>63</td>
</tr>
<tr>
<td>Hamon, S.</td>
<td>6</td>
</tr>
<tr>
<td>Haney, M.</td>
<td>117</td>
</tr>
<tr>
<td>Hanlon, C.A.</td>
<td>113</td>
</tr>
<tr>
<td>Hao, W.</td>
<td>68</td>
</tr>
<tr>
<td>Hao, Y.</td>
<td>19</td>
</tr>
<tr>
<td>Harding, I.H.</td>
<td>117</td>
</tr>
<tr>
<td>Hardy, S.L.</td>
<td>21, 70</td>
</tr>
<tr>
<td>Harmon, T.</td>
<td>84</td>
</tr>
<tr>
<td>Harrell, P.T.</td>
<td>68, 86</td>
</tr>
<tr>
<td>Harrell, R.E.</td>
<td>113</td>
</tr>
<tr>
<td>Harris, E.</td>
<td>7, 118</td>
</tr>
<tr>
<td>Harris, K.</td>
<td>24</td>
</tr>
<tr>
<td>Harrison, S.</td>
<td>27</td>
</tr>
<tr>
<td>Harrod, S.B.</td>
<td>61, 109</td>
</tr>
<tr>
<td>Harshbarger, T.</td>
<td>115</td>
</tr>
<tr>
<td>Hart, C.L.</td>
<td>58, 131</td>
</tr>
<tr>
<td>Harte-Hargrove, L.C.</td>
<td>5</td>
</tr>
<tr>
<td>Hartje, J.A.</td>
<td>70, 79, 86</td>
</tr>
<tr>
<td>Hartman, C.</td>
<td>73, 90</td>
</tr>
<tr>
<td>Hartwell, E.E.</td>
<td>92</td>
</tr>
<tr>
<td>Hartwell, K.J.</td>
<td>19, 22</td>
</tr>
<tr>
<td>Hartzell, R.R.</td>
<td>134</td>
</tr>
<tr>
<td>Hartzler, B.J.</td>
<td>18, 20, 122</td>
</tr>
<tr>
<td>Hasan, K.M.</td>
<td>113</td>
</tr>
<tr>
<td>Haskel, A.</td>
<td>93</td>
</tr>
<tr>
<td>Hasselquist, L.A.</td>
<td>134</td>
</tr>
<tr>
<td>Hasson, A.</td>
<td>121</td>
</tr>
<tr>
<td>Hatch-Maillette, M.A.</td>
<td>10</td>
</tr>
<tr>
<td>Hatsukami, D.K.</td>
<td>74, 104</td>
</tr>
<tr>
<td>Havens, J.R.</td>
<td>11, 69, 71, 72</td>
</tr>
<tr>
<td>Hawken, A.</td>
<td>2</td>
</tr>
<tr>
<td>Hawkins, R.</td>
<td>16, 59</td>
</tr>
<tr>
<td>Haynes, L.</td>
<td>56</td>
</tr>
<tr>
<td>Hays, L.R.</td>
<td>5, 16</td>
</tr>
<tr>
<td>Hazan, R.</td>
<td>112, 113</td>
</tr>
<tr>
<td>Hazim, R.</td>
<td>18</td>
</tr>
<tr>
<td>He, J.</td>
<td>105</td>
</tr>
<tr>
<td>He, S.</td>
<td>115</td>
</tr>
<tr>
<td>Heal, D.J.</td>
<td>63</td>
</tr>
<tr>
<td>Heath, A.C.</td>
<td>6</td>
</tr>
<tr>
<td>Hede-Brierley, L.</td>
<td>112</td>
</tr>
<tr>
<td>Heidbreder, C.</td>
<td>71</td>
</tr>
<tr>
<td>Heil, S.H.</td>
<td>6, 17, 21, 24, 73, 87, 108, 109, 121</td>
</tr>
<tr>
<td>Heilig, M.A.</td>
<td>28, 58</td>
</tr>
<tr>
<td>Heimer, R.</td>
<td>10</td>
</tr>
<tr>
<td>Heinrich, K.M.</td>
<td>22</td>
</tr>
<tr>
<td>Heinrichs, S.C.</td>
<td>29</td>
</tr>
<tr>
<td>Heinzerling, K.G.</td>
<td>15, 115</td>
</tr>
<tr>
<td>Heinzerling, K.H.</td>
<td>59</td>
</tr>
<tr>
<td>Heishman, S.J.</td>
<td>117, 133</td>
</tr>
<tr>
<td>Heitzeg, M.</td>
<td>6</td>
</tr>
<tr>
<td>Hellem, T.L.</td>
<td>113</td>
</tr>
<tr>
<td>Helmbrecht, S.</td>
<td>115</td>
</tr>
<tr>
<td>Hemby, S.E.</td>
<td>58</td>
</tr>
<tr>
<td>Hendricks, P.</td>
<td>19</td>
</tr>
<tr>
<td>Hengl, N.</td>
<td>79</td>
</tr>
<tr>
<td>Henningfield, J.E.</td>
<td>74, 120</td>
</tr>
<tr>
<td>Henry, C.</td>
<td>26</td>
</tr>
<tr>
<td>Henry, P.</td>
<td>75, 76</td>
</tr>
<tr>
<td>Herbeck, D.</td>
<td>11, 15, 60, 61</td>
</tr>
<tr>
<td>Herberholz, J.</td>
<td>60</td>
</tr>
<tr>
<td>Herbst, E.</td>
<td>84</td>
</tr>
<tr>
<td>Author(s)</td>
<td>Pages</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Herin, D.</td>
<td>27</td>
</tr>
<tr>
<td>Herman, D.</td>
<td>117</td>
</tr>
<tr>
<td>Herman, L.</td>
<td>91</td>
</tr>
<tr>
<td>Hernandez-Garcia, L.</td>
<td>115</td>
</tr>
<tr>
<td>Herrnitch, T.</td>
<td>70</td>
</tr>
<tr>
<td>Herrmann, E.</td>
<td>73</td>
</tr>
<tr>
<td>Hettema, J.E.</td>
<td>24</td>
</tr>
<tr>
<td>Hewitt, J.K.</td>
<td>73, 88, 90</td>
</tr>
<tr>
<td>Hibbeln, J.</td>
<td>103</td>
</tr>
<tr>
<td>Hickey, K.</td>
<td>118</td>
</tr>
<tr>
<td>Hick, T.</td>
<td>134</td>
</tr>
<tr>
<td>Hickman, M.</td>
<td>8, 92</td>
</tr>
<tr>
<td>Hickman, N.J.</td>
<td>87</td>
</tr>
<tr>
<td>Higgins, S.T.</td>
<td>6, 17, 21, 24, 73, 87, 108</td>
</tr>
<tr>
<td>Hile, M.G.</td>
<td>57</td>
</tr>
<tr>
<td>Hill, K.P.</td>
<td>117</td>
</tr>
<tr>
<td>Hiller, M.</td>
<td>70</td>
</tr>
<tr>
<td>Hillhouse, M.P.</td>
<td>9, 60, 61, 93, 121</td>
</tr>
<tr>
<td>Himes, M.</td>
<td>113</td>
</tr>
<tr>
<td>Hinchey, C.T.</td>
<td>92</td>
</tr>
<tr>
<td>Hirayama, S.</td>
<td>119</td>
</tr>
<tr>
<td>Hiremath, M.</td>
<td>106</td>
</tr>
<tr>
<td>Hirsh, J.B.</td>
<td>80</td>
</tr>
<tr>
<td>Hladky, K.</td>
<td>18</td>
</tr>
<tr>
<td>Ho, A.</td>
<td>25, 123</td>
</tr>
<tr>
<td>Ho, I.K.</td>
<td>93</td>
</tr>
<tr>
<td>Hobart, M.</td>
<td>88</td>
</tr>
<tr>
<td>Hodges, A.B.</td>
<td>63</td>
</tr>
<tr>
<td>Hodgkins, Y.</td>
<td>14</td>
</tr>
<tr>
<td>Hodgkinson, C.</td>
<td>115</td>
</tr>
<tr>
<td>Hoexter, M.</td>
<td>28</td>
</tr>
<tr>
<td>Hoffenberg, A.S.</td>
<td>73, 90</td>
</tr>
<tr>
<td>Hoffman, K.</td>
<td>79</td>
</tr>
<tr>
<td>Hogarth, L.</td>
<td>29</td>
</tr>
<tr>
<td>Holcomb, H.H.</td>
<td>59</td>
</tr>
<tr>
<td>Hole, A.V.</td>
<td>112</td>
</tr>
<tr>
<td>Holmes, B.W.</td>
<td>56</td>
</tr>
<tr>
<td>Holtz, N.A.</td>
<td>104, 110</td>
</tr>
<tr>
<td>Holzer, C.</td>
<td>22</td>
</tr>
<tr>
<td>Homer, E.</td>
<td>120</td>
</tr>
<tr>
<td>Homish, G.G.</td>
<td>20</td>
</tr>
<tr>
<td>Hommel, J.D.</td>
<td>61, 62, 109</td>
</tr>
<tr>
<td>Hong, A.</td>
<td>16</td>
</tr>
<tr>
<td>Hopfer, C.J.</td>
<td>73, 88, 90</td>
</tr>
<tr>
<td>Hord, L.L.</td>
<td>109</td>
</tr>
<tr>
<td>Horn, L.R.</td>
<td>64</td>
</tr>
<tr>
<td>Horner, M.S.</td>
<td>66</td>
</tr>
<tr>
<td>Horton, A.M.</td>
<td>15</td>
</tr>
<tr>
<td>Horton, D.</td>
<td>112</td>
</tr>
<tr>
<td>Horton, T.</td>
<td>80</td>
</tr>
<tr>
<td>Horvatic, P.K.</td>
<td>79, 80, 86</td>
</tr>
<tr>
<td>Houck, J.M.</td>
<td>18</td>
</tr>
<tr>
<td>Housman, A.</td>
<td>84</td>
</tr>
<tr>
<td>Howard, M.O.</td>
<td>104</td>
</tr>
<tr>
<td>Howell, H.</td>
<td>108</td>
</tr>
<tr>
<td>Hser, Y.</td>
<td>9, 12, 79, 81, 122</td>
</tr>
<tr>
<td>Hsieh, J.</td>
<td>9</td>
</tr>
<tr>
<td>Hsu, S.</td>
<td>116</td>
</tr>
<tr>
<td>Hu, M.</td>
<td>66</td>
</tr>
<tr>
<td>Huang, D.</td>
<td>12</td>
</tr>
<tr>
<td>Huang, M.</td>
<td>6</td>
</tr>
<tr>
<td>Huang, W.</td>
<td>19, 27</td>
</tr>
<tr>
<td>Huang, Y.</td>
<td>62</td>
</tr>
<tr>
<td>Huber, R.S.</td>
<td>113</td>
</tr>
<tr>
<td>Huebner, K.</td>
<td>16</td>
</tr>
<tr>
<td>Huestis, M.A.</td>
<td>102</td>
</tr>
<tr>
<td>Huffman, J.</td>
<td>116</td>
</tr>
<tr>
<td>Hughey, J.</td>
<td>22</td>
</tr>
<tr>
<td>Huizink, A.C.</td>
<td>66, 116</td>
</tr>
<tr>
<td>Hultbert, A.</td>
<td>22</td>
</tr>
<tr>
<td>Hull, L.C.</td>
<td>61</td>
</tr>
<tr>
<td>Hulvershorn, L.A.</td>
<td>88</td>
</tr>
<tr>
<td>Hung, L.W.</td>
<td>93</td>
</tr>
<tr>
<td>Hunter, B.D.</td>
<td>79</td>
</tr>
<tr>
<td>Hunter, D.</td>
<td>81</td>
</tr>
<tr>
<td>Hunter, S.</td>
<td>66</td>
</tr>
<tr>
<td>Hurlburt, W.</td>
<td>69</td>
</tr>
<tr>
<td>Husbands, S.</td>
<td>103</td>
</tr>
<tr>
<td>Hutchison, K.</td>
<td>77, 84, 91</td>
</tr>
<tr>
<td>Hutchison, M.</td>
<td>110</td>
</tr>
<tr>
<td>Hutson, L.W.</td>
<td>123</td>
</tr>
<tr>
<td>Huynh, L.</td>
<td>65</td>
</tr>
<tr>
<td>Hwang, J.</td>
<td>114</td>
</tr>
<tr>
<td>Hyland, A.</td>
<td>89</td>
</tr>
<tr>
<td>Ialongo, N.S.</td>
<td>105</td>
</tr>
<tr>
<td>Ianos-Rancovici, R.</td>
<td>120</td>
</tr>
<tr>
<td>Ibanez de Benito, S.</td>
<td>57</td>
</tr>
<tr>
<td>Ibanez, G.E.</td>
<td>73, 78</td>
</tr>
<tr>
<td>Igboekwu, J.L.</td>
<td>108</td>
</tr>
<tr>
<td>Iguchi, M.Y.</td>
<td>2, 8, 10, 79</td>
</tr>
<tr>
<td>Ikeda, K.</td>
<td>71</td>
</tr>
<tr>
<td>Ilgen, M.A.</td>
<td>72, 82, 85</td>
</tr>
<tr>
<td>Inciardi, J.A.</td>
<td>72</td>
</tr>
<tr>
<td>Indarte, M.</td>
<td>62, 83</td>
</tr>
<tr>
<td>Ingersoll, K.S.</td>
<td>24, 70, 77, 84, 91</td>
</tr>
<tr>
<td>Insana, M.</td>
<td>117, 118</td>
</tr>
<tr>
<td>Insúa, P.</td>
<td>86</td>
</tr>
<tr>
<td>Irons, J.</td>
<td>90</td>
</tr>
<tr>
<td>Ironside, K.</td>
<td>73</td>
</tr>
<tr>
<td>Ishiwari, K.</td>
<td>7</td>
</tr>
<tr>
<td>Islam, L.</td>
<td>19</td>
</tr>
<tr>
<td>Islam, M.A.</td>
<td>70</td>
</tr>
<tr>
<td>Isotani, K.</td>
<td>122</td>
</tr>
<tr>
<td>Itzhak, Y.</td>
<td>25</td>
</tr>
<tr>
<td>Iverson, E.</td>
<td>80</td>
</tr>
<tr>
<td>Izenwasser, S.</td>
<td>23, 64, 84</td>
</tr>
<tr>
<td>Jackson Bloom, J.</td>
<td>80</td>
</tr>
<tr>
<td>Jackson, L.</td>
<td>17</td>
</tr>
<tr>
<td>Jackson, M.</td>
<td>58</td>
</tr>
<tr>
<td>Jaffé, A.</td>
<td>80</td>
</tr>
<tr>
<td>Jaffé, J.H.</td>
<td>9, 121</td>
</tr>
<tr>
<td>Jagsch, R.</td>
<td>109</td>
</tr>
<tr>
<td>James, A.</td>
<td>114</td>
</tr>
<tr>
<td>Jan, R.K.</td>
<td>114</td>
</tr>
<tr>
<td>Janes, A.C.</td>
<td>6, 115</td>
</tr>
<tr>
<td>Jansson, L.M.</td>
<td>24</td>
</tr>
<tr>
<td>Jardin, B.</td>
<td>16</td>
</tr>
<tr>
<td>Jarmolowicz, D.P.</td>
<td>17</td>
</tr>
<tr>
<td>Jayadevappa, R.</td>
<td>22</td>
</tr>
<tr>
<td>Jayaram-Lindström, N.</td>
<td>69, 113</td>
</tr>
<tr>
<td>Jemal, A.</td>
<td>12</td>
</tr>
<tr>
<td>Jenab, S.</td>
<td>18, 81</td>
</tr>
<tr>
<td>Jensen, J.E.</td>
<td>115</td>
</tr>
<tr>
<td>Jentink, K.G.</td>
<td>61</td>
</tr>
<tr>
<td>Jentsch, J.</td>
<td>75, 76</td>
</tr>
<tr>
<td>Jeong, E.K.</td>
<td>113</td>
</tr>
<tr>
<td>Jernstom, A.</td>
<td>81</td>
</tr>
<tr>
<td>Jiang, H.</td>
<td>122</td>
</tr>
<tr>
<td>Jitnarin, N.</td>
<td>22</td>
</tr>
<tr>
<td>Jobes, M.L.</td>
<td>91</td>
</tr>
<tr>
<td>Joe, G.W.</td>
<td>69</td>
</tr>
<tr>
<td>Johanson, C.E.</td>
<td>15, 72, 117</td>
</tr>
<tr>
<td>Johnson, A.</td>
<td>81</td>
</tr>
<tr>
<td>Johnson, D.</td>
<td>67</td>
</tr>
<tr>
<td>Johnson, G.S.</td>
<td>5</td>
</tr>
<tr>
<td>Johnson, H.</td>
<td>24</td>
</tr>
<tr>
<td>Author</td>
<td>Pages</td>
</tr>
<tr>
<td>-----------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Kothari, P.</td>
<td>79</td>
</tr>
<tr>
<td>Koulousas, A.</td>
<td>120</td>
</tr>
<tr>
<td>Kousik, S.M.</td>
<td>112</td>
</tr>
<tr>
<td>Kowal, B.P.</td>
<td>21</td>
</tr>
<tr>
<td>Kozink, R.</td>
<td>77, 115</td>
</tr>
<tr>
<td>Kraemer, K.L.</td>
<td>9</td>
</tr>
<tr>
<td>Kramer, L.A.</td>
<td>113</td>
</tr>
<tr>
<td>Kranzler, H.R.</td>
<td>88, 116</td>
</tr>
<tr>
<td>Krauss, M.</td>
<td>65</td>
</tr>
<tr>
<td>Krausz, R.M.</td>
<td>89</td>
</tr>
<tr>
<td>Kreek, M.J.</td>
<td>25, 64, 123</td>
</tr>
<tr>
<td>Kreische, F.</td>
<td>60</td>
</tr>
<tr>
<td>Krentzel, A.A.</td>
<td>5</td>
</tr>
<tr>
<td>Krishnamurti, T.</td>
<td>17</td>
</tr>
<tr>
<td>Krishnan, B.</td>
<td>26</td>
</tr>
<tr>
<td>Krishnan-Sarin, S.</td>
<td>20, 30, 77, 89, 105</td>
</tr>
<tr>
<td>Kritz, S.A.</td>
<td>67</td>
</tr>
<tr>
<td>Kronberg, E.</td>
<td>114</td>
</tr>
<tr>
<td>Krupitsky, E.M.</td>
<td>23, 67</td>
</tr>
<tr>
<td>Kuhar, M.J.</td>
<td>2, 18</td>
</tr>
<tr>
<td>Kulakova, O.V.</td>
<td>27</td>
</tr>
<tr>
<td>Kumar, S.</td>
<td>61, 87</td>
</tr>
<tr>
<td>Kurtz, S.P.</td>
<td>14, 67, 72, 73, 78</td>
</tr>
<tr>
<td>Kusick, M.</td>
<td>78</td>
</tr>
<tr>
<td>Kuwabara, H.</td>
<td>59</td>
</tr>
<tr>
<td>Kuzumaki, N.</td>
<td>119</td>
</tr>
<tr>
<td>Kydd, R.R.</td>
<td>102, 114, 119</td>
</tr>
<tr>
<td>Kyle, T.</td>
<td>10</td>
</tr>
<tr>
<td>Lacadie, C.</td>
<td>104</td>
</tr>
<tr>
<td>Lacey, J.</td>
<td>22, 68, 85</td>
</tr>
<tr>
<td>Lack, A.</td>
<td>113</td>
</tr>
<tr>
<td>Lacy, R.T.</td>
<td>109</td>
</tr>
<tr>
<td>Laezza, F.</td>
<td>62</td>
</tr>
<tr>
<td>Lai, C.</td>
<td>116</td>
</tr>
<tr>
<td>Lamarre, N.</td>
<td>59</td>
</tr>
<tr>
<td>Lambiase, M.</td>
<td>117</td>
</tr>
<tr>
<td>Lamson, M.J.</td>
<td>13, 83</td>
</tr>
<tr>
<td>Landes, R.D.</td>
<td>17, 21</td>
</tr>
<tr>
<td>Lane, P.</td>
<td>70</td>
</tr>
<tr>
<td>Lane, S.D.</td>
<td>17, 58, 59</td>
</tr>
<tr>
<td>Langston, T.</td>
<td>84</td>
</tr>
<tr>
<td>Lanier, R.K.</td>
<td>15, 78</td>
</tr>
<tr>
<td>Lankenaus, S.</td>
<td>80</td>
</tr>
<tr>
<td>Lapinsky, D.J.</td>
<td>83</td>
</tr>
<tr>
<td>Larios, S.E.</td>
<td>9, 81, 120</td>
</tr>
<tr>
<td>Larkins, S.</td>
<td>10</td>
</tr>
<tr>
<td>LaRowe, S.D.</td>
<td>16, 27, 102</td>
</tr>
<tr>
<td>Larrabeiti, A.</td>
<td>11</td>
</tr>
<tr>
<td>Lash, S.</td>
<td>18</td>
</tr>
<tr>
<td>Lasher, B.A.</td>
<td>84</td>
</tr>
<tr>
<td>Latimer, W.W.</td>
<td>66, 68, 86</td>
</tr>
<tr>
<td>Latkin, C.</td>
<td>22</td>
</tr>
<tr>
<td>Laudet, A.B.</td>
<td>24, 60, 79</td>
</tr>
<tr>
<td>Laughlin, R.E.</td>
<td>76</td>
</tr>
<tr>
<td>Lawental, E.</td>
<td>80</td>
</tr>
<tr>
<td>Leal, E.</td>
<td>27</td>
</tr>
<tr>
<td>Lebeau, R.</td>
<td>69</td>
</tr>
<tr>
<td>Ledgerwood, D.M.</td>
<td>17, 21</td>
</tr>
<tr>
<td>Lee, B.</td>
<td>114</td>
</tr>
<tr>
<td>Lee, D.C.</td>
<td>115, 116</td>
</tr>
<tr>
<td>Lee, G.P.</td>
<td>105</td>
</tr>
<tr>
<td>Lee, K.</td>
<td>89</td>
</tr>
<tr>
<td>Lee, M.H.</td>
<td>105</td>
</tr>
<tr>
<td>Lee, S.</td>
<td>90</td>
</tr>
<tr>
<td>Lee, T.</td>
<td>76</td>
</tr>
<tr>
<td>Lehman, W.E.</td>
<td>69, 71, 121</td>
</tr>
<tr>
<td>Lehr, E.</td>
<td>82</td>
</tr>
<tr>
<td>Leite-Morris, K.A.</td>
<td>26, 29</td>
</tr>
<tr>
<td>Lejuez, C.W.</td>
<td>60, 65, 88, 105</td>
</tr>
<tr>
<td>LeNaour, M.</td>
<td>84</td>
</tr>
<tr>
<td>Lennox, A.</td>
<td>88</td>
</tr>
<tr>
<td>Leonard, J.R.</td>
<td>60</td>
</tr>
<tr>
<td>Leonard, K.E.</td>
<td>20</td>
</tr>
<tr>
<td>Leonard, L.</td>
<td>10</td>
</tr>
<tr>
<td>Leoutsakos, J.M.</td>
<td>119</td>
</tr>
<tr>
<td>Leoutsakos, J.S.</td>
<td>24, 121</td>
</tr>
<tr>
<td>Leoveau, V.</td>
<td>120</td>
</tr>
<tr>
<td>LeResche, L.</td>
<td>133</td>
</tr>
<tr>
<td>Leri, F.</td>
<td>6, 109</td>
</tr>
<tr>
<td>Lerner, B.</td>
<td>115</td>
</tr>
<tr>
<td>LeSage, M.G.</td>
<td>20</td>
</tr>
<tr>
<td>Leshner, A.R.</td>
<td>60</td>
</tr>
<tr>
<td>Letcher, A.</td>
<td>91</td>
</tr>
<tr>
<td>Leukefeld, C.G.</td>
<td>11, 71, 72, 101</td>
</tr>
<tr>
<td>Leung, K.S.</td>
<td>20, 69</td>
</tr>
<tr>
<td>Leventhal, A.M.</td>
<td>88</td>
</tr>
<tr>
<td>Levi-Minzi, M.A.</td>
<td>78</td>
</tr>
<tr>
<td>Levin, F.R.</td>
<td>13, 27, 58, 76, 88, 117, 118</td>
</tr>
<tr>
<td>Levin, K.H.</td>
<td>117</td>
</tr>
<tr>
<td>Levitin, T.</td>
<td>106</td>
</tr>
<tr>
<td>Levy, A.M.</td>
<td>109</td>
</tr>
<tr>
<td>Levy, M.</td>
<td>6</td>
</tr>
<tr>
<td>Levy-Cooperman, N.</td>
<td>11</td>
</tr>
<tr>
<td>Lewis, D.</td>
<td>105</td>
</tr>
<tr>
<td>Lewis, R.</td>
<td>22</td>
</tr>
<tr>
<td>Lewis, S.</td>
<td>73</td>
</tr>
<tr>
<td>Li, J.X.</td>
<td>9, 26, 28</td>
</tr>
<tr>
<td>Li, L.</td>
<td>12, 59, 83, 102</td>
</tr>
<tr>
<td>Li, M.</td>
<td>20</td>
</tr>
<tr>
<td>Li, M.D.</td>
<td>21, 115, 134</td>
</tr>
<tr>
<td>Li, X.</td>
<td>26</td>
</tr>
<tr>
<td>Li, Y.</td>
<td>77, 112, 113</td>
</tr>
<tr>
<td>Liao, D.</td>
<td>116</td>
</tr>
<tr>
<td>Liao, R.</td>
<td>64</td>
</tr>
<tr>
<td>Liddie, S.A.</td>
<td>25</td>
</tr>
<tr>
<td>Lieberman, R.L.</td>
<td>27</td>
</tr>
<tr>
<td>Lightfoot-Siordia, C.L.</td>
<td>63</td>
</tr>
<tr>
<td>Lile, J.A.</td>
<td>5, 16, 87, 113, 116</td>
</tr>
<tr>
<td>Lim, K.</td>
<td>76</td>
</tr>
<tr>
<td>Lin, A.</td>
<td>26</td>
</tr>
<tr>
<td>Lin, J.C.</td>
<td>114</td>
</tr>
<tr>
<td>Lin, K.</td>
<td>65</td>
</tr>
<tr>
<td>Lin, L.</td>
<td>93</td>
</tr>
<tr>
<td>Lin, M.</td>
<td>12, 67</td>
</tr>
<tr>
<td>Lin, P.S.</td>
<td>93</td>
</tr>
<tr>
<td>Lin, W.</td>
<td>101</td>
</tr>
<tr>
<td>Lin, Y.</td>
<td>65</td>
</tr>
<tr>
<td>Lindblad, R.</td>
<td>57</td>
</tr>
<tr>
<td>Lindsay, J.A.</td>
<td>16, 20, 58, 115</td>
</tr>
<tr>
<td>Ling, K.</td>
<td>17</td>
</tr>
<tr>
<td>Ling, W.</td>
<td>9, 14, 61, 93, 121</td>
</tr>
<tr>
<td>Linton, S.L.</td>
<td>67</td>
</tr>
<tr>
<td>Lipshultz, S.L.</td>
<td>108</td>
</tr>
<tr>
<td>Lipson, A.B.</td>
<td>60</td>
</tr>
<tr>
<td>Lipton, R.</td>
<td>85</td>
</tr>
<tr>
<td>Liss, A.</td>
<td>20, 89</td>
</tr>
<tr>
<td>Liss, T.</td>
<td>20, 105</td>
</tr>
<tr>
<td>Listerud, J.</td>
<td>86</td>
</tr>
<tr>
<td>Litvin, Y.</td>
<td>25</td>
</tr>
<tr>
<td>Liu, F.</td>
<td>113, 117</td>
</tr>
<tr>
<td>Liu, H.</td>
<td>70</td>
</tr>
<tr>
<td>Liu, S.</td>
<td>17</td>
</tr>
<tr>
<td>Liu, X.</td>
<td>134</td>
</tr>
<tr>
<td>Liu, Y.</td>
<td>64, 83</td>
</tr>
<tr>
<td>Lledó, M.</td>
<td>86</td>
</tr>
<tr>
<td>Llosa, L.</td>
<td>15</td>
</tr>
<tr>
<td>Llosa, T.</td>
<td>15</td>
</tr>
<tr>
<td>Lloyd, D.R.</td>
<td>64, 75, 110</td>
</tr>
</tbody>
</table>
Loch, C.  86
Lockhart, N.  101
Loescher, J.L.  15
Lofwall, M.R.  16, 28, 72, 92
Logan, B.K.  120
Lombard, C.  90
Lominac, K.D.  111
London, E.D.  6, 26, 59, 77, 114, 131
Long, E.C.  112
Long, L.  91
Lookatch, S.J.  12
Lopez, A.A.  87
Lopez, A.Y.  81
Lopez, J.C.  83
Lopez-Quintero, C.  91
Lopresti, B.  113
Loran, E.G.  81, 82
Lorenzetti, V.  114, 117
Losonczy, M.  56
Lott, D.C.  101
Louw, J.  90
Lovascio, B.  26
Love, M.  78
Lovingier, K.  11, 20, 60, 61, 69
Lowing, J.  7
Lozada, L.  19
Lozama, A.  104
Lozano, O.M.  80
Lu, S.E.  87
Lubman, D.I.  29, 87, 90, 114, 117
Luby, J.  21
Lukacs, N.W.  112
Lukas, S.E.  15, 19, 24, 28, 117
Lum, P.  58
Luna, B.  112
Lundahl, L.H.  19, 117
Lundberg, K.J.  113
Lupee, D.  120
Lurie, B.  58
Lv, X.  64
Lwin, A.  78
Lynch, K.G.  27, 106
Lynch, M.E.  87
Lynch, W.J.  103, 104
Lynskey, M.T.  116
Lyoo, I.  114
Lysle, D.T.  123
Ma, J.Z.  21, 115
Ma, L.  113
Maan, R.  7, 118
Macatee, R.J.  88
MacGraw, L.  93
Machado, C.  68
MacKerrell, A.  83
MacKillop, J.  65
Mackowick, K.  91
MacLean, K.A.  102, 119
MacLean, M.  116
MacLean, S.  104
MacPherson, L.  65, 66
Madras, B.K.  6, 62
Madry, L.  12
Madura, J.D.  62, 83
Magland, J.  112
Magruder, K.  67
Magura, S.  89
Mahoney, III, J.J.  15, 16, 27, 59
Mahony, A.  88
Maili, L.  6
Maire, C.  87
Malcolm, R.J.  16, 27
Malivert, M.  88
Mallik, S.  24
Malotte, K.  10
Malow, R.  115
Mamczur, A.K.  118
Man, H.Y.  26
Manari, A.  83, 92
Mancha, B.E.  68, 86
Mancino, M.J.  16, 91
Mandler, R.N.  78, 135
Manubay, J.M.  13, 28, 91, 82
Manuel, J.K.  18, 120
Marchi, N.C.  11
Marcus, B.A.  19
Mariani, J.J.  13, 27, 58, 117, 118
Marienfeld, C.  118
Marin, I.A.  5
Marinelli-Casey, P.  60
Markman, J.  79
Marks, K.  19
Marlowe, D.B.  78, 135
Marmorstein, N.R.  76
Marrone, G.F.  133
Marsch, L.A.  89, 101, 105
Marsden, J.  102
Martin, C.A.  87, 113, 116
Martin, L.  114
Martin, N.G.  6, 116
Martin, P.  108, 109
Martin, P.R.  24, 108, 109, 121
Martin, R.A.  69
Martinez, D.  28, 101, 113
Martinez, G.  19
Martin-Fardon, F.  110
Martinez-Riera, R.  60, 85, 87
Martinez-Sanvisens, D.  60, 85, 87
Martin-Fardon, R.  84
Martins, S.S.  14, 28, 73, 82, 105
Marusich, J.A.  64, 110, 116
Masci, J.S.  20
Mashhoon, Y.  115
Mason, M.D.  83
Mason, N.S.  113
Massey, L.S.  90
Masson, C.L.  9, 25, 79
Mateu-Gelabert, P.  10
Matheson, T.  56
Mathew, T.  81
Mathison, A.  92
Mathis, C.  113
Matos, J.  64
Matsumoto, R.  83
Matthews, A.G.  80
Matusow, H.  89
Maurer, L.  22
Maxwell, J.C.  22
May, J.  80
May, P.  68
Mayes, L.C.  5
Mazlan, M.  68
<table>
<thead>
<tr>
<th>Author</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mazure, C.</td>
<td>77</td>
</tr>
<tr>
<td>McCabe, S.E.</td>
<td>105</td>
</tr>
<tr>
<td>McCaffrey, D.</td>
<td>66, 89</td>
</tr>
<tr>
<td>McCain, K.R.</td>
<td>72</td>
</tr>
<tr>
<td>McCambridge, J.E.</td>
<td>58, 82</td>
</tr>
<tr>
<td>McCann, D.</td>
<td>30</td>
</tr>
<tr>
<td>McCart, M.R.</td>
<td>30</td>
</tr>
<tr>
<td>McCarty, C.</td>
<td>60</td>
</tr>
<tr>
<td>McCarty, D.</td>
<td>79</td>
</tr>
<tr>
<td>McClatchey, B.</td>
<td>67</td>
</tr>
<tr>
<td>McClernon, F.J.</td>
<td>20, 77, 115</td>
</tr>
<tr>
<td>McEauchern, A.D.</td>
<td>77, 84, 91</td>
</tr>
<tr>
<td>McGaugh, J.</td>
<td>16</td>
</tr>
<tr>
<td>Mc Gee, E.</td>
<td>61</td>
</tr>
<tr>
<td>McGinnis, A.G.</td>
<td>62, 83</td>
</tr>
<tr>
<td>McGinnis, K.A.</td>
<td>9</td>
</tr>
<tr>
<td>McGlade, E.C.</td>
<td>113</td>
</tr>
<tr>
<td>McGlennen, K.M.</td>
<td>77</td>
</tr>
<tr>
<td>McGorry, P.D.</td>
<td>87</td>
</tr>
<tr>
<td>McIntosh, S.</td>
<td>58</td>
</tr>
<tr>
<td>Mcke, S.</td>
<td>77</td>
</tr>
<tr>
<td>McKenna, C.L.</td>
<td>115</td>
</tr>
<tr>
<td>McKenzie, T.L.</td>
<td>17</td>
</tr>
<tr>
<td>McKnight, C.</td>
<td>9, 10</td>
</tr>
<tr>
<td>McLaughlin, G.</td>
<td>30</td>
</tr>
<tr>
<td>McLaughlin, J.P.</td>
<td>134</td>
</tr>
<tr>
<td>McMahon, L.R.</td>
<td>5, 133</td>
</tr>
<tr>
<td>McNaughton, E.C.</td>
<td>15</td>
</tr>
<tr>
<td>McNeeley, J.</td>
<td>80</td>
</tr>
<tr>
<td>McNeeley, M.</td>
<td>80</td>
</tr>
<tr>
<td>McQueen, M.</td>
<td>73, 90</td>
</tr>
<tr>
<td>McRae-Clark, A.L.</td>
<td>16, 22</td>
</tr>
<tr>
<td>McWhite, C.B.</td>
<td>104, 117</td>
</tr>
<tr>
<td>Mead, H.</td>
<td>77, 84, 91</td>
</tr>
<tr>
<td>Mehta, S.H.</td>
<td>67</td>
</tr>
<tr>
<td>Mehtani, S.</td>
<td>16, 59</td>
</tr>
<tr>
<td>Meissler, J.J.</td>
<td>134</td>
</tr>
<tr>
<td>Mello, N.</td>
<td>58</td>
</tr>
<tr>
<td>Mendelson, J.</td>
<td>16, 59, 83, 102, 131</td>
</tr>
<tr>
<td>Mendez, I.A.</td>
<td>20</td>
</tr>
<tr>
<td>Mennemeyer, S.</td>
<td>28</td>
</tr>
<tr>
<td>Mennis, J.</td>
<td>70</td>
</tr>
<tr>
<td>Merchan-Hamann, E.</td>
<td>27</td>
</tr>
<tr>
<td>Meredith, S.</td>
<td>21</td>
</tr>
<tr>
<td>Mericle, A.A.</td>
<td>79</td>
</tr>
<tr>
<td>Merikangas, K.R.</td>
<td>105</td>
</tr>
<tr>
<td>Merlo, L.J.</td>
<td>11, 14, 15</td>
</tr>
<tr>
<td>Messena, N.</td>
<td>12</td>
</tr>
<tr>
<td>Messiah, S.E.</td>
<td>108</td>
</tr>
<tr>
<td>Messina, N.P.</td>
<td>56, 69, 135</td>
</tr>
<tr>
<td>Metsch, L.R.</td>
<td>10, 56, 73</td>
</tr>
<tr>
<td>Metz, V.</td>
<td>109</td>
</tr>
<tr>
<td>Metzger, D.S.</td>
<td>22, 135</td>
</tr>
<tr>
<td>Meyers, J.</td>
<td>116</td>
</tr>
<tr>
<td>Miczek, K.</td>
<td>132</td>
</tr>
<tr>
<td>Miescher, A.</td>
<td>24</td>
</tr>
<tr>
<td>Mignone, T.</td>
<td>12</td>
</tr>
<tr>
<td>Migúeñas, M.</td>
<td>112</td>
</tr>
<tr>
<td>Mikulich-Gilbertson, S.K.</td>
<td>11, 73, 77, 90</td>
</tr>
<tr>
<td>Milam, A.J.</td>
<td>105</td>
</tr>
<tr>
<td>Milby, J.B.</td>
<td>28</td>
</tr>
<tr>
<td>Miller, B.W.</td>
<td>111, 115</td>
</tr>
<tr>
<td>Miller, C.</td>
<td>75</td>
</tr>
<tr>
<td>Miller, G.M.</td>
<td>6, 56, 62</td>
</tr>
<tr>
<td>Miller, L.L.</td>
<td>81</td>
</tr>
<tr>
<td>Miller, T.L.</td>
<td>108</td>
</tr>
<tr>
<td>Miller, W.R.</td>
<td>112</td>
</tr>
<tr>
<td>Milligan, G.N.</td>
<td>134</td>
</tr>
<tr>
<td>Min, A.</td>
<td>9</td>
</tr>
<tr>
<td>Min, M.</td>
<td>60, 108</td>
</tr>
<tr>
<td>Min, S.</td>
<td>9, 90</td>
</tr>
<tr>
<td>Miñarro, J.</td>
<td>64, 110</td>
</tr>
<tr>
<td>Miner, J.L.</td>
<td>58</td>
</tr>
<tr>
<td>Minnes, S.</td>
<td>108</td>
</tr>
<tr>
<td>Minnix-Cotton, C.</td>
<td>24</td>
</tr>
<tr>
<td>Mintzer, M.Z.</td>
<td>76</td>
</tr>
<tr>
<td>Mishani, E.</td>
<td>77</td>
</tr>
<tr>
<td>Mitchell, M.R.</td>
<td>63</td>
</tr>
<tr>
<td>Mitchell, S.G.</td>
<td>86, 121</td>
</tr>
<tr>
<td>Mitchell, S.H.</td>
<td>84</td>
</tr>
<tr>
<td>Mitcheson, L.</td>
<td>102</td>
</tr>
<tr>
<td>Mitzelfelt, J.D.</td>
<td>64</td>
</tr>
<tr>
<td>Moeller, F.G.</td>
<td>17, 27, 58, 59, 61, 62, 93, 111, 113, 132</td>
</tr>
<tr>
<td>Mogali, S.</td>
<td>92</td>
</tr>
<tr>
<td>Mokri, A.</td>
<td>92</td>
</tr>
<tr>
<td>Molina, B.S.</td>
<td>88, 116</td>
</tr>
<tr>
<td>Montgomery, L.</td>
<td>79</td>
</tr>
<tr>
<td>Monti, P.</td>
<td>69</td>
</tr>
<tr>
<td>Moody, D.E.</td>
<td>58, 82, 106</td>
</tr>
<tr>
<td>Moon, M.</td>
<td>81</td>
</tr>
<tr>
<td>Mooney, L.J.</td>
<td>60, 121, 132</td>
</tr>
<tr>
<td>Mooney, M.</td>
<td>88</td>
</tr>
<tr>
<td>Moore, B.A.</td>
<td>82, 122</td>
</tr>
<tr>
<td>Moore, C.</td>
<td>68</td>
</tr>
<tr>
<td>Moore, S.</td>
<td>89, 105</td>
</tr>
<tr>
<td>Moore, T.</td>
<td>11</td>
</tr>
<tr>
<td>Morales, A.M.</td>
<td>114</td>
</tr>
<tr>
<td>Morales-Manrique, C.C.</td>
<td>85</td>
</tr>
<tr>
<td>Moran, C.</td>
<td>72</td>
</tr>
<tr>
<td>Moran-Santa Maria, M.</td>
<td>104</td>
</tr>
<tr>
<td>Morasco, B.J.</td>
<td>82</td>
</tr>
<tr>
<td>Morgado, M.</td>
<td>22</td>
</tr>
<tr>
<td>Morgan, A.J.</td>
<td>61, 109</td>
</tr>
<tr>
<td>Morgan, A.T.</td>
<td>59</td>
</tr>
<tr>
<td>Morgan, D.</td>
<td>62, 64</td>
</tr>
<tr>
<td>Morgen, K.</td>
<td>70</td>
</tr>
<tr>
<td>Morig, N.</td>
<td>71</td>
</tr>
<tr>
<td>Mori, T.</td>
<td>122</td>
</tr>
<tr>
<td>Morisano, D.</td>
<td>80</td>
</tr>
<tr>
<td>Morral, A.</td>
<td>66, 89</td>
</tr>
<tr>
<td>Morris Bobzean, S.A.</td>
<td>29</td>
</tr>
<tr>
<td>Morris, L.A.</td>
<td>122</td>
</tr>
<tr>
<td>Morris, M.D.</td>
<td>19</td>
</tr>
<tr>
<td>Morrison, J.</td>
<td>82</td>
</tr>
<tr>
<td>Morrow, C.E.</td>
<td>66</td>
</tr>
<tr>
<td>Mortensen, P.</td>
<td>119</td>
</tr>
<tr>
<td>Moseley, A.</td>
<td>86</td>
</tr>
<tr>
<td>Moser, P.</td>
<td>64</td>
</tr>
<tr>
<td>Moskowitz, J.T.</td>
<td>73</td>
</tr>
<tr>
<td>Motel, W.</td>
<td>83</td>
</tr>
<tr>
<td>Moyers, T.B.</td>
<td>13, 18</td>
</tr>
<tr>
<td>Moynihan, M.</td>
<td>57</td>
</tr>
<tr>
<td>Mueller, E.T.</td>
<td>21</td>
</tr>
<tr>
<td>Mulpur, S.</td>
<td>20</td>
</tr>
<tr>
<td>Muñiz, A.K.</td>
<td>133</td>
</tr>
<tr>
<td>Muñoz, R.</td>
<td>110</td>
</tr>
<tr>
<td>Murphy, A.Z.</td>
<td>133</td>
</tr>
<tr>
<td>Murphy, J.G.</td>
<td>65</td>
</tr>
</tbody>
</table>
Murphy, S.A. 106
Murray, J. 91
Myers, A.M. 110
Myers, B. 90
Myers, C.P. 121
Myerson, J. 110
Myrick, H. 102
Nader, M.A. 5
Nagase, H. 119
Nair, M.P. 56, 67, 84, 115, 134
Nakama, H. 19
Nakamura, K. 71
Nakamura, R.K. 26
Nakazawa, M. 79
Namjoshi, O. 7
Napier, T.C. 112, 123
Narasimhan, D. 112
Narayana, P.A. 113, 132
Narendran, R. 113
Narita, M. 119, 122
Natal, N.O. 116
Natarajan, A. 62
Natividad, L.A. 133
Navarro, H.A. 84
Navas, III, F. 110
Nawata, Y. 110
Necrason, E. 122
Neduzhko, O.O. 71
Neelakantan, H. 5
Negus, S.S. 122
Neilsen, S. 121
Necsawder, J.L. 25, 63, 132, 134
Nelson, E. 93
Nemes, S. 56
Nerutamalla, C.S. 17, 59
Nestler, E.J. 29, 111
Neufeld, K. 81
Neumark, Y. 91
Newman, J. 58
Newton, M. 90
Newton, T.F. 15, 16, 17, 27, 59
Newville, H. 120
Neylan, T.C. 84
Nguyen, J.D. 7
Nic Dhonnchadha, B. Áine 25, 26, 112
Nich, C. 12, 24, 118
Nicholas, K.S. 117
Nick, C.E. 12
Nickel, K.B. 20, 69
Nielsen, D.A. 6, 19, 115
Nielsen, S. 121
Noble-Desy, P. 121
Noel, J.G. 57
Noel, J.K. 20
Nolan, T.L. 62, 83
Noll, D.C. 115
Noon, K.R. 112
Nora, P. 61, 80
Norberg, M.M. 117, 118
Noriega, M. 67
Northrup, T. 93
Nouri, S.D. 5
Nunes, E.V. 10, 13, 16, 27, 66, 79, 92, 113, 118
Nurmi, E.L. 6
Nuzzo, P.A. 16, 28, 92
Nyberg, E. 114
Nygard, S.K. 18
O’Brien, B. 20
O’Brien, C.P. 23, 27, 70, 77, 112, 113
O’Connell, M.M. 61
O’Dell, L.E. 133
O’Donnell, L. 10
O’Grady, K.E. 9, 121
O’Leary, C.C. 20, 56, 69, 135
O’Malley, P.W. 81
O’Malley, S. 77
O’Neill, J. 114
O’Sullivan, A. 22
Ober, A.J. 10, 12
Obomanu, B. 63
Ogai, Y. 71
Ogawa, L.M. 56
Ogeil, R.P. 119
Oh Min, M. 60
O’Keefe, V. 68
Olaer, M. 79
Olaizola, C. 86
Oliveto, A. 16, 91
Olsen, J.H. 19
Olsen, Y.K. 121
Omar, Y. 17
Ompad, D.C. 67, 73, 78
Ondersma, S.J. 19, 24, 80, 101
Orme, J. 66, 116
Orslin, D.W. 86, 88, 106
Ostos, M. 25
Ostrow, D.G. 82
Oswald, L. 59
Otaishvili, D. 9
Ouljet, L.J. 10
Owens, D. 70
Ozechowski, T.J. 66
Pachas, G. 115
Painter, M.R. 134
Pajtek, S. 112
Palacios, I. 57
Palfai, T. 80
Palma, J. 29
Palmer, M. 86
Pampanini, T. 113
Pande, P.G. 57, 83
Pankow, J. 69
Pantelis, C. 87, 114
Paris, E.M. 120
Park, S. 119
Parker, S. 86
Parrino, M. 13
Parry, T. 59
Parsons, J.T. 22
Partilla, J.S. 63
Passik, S. 25
Pasternak, G. 103
Patak, M. 65
Patel, N. 92
Pat-Horenczyk, R. 27
Patrick, M.E. 21
Patterson, T.L. 60
Pattison, L.P. 58
Paulsen, B.J. 27
Pavlicova, M. 27, 66
Payer, D.E.  6
Payne, T.J.  21
Paz, A.  25
Peal, A.  65
Pearce, V.J.  12
Peartree, N.A.  133, 134
Peavy, K.M.  20, 122
Pechansky, F.  11, 28, 60, 68, 81, 85, 104
Pecoraro, A.  67, 80
Pedroza, C.  58
Peirce, J.M.  10, 27, 81, 89, 122
Pelham, W.E.  88, 116
Peltier, S.J.  115
Penate, J.  132
Penetar, D.M.  15, 24
Peng, X.  26
Pennington, L.E.  18
Pentel, P.R.  84
Pentkowski, N.S.  25, 63, 134
Pérez de los Cobos, J.C.  11
Perez, P.  8
Pericot-Valverde, I.  101
Perkins, A.C.  20, 21, 70
Perl, H. I.  13
Perree, A.  57
Perrey, D.  84
Perrine, S.A.  113
Perry, B.  61
Perry, J.  18
Perry-Parish, C.  89
Perry-Parrish, C.  89
Person, A.  76
Peters, E.N.  118
Peterson, B.S.  113
Peterson, J.B.  80
Peterson, T.  86
Petry, N.M.  21
Pettinati, H.M.  27
Pfaff, D.  25
Pfleger, J.  89
Pham, A.  60
Phan, K.L.  115
Phillips, B.  23
Phillips, K.A.  73, 91, 101
Picciotto, M.  77
Picetti, R.  123
Pichili, V.B.  84, 134
Pickover, A.  60
Pihl, R.O.  80
Pipkin, J.A.  109
Piray, P.  92
Pires, D.V.  11
Pirie, P.  65
Pitts, E.G.  131
Pixton, G.C.  13
Plankey, M.W.  82
Platt, D.M.  112
Plebani, J.G.  60
Pletcher, M.  59, 88
Ploense, K.  111
Ploutz-Snyder, R.  88
Pockros, L.A.  25
Polanowska-Grabow, R.  134
Poldrack, R.A.  77
Poling, J.  5
Pollack, L.M.  73
Poole, M.M.  59
Popa, S.C.  120
Porrino, L.J.  113, 114
Portoghese, P.S.  84
Poston, W.C.  22
Potenza, M.N.  104
Potter, J.S.  14, 82, 93
Prado, C.M.  12, 13
Prathikanti, S.  58
Pravetoni, M.  84
Prendergrast, M.  121
Prescot, A.P.  115
Pressley, D.P.  57
Preston, D.  70
Preston, K.L.  91, 101, 107
Pribasvign, A.  109
Price, K.L.  16, 117
Price, L.  116
Price, R.K.  6, 118
Prieto-López, R.  27
Prince van Leeuwen, A.  66
Prieolou, C.  57
Prisinzano, T.E.  63, 102, 104
Prochaska, J.J.  22, 87
Protas, J.S.  68
Prow, M.  63
Prussack, A.N.  119
Pulaski, A.R.  91
Purohit, V.  133
Pusateri, L.  12
Quinn, L.  64
Quinones-Jenab, V.  18, 81
Rabkin, J.  64
Raby, W.N.  16
Radovanovic, M.  86
Rahmadi, M.  119
Raiff, B.R.  21
Raihan, A.  11, 60
Rainey, P.M.  58
Raj, A.  67
Raj, V.  119
Rajaratanam, S.M.  119
Raleigh, M.  84
Ramamurthy, S.  82
Ramchand, R.  10, 66, 89
Ramirez, K.  93
Ramirez, M.D.  5
Ramo, D.  22
Ramoa, C.  103, 104
Ramos, E.M.  88
Randall, S.  7, 118
Ransom, J.  83, 92
Rapaka, R.  103, 106
Rapoza, M.  56
Rapp, L.E.  14
Rasmussen, B.  26
Ratcliffe, S.  107
Raval, A.P.  134
Rawls, S.  26
Rawson, R.A.  9, 10, 12, 60, 86, 132
Ray, A.  67
Ray, L.  115
Raymond, K.M.  77
Realmuto, G.  90
Reddy, P.V.  67
Redish, A.  132
Reed, C.  104
Reed, S.C.  76, 93
Rees, V.W.  20, 74, 83

155
Reggio, P.H.  110  
Regier, P.  75  
Rehm, J.  69  
Reichel, C.M.  103, 104  
Reid, P.  27  
Reissig, C.R.  102  
Relyea, G.  11  
Renshaw, P.F.  103, 113, 114, 115  
Reynolds, B.  65  
Reynolds, C.R.  15  
Reynolds, E.  105  
Reynolds, M.D.  116  
Rhode, P.  105  
Rhodes, A.G.  70  
Rice, K.C.  2, 7, 111  
Rice, T.M.  73  
Richards, J.B.  64, 75, 110  
Richards, J.M.  19, 60  
Richman, J.  59  
Ridderinkhof, K.R.  77  
Riddle, J.R.  123  
Ridenour, T.A.  66, 76, 112  
Rieckmann, T.  19  
Rigg, K.  14  
Riggs, P.D.  70, 105  
Riley, A.L.  23, 58, 110, 111, 122  
Rinker, J.A.  58  
Rios, V.  64  
Ritter, A.  8, 78  
Rivera, A.  67, 73  
Rivera-Quinones, S.K.  70  
Roane, D.  81, 82  
Robbins, C.G.  116  
Robble, M.A.  64, 75, 110  
Roberts, D.C.  25, 110, 111  
Robertson, L.M.  19  
Robertson, M.J.  22  
Robinson, C.  59  
Robinson, S.  18  
Rocha, B.  31, 71  
Rocha, N.S.  81  
Roche, D.  28  
Roddy, J.K.  69  
Rodolico, J.M.  15, 56, 117  
Rodriguez-Arias, M.M.  64, 110  
Rodrigues, S.  56, 88  
Rodriguez, A.  73  
Roebke, P.V.  58  
Roehrs, T.  7, 118  
Rogers, B.P.  119  
Roget, N.A.  70, 79, 86  
Rohde, L.  28  
Rohsenow, D.  69  
Rojewski, A.  21  
Roll, J.  18  
Rolleri, R.L.  13  
Romach, M.K.  7, 11, 107, 116, 120  
Romano, E.  68, 85  
Rongey, C.R.  22  
Rooke, S.  118  
Rosa, M.C.  11, 81  
Rose, J.  115  
Rosen, D.  78  
Rosen, K.  82, 93  
Rosen, M.I.  65  
Rosenberg, E.  80  
Rosenberg, R.  115  
Rosenblum, A.  13, 89  
Rosenfeld, E.  58  
Ross, A.L.  5  
Ross-Durow, P.  105  
Rossi, P.  60, 85, 87  
Roth, T.L.  7, 27, 118  
Rothman, R.B.  63, 102, 122, 133  
Rotrosen, J.  80  
Rounsaville, B.J.  24, 108, 122  
Roux, P.  91  
Rowan-Szl, G.A.  69, 71  
Rowlett, J.K.  7, 25  
Royer, M.S.  9  
Rudy, N.  111  
Ruffalo, M.  11  
Rus Makovec, M.  86  
Rus, V.  86  
Rush, B.  89  
Rush, C.R.  16, 59  
Russell, B.R.  102, 114, 119  
Rutkowski, B.  10  
Ryan, E.T.  15  
Ryan, S.R.  114  
Saavedra, J.  68  
Sabbinevi, A.  84  
Sabet, M.  65  
Sabharwal, S.  57  
Sacco, P.  28, 91  
Sacks, S.  101  
Sacramento, A.D.  111  
Saenz, E.  57  
Safford, L.  80  
Safford, M.  88  
Sagar, K.  28  
Sage, R.  12  
Said, M.  70  
Saine, S.K.  122  
Saizt, R.  80  
Saijed, Z.M.  84, 134  
Sakai, J.  73, 90  
Saladin, M.E.  16, 19  
Salisbury, E.  93  
Salkeld, M.D.  119  
Saloum, I.M.  87, 88, 114  
Salomonsen-Sautel, S.  73, 90  
Saltino, D.  117  
Salvatore, M.F.  110  
Samet, J.H.  67, 80  
Samikkannu, T.  84, 134  
Samos, P.  60  
Samudra, P.  6  
Sanchez, C.  13  
Sánchez-Hervás, E.  17  
Sanders, N.  91  
Sandoval, M.  10  
Sandstrom, L.  122  
Sanfilippo, L.  16  
Sanghera, S.  69  
Sannerud, C.A.  57  
Santa Ana, E.J.  16  
Sapag, J.  27  
Saria, A.  111  
Sarton, E.Y.  133  
Saucerman, J.  134  
Saulsgiver, K.A.  6, 8, 21  
Saurer, T.B.  123  
Savant, J.  82, 89  
Sawh, L.  56  
Saykao, A.T.  63  
Scavone, M.  93  
Schackman, B.R.  73
Scheidweiler, K.  102
Scherer, M.  68, 86
Schiiff, M.  27
Schiller, C.E.  19
Schlebecker, K.  56
Schlussman, S.D.  64
Schmaal, L.  113
Schmitz, J.  27, 58, 93
Schmitz, J.M.  17, 59
Schmoutz, C.D.  111
Schnieder, T.  81
Schnoll, S.H.  120
Schoedel, K.A.  7, 11, 13, 107, 116, 120
Schoenhard, G.L.  83
Schootman, M.  65
Schori, M.  80
Schottenfeld, R.  68, 76, 82, 89, 118, 121, 122
Schreiber, W.F.  66
Schretlen, D.J.  19
Schroeder, S.M.  9, 61
Schrott, L.M.  5, 109
Schuetz, C.G.  89
Schulze, D.R.  5
Schumacher, J.  28, 59, 88
Scholes, P.  11, 60, 61
Seal, M.L.  114, 117
Seale, J.P.  81
Sears, R.  61, 62
Seaver, R.  71
Secades-Villa, R.  17, 65, 101
See, R.E.  104
Seewald, R.M.  9, 81, 82
Seibyl, J.  77, 115
Seidenberg, A.  83
Seitz, P.K.  62, 83
Selby, P.  108, 109
Sellers, E.M.  7, 11, 13, 74, 107, 120
Seltzman, H.H.  110
Semaan, S.  10
Semple, S.J.  60
Sen, S.  79
Senese, N.B.  19
Senoo, E.  71
Sepulveda, A.  61, 108
Serafine, K.M.  111
Serper, M.  88
Setlow, B.  20, 63
Setnik, B.  8, 116
Shafaei, E.M.  80
Shafere, M.S.  121
Shaftman, S.R.  13, 19
Shah, S.  89
Shah, Y.S.  115
Shamandi, Z.  122
Shannon, L.M.  69
Shapiro, D.  13
Sharma, A.  63
Shashack, M.  83
Shaumar, B.  57
Shaver, K.  14
Shavkunov, A.  62
Shay, C.F.  134
Sheafl, P.  11, 60, 61
Sheikhattari, P.  21
Shelley, D.  80
Shen, X.  81
Shen, Y.  64
Shepard, D.S.  78
Sherrill, L.  63
Shi, X.  113
Shih, C.  28
Shihadeh, A.  61
Shin, J.  77, 112, 113
Shin, S.H.  91
Shinday, N.M.  25
Shivers, K.Y.  81
Shoaib, M.  29
Shopshire, M.  79
Shoptaw, S.J.  10, 15, 17, 59, 115
Short, E.J.  108
Shorter, D.I.  58
Shram, M.J.  116
Shrestha, N.  26
Sirikantraporn, S.  10
Sivipurapu, K.  112
Sivesind, D.  81, 82
Skanderson, M.  9
Skelly, J.M.  17, 24, 87
Skinstad, A.H.  10, 57, 79, 86
Skolnick, P.  30, 71
Slavutzy, S.B.  11, 81
Slavutzy, S.M.  11
Slaymaker, V.  76
Slesnick, N.  65, 91
Small, M.  83
Smelstion, D.  56, 88, 92
Smith, C.  24
Smith, J.L.  79, 118
Smith, L.M.  78, 115
Smith, M.A.  93, 131, 132
Smith, M.T.  91
Smith, P.  70
Smith, P.H.  20
Smithies, V.  102
Smoller, J.W.  6
Sobell, L.  18
Sobell, M.  18
Shuster, K.P.  80
Shutter, T.  16
Shi, X.  21
Siegal, N.  18
Siegel, A.J.  18
Simpson, A.N.  16, 22
Simpson, D.D.  69
Sindich, N.  119
Singer, L.T.  108
Singh, H.H.  106
Singleton, L.M.  13
Singley, E.D.  58
Sinha, R.  16, 115
Sink, J.R.  63
Siñol, N.  11
Sirikantraporn, S.  10
Srikandantrapat, K.  112
Sirikantraporn, S.  10
Sivipurapu, K.  112
Sivesind, D.  81, 82
Skanderson, M.  9
Skelly, J.M.  17, 24, 87
Skinstad, A.H.  10, 57, 79, 86
Skolnick, P.  30, 71
Slavutzy, S.B.  11, 81
Slavutzy, S.M.  11
Slaymaker, V.  76
Slesnick, N.  65, 91
Small, M.  83
Smelstion, D.  56, 88, 92
Smith, C.  24
Smith, J.L.  79, 118
Smith, L.M.  78, 115
Smith, M.A.  93, 131, 132
Smith, M.T.  91
Smith, P.  70
Smith, P.H.  20
Smithies, V.  102
Smoller, J.W.  6
Sobell, L.  18
Sobell, M.  18
<table>
<thead>
<tr>
<th>Author Name</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sofuoglu, M.</td>
<td>5</td>
</tr>
<tr>
<td>Sokoloff, J.</td>
<td>19</td>
</tr>
<tr>
<td>Sokolowska, M.</td>
<td>31</td>
</tr>
<tr>
<td>Solhkhah, R.</td>
<td>105</td>
</tr>
<tr>
<td>Solomon, L.J.</td>
<td>87</td>
</tr>
<tr>
<td>Solowij, N.</td>
<td>87, 114, 117</td>
</tr>
<tr>
<td>Somoza, E.</td>
<td>105</td>
</tr>
<tr>
<td>Sonne, S.</td>
<td>67, 105</td>
</tr>
<tr>
<td>Sophis, E.</td>
<td>92</td>
</tr>
<tr>
<td>Sordi, A.O.</td>
<td>60</td>
</tr>
<tr>
<td>Sorensen, J.L.</td>
<td>9, 73, 79, 81, 120</td>
</tr>
<tr>
<td>Sorg, J.</td>
<td>86</td>
</tr>
<tr>
<td>Soto, G.G.</td>
<td>80</td>
</tr>
<tr>
<td>Spadola, C.</td>
<td>56, 67</td>
</tr>
<tr>
<td>Spann, S.</td>
<td>110</td>
</tr>
<tr>
<td>Sparenborg, S.</td>
<td>57</td>
</tr>
<tr>
<td>Spealman, R.D.</td>
<td>112</td>
</tr>
<tr>
<td>Speck, K.</td>
<td>79</td>
</tr>
<tr>
<td>Specker, S.</td>
<td>76</td>
</tr>
<tr>
<td>Spitznagel, E.L.</td>
<td>6, 65</td>
</tr>
<tr>
<td>Springer, J.R.</td>
<td>58</td>
</tr>
<tr>
<td>Sproule, B.</td>
<td>69</td>
</tr>
<tr>
<td>Srivastava, R.</td>
<td>26</td>
</tr>
<tr>
<td>Stafford, J.</td>
<td>93</td>
</tr>
<tr>
<td>Stagg, M.</td>
<td>64</td>
</tr>
<tr>
<td>Stahler, G.</td>
<td>70, 135</td>
</tr>
<tr>
<td>Staios, G.</td>
<td>69</td>
</tr>
<tr>
<td>Stairs, D.J.</td>
<td>133, 134</td>
</tr>
<tr>
<td>Staley, J.</td>
<td>77, 115</td>
</tr>
<tr>
<td>Stall, R.C.</td>
<td>82</td>
</tr>
<tr>
<td>Stallings, M.C.</td>
<td>73, 88, 90</td>
</tr>
<tr>
<td>Stanger, C.</td>
<td>30, 65, 101, 114</td>
</tr>
<tr>
<td>Stanikzai, M.R.</td>
<td>57</td>
</tr>
<tr>
<td>Stanley, E.</td>
<td>61</td>
</tr>
<tr>
<td>Starosciak, A.K.</td>
<td>64</td>
</tr>
<tr>
<td>Staton-Tindall, M.</td>
<td>11, 69, 101</td>
</tr>
<tr>
<td>Steensland, P.</td>
<td>84</td>
</tr>
<tr>
<td>Stein, J.A.</td>
<td>82</td>
</tr>
<tr>
<td>Stein, L.</td>
<td>69, 121</td>
</tr>
<tr>
<td>Stein, M.</td>
<td>117</td>
</tr>
<tr>
<td>Stein, M.D.</td>
<td>73</td>
</tr>
<tr>
<td>Steinberg, J.L.</td>
<td>113</td>
</tr>
<tr>
<td>Steinmiller, C.L.</td>
<td>17, 117</td>
</tr>
<tr>
<td>Stinchfield, R.</td>
<td>91</td>
</tr>
<tr>
<td>Stine, S.M.</td>
<td>24, 108, 109, 121</td>
</tr>
<tr>
<td>Stitzer, M.L.</td>
<td>5, 117</td>
</tr>
<tr>
<td>Stockman, J.K.</td>
<td>60</td>
</tr>
<tr>
<td>Stoica, I.G.</td>
<td>120</td>
</tr>
<tr>
<td>Stoller, K.</td>
<td>109</td>
</tr>
<tr>
<td>Stone, A.M.</td>
<td>14</td>
</tr>
<tr>
<td>Stoops, W.W.</td>
<td>16, 59</td>
</tr>
<tr>
<td>Storr, C.L.</td>
<td>28, 65, 105</td>
</tr>
<tr>
<td>Stotts, A.</td>
<td>82, 93</td>
</tr>
<tr>
<td>Strain, E.C.</td>
<td>28, 71, 76, 91, 92</td>
</tr>
<tr>
<td>Strang, J.</td>
<td>92</td>
</tr>
<tr>
<td>Strathdee, S.A.</td>
<td>19, 60</td>
</tr>
<tr>
<td>Strehlow, A.J.</td>
<td>22</td>
</tr>
<tr>
<td>Strickler, G.</td>
<td>78</td>
</tr>
<tr>
<td>Strike, C.</td>
<td>27</td>
</tr>
<tr>
<td>Striely, C.W.</td>
<td>14, 20, 56, 69, 135</td>
</tr>
<tr>
<td>Stutz, S.J.</td>
<td>26, 61, 62, 109, 111, 112</td>
</tr>
<tr>
<td>Suarez, M.</td>
<td>65</td>
</tr>
<tr>
<td>Sud, R.</td>
<td>80</td>
</tr>
<tr>
<td>Sugarman, D.E.</td>
<td>5</td>
</tr>
<tr>
<td>Sugita, W.</td>
<td>86</td>
</tr>
<tr>
<td>Suh, J.J.</td>
<td>77, 112, 113</td>
</tr>
<tr>
<td>Sullivan, L.E.</td>
<td>58, 82, 122</td>
</tr>
<tr>
<td>Sullivan, M.A.</td>
<td>23, 28, 82, 91, 92</td>
</tr>
<tr>
<td>Summers, K.</td>
<td>57</td>
</tr>
<tr>
<td>Sun, P.</td>
<td>85</td>
</tr>
<tr>
<td>Sunahara, R.K.</td>
<td>112</td>
</tr>
<tr>
<td>Sung, Y.H.</td>
<td>113</td>
</tr>
<tr>
<td>Surratt, C.K.</td>
<td>62, 83</td>
</tr>
<tr>
<td>Surratt, H.L.</td>
<td>14, 67, 72, 73, 78</td>
</tr>
<tr>
<td>Susick, L.</td>
<td>7</td>
</tr>
<tr>
<td>Suzuki, T.</td>
<td>119, 122</td>
</tr>
<tr>
<td>Svikis, D.</td>
<td>11, 19, 24, 61, 80, 101, 108</td>
</tr>
<tr>
<td>Swanson, A.N.</td>
<td>15, 59, 115</td>
</tr>
<tr>
<td>Sweeney, C.G.</td>
<td>56</td>
</tr>
<tr>
<td>Swieter, M.</td>
<td>106</td>
</tr>
<tr>
<td>Swinford, S.E.</td>
<td>62</td>
</tr>
<tr>
<td>Swoeger, M.T.</td>
<td>69</td>
</tr>
<tr>
<td>Sypek, E.I.</td>
<td>134</td>
</tr>
<tr>
<td>Szalay, J.J.</td>
<td>63</td>
</tr>
<tr>
<td>Szczytkowski, J.L.</td>
<td>123</td>
</tr>
<tr>
<td>Sobot, C.M.</td>
<td>28</td>
</tr>
<tr>
<td>Szombathyne Meszaros, Z.</td>
<td>88</td>
</tr>
<tr>
<td>Szuces-Reed, R.</td>
<td>77, 112, 113</td>
</tr>
<tr>
<td>Szumlinski, K.K.</td>
<td>25, 26, 111, 115</td>
</tr>
<tr>
<td>Taffe, M.A.</td>
<td>64, 102</td>
</tr>
<tr>
<td>Tai, B.</td>
<td>57</td>
</tr>
<tr>
<td>Takagi, M.J.</td>
<td>87, 90, 114, 117</td>
</tr>
<tr>
<td>Takeda, K.</td>
<td>119</td>
</tr>
<tr>
<td>Talbot, J.N.</td>
<td>83</td>
</tr>
<tr>
<td>Talboy, E.</td>
<td>10</td>
</tr>
<tr>
<td>Tallarida, R.J.</td>
<td>59</td>
</tr>
<tr>
<td>Talpins, S.K.</td>
<td>120</td>
</tr>
<tr>
<td>Tamagnan, G.</td>
<td>115</td>
</tr>
<tr>
<td>Tanabe, J.</td>
<td>11, 114</td>
</tr>
<tr>
<td>Tandon, M.</td>
<td>21</td>
</tr>
<tr>
<td>Tang, Q.</td>
<td>68</td>
</tr>
<tr>
<td>Tapi, C.</td>
<td>89</td>
</tr>
<tr>
<td>Tarter, R.E.</td>
<td>66, 116</td>
</tr>
<tr>
<td>Tau, G.</td>
<td>113</td>
</tr>
<tr>
<td>Taxman, F.S.</td>
<td>70</td>
</tr>
<tr>
<td>Teixeira, L.P.</td>
<td>7</td>
</tr>
<tr>
<td>Tejani, E.</td>
<td>68</td>
</tr>
<tr>
<td>Tek, E.</td>
<td>118</td>
</tr>
<tr>
<td>Telesca, D.</td>
<td>59</td>
</tr>
<tr>
<td>Tella, S.R.</td>
<td>57</td>
</tr>
<tr>
<td>Terplan, M.</td>
<td>18</td>
</tr>
<tr>
<td>Terrell, D.</td>
<td>108</td>
</tr>
<tr>
<td>Teruya, C.</td>
<td>79</td>
</tr>
<tr>
<td>Teter, C.J.</td>
<td>105</td>
</tr>
<tr>
<td>Tetrault, J.M.</td>
<td>58</td>
</tr>
<tr>
<td>Thakur, P.</td>
<td>109</td>
</tr>
<tr>
<td>Thamotharan, S.</td>
<td>65</td>
</tr>
<tr>
<td>Thangavel, S.</td>
<td>67</td>
</tr>
<tr>
<td>Thau, K.</td>
<td>109</td>
</tr>
<tr>
<td>Thiel, K.J.</td>
<td>63, 134</td>
</tr>
<tr>
<td>Thomas, B.F.</td>
<td>57, 83, 84</td>
</tr>
<tr>
<td>Thomas, C.</td>
<td>121</td>
</tr>
<tr>
<td>Thomas, D.M.</td>
<td>119</td>
</tr>
<tr>
<td>Thomas, S.</td>
<td>22</td>
</tr>
<tr>
<td>Thompson, A.C.</td>
<td>65</td>
</tr>
<tr>
<td>Thompson, L.L.</td>
<td>11</td>
</tr>
<tr>
<td>Thornton, B.</td>
<td>9, 61, 93</td>
</tr>
<tr>
<td>Thorsell, A.</td>
<td>58</td>
</tr>
<tr>
<td>Thostenson, J.</td>
<td>16, 65</td>
</tr>
<tr>
<td>Thurstone, C.</td>
<td>73, 90</td>
</tr>
<tr>
<td>Tian, F.</td>
<td>113</td>
</tr>
<tr>
<td>Tidey, J.W.</td>
<td>65, 87</td>
</tr>
<tr>
<td>Tiffany, S.T.</td>
<td>107</td>
</tr>
<tr>
<td>Timko, C.</td>
<td>85</td>
</tr>
<tr>
<td>Tindall, C.</td>
<td>91</td>
</tr>
<tr>
<td>Tjoa, C.</td>
<td>112</td>
</tr>
<tr>
<td>Todman, M.</td>
<td>81, 82</td>
</tr>
</tbody>
</table>
CPDD AUTHOR INDEX

Toll, L.  131
Tolliver, B.K.  16
Tomas Rosello, J.  57
Tomiyama, K.  116
Tompkins, D.A.  91
Tonigan, J.S.  86
Torigoe, K.  122
Torrens, M.  60, 85, 87
Torres, O.V.  133
Torres-Sanchez, T.  113
Toto, L.H.  24, 117
Tracy, E.  60
Tracy, K.  24
Tracy, M.  68
Travers, M.  89
Traynor, J.  103
Treatnet Mastertrainers, 1.  57
Treatnet Trainers, 2.  57
Tregellas, J.  114
Trenz, R.C.  68, 86
Tristan, S.  18
Trivedi, M.H.  12
Trksak, G.  117
Troost, J.P.  22
Tross, S.  10, 66
Trudell, M.L.  84
Truitt, D.  84
Trujols, J.  11
Tsai, H.  116
Tsao, J.C.  82
Tseng, K.C.  93
Tseng, K.C.  93
Tseng, K.C.  93
Tucker, J.  59, 88
Tuller, A.  12
Turncliff, R.  83, 92
Turner, C.W.  105
Tuten, M.  12, 24, 121
Tyrka, A.  116
Tyson, A.  65
Tzall, D.  18

Ueda, H.  75
Ulibarri, M.D.  60
Umbricht, A.  76, 91, 92, 121
Unger, A.  109
Unser, A.  24
Unterwald, E.M.  62, 111
Urada, D.  12

Vaillencourt, B.  64
Valderrama-Zurián, J.C.  85
Valencia, F.D.  134
Valenstein, H.R.  85
Valentine, J.M.  64, 109
Vallender, E.J.  6, 56, 62
Vallone, D.  86
van den Brink, W.  77, 113, 114
Van Linn, M.L.  7
van Oort, F.  116
Van Roijen, M.  104
Vandewater, S.A.  64
Vandrey, R.  5, 117
VanNess, R.D.  86
Vansickel, A.R.  20, 59, 61
Vasconcelos, L.  11
Vásquez-Espinosa, E.  27
Vazan, P.  12
Vazirian, M.  121
Veenstra, R.  116
Veltman, D.J.  77, 113, 114
Venheim, E.R.  63
Venner, K.  68, 120
Vera, A.  19
Verduin, M.  102
Verendeev, A.  23
Verhulst, F.C.  66, 116
Verma, A.  84
Verotta, D.  83
Veselenak, R.L.  62
Vessella, J.  88
Vetter, C.  117
Vialou, V.  29
Vickerman, P.  92
Vickers, S.P.  63
Vicknasingam, B.  92, 122
Vidal-Infer, A.  64
Vidot, D.C.  108
Viernes, J.  86
Villafuerte, S.  6
Vincent, P.C.  117, 118
Virens, J.  86
Vogel, H.  89
Vogenthaler, N.  73

Vollebergh, W.  116
Von Diemen, L.  11
Vosburg, S.K.  13, 28, 82, 91, 117

Wada, K.  116
Wade, D.  84
Wagner, F.A.  21
Wagner, F.P.  59
Wagner, K.  80
Wahlestedt, C.  131
Waldman, A.J.  19
Waldron, H.B.  66, 105
Waldron, M.  6
Waldrop, A.E.  84
Walker, D.D.  101
Walker, E.A.  5, 26, 110
Walker, M.D.  57
Walker, R.  12
Wall, D.  21
Wallace, D.  28
Walley, A.Y.  67
Walsh, B.  71
Walsh, R.  121
Walsh, S.L.  16, 28, 71, 92
Walton, M.A.  90, 91
Wand, G.S.  59
Wang, J.  122, 134
Wang, J.D.  93
Wang, P.  113
Wang, S.  93
Wang, Z.  7, 77, 112, 113
Ward, K.  11
Ward, S.J.  5, 26
Warda, U.  69
Warner, K.  84
Wasarhaley, N.E.  69
Washio, Y.  17, 73, 87
Watanabe, T.  71
Waters, A.J.  59
Watkins, T.J.  119
Watson, C.S.  62
Weaver, M.F.  61
Webb, L.  11
Webb, S.M.  111
Webster, J.M.  68
Webster, L.  8, 13
<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Webster, M.</td>
<td>69, 101</td>
</tr>
<tr>
<td>Wei, L.</td>
<td>75</td>
</tr>
<tr>
<td>Weiland, B.</td>
<td>6</td>
</tr>
<tr>
<td>Weinstein, A.M.</td>
<td>24, 77</td>
</tr>
<tr>
<td>Weiss, F.</td>
<td>84, 110</td>
</tr>
<tr>
<td>Weiss, R.D.</td>
<td>14, 19</td>
</tr>
<tr>
<td>Weiss, S.</td>
<td>2</td>
</tr>
<tr>
<td>Weizman, A.</td>
<td>77</td>
</tr>
<tr>
<td>Wells, E.A.</td>
<td>20, 122</td>
</tr>
<tr>
<td>Welsh, W.</td>
<td>70</td>
</tr>
<tr>
<td>West, B.T.</td>
<td>105</td>
</tr>
<tr>
<td>West, J.</td>
<td>59</td>
</tr>
<tr>
<td>Westmoreland, S.</td>
<td>25</td>
</tr>
<tr>
<td>Wetherington, C.</td>
<td>5, 133</td>
</tr>
<tr>
<td>Whaley, J.</td>
<td>112</td>
</tr>
<tr>
<td>Wheat, A.</td>
<td>14</td>
</tr>
<tr>
<td>Whiteside, L.</td>
<td>90</td>
</tr>
<tr>
<td>Whitfield, N.</td>
<td>15</td>
</tr>
<tr>
<td>Widner, G.</td>
<td>6, 118</td>
</tr>
<tr>
<td>Wiedemann, A.A.</td>
<td>21</td>
</tr>
<tr>
<td>Wiers, R.W.</td>
<td>77, 114</td>
</tr>
<tr>
<td>Wiest, K.</td>
<td>73</td>
</tr>
<tr>
<td>Wiley, J.</td>
<td>72, 116</td>
</tr>
<tr>
<td>Wiley, J.L.</td>
<td>72, 83, 110</td>
</tr>
<tr>
<td>Wilhelm, M.A.</td>
<td>86</td>
</tr>
<tr>
<td>Willard, D.</td>
<td>112, 113</td>
</tr>
<tr>
<td>Williams, D.K.</td>
<td>16</td>
</tr>
<tr>
<td>Williams, E.</td>
<td>65</td>
</tr>
<tr>
<td>Williams, J.M.</td>
<td>87</td>
</tr>
<tr>
<td>Williams, J.W.</td>
<td>61</td>
</tr>
<tr>
<td>Wills, A.</td>
<td>69</td>
</tr>
<tr>
<td>Wilson, D.</td>
<td>11, 19</td>
</tr>
<tr>
<td>Wilson, J.</td>
<td>10</td>
</tr>
<tr>
<td>Wilson, K.</td>
<td>13</td>
</tr>
<tr>
<td>Wilson, S.A.</td>
<td>6, 118</td>
</tr>
<tr>
<td>Wilson, S.C.</td>
<td>122</td>
</tr>
<tr>
<td>Wilson-Murphy, M.M.</td>
<td>121</td>
</tr>
<tr>
<td>Windsor, L.</td>
<td>12</td>
</tr>
<tr>
<td>Winhusen, T.</td>
<td>105</td>
</tr>
<tr>
<td>Winklbaur, B.</td>
<td>24, 109</td>
</tr>
<tr>
<td>Winstock, A.R.</td>
<td>102</td>
</tr>
<tr>
<td>Winters, K.</td>
<td>57, 90, 91</td>
</tr>
<tr>
<td>Winzer-Serhan, U.</td>
<td>20</td>
</tr>
<tr>
<td>Wittas, J.</td>
<td>80</td>
</tr>
<tr>
<td>Wojnar, M.</td>
<td>85</td>
</tr>
<tr>
<td>Wolinsky, T.</td>
<td>64</td>
</tr>
<tr>
<td>Wong, D.F.</td>
<td>59</td>
</tr>
<tr>
<td>Wong, L.L.</td>
<td>57</td>
</tr>
<tr>
<td>Wood, M.</td>
<td>75</td>
</tr>
<tr>
<td>Wood, S.J.</td>
<td>87</td>
</tr>
<tr>
<td>Wooditch, A.</td>
<td>70</td>
</tr>
<tr>
<td>Woods, J.H.</td>
<td>112</td>
</tr>
<tr>
<td>Woods, W.J.</td>
<td>73</td>
</tr>
<tr>
<td>Woods, W.L.</td>
<td>70, 79</td>
</tr>
<tr>
<td>Woodward, N.</td>
<td>111</td>
</tr>
<tr>
<td>Woody, G.E.</td>
<td>22, 67, 80</td>
</tr>
<tr>
<td>Woolson, R.</td>
<td>16</td>
</tr>
<tr>
<td>Woolverton, B.V.</td>
<td>63</td>
</tr>
<tr>
<td>Woolverton, W.L.</td>
<td>58, 110</td>
</tr>
<tr>
<td>Wooten, D.</td>
<td>24</td>
</tr>
<tr>
<td>Worley, M.J.</td>
<td>88</td>
</tr>
<tr>
<td>Wright, C.</td>
<td>15, 78</td>
</tr>
<tr>
<td>Wright, L.</td>
<td>10</td>
</tr>
<tr>
<td>Wright, M.G.</td>
<td>27</td>
</tr>
<tr>
<td>Wright, M.J.</td>
<td>64, 102</td>
</tr>
<tr>
<td>Wright, P.A.</td>
<td>80</td>
</tr>
<tr>
<td>Wright, S.</td>
<td>80</td>
</tr>
<tr>
<td>Wright, T.E.</td>
<td>118</td>
</tr>
<tr>
<td>Wu, H.</td>
<td>22</td>
</tr>
<tr>
<td>Wu, X.Y.</td>
<td>76</td>
</tr>
<tr>
<td>Wu, Y.</td>
<td>81</td>
</tr>
<tr>
<td>Wunsch, M.J.</td>
<td>14</td>
</tr>
<tr>
<td>Würzl, J.</td>
<td>109</td>
</tr>
<tr>
<td>Wyman, Z.</td>
<td>92</td>
</tr>
<tr>
<td>Xi, Z.</td>
<td>26</td>
</tr>
<tr>
<td>Xi, Z.X.</td>
<td>110</td>
</tr>
<tr>
<td>Xu, Q.</td>
<td>20</td>
</tr>
<tr>
<td>Xue, L.</td>
<td>66, 108</td>
</tr>
<tr>
<td>Yamamoto, T.</td>
<td>110</td>
</tr>
<tr>
<td>Yamutewa, Y.</td>
<td>120</td>
</tr>
<tr>
<td>Yang, A.</td>
<td>15, 101</td>
</tr>
<tr>
<td>Yang, B.</td>
<td>115</td>
</tr>
<tr>
<td>Yang, F.</td>
<td>64</td>
</tr>
<tr>
<td>Yang, X.</td>
<td>85</td>
</tr>
<tr>
<td>Yang, Y.</td>
<td>115</td>
</tr>
<tr>
<td>Yankelevitz, R.L.</td>
<td>84</td>
</tr>
<tr>
<td>Yanli, H.</td>
<td>27</td>
</tr>
<tr>
<td>Yao, W.</td>
<td>25</td>
</tr>
<tr>
<td>Yates, J.R.</td>
<td>110</td>
</tr>
<tr>
<td>Yau, W.</td>
<td>6</td>
</tr>
<tr>
<td>Yi, R.</td>
<td>17, 21</td>
</tr>
<tr>
<td>Yi, S.G.</td>
<td>115</td>
</tr>
<tr>
<td>Yndart-Arias, A.</td>
<td>84, 134</td>
</tr>
<tr>
<td>Yonkers, K.A.</td>
<td>108</td>
</tr>
<tr>
<td>Yoon, J.H.</td>
<td>17</td>
</tr>
<tr>
<td>Yoon, S.J.</td>
<td>114</td>
</tr>
<tr>
<td>Yoshizawa, K.</td>
<td>119, 122</td>
</tr>
<tr>
<td>Young, A.M.</td>
<td>71, 105</td>
</tr>
<tr>
<td>Young, C.</td>
<td>9</td>
</tr>
<tr>
<td>Young, K.C.</td>
<td>65, 66</td>
</tr>
<tr>
<td>Young, S.</td>
<td>73, 90</td>
</tr>
<tr>
<td>Yücel, M.</td>
<td>87, 90, 114, 117</td>
</tr>
<tr>
<td>Yurgelun-Todd, D.A.</td>
<td>113</td>
</tr>
<tr>
<td>Zaatari, G.</td>
<td>120</td>
</tr>
<tr>
<td>Zajac, G.</td>
<td>70</td>
</tr>
<tr>
<td>Zamanian, B.</td>
<td>92</td>
</tr>
<tr>
<td>Zavala, R.</td>
<td>67</td>
</tr>
<tr>
<td>Zaveri, N.</td>
<td>131</td>
</tr>
<tr>
<td>Zeman, L.</td>
<td>67</td>
</tr>
<tr>
<td>Zeng, H.</td>
<td>76</td>
</tr>
<tr>
<td>Zerger, S.</td>
<td>22</td>
</tr>
<tr>
<td>Zernig, G.</td>
<td>111</td>
</tr>
<tr>
<td>Zhai, Z.</td>
<td>112</td>
</tr>
<tr>
<td>Zhang, H.</td>
<td>116, 122</td>
</tr>
<tr>
<td>Zhang, L.</td>
<td>64</td>
</tr>
<tr>
<td>Zhang, Y.</td>
<td>64, 84</td>
</tr>
<tr>
<td>Zhao, C.</td>
<td>64</td>
</tr>
<tr>
<td>Zhao, M.</td>
<td>93, 122</td>
</tr>
<tr>
<td>Zheng, G.</td>
<td>112</td>
</tr>
<tr>
<td>Zhou, H.</td>
<td>28</td>
</tr>
<tr>
<td>Zhou, L.</td>
<td>104</td>
</tr>
<tr>
<td>Zhou, Y.</td>
<td>25</td>
</tr>
<tr>
<td>Zians, J.K.</td>
<td>60</td>
</tr>
<tr>
<td>Ziedonis, D.</td>
<td>56, 88</td>
</tr>
<tr>
<td>Zimmer, B.A.</td>
<td>110</td>
</tr>
<tr>
<td>Zimmerman, M.A.</td>
<td>90, 91</td>
</tr>
<tr>
<td>Zlebnik, N.</td>
<td>63</td>
</tr>
<tr>
<td>Zubaran, C.</td>
<td>80</td>
</tr>
<tr>
<td>Zubieta, J.K.</td>
<td>6, 101, 115</td>
</tr>
<tr>
<td>Zucker, R.A.</td>
<td>6, 91</td>
</tr>
<tr>
<td>Zule, W.A.</td>
<td>10</td>
</tr>
<tr>
<td>Zumberg, K.M.</td>
<td>19</td>
</tr>
<tr>
<td>Zur, J.B.</td>
<td>66</td>
</tr>
</tbody>
</table>
INRC INDEX

Abe, M. 130
Aceto, M.D. 97
Adelson, M. 98, 127
Ahmed, T. 130
Akbarali, H. I. 97
Aldrich, J.V. 94, 95
Altamura, A.C. 130
Amasheh, S. 128
Anderson, E.M. 128
Ansonoff, M. 137
Ansonoff, M. 129
Araki, K. 129, 130
Arnelle, D. 125
Artemenko, K.A. 96
Arttamangkul, S. 94, 140
Assis, M.A. 125
Azar, M.R. 94
Bagley, E. 141
Bailey, C.P. 98, 100
Bakalkin, G. 75, 96, 127, 129
Baker, A. 128
Barbier, E. 97
Bartos, M. 125
Basbaum, A.I. 139
Bastias Candia, S. 130
Bazov, I. 96, 127
Beaudry, H. 128
Becerra, L. 101
Becker, A. 97
Beckerman, M.A. 126
Benovic, J. 136
Berezowska, I. 95
Berg, K. 124
Berg, K.A. 127
Bidlack, J.M. 94, 95, 125
Bilsky, E.J. 94
Birdsong, W. 94
Blendy, J. 126, 138
Bobeck, E.N. 128, 136
Bohn, L. 98, 140
Brack, A. 128
Brissett, D.I. 124
Brothers, S. 131
Bruchas, M. 140
Bryant, C.D. 127
Bull, G. 96
Burgman, M. 129
Bushlin, I. 128
Butelman, E.R. 96, 124
Cabañero, D. 128
Cancela, L.M. 125
Candeletti, S. 130
Carai, M.A.M. 97
Carlezon, B. 139
Carlsson, A. 96, 97
Carlton, S.M. 128
Carroll, I. 139
Cassells, R.C. 125
Cassid, M.P. 136
Cassin, J. 96
Caudle, R.M. 128
Cazares, M. 94, 95
Chait, B.T. 96
Chakraborty, B. 124
Chapleau, J.D. 100
Chavkin, C. 140
Chen, C.K. 136
Chen, N.L. 124
Chen, S. 124
Chen, Y.-J. 136
Chieng, B. 100
Chiou, L.-C. 128
Chiou, L.-C. 99
Christie, M.J. 100
Chung, N.N. 95
Ciccocioppo, R. 131
Clarke, W. 124
Clarke, W.P. 127
Cohen, D.J. 95
Cole, S.L. 125
Colombo, G. 97
Comer, S. 103
Cordero, K.A. 125
Cordery, S. 98
Cortini, F. 130
Cowan, A. 139
Cox, B.M. 96
Crawford, C. 127
Crystal, H. 99
Cunningham, J.I. 94
D’Addario, C. 130
Dang, V.C. 100
Dean, R.L. 94, 125
Deaver, D.R. 94
Deaver, D.R. 125
Delgado-Charro, M.B. 98
Dell’Osso, B. 130
Desai, N. 127
Dever, S.M. 130
Devi, L.A. 128
Dewey, B. 140
Devey, W.L. 97
DeWire, S.M. 136
Di Benedetto, M. 130
Diener, K.R. 98
Doll, C. 97, 100, 136
Donica, C. L. 124
Dooley, C. 100
Dooley, C. 94, 95
Dorn, M. 99
Dubois, D. 128
Ducat, E. 127
Eans, S. 94, 100
Egbuta, O. 127
Eitan, S. 125
El-Hage, N. 130
Enhamre, E. 95, 97
Enquist, J. 100
Evans, C. 127
Evert, D.J. 125
Eyerman, D.J. 94
Fang, N.Z. 124
Fink, D. 99
Fischer, O. 129
Ford, C. 141
Fromm, M. 128
Galimberti, D. 130
Ganno, M.L. 94, 125
Gendron, L. 128
Gessa, G.L. 97
Gibbins, T. 95
Gintzler, A. 133
Giulianotti, M. 95
Giuvellis, D. 94
Glass, M. J. 126
Goli, V. 124
Gonzales, K. L. 100
Gorelick, D. 101
Gould, T.J. 125
Gouty, S. 96
Grant, S. 101
Grecksch, G. 97
Grinnell, S.G. 129
Grönbladh, A. 95, 97, 126
Gupta, A. 128
Gurevich, V. 136
Guy, R.H. 98
Hackel, D. 128
Hall, F.S. 126
Hallberg, M. 95, 97, 126
Hamon, S. 127
Hao, S. 99
Harris, L.S. 97
Hasegawa, M. 130
Haseman, R.A. 128
Hauser, K.F. 96, 98, 99, 130
Hayball, J.D. 98
He, Y. 136
Heang, K.A. 125
Heilig, M. 138
Henderson, G. 136
Hentges, S.T. 100
Ho, A. 95, 96, 97, 98, 99, 127
Hofford, S.R. 125
Höllt, V. 97, 100, 126
Hoot, M.R. 124
Horiuchi, H. 128, 130
Houghten, R. 94, 139
Howells, R.D. 139
Huang, E.Y.-K. 130
Huang, P. 126
Hughes, L.D. 97
Husbands, S. 103
Husbands, S.M. 98
Hutchinson, M.R. 98
Ide, S. 126
Imai, S. 128, 130
Imhof, A.-K. 97
Ingram, S.L. 128, 136
Inturrisi, C.E. 126
Jaehne, E.J. 98
Jayawardene, W. 98
Jernberg, J.N. 95

162
INRC INDEX

Jezierska, J. 96
Jira, J.A. 129
Johansson, B-M. 95, 97
Johansson, J. 95, 126
Journigan, V. 94
Just, S. 97
Jutkiewicz, E. 126
Jutkiewicz, E.M. 129
Kahl, E. 126
Kalyuzhny, A.E. 136
Kang, M. 97
Kasahara, Y. 126
Kash, T. 141
Katayama, T. 130
Kato, A. 130
Kelly, E. 136
Kelter, D. 100
Kieffer, B.L. 138, 139
Kiguchi, N. 129
Kirkmire, C.M. 94
Kishioka, S. 129
Knapp, B.I. 125
Knapp, C.M. 129
Knapp, P.E. 98, 99
Ko, H. 131
Kobayashi Y. 129
Koch, T. 97, 100, 126
Koek, W. 124
Komatsu, H. 126
Konietzko, J. 100, 126
Kononenko, O. 127
Koob, G. 94
Kornetsky, C. 129
Kreek 99
Kreek, M.J. 95, 96, 97, 98, 99, 124, 127
Krishtal, O. 96, 129
Krug, S. 128
Kulkarni, S. 95
Kulkarni, S.S. 94
Kulyk, V. 129
Kuzumaki, N. 125, 128, 130
Labuda, C.J. 136
Lamberts, J. 126
Lark, M. W. 136
LaVoi, T. 95
Le Rouzic, V. 129
Lee, H.-J. 128
Lee, P.-H. 130
Lefever, M. 94
Lemieux, C. 95
LeResche, L. 133
Levitt, E. 97
Levran, O. 96, 127
Levy-Cooperman, N. 124
Li, L. 100
Li, Y. 94
Liao, Y.-Y. 128
Lichtman, A.H. 97
Lin, W. 101
Linzy, S. 98
Liu-Chen, L-Y. 126
Liu, J. 126
Liu, L. 98
Liu, S. 99
Lovell, K. 124
Lowe, J. D. 100
Lu, H.W. 140
Lupp, A. 97
M. Tan
Maccarrone, M. 130
MacDermott, A.B. 139
Macey, T.A. 136
Madhavan, A. 100
Maeda, T. 129
Maguma, H. 97
Maida, L. 95
Majumdar, S. 129
Mankura, M. 130
Margolis, E.B. 141
Martinez, D. 101
Massotte, D. 138
Mata, M. 99
Matsui, A. 99
Matsumoto, K. 130
Mayer-Blackwell, B. 124
McEwen, B.S. 100
McGuire, B.A. 127
McLaughlin, J. 94, 95, 100, 124, 125
Milan-Lobo, L. 100
Miller, C. 75
Miller, G.M. 127
<table>
<thead>
<tr>
<th>Author</th>
<th>Page Numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miller, L.K.</td>
<td>128</td>
</tr>
<tr>
<td>Milner, T.A.</td>
<td>100</td>
</tr>
<tr>
<td>Minami, K.</td>
<td>130</td>
</tr>
<tr>
<td>Misler, J.</td>
<td>94, 95, 100</td>
</tr>
<tr>
<td>Mittal, N.</td>
<td>127</td>
</tr>
<tr>
<td>Mizoguchi, H.</td>
<td>96</td>
</tr>
<tr>
<td>Mongi Bragato, B.</td>
<td>125</td>
</tr>
<tr>
<td>Morales, A.</td>
<td>95</td>
</tr>
<tr>
<td>Morari, M.</td>
<td>139</td>
</tr>
<tr>
<td>Morgan, M.M.</td>
<td>128, 136</td>
</tr>
<tr>
<td>Morgello, S.</td>
<td>99</td>
</tr>
<tr>
<td>Morón-Concepción, J.</td>
<td>126, 128, 141</td>
</tr>
<tr>
<td>Mousa, S.A.</td>
<td>128</td>
</tr>
<tr>
<td>Mukae, T.</td>
<td>129</td>
</tr>
<tr>
<td>Murphy, A.Z.</td>
<td>133</td>
</tr>
<tr>
<td>Murray, T.F.</td>
<td>94</td>
</tr>
<tr>
<td>Muthu, D.</td>
<td>94</td>
</tr>
<tr>
<td>Nagasawa, A.</td>
<td>125</td>
</tr>
<tr>
<td>Nagase, H.</td>
<td>126</td>
</tr>
<tr>
<td>Nakamoto, K.</td>
<td>130</td>
</tr>
<tr>
<td>Nakamura, A.</td>
<td>130</td>
</tr>
<tr>
<td>Nakamura, J.</td>
<td>129</td>
</tr>
<tr>
<td>Narita, M.</td>
<td>125, 128, 130</td>
</tr>
<tr>
<td>Neelakantan, H.</td>
<td>125</td>
</tr>
<tr>
<td>Nestler, E.</td>
<td>136, 138</td>
</tr>
<tr>
<td>Nguyen, T.M.-D.</td>
<td>95</td>
</tr>
<tr>
<td>Niikura, K.</td>
<td>95, 97, 128, 130</td>
</tr>
<tr>
<td>Nishinaka, T.</td>
<td>130</td>
</tr>
<tr>
<td>Nishiyori, A.</td>
<td>130</td>
</tr>
<tr>
<td>Nishiyori, M.</td>
<td>129</td>
</tr>
<tr>
<td>Nitsche, J.</td>
<td>137</td>
</tr>
<tr>
<td>Nyberg, F.</td>
<td>95, 96, 97, 126</td>
</tr>
<tr>
<td>Nylander, I.</td>
<td>95</td>
</tr>
<tr>
<td>O’Neill, K.S.</td>
<td>125</td>
</tr>
<tr>
<td>Okada, Y.</td>
<td>125</td>
</tr>
<tr>
<td>Okano, H.</td>
<td>125</td>
</tr>
<tr>
<td>Okano, H.J.</td>
<td>125</td>
</tr>
<tr>
<td>Olker, C.</td>
<td>127</td>
</tr>
<tr>
<td>Ott, J.</td>
<td>99</td>
</tr>
<tr>
<td>Ott, J.</td>
<td>99</td>
</tr>
<tr>
<td>Palm, S.</td>
<td>95</td>
</tr>
<tr>
<td>Palmer, A.A.</td>
<td>127</td>
</tr>
<tr>
<td>Pan, Y.-X.</td>
<td>126</td>
</tr>
<tr>
<td>Pasternak, G.W.</td>
<td>103, 126, 129</td>
</tr>
<tr>
<td>Patkar, K.A.</td>
<td>125</td>
</tr>
<tr>
<td>Peles, E.</td>
<td>98, 127</td>
</tr>
<tr>
<td>Pennock, R. L.</td>
<td>100</td>
</tr>
<tr>
<td>Picetti, R.</td>
<td>98</td>
</tr>
<tr>
<td>Pierce, J.P.</td>
<td>100</td>
</tr>
<tr>
<td>Pierstorff, C.</td>
<td>97</td>
</tr>
<tr>
<td>Pintar, J.E.</td>
<td>129, 137</td>
</tr>
<tr>
<td>Platt, D.M.</td>
<td>127</td>
</tr>
<tr>
<td>Podhaizer, E.M.</td>
<td>98</td>
</tr>
<tr>
<td>Polgar, W.</td>
<td>94</td>
</tr>
<tr>
<td>Polikar, L.</td>
<td>129</td>
</tr>
<tr>
<td>Pöl, F.</td>
<td>100, 136</td>
</tr>
<tr>
<td>Polt, R.</td>
<td>94, 139</td>
</tr>
<tr>
<td>Portoghese, P.S.</td>
<td>136</td>
</tr>
<tr>
<td>Portugal, G.S.</td>
<td>126</td>
</tr>
<tr>
<td>Premaratne, I.D.</td>
<td>97</td>
</tr>
<tr>
<td>Prisinzano, T.E.</td>
<td>98, 124, 139</td>
</tr>
<tr>
<td>Proudnikov, D.</td>
<td>99</td>
</tr>
<tr>
<td>Purohit, V.</td>
<td>133</td>
</tr>
<tr>
<td>Raehal, K. M.</td>
<td>98</td>
</tr>
<tr>
<td>Randesi, M.</td>
<td>99, 127</td>
</tr>
<tr>
<td>Rasakham, K.</td>
<td>124</td>
</tr>
<tr>
<td>Ray, B.</td>
<td>127</td>
</tr>
<tr>
<td>Reed, B.</td>
<td>96, 124</td>
</tr>
<tr>
<td>Reilley, K.</td>
<td>100</td>
</tr>
<tr>
<td>Reilley, K.J.</td>
<td>94</td>
</tr>
<tr>
<td>Rice, K.</td>
<td>94</td>
</tr>
<tr>
<td>Rice, K.C.</td>
<td>98</td>
</tr>
<tr>
<td>Righard, L.</td>
<td>96</td>
</tr>
<tr>
<td>Rittner, H.L.</td>
<td>128</td>
</tr>
<tr>
<td>Rodriguez-Martin, I.</td>
<td>136</td>
</tr>
<tr>
<td>Romach, M.K.</td>
<td>124</td>
</tr>
<tr>
<td>Roman, E.</td>
<td>95</td>
</tr>
<tr>
<td>Romualdi, P.</td>
<td>130</td>
</tr>
<tr>
<td>Ross, G.R.</td>
<td>97</td>
</tr>
<tr>
<td>Ross, N.C.</td>
<td>94, 95, 125</td>
</tr>
<tr>
<td>Rossi, G.C.</td>
<td>126</td>
</tr>
<tr>
<td>Rowan, M.</td>
<td>124</td>
</tr>
<tr>
<td>Rus, S.</td>
<td>124</td>
</tr>
<tr>
<td>Saeki, M.</td>
<td>130</td>
</tr>
<tr>
<td>Sakaguchi, G.</td>
<td>130</td>
</tr>
<tr>
<td>Sakurada, S.</td>
<td>96</td>
</tr>
<tr>
<td>Samano, K. L.</td>
<td>99</td>
</tr>
<tr>
<td>Sarton, E.Y.</td>
<td>133</td>
</tr>
<tr>
<td>Sasaki, K.</td>
<td>126</td>
</tr>
<tr>
<td>Saxena, K.</td>
<td>136</td>
</tr>
<tr>
<td>Scarlota, L.</td>
<td>124</td>
</tr>
</tbody>
</table>
Scarpini, E. 130
Scherrer, G. 139
Schiller, P.W. 95
Schimmel, J.S. 128
Schlussman, S.D. 96
Schoedel, K. 124
Schulz, S. 97, 100, 136
Sellers, E.M. 124
Selley, D.E. 136
Senadheera, S.N. 94
Setnik, B. 124
Shimada, M. 126
Silveira, J.T. 96
Sim-Selley, L.J. 136
Simone, D. 129
Singh, H.D. 125
Smith, T.H. 97
Sommerville, K. 124
Somogyi, A.A. 98
Sora, I. 126
Spahn, V. 129
Standifer, K. M. 124
Stockton Jr., S.D. 128
Stumm, R. 97
Suchland, K.L. 136
Sun, J. 99
Sun, Y. 129
Suzuki, A. 125
Suzuki, T. 125, 128, 130
T-Narita, M. 125, 130
Takemura, Y. 128
Tao, P.-L. 130
Tapan, S. 129
Taqi, M.M. 96
Taqi, M.M.H. 127
Taverner, A. 98
Thompson, J. 94
Todtenkopf, M.S. 94, 125
Tokuyama, S. 130
Toll, L. 94, 131
Tomii, T. 130
Tominaga, S. 129
Torabi, M. 98
Torigoe, K. 128
Torres-Reveron, A. 100
Tozier, L. 129
Traynor, J.R. 103, 126, 127, 129
Tung, L.-W. 99
Turek, F.W. 127
Uchida, H. 130
Ueda, H. 75, 129, 130
Uhl, G.R. 126
Ung, A. 126
Unterwald, E. 138
Vallender, E.J. 127
Van Rijn, R. 139
van Rijn, R. M. 124
VanAlstine, M.A. 95
Verbeek, D.S. 96
Violin, J.D. 136
Vitaterna, M.H. 127
Volkow, N. 75
Wahlestedt, C. 131
Walker, E.A. 125
Walwyn, W. 127
Wang, J.B. 97, 138
Wang, Q. 127
Wang, Y-J. 126, 127
Wang, Z. 136
Wang, Z.J. 140
Ward, S.J. 125
Watanabe, H. 96, 97, 127
Waters, E.M. 100
Watkins, L.R. 98
Wei, L.-N. 75
Wellman, P.J. 125
Weltrowska, G. 95
Wen, T. 137
Wentland, M.P. 95
Wetherington, C.L. 133
Whistler 124
Whistler, J. 138
Whistler, J.L. 100
Wilkes, B.C. 95
Williams, J. 94, 97
Williams, J.T. 99, 140
Williams, T.J. 100
Wise, L.E. 97
Wood, M. 75
Wrede, E.J. 128
Wu, Y. 98
Xia, Y. 126, 128
INRC INDEX

Xiang Pan, X. 129
Xie, T. 127
Xie, Z. 127
Xu, J. 126
Xu, M. 126
Yakovleva, T. 96, 127
Yamamizu, K. 125
Yamashita, A. 125, 128, 130, 136
Yamazaki, M. 128
Yanase, M. 130
Yekkirala, A.S. 136
Youssef Agha, A. 98
Yuferov, V. 99
Zachariou, V. 136, 140
Zadina, J.E. 95
Zaveri, N. 131
Zaveri, N.T. 94
Zhang, X. 95
Zhang, Y. 96, 98, 130
Zheng, X. 99
Zhou, L. 127
Zhou, S. 128
Zhou, Y. 95, 97, 124
Zimmer, A. 125, 138
Zöllner, C. 129
Zubieta, J.-K. 101
I. Prenatal cocaine exposure in animals and humans: Sex differences across the lifespan  
Chairs: Cora Lee Wetherington and Samia Dawud Noursi

The purpose of this translational symposium is to present new data on sex differences in the effects of prenatal cocaine exposure and concomitant factors on a variety of endpoints across the lifespan. Data analyzed by sex/gender will be presented from two animal models and from two longitudinal cohorts. Dr. Dow-Edwards will present data from adolescent rats that were prenatally exposed to cocaine and at weaning were housed either under isolated or enriched (3 rats/cage with toys) conditions. At adolescence, they were tested for the effects of these variables on cocaine conditioned place preference and dopamine and serotonin transporters. Dr. Nader will discuss data from adult rhesus monkeys prenatally exposed to cocaine and aged 13-14 years old upon arrival in his lab. Outcomes include behavioral data (measures of impulsivity, operant behavior and cocaine self-administration), unconditioned behaviors elicited by drugs (quinpirole and SKF 38393) and brain imaging studies using PET and dopamine D2 receptors. Dr. Bandstra will describe birth through adolescence outcomes of prenatal cocaine exposure focusing on cognitive/neuropsychological (e.g., IQ, language, learning disabilities, attention, executive function, memory) and behavioral outcomes (e.g., childhood behavioral disorders, adolescent drug involvement and risky sexual activity). This longitudinal study has completed 13 prior waves of assessments through age 16/17 with an ongoing assessment at age 18/19 years. Lastly, Dr. Mayes will present fMRI data regarding relationships among prenatal cocaine exposure and later stress reactivity in adolescence (ages 14-17) as mediated by adverse early experiences. She will also describe how adolescent drug use and related risk taking are impacted by prenatal exposure, early stressors, and individual differences in brain activation in response to stress and appetitive imagery. Collectively these four presentations will underscore the variety of domains in which offspring can be impacted by exposure to prenatal cocaine and concomitant factors, both short-term and long-term, and the differential impact on males and females.

II. Naltrexone in the treatment of opioid addiction: Current research and novel applications  
Chairs: Kenneth Silverman and Sandra D. Comer

Opioid addiction is a chronic disorder that can require long-term treatment. Naltrexone is an opioid antagonist that could be an ideal medication for the long-term treatment of opioid addiction; however, naltrexone’s utility has been limited because many patients discontinue its use prematurely. Recent development of sustained release naltrexone has renewed interest in using naltrexone to treat opioid addiction. This symposium will review research on available naltrexone formulations for the treatment of opioid addiction. Dr. Sullivan will review a decade of laboratory and clinical trials aimed at optimizing the use of naltrexone, including research on a behavioral therapy for naltrexone treatment and trials of depot naltrexone. Dr. Krupitsy will review clinical trials conducted in Russia over 12 years, including studies of oral naltrexone, sustained release implant naltrexone, and sustained release injectable naltrexone. Dr. O’Brien will review naltrexone studies in criminal justice populations and advance a novel and potentially cost-effective proposal in which selected non violent offenders could be offered monthly naltrexone injections in lieu of prison or as a condition for early release. Dr. Silverman will review clinical trials which show that employment can be highly effective in
motivating both oral and sustained release naltrexone adherence if individuals are required to take scheduled naltrexone doses to gain and maintain access to the workplace. Dr. Comer will discuss the presentations and address ethical issues surrounding antagonist maintenance. The symposium will provide an in-depth review of current research and novel applications of oral and sustained release naltrexone for the treatment of opioid addiction.

III. Plasticity in reward circuits during adolescence: Effects of early drug exposure
Chairs: Sari Izenwasser and Kathleen Kantak

Adolescence is a vulnerable period associated with a high incidence of drug abuse initiation and an increased risk for developing dependence and addiction. Factors that modulate and are a consequence of the effects of drugs of abuse during this critical period of development will be discussed. Dr. Sari Izenwasser will present data on sex and age differences in the behavioral and neurochemical effects of social/environmental enrichment in adolescent rats on cocaine, nicotine and MDMA. Dr. Kathleen Kantak will present studies on the effects of self-administered cocaine on cognitive functioning in rats. She has shown that when exposure to self-administered cocaine is initiated during adolescence, stimulus-reward learning is unaffected, non-spatial working memory is disrupted and reversal learning is improved relative to passively yoked-control rats. This profile is different from that observed when exposure to cocaine is initiated during adulthood. Age-dependent regional differences in cocaine-induced neuroplasticity may underlie these distinct profiles. Dr. Emilio Ambrosio will present data on the effects of adolescent exposure to cannabinoids in morphine and cocaine self-administration behavior of adult male and female rats, as well as in several regulatory elements of opioidergic, dopaminergic, glutamatergic and GABAergic transmission, and in brain glucose metabolism measured by microPET.

IV. Epidemiology of chronic pain and clinical management among individuals with a substance use disorder
Chairs: Lara Dhingra and Carmen Masson

Patients with substance use disorders (SUD) commonly experience chronic pain. However, there is limited research examining the issue of chronic pain management in this population. To address this gap in the literature, more research is needed to identify the epidemiology of pain in different subpopulations with SUD and to develop effective, tailored pharmacological and behavioral pain management strategies for specific patients. The session will include presentations from an interdisciplinary group of clinical researchers in pain and addictions medicine from academic medical settings and the National Institute on Drug Abuse (NIDA). The specific aims of the session are to: (1) present original data on the prevalence and correlates of pain in a multi-site sample of individuals undergoing methadone maintenance therapy in New York and San Francisco; (2) evaluate associations among pain, psychological distress, quality of life, and substance use in this population; (3) discuss clinical aspects of risk management for opioid therapy to improve chronic pain in SUD populations; and (4) evaluate the feasibility of novel behavioral interventions for the treatment of pain and comorbid SUD. The discussant for the session will synthesize the information from these presentations,
discuss NIDA’s research portfolio on pain and addiction, and outline new funding opportunities. This session will inform the development of novel interventions to improve pain management among vulnerable patients with addictive disorders, highlight strategies to reduce the risk of prescription opioid abuse in this population, and guide research and clinical efforts to improve public health related to pain control and addiction treatment.

V. Drug related attentional bias and cue reactivity: Neuropsychological mechanisms and clinical relevance
Chairs: Lee Hogarth and Marcus Munafo

This symposium will examine the role of drug related attentional bias and drug cue reactivity in addictive behaviour, addressing the neuropsychological mechanisms, clinical application and animal modeling of these phenomena. The talk by Hogarth will describe recent work on the associative basis of drug cue reactivity using human drug conditioning procedures translated from animal behavioural neuroscience. The talk by Adams will address the reliability of two standard assays of attentional bias, the Stroop task and the dot probe task, and will point the way to developing more sensitive measures of drug related attentional bias. The talk by Garavan will address the neural mechanisms of the attentional bias, its inhibition by cognitive control processes, and how this inhibitory capacity may be important for maintaining abstinence. The talk by Lubman will describe recent evidence that differential reactivity to drug cues versus natural reward cues is a key predictor of abstinence following drug treatment. Finally, the talk by Shoaib will examine animal models of drug cue reactivity and the utility of these models for screening candidate medications for addiction. Overall, the symposium will encompass the translational breadth of attentional bias and drug cue reactivity research in contemporary addiction science.

VI. K2/Spice – synthetic cannabinoids as emerging drugs of abuse
Chairs: William Fantegrossi and Jenny Wiley

K2 / Spice is an emerging drug of abuse, often touted as “legal marijuana”. Most K2 products are plant materials laced with synthetic cannabinoids with psychoactive properties similar to those of Δ^9-tetrahydrocannabinol (Δ^9-THC). The synthetic compounds in K2 products are aminoalkylindole (AAI) derivatives, and, like Δ^9-THC, these compounds bind and activate cannabinoid CB1 receptors in the CNS. Many different K2-AAIs are present in various K2 preparations, but because AAIs are structurally distinct from Δ^9-THC, governmental regulation of K2 products is inconsistent or totally lacking in many states, and traditional urine drug screens fail to detect K2 use. This symposium is designed to present a highly translational view of what is currently known about K2 / Spice. The chemistry of the compounds typically found in K2 will be reviewed, paying particular attention to how this influences regulatory decisions (Boos). Efforts to survey K2 products and develop analytical techniques useful for determining identities and amounts of active compounds in these products, as well as detection of K2 metabolites excreted in urine, will also be presented (Moran.) Clinical signs and symptoms associated with acute K2 intoxication will be discussed, and compared with marijuana intoxication (McCain). The unique receptor binding, intrinsic activity, and in
vivo effects of cannabinoids commonly found in K2 will be described (Fantegrossi). Finally, a historical perspective will be applied to the study of K2 constituents, comparing and contrasting their actions with those of more traditional cannabinoids (Wiley). This timely symposium will be of interest to clinicians and basic scientists alike.

VII. Abuse liability and product appeal assessment of tobacco products
Chairs: Dorothy Hatsukami and Jack Henningfield

Abuse liability assessment of tobacco products has become critical because of the recent passage of the Family Smoking Prevention and Tobacco Control Act. While valid experimental methods of abuse liability assessment (ALA) are used for testing medications or drugs that might pose a risk for abuse, there is less experience in the application of ALA to tobacco products. Furthermore, tobacco products pose special challenges compared to most medications (e.g., tobacco products are complex mixture of constituents in products; new substances are present in the emissions; sensory factors can further influence nicotine intake, self-administration patterns and reinforcing efficacy of the product). Although non-pharmacological factors are important determinants of use, abuse, and addiction to drugs, such factors (e.g., product packaging and advertising, product claims, consumer perceptions) appear of even greater importance as determinants of use and addiction to tobacco products. Such consumer or product appeal factors are not included in traditional abuse liability assessment. The goals of this symposium will be to summarize the proceedings of a meeting on this topic that was co-sponsored by CPDD. We will discuss what we know about the assessment of pharmacological abuse liability of tobacco products (L. Carter), provide a conceptual framework that will allow us to identify and assess additional factors that influence use and addiction to tobacco products such as consumer marketing and product appeal (V. Rees), discuss the nature of post-marketing surveillance of tobacco products (J. Henningfield) and identify research needs and recommend a regulatory framework (E. Sellers).

VIII. The role of parental mental disorders and parental rearing behavior for cannabis use and cannabis use disorders in offspring
Chairs: Silke Behrendt and Ty A. Ridenour

By early adulthood, nearly all incidence of cannabis use (CU) and cannabis use disorders (cannabis abuse and dependence; CUD) has occurred. Although evidence demonstrates a familial aggregation of CUD, few studies have investigated the roles of parental psychiatric disorders (i.e. anxiety, mood and substance use disorders), rearing style and their possible interplay in the etiology of offspring CU and progression to CUD using prospective-longitudinal designs. This symposium will elucidate these relationships with four investigations, each emphasizing different elements of these variables, using international samples of varying ages. All four studies are prospective-longitudinal (three community samples and one high-risk sample), covering a developmental interval from late childhood through early adulthood. The first study addresses the role of parental monitoring for offspring first CU and regular CU in a large epidemiological Dutch study. Using a U.S. community-based family study, the second contribution specifically addresses the association between parental major depression and CUD and these same
disorders in offspring, focusing on how risk differs for adopted and biological offspring. The third study investigates the role of paternal and maternal psychiatric disorders (substance and non-substance disorders), rearing style and their combinations for CU/CUD in offspring in a high-risk U.S. sample of offspring from ages 10-12 through 22. Lastly, a German community study focuses on associations between parental substance use, anxiety and affective disorders and offspring CU/CUD taking into account parental rearing style. The discussion will concentrate on converging/divergent results among studies, etiological importance of the findings and implications for family-based prevention programming.

IX. Nutrition and Addiction: Food for thought
Chairs: Rao Rapaka and David Shurtleff

In addition to being highly palatable and rich in calories, the Western diet is generally poor in many micronutrients – vitamins, minerals, lipids and others – that are essential for human health. Moreover, it is becoming clear that excessive consumption of palatable food can drive reward dysfunction and, thereby, contribute to diet-induced obesity. It is also becoming increasingly clear that chronic micronutrient deficiencies can produce subtle but persistent damage to multiple organs of the human body, including the brain. Prolonged deficiencies of minerals such as iron, zinc and selenium can disrupt brain development and brain function. Lower-than-normal intake of vitamins (e.g., D and B12), lipids (e.g., omega-3 polyunsaturated fatty acids), essential metabolites and enzyme cofactors (e.g., choline and homocysteine) are also thought to exert harmful effects on attention, memory and mood. This dietary imbalance is largely due to the increasing prevalence of processed food products. Thus, long-term micronutrient deficits and chronic consumption of palatable food might lead to dysregulated neural networks that are involved in cognition and may manifest as severe psychiatric disorders including addiction, major depression, impulse control disorders and suicide. Similarly, drugs of abuse can cause a reduction in key micronutrients (e.g., choline, creatine) that can affect neuronal function. The goal of this symposium is to highlight the role of micronutrient deficits and palatable food consumption on brain function and disorders of addiction. In addition, the symposium will explore how micronutrient replacement might be used to improve brain function and treat addiction disorders.

X. CPDD International Committee Symposium: Volatile substance misuse: A global call for action
Chairs: Flavio Pechansky and Colleen Anne Dell

When compared with other drugs used at a similar prevalence, the misuse of volatile substances (VSM) has attracted relatively little research effort. The goal of bringing together experienced voices from across the globe in this second symposium of the International Committee of CPDD is to increase understanding of, and put forth a call for action toward, VSM as an important public health issue. Volatile substances are a large and diverse group of chemical compounds contained in hundreds of household and industrial products. As such, they are among the first drugs of choice used by children and youth. VSM has diverse as well as common effects on the health and welfare of
users, their families and communities across the globe. In this session, cross-country concerns are examined, alongside recent advances in understanding and responses. Dr. Howard's presentation will review the epidemiology, phenomenology, and natural history of inhalant use. The focus will be on recently published investigations in these areas and potential avenues for future research investigations. Dr. Silvia Cruz will approach the topic from the neuro-biological perspective. And Dr. Sarah MacLean will discuss therapeutic interventions with VSM. Dr. Robert Balster will be the session discussant, leading a conversation about prevention policies and key research aspects. Participants will be encouraged to re-evaluate and expand their knowledge about volatile substance misuse. The presenters in this session are all contributors to a forthcoming special VSM issue of the journal of Substance Use & Misuse.

XI. Rethinking the effects of methamphetamines
   Chairs: Hedy Kober and Matthew Kirkpatrick

Methamphetamine abuse continues to be a significant worldwide problem and the possible deleterious effects of methamphetamine use on cognition and mood have received much empirical and popular attention. With slogans like “not even once,” the modal view suggests that methamphetamine is dangerous, use is uncontrollable, and chronic use leads to neurocognitive deficits. Indeed, a large human literature associates methamphetamine to psychological disturbances (Grelotti et al., 2010) and cognitive impairments (Baicy and London, 2007), and it has been suggested that methamphetamine-related cognitive impairments may be associated with adverse treatment outcomes (Sofuoglu, 2010). Importantly, however, the impact of illicit methamphetamine use on cognition and mood has not been fully elucidated. For example, in many investigations of the long-term cognitive effects of methamphetamine abuse, users performed within the normal range for their age group and educational background (Chang et al., 2002; Johanson et al., 2006). Additionally, in studies examining the acute effects of the drug, methamphetamine improved performance on wide range of tasks (Wiegmann et al., 1996; Silber et al., 2006). Given these discrepancies, do we need to rethink the cognitive effects of methamphetamines? The aim of this symposium is to present emerging work on the effects of methamphetamine on behavior, cognition, and mood, in order to explore the apparent contradicting results of previous research. Speakers will discuss both the acute and long-term effects of methamphetamine on cognition and mood, the diverse neural mechanisms that underlie reinforcing and cognitive effects, and the implications of these effects for treatment efficacy.

XII. Social environment and drug-seeking: Neurobiological factors
   Chairs: Linda Dykstra and Mark Smith

The social environment plays a key role in shaping an individual’s attitudes, preferences, and choices regarding drug use. Studies in genetics and imaging, coupled with traditional pharmacological lines of investigation, are revealing how neurobiological factors interact with the social environment to influence drug-seeking behavior. For instance, scientists are now beginning to understand the neurocircuitry and neuropharmacology mediating the effects of social stress on drug self-administration. Scientists are also beginning to
understand the molecular mechanisms by which social and environmental enrichment produces protective effects on drug-seeking behavior. Finally, scientists are beginning to understand how these biological factors interact with sex and social rank to determine an individual’s sensitivity to various drugs of abuse. Knowledge of all these factors will be critical as substance abuse researchers and clinicians begin to tailor prevention and treatment interventions for specific populations. The aims of this symposium are to (1) demonstrate how recent research in genetics, imaging, and neuropharmacology is revealing the mechanisms by which the social environment influences drug-seeking behavior, (2) determine how the social environment interacts with the neurobiology of the organism to influence drug-seeking behavior, and (3) discuss how knowledge of the interplay between neurobiology and the social environment can be used to guide the development of new interventions for the prevention and treatment of substance use disorders.

XIII. Neurocognitive dysfunction in addiction: Mechanisms and interventions  
Chairs: Warren K. Bickel and Will M. Aklin

Addiction is a complex disorder in which numerous factors come into play (e.g., behavioral economic, developmental, environmental, genetic, etc). One factor that has begun to be increasingly recognized as an important process in addiction is neurocognitive dysfunction (also referred to as executive dysfunction). Neurocognitive dysfunction refers to deficiencies in variety of neurocognitive/executive functions including attention, valuation of delayed outcomes, planning and memory. A growing number of studies are showing that neurocognitive dysfunction appears to be a part of the addiction process and predictive of treatment outcomes. The next step in the study of these dysfunctions is to describe the specific processes and mechanisms associated with neurocognitive dysfunction and develop potential therapeutics to improve them. This translational symposium describes recent advances in the study of neurocognitive dysfunction in addiction, the underlying mechanism, and novel therapeutic approaches to improving cognitive dysfunction. Specifically, our speakers will present their recent findings that employ computational neuroscience, and human laboratory studies of cognitive dysfunction in addiction, and efforts to improve those dysfunctions via medication and neurocognitive rehabilitation processes. These findings will illustrate the importance of addressing neurocognitive dysfunction and set the occasion for additional research that will explore the genetics of neurocognitive dysfunction, the specific targets for therapeutic development, the role of developmental processes, and environment modulation of these processes. At the conclusion of this symposium discussion will address the mechanisms of dysfunction, development of potential candidate therapeutics, and their role in addiction treatment.

XIV. Brain imaging as a tool for treatment development in stimulant abuse  
Chairs: F. Gerald Moeller and Perry F. Renshaw

In spite of substantial strides in our understanding of the basic neuroscience of addictions, development of effective treatments, especially effective pharmacotherapies for addictions, has developed less rapidly. Recently, there is data that brain imaging may be
useful as a tool in development of effective treatments for addictions. The goal of this symposium is to present data from clinical and preclinical studies using a variety of magnetic resonance (MR) imaging techniques showing the potential utility of brain imaging as a tool in treatment development research in addictions, with a focus on stimulant abuse. Data will be presented from functional MRI, pharmacoMRI, diffusion tensor imaging, and MR spectroscopy. Using these imaging methods, data will be presented showing that brain imaging can be used to gain a greater understanding of risk for development of addiction and relapse, as well as the interaction between brain function and treatment response in stimulant abuse. In addition, data will be presented showing that brain imaging can be used to examine acute and chronic effects of potential therapeutic agents in stimulant abuse to aid in medication development. Challenges and potential rewards of using brain imaging as a tool for treatment development will also be discussed.
I. 17th Annual Contingency Management Working Group
   Chairs: Kelly Dunn and Kathryn Saulsgiver

The Contingency Management (CM) Working Group, held annually during the CPDD convention, is an opportunity for the dissemination and discussion of current research regarding the use of CM interventions to promote behavior change and reduce drug use. CM is a behavioral treatment strategy that has demonstrated consistent success in promoting abstinence from a wide-range of drugs and across many different treatment populations. It is also being used to promote change in behaviors impacting the course of other chronic diseases (e.g., obesity, diabetes). At the 17th Annual Meeting of the CM Working Group, junior and senior researchers will present preliminary data from ongoing studies involving CM. The goal for this working group is to provide an informal outlet for discussion of ongoing CM research, with an emphasis on developing or improving research strategies by seeking audience input, and providing opportunities for junior and senior researchers to interact. As the goal for this working group has always been to provide an informal outlet for discussion of CM data, names of presenters are not included with this submission. Rather, participants and topics will be chosen during the Spring of 2011 in order to capture the most current data in contingency management for presentation at our annual working group.

II. Media Training
   Chairs: Kathleen Brady and Martin Y. Iguchi

This workshop is designed to help participants prepare for interviews with media, including advice on how to prepare for interviews, pitfalls to avoid, and strategies for effective communication. Facilitators include Tom Linden, M.D. Glaxo Wellcome Distinguished Professor of Medical Journalism in the School of Journalism and Mass Communication at the University of North Carolina at Chapel Hill as well as several newspaper and television reporters. As director of the Medical and Science Journalism Program at UNC-CH, Dr. Linden teaches courses for both undergraduate and graduate students and administers one of the nation's first master's programs in medical journalism. Participants are encouraged to bring in specific examples of situations that they have encountered with the media for discussion.

III. Assessing and monitoring risk for prescription opioid abuse across diverse populations
   Chairs: Andrea Barthwell and Lynn Webster

Predicting and assessing risk for prescription opioid abuse across different populations can be challenging and approaches may require adaptation based on the type of population being assessed. Particular populations that may be vulnerable to prescription abuse include adolescents and persons abusing drugs and alcohol for recreational purposes, pain patients that are exposed to these medications for treatment, as well as persons with addictive disorders. Identifying and mitigating the risks associated with drug
abuse is critical, given the growing rates and societal implications of drug abuse. Manifestations of behaviors around prescription opioid abuse vary with each population type, and tools used for clinical assessment need to be adaptable. Outcomes and limitations of both objective and subjective tools need to be carefully considered. Furthermore, tools need to be selective to differentiate abuse from misuse, and in the case of pain patients, distinguish drug-seeking behavior related to pseudo-addiction or the under-treatment of pain. In addition, standardization of definitions for abuse, misuse, and recreational drug use are needed. This symposium will review current definitions, current tools available that can be appropriately used in different populations, and the limitations and critical gaps in this area.

IV. *Frontiers in systems modeling: Bridging science and policy*
   Chairs: Alison Ritter and Georgiy Bobashev

The use of modeling techniques, including agent-based modeling and mathematical modeling have become central to advancing knowledge and policy in the area of drug dependence. Modeling symposia and workshops have been held at CPDD for the last several years. Given the field advances and the vast increase in modeling use for policy evaluation, the 2011 workshop will emphasize the applications of modeling methods by showcasing a range of models of interest to the broad CPDD public who do not need to be mathematicians to appreciate the utility of the models to research and policy making. This workshop brings a fresh group of internationally recognized presenters to CPDD, all of whom have extensive expertise in modeling. The aims of the workshop are to 1) engage the delegates in both the theory and practice of modeling in the area of drug abuse and dependence; 2) demonstrate different types of modeling approaches and the diverse methodological approaches; and 3) articulate both the practice and policy implications that arise from the models presented. An important feature of the carefully selected presenters and discussant is the focus on the modeling policy and practice implications; the discussant having worked in government, in clinical practice and used models actively. It is through the application of this scientific method that we will demonstrate the ways in which models contribute to the evidence-base and can sit alongside randomized controlled trials and other forms of ‘evidence’ to inform better practice and policy responses.

V. *SASATE*
   Chairs: Catherine Stanger and Michael Dennis

Contingency management has been successfully used to target adolescent marijuana and tobacco use. However, the literature in adolescents is in its early stages compared to CM applications with adult substance abuse. There are unique issues relevant to the use of CM with adolescent populations. The success of CM interventions will be influenced by at least 5 factors: the schedule used to deliver incentives, the magnitude of the incentives, the choice of the target behavior, the selection of the type of consequence, and the monitoring of the target behavior. These dimensions are important to consider in developing, testing, and disseminating CM interventions. This workshop will involve a series of presentations on recent adolescent substance abuse research on CM approaches in outpatient and school settings with a focus on the technical aspects of CM development, implementation and dissemination issues. Participants will learn 1) How to identify
important methodological issues likely to influence the efficacy of CM interventions for adolescent substance use; 2) outcomes of studies examining CM approaches in clinical and school settings; and 3) Predictors of successful CM adoption in community settings. Following the panel discussion will be a brief business meeting for the Society for Adolescent Substance Abuse Treatment Effectiveness (SASATE) chaired by Dr. Michael Dennis.

VI. Career development: A perspective from junior and senior researchers
   Chairs: Gerald McLaughlin and Scott Chen

Developing a career involves a series of decisions, often made with limited information or assistance. The purpose of this workshop is to provide a forum for thinking more creatively and systematically about one’s career decisions by inviting both junior and more senior scientists to reflect on their own career choices and experiences, as well as those of their colleagues, and encouraging substantial audience participation. Topics such as mentor/mentee suggestions; networking; advantages of academic, industry or government positions; and job interview guides will be considered. About half the time will be allotted for presentations by speakers with a spectrum of backgrounds, and half the time is available for audience discussion/questions. We encourage potential attendees to submit topics of interest to the workshop chairs before the CPDD meeting so that these can be shared with the speakers and participants.

VII. NIDA Medications Development Workshop 2011
   Chairs: David McCann and Phil Skolnick

This workshop will provide an opportunity for two-way communication between NIDA staff and researchers in the field of medications development. Three NIDA presentations will focus on topics of importance to the field: 1) an FDA-suggested endpoint for trials evaluating medications for cocaine and methamphetamine addiction treatment; 2) medication non-compliance in clinical trials and methods for addressing the problem; and 3) promising new pharmacotherapies in late preclinical and Phase I development. Approximately 20 minutes at the end of the workshop will be devoted to comments from the field. Attendees will be asked to share their perceptions of the biggest challenges facing the field of medications development.

VIII. FDA draft guidance on testing of the abuse potential of compounds:
      Dialogue between industry and the FDA Controlled Substance Staff
      Chairs: Beatriz Rocha and Silvia Calderon

In 2008 the Cross Company Abuse Liability Consortium (CCALC) held a first Dialogue Session on abuse potential assessment with the FDA Controlled Substance Staff (CSS). Participants were representatives from more than 25 pharmaceutical companies, CSS, and from CDER Review Division and Management. The meeting focused on the prospective assessment of abuse potential, both preclinical and clinical, and successfully furthered industry-FDA understanding regarding requirements for abuse potential assessment. It was especially useful and important given the lack of published guidance on abuse potential assessment at the time. CPDD had the unique opportunity to be updated on
such discussions through a workshop held during the 71st Annual Meeting. In January, 2010 FDA published the Draft Guidance on Testing of the Abuse Potential of Compounds, and since then the CSS has been receiving public comments. A second Dialogue Session between the CCALC and FDA took place in November 2010. This Dialogue represents CSS outreach to the CCALC in seeking to have a collaborative discussion about the Draft Guidance. Procedural issues, including the role of NIDA during a New Drug Application (NDA) review, were discussed, and numerous questions submitted to the FDA from various stakeholders were addressed. Other issues discussed included preclinical, clinical and post marketing studies evaluating abuse potential of new products.

IX. Getting SMART about developing individualized sequences of health interventions
Chairs: Susan A. Murphy and Daniel Almirall

The effective management of a wide variety of substance use disorders often requires individualized, sequential decision making, whereby treatment is dynamically adapted over time based on an individual’s changing course. Adaptive health interventions operationalize individualized, sequential, decision making via a sequence of decision rules that specify whether, how, for whom, and when to alter the intensity, type, or delivery of psychosocial, behavioral, and/or pharmacological treatments at critical decision points in the management of chronic disorders. Adaptive health interventions can be used to develop or supplement clinical treatment guidelines. The aim of this workshop is to describe and discuss the use of a novel experimental design—sequential multiple assignment randomized trials, or SMART—intended specifically for the purpose of developing and optimizing adaptive health interventions. Specifically, the workshop will involve three presentations. The first presentation will define adaptive health interventions, discuss why they are important, and will introduce SMART designs, including a description of basic SMART design principles and the types of primary and secondary scientific questions that can be addressed in a SMART. The second and third presentations will discuss experiences and issues related to the motivation for, planning, conduct, and/or data analysis of two SMART studies currently in the field. Ample time will be set aside for questions, comments, and in-depth discussion. Participants will be encouraged to share experiences and ideas from their own research as a way to connect with the material. Participants attending this seminar should be familiar with the basic principles of experimental design.

X. NIDA research resources: An update on the NIDA Drug Supply and Analytical Services Program
Chairs: Hari H. Singh and Rao S. Rapaka

The National Institute on Drug Abuse (NIDA) provides an array of services at no cost to qualified research investigators through its Drug Supply and Analytical Services Program. Although this program has been in existence for quite some time, many research investigators, particularly early career investigators are not aware of this program. The proposed workshop will give CPDD attendees an opportunity to learn about this program and make them aware of various services provided by NIDA free of cost. Highlighted topics will include 1) an overview of NIDA’s Drug Supply and
Analytical Services Program which include the supply of DEA controlled drugs and other chemical substances that may or may not be controlled, but serve as biological probes for basic research and help in developing possible therapeutics for the treatment of drug addiction, (2) procedures for the acquisition of inventoried substances, their storage and distribution under controlled environment; 3) procedure for X-ray crystallography of chemical compound and biological substrates, and finally 4) procedures for analysis of experimental samples received from NIDA-supported studies. Overall the NIDA-sponsored workshop will provide a detailed and updated overview of the NIDA Drug Supply and Analytical Services Program’s purpose, procedures, and functioning, so that new and experienced investigators can take advantage of these freely available supplies to facilitate their research.

XI. What’s new at NIDA and NIH: Peer review and other policies that affect applicants
Chairs: Meena Hiremath, Mark Swieter, and Teri Levitin

This workshop is intended to provide an opportunity for participants to learn about new policies and procedures at NIH and NIDA that are relevant to them. Topics will include changes in the peer review process at NIDA and the Center for Scientific Review (CSR) associated with the implementation of Enhancing Peer Review, tips on grant preparation, and how to find somebody to help you with your application. Other topics and questions of interest to the audience will be addressed. This is very much an interactive, audience-directed activity. We see this workshop as a public service to the CPDD community, with issues we discuss determined by audience interest. Although we will have a list of topics of interest, as is always the case with these presentations, audience members may ask about the budget, recent Advisory Council reports, new research directions at NIDA, various NIH support mechanisms, or any other subject.

XII. A systematic approach to selection and measurement in clinical trials research
Chairs: George Bigelow and Carmen Rosa

Drug use dependence continues to be a major public health problem. Clinical trials test the efficacy of behavioral and pharmacological interventions in dependent individuals. There is no consensus about the most appropriate outcome(s) to consider in determining treatment efficacy or on the most appropriate methods for assessing the selected outcome(s). Having a commonly employed outcome (or a set of common outcomes) that could be used consistently across all clinical trials would facilitate treatment research. Discussions among experts suggests that the most appropriate outcome will vary as a function of salient variables inherent in the particular clinical trial, such as the type of intervention, its target, the treatment goals (e.g., abstinence or harm reduction drug use goals, improved psychosocial function), and the perspective being taken (e.g., researcher, clinical program, patient, society). This workshop will provide a discussion venue for researchers and practitioners to discuss the value of developing a decision tree approach, based on these trial variables, to guide the selection of primary and secondary outcomes, as well as the methods to assess them. Speakers will discuss 1) issues around drug use as primary outcome, 2) measuring drug use, 3) what other outcomes are clinically significant and should be evaluated in clinical trials as a set of common outcomes; and 4) recommendations.
XIII. *When clinical adverse events signal drug abuse potential*
   Chairs: Edward M. Sellers and Kerri A. Schoedel

As human abuse liability studies are typically conducted in recreational drug-using populations, clinical evaluations of abuse/dependence in healthy volunteer and patient populations are based primarily on spontaneously reported abuse- and discontinuation-related adverse events observed in clinical trials. Although these events can signal the presence of mood-elevating, sedative, stimulant and hallucinogenic properties, or neuroadaptation and physical dependence, the evaluation of abuse- and dependence-related events has not yet been rigorously studied. Further research is needed to establish correlations between adverse events reported in clinical trials and controlled psychometric assessments, and to identify which events may be predictive of actual abuse or dependence. In addition, structured assessments of CNS effects (e.g., visual analogue scales, structured interviews) may be more sensitive for detecting abuse-related effects but are generally not implemented in large-scale trials. Although these data represent essentially the only pre-market opportunity to risk in intended therapeutic populations, a consensus review is needed in order to achieve greater standardization for the analysis and presentation of abuse and dependence-related data from clinical trials. Therefore, the aim of this workshop is to initiate discussion of issues surrounding the collection and interpretation of adverse event terms of interest, investigator training, case report management, and the potential use of alternative scales, with input from industry, academic, investigator and regulatory perspectives.
**EPIGENETICS**

**DNA methylation: a dynamic and stable regulator of memory**

C.A. Miller, Department of Metabolism & Aging, Department of Neuroscience, The Scripps Research Institute, Jupiter, FL, USA

A new line of neuroscience research suggests that epigenetics may be the site of nature and nurture integration by providing the environment with a mechanism to directly influence the read-out of our genome. Epigenetic mechanisms in the brain are a series of post-translational chromatin and DNA modifications driven by external input. Given the critical hub of epigenetics, neuroscientists have come to suspect its fundamental influence on how our minds change in response to our unique environment and, in turn, how these changes can then impact our future interactions with the environment. We are particularly interested in the role that associative memory plays in driving relapse to drug use, as well as the epigenetic influences on the long-term maintenance of this behavior. Because neuroepigenetics was such a young field at the time we began, we first investigated the mechanisms of simple associative fear memories. Our approach was particularly focused on an epigenetic transcriptional silencing mechanism that has been studied extensively as a lifelong molecular information storage mechanism put in place during development, DNA methylation. We found that learning is associated with hippocampal upregulation of the enzymes responsible for methylation (DNA methyltransferase; DNMT), as well as a rapid increase in the methylation of memory-associated genes. Specifically, a memory suppressing phosphatase, PP1, is transcriptionally silenced through methylation, while a memory promoting gene, reelin, is activated. Further, formation of the associative memory is blocked by intra-hippocampal administration of a DNMT inhibitor. Interestingly, these hippocampal changes return to baseline less than a day after learning. This shifted our focus to the cortex, where many types of memories are thought to reside in the long-term. We found that persistent, gene-specific hypermethylation is induced in the cortex by a single, hippocampus-dependent associative learning experience. Further, pharmacologic inhibition of methylation one month after learning disrupts long-term memory maintenance. We are currently taking this new knowledge of neuronal DNA methylation’s roles in memory and applying it to animal models of relapse to drug-seeking. Funding provided by NIDA (4R00DA024761-03).

**The role of chromatin modifying enzymes in the acquisition and extinction of context-drug associated memory**

M. Malvaez, S.C. McQuown, G.A. Rogge, M.A. Wood, Dept. of Neurobiology and Behavior, Center for the Neurobiology of Learning & Memory, Univ. of California Irvine, CA, USA

Repeated use of drugs of abuse causes persistent alterations in gene expression responsible for the long-term behavioral and structural changes in central reward pathways. Recently, it has been suggested that epigenetic mechanisms are responsible, in part, for these drug-induced changes in gene expression. Epigenetic regulation of gene expression may provide transient and potentially stable conditions, which in turn may ultimately participate in the molecular mechanisms required for neuronal changes subserving long-lasting changes in drug-seeking behavior. Our research is focused on understanding the role of chromatin modifying enzymes in the acquisition and extinction of context-drug associated memory formation. In particular, we examine how the histone
acetyltransferase CREB-binding protein (CBP) and the histone deacetylase 3 (HDAC3) are pivotally involved in regulating histone acetylation required for transcription underlying context-cocaine associated memory formation using the conditioned place preference (CPP) paradigm. One exciting result of this research is that HDAC inhibition after establishing a CPP significantly facilitates extinction of drug-seeking behavior in a manner that is refractive to reinstatement. Thus, understanding chromatin modifying mechanisms that establish and maintain drug-dependent plasticity changes may lead to a better understanding of substance abuse disorders as well as novel approaches for treatment. Supported by NIDA (DA025992) and NIMH (MH081004) grants to M.A.W., an NRSA fellowship (DA029368) to M.M., and Repligen Corporation.

Epigenetics of opioid receptor genes – nutrients, drugs and behavior

L.-N. Wei, Department of Pharmacology, University of Minnesota Medical School, Minneapolis, MN 55455, USA

The three opioid receptor genes, MOR, DOR and KOR, are differentially regulated but share a highly conserved genomic structure and promoter feature. Classical studies established various combinations of transcription factors in regulating these genes in different cellular contexts. Recent studies uncovered fundamentally important roles for chromatin remodeling in the manifestation of these genes’ plasticity, which underlines distinct behavior of the three opioid receptor genes in response to different transcription factors’ action and in various biological contexts. Diets, drugs and behavior all can potentially modulate these genes’ chromatin remodeling processes, thereby altering their chromatin conformation that is principally responsible for the gene’s activity. This paper will present findings supporting epigenetic regulation of opioid receptor genes by various environmental factors, and discuss studies that have begun to examine the molecular mechanisms.

Acknowledgment: This work is supported by NIH grants DA11190, DA11806, DK54733, DK60521 and K02-DA13926, and the Distinguished McKnight University Professorship to LNW.

Chromatin plasticity in addicted brain: prodynorphin upregulation in human alcoholics


Genetic, epigenetic and environmental factors may influence the risk for neuropsychiatric disease through their effects on gene transcription. We hypothesize that these effects may be integrated through changes in chromatin states involving methylation of CpG dinucleotides that overlap with single-nucleotide polymorphisms (SNPs) associated with a disorder. We addressed this hypothesis by analyzing methylation of prodynorphin (PDYN) CpG-SNPs, reported to be associated with alcohol dependence, in the brain of human alcoholics. Analysis of postmortem human brain specimens demonstrated that PDYN expression is activated in discrete brain loci including the dl-PFC in alcoholics. This activation may contribute to cognitive dysfunctions relevant for “preoccupation / anticipation” stages of addiction and disrupted inhibitory control. Three of five PDYN SNPs associated with alcohol dependence were found to overlap with CpG dinucleotides. Methylation of these three CpG-SNPs was analyzed by pyrosequencing in the dl-PFC and
motor cortex (MC; no expression changes) from 14 alcohol dependent and 14 control subjects. In the dl-PFC but not in the MC of alcoholics, methylation levels of one of these three CpG-SNPs, the C, non-risk variant of 3´-untranslated region (3´-UTR) SNP (rs2235749; C>T) were increased (P < 0.001). This methylation positively correlated with PDYN mRNA and dynorphins (P < 0.05). A DNA-binding factor that differentially targeted the T, risk allele and methylated and unmethylated C allele of this SNP was identified. This factor may be involved in PDYN transcription through binding to the methylated 3´-UTR SNP C or T allele. The findings suggest a causal link between alcoholism-associated PDYN 3´-UTR CpG-SNP methylation, activation of PDYN transcription, and vulnerability to develop alcohol dependence in subjects with the non-risk SNP variant. Methylation of CpG-SNPs associated with a disease under environmental influences may be a general phenomenon affecting gene expression and contributing to disease susceptibility. Supported by the Swedish Council for Working Life and Social Research, and the Swedish Science Research Council.

BRAIN IMAGING

Imaging opioid effects on brain systems

Lino Becerra, Center for Pain and the Brain, Harvard Medical School, Boston, USA

Imaging has provided opportunities to evaluate drug effects on brain function and structure. Opioids, classically used as analgesics are also drugs of abuse. In this session we will discuss two aspects of opioid actions on brain function. The first will discuss different opioid agonist and antagonist phMRI results, showing that specific features of opioid subtypes may be evaluated using functional and phMRI. The second will discuss potential long-term effects of opioids on brain structure and function.


Mu-opioid receptors and cocaine addiction

D.A. Gorelick, Intramural Research Program, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, USA

Mu-opioid receptors (mOR) are expressed on neurons in several brain regions considered to play a role in cocaine use and craving, and are up-regulated by binge administration of cocaine to rodents. We conducted a series of studies, in collaboration with the Johns Hopkins PET Center, evaluating regional brain mOR binding potential (BP) in healthy adults with current cocaine abuse or dependence, no other current psychiatric disorder (except nicotine dependence), and minimal recent use of other drugs (except cigarettes). The PET radioligand was [11C]carfentanil, a selective mOR agonist. The initial study of 10 men found significantly increased (10-50%) mOR BP, compared to 7 non-addicted controls, in frontal, temporal, and anterior cingulate cortex and striatum after 1-4 days of abstinence. Increased BP in most regions was positively correlated with cocaine craving, and declined towards normal in most subjects after 28 days of abstinence. A second study in 17 non-treatment-seeking cocaine users and 16 healthy controls found increased mOR BP in frontal, anterior cingulate, and lateral temporal cortex after 1 days of abstinence, which correlated with cocaine craving and amount of cocaine use in the 2 weeks prior to admission. Binding remained elevated after 1 week in the frontal cortex, and after 12 weeks in the anterior cingulate and anterior frontal cortex. A shorter interval
before relapse to cocaine use (after discharge from the secure research ward) was associated with increased mOR BP in frontal and temporal cortex and with lesser decrease in BP between 1 and 12 weeks. A third study in 25 outpatients receiving psychosocial treatment for cocaine addiction found significant associations between increased mOR BP in medial and middle frontal gyri and greater cocaine use and shorter duration of cocaine abstinence during the 12 weeks of treatment. These findings suggest that brain mOR play an important role in human cocaine addiction and may offer a therapeutic target for developing new treatments. Supported by the IRP, NIH, NIDA and NIH grants R01-DA 09479, DA-11774, & DA-12274.

**Development and clinical use of a PET radioligand for the kappa receptor**

D. Martinez¹, F. Liu¹, Y. Huang², D.R. Hwang¹, R. Narendran³, R. Carson² and M. Slifstein¹, ¹Division on Substance Abuse, Columbia University/New York State Psychiatric Institute; ²Positron Emission Tomography Center; Yale University School of Medicine; ³Department of Radiology, University of Pittsburgh, USA

Both pre-clinical and postmortem human studies investigating kappa receptor binding in cocaine abuse shown that the kappa receptor plays an important role in addiction. Thus, we developed a radiotracer to image this receptor in humans. The initial work performed in baboons showed that this radiotracer was able to cross the blood brain barrier, and had a good ratio of specific to non-specific binding. In addition, the uptake kinetics showed that significant washout occurred within the time frame of the PET experiment. PET blocking studies with naltrexone showed that the cerebellum could be used as a reference region. Subsequent to this, biodistribution studies were performed in human volunteers, in order to measure the organ exposure, which showed that the radiotracer could be used in clinical studies that required multiple scans. Based on these findings, brain imaging studies were performed in human volunteers. To date, studies in control subjects show that kinetics of the radiotracer vary significantly from the baboon studies, such that long scan times are required. In addition, there is no observable reference region in human subjects, such that scans with naltrexone are needed to obtain the non-specific distribution volume. Thus, while clinical studies performed with this radiotracer remain feasible, these issues must be taken into consideration when developing a PET imaging study with this radiotracer. Supported by the National Institute on Drug Abuse.

**Endogenous opioid system modulation of motivation circuitry**

J.K. Zubieta ¹,², T.F. Love², M. Peciña², C.S. Stohler³, ¹Department of Psychiatry and ²Molecular and Behavioral Neuroscience Institute, University of Michigan, and ³School of Dentistry, University of Maryland, USA

The endogenous opioid system, together with dopaminergic circuits, is emerging as a principal site of action of most drugs of abuse, including alcohol, opiates, psychostimulants and marihuana. Within the 3 receptor types involved in opioid neurotransmission, the μ-opioid receptor has been the best studied in humans. Using external imaging with positron emission tomography and selective radiotracers, studies in healthy humans have shown that there is substantial interindividual variation in the function of this neurotransmitter system, both in the in vivo availability of the receptors, as well as in the release of opioid peptides (e.g., β-endorphin, enkephalins, endomorphins) interacting with the μ receptor. In response to a stressful challenge,
variations in the concentration of receptors and in the magnitude of neurotransmitter release have been linked to the capacity to regulate the stressful experience. These variations have been linked to specific genetic polymorphisms (e.g., COMT val158met) enriched in substance abusing samples, suggesting that they may underlie variations in the propensity to use drugs and the development of addictions. For example, and in healthy subjects, trait impulsiveness was highly associated with resting and stress-induced μ-opioid system functional measures in the medial and orbitofrontal cortex, anterior cingulate, thalamus, nucleus accumbens and amygdala, accounting for up to 50% of the variance in that personality trait. Patient groups that present high levels of comorbidity with the addictions, such as borderline personality disorder, also present similar alterations in the function of this neurotransmitter system even in the absence of a frank diagnosis of drug dependence. Last, variations in the function of μ-opioid receptors also appear to impact on other neurotransmitter systems, such as the dopaminergic. A common genetic polymorphism in the μ-opioid receptor gene was associated with greater dopaminergic responses to nicotine in tobacco smokers. These data suggest that variation in this neurotransmitter system is implicated in both risk for the addictions and variation in the neural effects to substances of abuse. Supported by grants R01 DA016423, R01 DA027494, R21 DA027066, and R21 MH 069612

BUPRENORPHINE

The unique pharmacology of buprenorphine

J. Traynor, Department of Pharmacology and Substance Abuse Research Center, University of Michigan, Ann Arbor, MI 48109, USA

Since its introduction into clinical medicine in the 1970’s in the U.K., buprenorphine has been much studied for its unique pharmacology; properties that have lead to its successful introduction into the opiate abuse medication armamentarium, but properties that still remain to be fully explained. Important assets of buprenorphine include its low rate of dissociation from the mu-opioid (MOP) receptor and its profile as a MOP receptor agonist and kappa opioid receptor antagonist; it also has very low delta opioid receptor efficacy. Of special interest has been the bell-shaped dose-response relationship that is observed in many behavioral assays, including antinociception. This means that high doses show less robust effects and a shorter duration of agonist action than lower doses. Whether a bell-shaped dose-response curve is seen for buprenorphine in rodent models of antinociception is dependent on both the dose and timing of drug administration. The phenomenon has most recently been explained by extensive data supporting an antinociceptive action via MOP receptors at low doses and a physiological antagonism by an action at nociceptin/orphanin FQ (NOP) receptors at higher doses. However, this contradicts the fact that in vitro assays buprenorphine has low affinity and low efficacy at NOP receptors. Thus, for example across all brain regions of the rat when assayed using [35S]GTPgammaS autoradiography buprenorphine acts only as an antagonist. In addition, earlier findings showed that both the ascending and descending arms of the buprenorphine dose-effect curve are sensitive to naloxone antagonism, suggesting an interaction at classical opioid receptors, and structurally dissimilar opiates that also give a bell-shaped dose-effect curve, such as methoclocinnamox, have even lower affinity for, and efficacy at, NOP receptors. These apparent contradictions suggest we still have a lot to learn about the pharmacology of buprenorphine. Supported by NIDA grant DA04087.
New ligands from an old friend
S.M. Husbands, Department of Pharmacy and Pharmacology, University of Bath, Bath, UK
The use of buprenorphine in the treatment of opiate abuse and dependence by detoxification, substitution and maintenance, is the most noteworthy recent addition to the repertoire of methods available for the treatment of substance abuse disorders. In addition to its activity as a mu opioid (MOP) receptor partial agonist, buprenorphine is a kappa/delta (KOP/DOP) receptor antagonist and more recently profiled as a partial agonist at the nociceptin/orphanin FQ (NOP) receptor. It has been postulated that buprenorphine-like ligands with higher NOP receptor activity might have efficacy as non-addicting analgesics and potential drug abuse medications, while buprenorphine-like compounds with lower, or no, MOP receptor efficacy may have utility as relapse prevention agents in the treatment of drug abuse. Control over efficacy at four different receptors is difficult to manage, but notable successes have been achieved within the orvinol series. In the search for MOP/NOP receptor partial agonists, ligands with affinities from 8 nM – 133 nM at NOP receptors were generated (buprenorphine KiNOP 77 nM). Of the compounds with appreciable NOP receptor affinity, efficacy at this receptor ranged from very low (5% of nociceptin) to moderate (58% of nociceptin) with buprenorphine being intermediate in this range (21% of nociceptin). One compound, BU08028, was found to have comparable affinity at opioid and NOP receptors (all between 1.6 – 8.5 nM) and very similar activity to buprenorphine in the [35S]GTPγS assay, but with higher efficacy (48% of nociceptin) at NOP receptors. In the search for NOP partial agonists with antagonist activity at MOP and KOP receptors, ligands have been developed with the desired profile in vitro. The further evaluation of these ligands, including initial in vivo evaluations, will be presented and the recent developments in our understanding of structure-activity relationships in this remarkable series discussed. This work was supported by NIDA grants DA020469 & DA007315 (SMH) and DA023281 (L. Toll).

Buprenorphine: a novel receptor target and mechanism of action
S. Grinnell, S. Majumdar, Y.-X. Pan and G.W. Pasternak, Molecular Pharmacology and Chemistry Program and the Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA
Buprenorphine is a potent analgesic whose use is becoming increasingly widespread, due in part to a number of advantages over traditional mu opioids. However, a number of features of this agent have raised questions regarding its mechanism of action. It is often considered a partial mu agonist. Yet, it also has high affinity for other classes as well. Interestingly, it has a methyl-c-propyl substituent on the nitrogen, similar to naltrexone, but still remains an analgesic. Furthermore, many investigators have suggested that its actions are less easily reversed by the potent opioid antagonist naloxone. These observations led us to examine its mechanism of action. In our hands, buprenorphine is a potent analgesic. However, in a MOR-1 knockout model in which exon 11 and its associated splice variants are eliminated, buprenorphine shows no analgesic actions at doses many fold higher than its normal ED50. This contrasts with morphine and methadone which retain full analgesic activity in these same exon 11 knockout mice.
Although there are several exon 11-associated variants of the mu opioid receptor Oprm1 that predict full length, 7 transmembrane receptors, most predict truncated variants containing only 6 TM domains. Evidence from our group suggests that these truncated variants offer a unique target in the design of opioid anaaglesics and our current results suggest that much of the analgesic actions of buprenorphine can be attributed to these new targets, explaining much of the overall pharmacology. Supported by grants from the National Institute on Drug Abuse (DA02615, DA06241, DA07242) to GWP and a core grant from the NCI (CA08748) to MSKCC.

Abuse liability of buprenorphine in humans under various states of opioid physical dependence
S.D. Comer, M.A. Sullivan, S.K. Vosburg, J.M. Manubay, Z.D. Cooper, and J.D. Jones, NYSPI and Columbia University, New York, NY, USA
The abuse potential of buprenorphine (bup) as well as buprenorphine/naloxone (bup/nx) is unclear given the unique pharmacology of bup. Therefore, we conducted a series of studies to assess the abuse potential of bup and bup/nx under various states of opioid physical dependence. Heroin-dependent volunteers, who lived in the hospital for the duration of the studies, were given the opportunity to work for either drug or money using a progressive ratio self-administration procedure. None of the participants were interested in treatment for their drug use and were paid for their participation. The volunteers were detoxified from heroin, maintained on morphine, or maintained on sublingual bup. During a sample session, participants received $20 and a dose of the test drug. During a subsequent choice session, participants could work for the test drug or money they had sampled by making finger press responses. In recently detoxified individuals, bup was self-administered as much as methadone and ratings of drug liking were similar for bup and methadone. When bup was compared to bup/nx in recently detoxified individuals, both drugs were self-administered at the same levels. However, ratings of liking for bup/nx were not different from saline. Instead, participants reported that they self-administered bup/nx because it alleviated mild withdrawal. In morphine-maintained participants, bup alone increased both positive and negative subjective effects, but it was not self-administered at any dose that was tested. In bup-maintained individuals, self-administration of bup/nx was lower than bup alone and heroin. Drug liking and desire to take the drug again also were lower for bup/nx. Consistent with its partial agonist profile, the abuse liability of bup varied depending on the state of opioid physical dependence. The addition of naloxone further reduced the abuse liability of bup under the various experimental conditions. Supported by NIDA (DA09236, DA10909), Schering-Plough, and Reckitt Benckiser.

To mix or not to mix: modulation of opioid activity by nociceptin receptor ligands
Nociceptin/orphaninFQ via its cognate receptor NOP, modulates several opioid-mediated actions, particularly in reward and nociceptive pathways. We have hypothesized that modulation of opioid activity by NOP ligands could lead to non-addicting analgesics and drug abuse medications. To investigate this hypothesis for therapeutic development, we designed bifunctional NOP/mu-opioid receptor ligands that have varying selectivity and
functional efficacy at both these receptors. These compounds were evaluated in a mouse thermal antinociception assay, and in the mouse conditioned place preference paradigm (CPP) against morphine. Our results showed that a NOP/MOP agonist showed significant MOP-mediated analgesia, but NOP agonist efficacy, and preferably NOP selectivity, was required to attenuate the MOP-mediated reward in the same molecule or morphine-induced CPP, when co-administered with morphine. On the other hand, a NOP full agonist with low or negligible efficacy at MOP, attenuated morphine CPP and had no CPP on its own. Our recent studies with buprenorphine, a MOP partial agonist, which has low affinity and efficacy at NOP, showed that its NOP agonist activity can attenuate its MOP-mediated antinociceptive potency, particularly at higher doses, leading to its well-noted inverted U-shaped dose response curve for antinociception. However, buprenorphine induces a place preference in the CPP paradigm, indicating that its low NOP efficacy and selectivity does not attenuate its rewarding effects. It appears therefore, that a bifunctional NOP/MOP agonist profile with a higher balance of NOP selectivity and efficacy, may be suitable as a non-addicting analgesic, whereas full NOP agonist activity is required to attenuate the rewarding effects of opioids. The effect on other opioid-mediated actions such as locomotion and opioid tolerance is still under investigation, and will likely play a role in the therapeutic application of such multitargeted compounds. Supported by grants DA14026, DA027811(NZ) and DA023281(LT).

Therapeutic potential of NOP ligands as spinal analgesics
M.C. Ko, Department of Pharmacology, University of Michigan Medical School, Ann Arbor, MI, USA

Itch/pruritus is the most common side effect derived from spinal administration of mu opioid receptor (MOP) agonists. Given that intrathecal administration of morphine dose-dependently produces antinociception with simultaneous itch/scratching responses in monkeys, this non-human primate model provides a valuable tool to identify a viable target as spinal analgesics. The nociceptin/orphanin FQ (N/OFQ) receptor (NOP) is defined as the 4th member within the opioid receptor family. Although the actions of N/OFQ have much in common with those of classical opioids at the cellular level, the in vivo pharmacological profiles of N/OFQ and NOP-related ligands are not fully known in primates. This presentation provides an overview of recent studies of NOP- and MOP-related ligands in rhesus monkeys. First, intrathecal N/OFQ over a wide dose range produced antinociception without hyperalgesia, scratching, sedation, and muscle relaxation. In contrast, intrathecal MOP agonists such as morphine and DAMGO produced antinociception with profound scratching. When N/OFQ was combined with morphine intrathecally, this combination produced greater antinociceptive effect. Second, Ro 64-6198, a nonpeptidic NOP agonist, produced antinociceptive effects that are independent of MOP. Like the MOP agonist alfentanil, systemic Ro 64-6198 produced morphine-comparable antinociception. Unlike alfentanil, Ro 64-6198 did not produce reinforcing, respiratory depressant, or pruritic effects. Intrathecal Ro 64-6198 also produced NOP-mediated antinociception. Third, intrathecal UFP-112, a chemical modification of N/OFQ, produced long-lasting antinociception against acute noxious stimulus and capsaicin-induced allodynia. Antinociceptive effects of UFP-112 were antagonized by the NOP antagonist, J-113397, but not by the MOP antagonist,
naltrexone. In addition, intrathecal combination of inactive doses of UFP-112 and morphine significantly produced antinociception. Taken together, these findings strongly support the therapeutic potential of NOP agonists as spinal analgesics. Supported by U.S. Dept of Defense, Grant W81XWH-07-1-0162.

**The Nociceptin/Orphanin FQ system, as a treatment target for addiction.**
R. Ciccochioppo, School of Pharmacy, Pharmacology Unit, University of Camerino, Italy. Nociceptin/orphanin FQ (N/OFQ), the endogenous ligand of the NOP receptor, previously referred to as opioid receptor-like1 (ORL1) receptor, is a 17 aminoacid neuropeptide structurally related to the opioid peptide dynorphin A. From a functional point of view, N/OFQ possesses antiopiod properties and, acting as a presynaptic neuron inhibitor, it is able to control dopaminergic, noradrenergic and glutamatergic neurotransmission in different brain sites. In addition, it has been shown that N/OFQ possesses marked anxiolytic and anti-stress properties presumably mediated by its ability to blunt extrahypotalamic corticotropin releasing factor (CRF) activity. Altogether, these findings point at the N/OFQ–NOP receptor as a system potentially involved in the regulation of reward and drug abuse processes. Indeed, several studies demonstrate that activation of this system results in reduction of the rewarding properties of ethanol, morphine and cocaine. Recent rodent data suggest also that central administration of N/OFQ reduces reinstatement of alcohol-seeking behavior elicited by stress and by environmental conditioning factors. Buprenorphine has long been in clinical use for treatment of moderate-to-severe pain and its use for maintenance treatment of heroin dependence has been approved in several countries. This drug has long been known to be a partial agonist at m-opioid receptors but has also antagonistic or agonistic properties at k and d opioid receptors. In an unexpected development, it has recently been realized that buprenorphine also is agonist/partial agonist at the NOP receptors. Consistent with these findings we found that in rats this drug reduces excessive alcohol drinking via activation of NOP receptors. Based on these data we suggest that NOP receptors may represent a suitable target for addiction treatment development. Support: NIH/NIAAA grant AA014351.

**Discovery and development of nociceptin receptor agonists in alcohol dependence**
S.P. Brothers1,2,3, Y.T. Chen1, H. Salah-Uddin1,2,3, M. Cameron1, A. Thorsell4, M. Roberto5, T. Bannister1, M. Heilig4, C. Wahlestedt1,2,3, 1Molecular Therapeutics, The Scripps Research Institute - Scripps Florida, Jupiter, FL, USA, 2Department of Neuroscience, The Scripps Research Institute - Scripps Florida, Jupiter, FL, USA, 3Department of Psychiatry and Behavioral Sciences and the Hussman Institute for Human Genomics, University of Miami, Miami, FL, USA (current affiliation), 4National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda MD, USA, 5Committee on the Neurobiology of Addictive Disorders, The Scripps Research Institute, La Jolla, CA, USA

Alcohol dependence and abuse represents a considerable health and economic burden on society with available pharmacotherapies demonstrating insufficient efficacy. We designed novel, potent, and selective NOP agonists as tools for research on alcohol dependence with potential as clinically effective therapeutic agents. Currently available NOP small molecule agonists all have some mu or kappa opioid receptor activity,
limiting their usefulness as research tools. Our unpublished data show several promising novel molecules that are selective for the nociceptin receptor over the mu and kappa opioid receptors. Our molecules have been tested for in vitro activity and pharmacokinetic parameters. While our compounds are not orally bioavailable, they do show a high brain penetrance, and long half life in vivo. Our compounds also act in the central amygdala to reduce an ethanol dependant increase in GABA transmission. Finally, in animal models of hangover anxiety, our compounds show promising results that suggest some potential for future clinical translation. These studies were supported by NIH/NIAAA grant 5R01AA017943-02.

**SEX DIFFS PAIN**

**Gender differences in pain**  
L. LeResche, Dept. of Oral Medicine, University of Washington, Seattle, WA, USA

Although age- and sex-specific prevalence patterns differ for different pain conditions, prevalence rates of most common chronic pain conditions are higher in women than in men. For example, in population-based studies of adults, female:male ratios for headache, neck, shoulder, knee and back pain average around 1.5:1; for orofacial pains, ratios are about 2:1; for migraine headache, 2.5:1; and for fibromyalgia the ratio is over 4:1. Women are also more likely than men to experience multiple pains simultaneously. Having multiple pain problems (as opposed to a single pain condition) is associated with higher levels of disability and psychological distress, as well as higher risk of onset for new pain conditions. Differences in pain prevalence in men and women could be due to biological sex differences in nociceptive or perceptual mechanisms or to gender differences in pain appraisal, pain behavior or social roles. The gonadal hormone estrogen clearly plays a role in some pain conditions in women (migraine headache, temporomandibular pain). For other pain problems, evidence of hormonal involvement is less clear. However, rates of many pain conditions increase as girls pass through puberty, whereas rates for adolescent boys are stable or rise less steeply than for girls. Pain-related behavior differs by gender; women are more likely than men to seek health care for pain, resulting in a high proportion of women in many pain treatment settings. The higher rate of treatment seeking may in part be due to the fact that pain is more often severe for women than for men. Women’s higher pain intensity also seems to be a major factor influencing clinicians’ treatment decisions, especially prescription of medications for acute pain – although evidence suggests that clinicians’ gender stereotypes also play a role in these decisions, independent of the patient’s pain level. Women, particularly elderly women, are more likely than men to be prescribed opioid medications for pain and to use opioids long term. Understanding both biological and social contributions to gender differences in pain may help optimize treatment for people of both sexes. Supported by R01AG034181.

**Opioid analgesia and sex differences: An overview**  
E. Sarton, Department of Anesthesiology, Leiden University Medical Center, 2300 RC Leiden, The Netherlands

Although a contribution of sex in opioid efficacy has garnered much attention, the confirmation and direction of any such difference remain elusive. We performed a systematic review of the available literature on sex differences in μ and mixed μ/κ opioid
effect on acute and experimental pain. Fifty unique studies (including three unpublished studies) were included in the analyses. Across the 25 clinical studies on μ-opioids there was no significant sex-analgesia association. Restricting the analysis to patient-controlled analgesia (PCA) studies (irrespective of the opioid) yielded greater analgesia in women (n=15, effect size 0.22, 95% c.i. 0.02-0.42, P=0.028). Further restricting the analysis to PCA morphine studies yielded an even greater effect in women (n=11, effect size=0.36, 95% c.i. 0.17-0.56, P=0.003). Meta-regression indicated that the longer the duration of PCA, the difference in effect between the sexes further increased. Across experimental pain studies on μ-opioids women had greater antinociception from opioids (n=11, effect size=0.35; 95% c.i. 0.01-0.69, P=0.047), which was predominantly due to 6 morphine studies. Female patients had greater μ/κ opioid analgesia (n=7, effect size 0.84; 95% c.i. 0.25-1.43, P=0.005), but no sex-analgesia association was present in experimental studies (n=7). Sex differences exist in morphine-induced analgesia in both experimental pain studies and clinical PCA studies, with greater morphine efficacy in women. The data on non-morphine μ and mixed μ/κ-opioids are less convincing and require further study.

**Impact of age and sex in the antihyperalgesic actions of morphine: Role of periaqueductal gray**

A. Z. Murphy, Neuroscience Institute, Georgia State University, Atlanta, GA, USA

Opioid-based narcotics are the most widely prescribed therapeutic agent for the alleviation of persistent pain; however, it is becoming increasingly clear that morphine is significantly less potent in females compared to males. Indeed, studies from our lab using a variety of pain assays, including somatic, visceral and orofacial pain, have consistently shown that females require approximately twice the amount of morphine as a male to produce comparable levels of pain relief. The midbrain periaqueductal gray (PAG), via its descending projections to the rostral ventromedial medulla and the dorsal horn of the spinal cord, is considered an essential neural substrate for opioid-based analgesia. The PAG contains a dense population of mu opioid receptor (MOR) expressing neurons, and we hypothesized that MOR expression in the PAG was sexually dimorphic, and that these sex differences in opioid receptor levels contribute to the observed sex differences in morphine potency. Using a variety of techniques, including immunohistochemistry, western binding and autoradiography, we found that males have significantly higher levels of MOR expression in the ventrolateral PAG compared to cycling females. Inflammatory hyperalgesia induced by intraplantar administration of Complete Freund’s Adjuvant (CFA) was significantly reversed in males following direct administration of morphine into the PAG. By contrast, the antihyperalgic actions of morphine were significantly attenuated in proestrus and estrus females. Additional studies by our lab have shown that selective lesions of MOR-expressing neurons in the ventrolateral PAG significantly reduces the antihyperalgesic effects of systemic morphine in males only, and this reduction was positively correlated with the level of MOR expression in the ventrolateral PAG. Together, our studies suggest that sex differences in PAG MOR expression may provide the biological bases for the observed sexually dimorphic actions of morphine. Funded by NIH grant DA16272.
The importance of sex in pain; sexual dimorphic expression in spinal cord of mu-opioid and kappa-opioid receptor heterodimers.
AR. Gintzler, State Univ. NY, Downstate Medical Center, Brooklyn, NY, USA

Sexually dimorphic nociception and opioid antinociception has been extensively demonstrated. In particular, the nociceptive vs. antinociceptive consequences of kappa opioid receptor (KOR) activation is sexually dimorphic. Although it has been established for some time that KOR agonists have weaker analgesic activity and produce greater nociception in males vs. females, determinants of the balance between nociceptive and antinociceptive properties of KOR agonists remain largely unknown. My laboratory had demonstrated that the concomitant activation of spinal μ-opioid receptors (MOR) and KOR is necessary for spinal morphine antinociception in females, but not males. This sexual dimorphism can be explained by spinal cord expression of a MOR/KOR heterodimer that is vastly more prevalent in the spinal cord of females vs. males. Cross-linking experiments in combination with in vivo pharmacological analyses indicate that heterodimeric MOR/KOR utilizes spinal dynorphin 1-17 as a substrate and is likely to be the molecular transducer for the female-specific KOR component of spinal morphine antinociception. The existence of heterodimeric MOR/KOR provides a mechanism for activating spinal KOR-mediated antinociception without the concomitant pro-nociceptive functions that monomeric KOR also subserves. The presence of an ovarian sex steroid-dependent functional interaction of KOR with MOR, suggested by the dependence of MOR/KOR expression on stage of cycle, can explain sexually dimorphic analgesic mechanisms solicited by spinal morphine as well as male female differences in the balance between pro-nociceptive vs. antinociceptive responsiveness to KOR agonists. Supported by R01 DA027663.

GENETIC MICE

Functional characterization of the OPRM1 A112G SNP in mice
S. D. Mague 1, J. R. Turner 1, G. Carlson 2, J. A. Blendy 1, Departments of 1Pharmacology and 2Psychiatry, University of Pennsylvania, Philadelphia, PA, USA

A single nucleotide polymorphism (SNP) in the human μ-opioid receptor gene (OPRM1 A118G) has been widely studied for its association in a variety of drug addiction and pain sensitivity phenotypes; however, the extent of these adaptations and the mechanisms underlying these associations remain elusive. To clarify the functional mechanisms linking the A118G SNP to altered phenotypes, we derived a mouse model possessing the equivalent nucleotide substitution (A112G), which corresponds to the same amino acid replacement in the Oprml gene. These mice have alterations in basal and morphine-evoked responses in a variety of behavioral tasks, including nociception, behavioral sensitization and conditioned place preference. Some of these behavioral differences may be explained by reductions in MOPR expression levels, however MOPRs are reduced in a sub-set, but not all, brain regions. Specifically, the levels of MOPRs in the hippocampus are not different between genotypes. The hippocampus is an ideal structure to evaluate circuit function. Therefore, to investigate if this SNP impacts a functional response in the absence of reduced receptor levels, we utilized voltage-sensitive dye imaging in hippocampal slices before and after MOPR stimulation with DAMGO. Utilizing several analytical methodologies, we found significant reductions in DAMGO-mediated
responses in animals with the G112 allele. These data further support claims that this SNP results in a loss of receptor function. Supported by DA-027066.

**The role of OPRM1 variation for alcohol reward examined using a reverse translational approach**

M. Heilig, A. Thorsell. Laboratory of Clinical and Translational Studies, NIAAA, Bethesda MD, USA

Purpose: Mu-opioid (OPRM1) receptors are key to rewarding properties of alcohol, and the target for the approved alcoholism medication naltrexone. Based on secondary analyses of clinical trials, A118G variation at the OPRM1 locus has been suggested to moderate therapeutic efficacy of naltrexone, but this notion remains highly controversial. The purpose of the present set of studies was to examine the role of OPRM1 A118G variation for alcohol related behaviors using a reverse-translational approach. Humanized mouse lines carrying the human 118A and 118G variants, respectively, were generated on a C76BL/6 background. Ligand affinity was determined using displacement of [3H]DAMGO in cloned CHO-cells. Distribution, binding density and signaling were determined using autoradiography. A standard behavioral phenotyping battery was carried out. Alcohol-induced DA-release was examined using microdialysis, and alcohol consumption was assessed using two-bottle free-choice drinking. Both humanized receptor variants showed normal ligand affinity, distribution, binding density, and signaling, with no differences by genotype. In the basic behavioral phenotyping battery, 118GG mice were more bold/exploratory than 118AA mice. Similar to our human 11C-raclopride PET data, alcohol-induced DA-release was greater in male 118GG than male 118AA mice. Male, but not female 118GG mice consumed higher amounts of alcohol than 118AA mice of the corresponding sex, in particular at higher alcohol concentrations. The functional OPRM1 118G variant is sufficient to confer greater alcohol-induced DA-release and consumption. These findings are consistent with a role of this variant to predispose human carriers to endorphin-dependent alcoholism, but also to render patients more responsive to opioid antagonist treatment.

**Direct visualization of delta opioid receptor internalization under physiological conditions**

D. Massotte¹, L. Faget¹, E. Erbs¹, J. Le Merrer¹, G. Scherrer², A. Matifas¹, J.-L. Vonesch³, F. Noble⁴, B. L. Kieffer¹, ¹Dept of Neurobiology and Genetics, IGBMC, Illkirch-Graffenstaden, France, ²Dept of Physiology and Cellular Biophysics, Columbia University, New York, NY 10032, USA, ³Imaging Center, IGBMC, Illkirch-Graffenstaden, France, ⁴Neuropsychopharmacologie des addictions, Université Paris Descartes, Paris, France.

Drug addiction is a complex disorder involving gradual and long-term adaptations of the brain in response to repeated drug exposure. This entails modifications of neuronal connectivity, signaling and plasticity. In heroin addicts, re-exposure to environmental elements previously associated with heroin abuse induce intense drug craving. Therefore, numerous behavioral studies addressed the impact of environmental cues on drug seeking. We developed a protocol in which morphine was repeatedly administered in a given environment at a dose leading to physical dependence. This paradigm elicited context-induced withdrawal upon re-exposure of drug-free animals and induced
activation of the hippocampus. Using knock-in mice expressing a functional fluorescent delta opioid receptor (DOR-eGFP), we then investigated delta receptor activation and subsequent internalization by fluorescence microscopy to address in vivo dynamics of the receptor under physiological conditions. The authors acknowledge NIDA support to the Center for Opioid Receptors and Drugs of Abuse (#DA 005010), ANR, CNRS, INSERM, the University of Strasbourg and the Alsace region.

Opioids induced cellular and behavioral changes in MOPr phosphorylation-deficient (PD) mice

J.B. Wang¹, E. Barbier¹, Y. Chiu², and L.Y. Liu-Chen², ¹Dept. of Pharmaceut. Sci. Univ. of Maryland Baltimore, Sch. of Pharmacy, ²Dept. of Pharmacol, Temple Univ Med Sch., Philadelphia, PA, USA

Acute or chronic opioid treatment produces major behavioral responses. Upon exposure to agonists, MOPr undergoes phosphorylation in cultured cells, which is related to desensitization and internalization. To assess contributions of in vivo MOPr phosphorylation to regulation of opioid induced behaviors, we have generated a knockin mouse with the putative key phosphorylation residue T349 in MOPr mutated to alanine. Our study revealed that the MOPr –phosphorylation deficient (PD) mice displayed interesting phenotypes at both behavioral and cellular levels. MOPr-PD mice showed attenuated acute tolerance to morphine and etorphine-induced analgesia and different withdrawal responses compared with their wild type littermates. At cellular levels, MOPr internalization in the spinal cord following systemic etorphine was diminished in the MOPr-PD mice. 2D DIGE analysis of the brain tissue from the MOPr-PD mice will provide a further insight regarding the role of receptor phosphorylation for the actions of different opioids. Therefore, the MOPr-PD mice serve as a unique animal model to validate and more importantly extend our understanding of regulation of MOPr functions by opioid drugs from cellular models to whole animals. [supported by NIH grants DA011925 to JBW and DA17302 to LYLC]

Dynorphins regulate the intensity of fear memory: from mice to men

A. Bilkei-Gorzo¹, S. Erk², K. Michel¹, B. Schürmann¹,², H. Boecker², L. Scheef³, H. Walter², and A. Zimmer¹, ¹Institute of Molecular Psychiatry, ²Department of Psychiatry and ³Functional Neuroimaging Group, Department of Radiology, University of Bonn, Sigmund-Freud-Str. 25, 53127 Bonn, Germany

The formation of fear memories and their extinction are necessary for the adaptation to a changing environment. Here with a translational approach we investigated the role of dynorphins in the dynamic change in fear memories in mice and in humans. In mice, genetic deletion of the dynorphin encoding gene Pdyn in mice resulted in enhanced cue-dependent fear conditioning, as well as delayed extinction in contextual and cue conditioning/extinction paradigms. The pharmacological blockade of kappa opioid receptors produced a similar effect on fear extinction as the dynorphin deletion. The behavioral data are supported by the analysis of the induction of the immediate early gene c-fos, which demonstrated that the absence of dynorphin results in reduced neuronal activity in key limbic structures during extinction. Translating these findings into the human domain, we could demonstrate that a polymorphism in the dynorphin encoding gene Pdyn impacts the activity of the amygdala, functional coupling between amygdala
and the prefrontal cortex and the intensity of stress responses during extinction. Our findings establish a role of Pdyn/KOR signaling in fear extinction and suggest a biological mechanism for the success of trauma exposure therapy.

**DELTA**

**Dual efficacy of DOR subtype selective ligands for ethanol consumption and its side effects of withdrawal-induced anxiety and hyperalgesia**

J. L. Whistler and R. van Rijn, Ernest Gallo Clinic and Research Center at the University of California San Francisco, USA

A strong co-morbidity exists between alcoholism and anxiety disorders. Indeed, alcohol withdrawal-induced anxiety is a primary contributing factor for relapse, and anxiolytics are a common adjuvant therapy prescribed for treatment-seeking alcoholics. Treatment for anxiety disorders and alcoholism exist but are not universally effective. The delta opioid receptor (DOR) has been shown to play a role in both alcohol consumption and anxiety in preclinical animal models making it a very interesting clinical target. Although, there is only one gene that encodes the DOR, there are two distinct pharmacologically-defined subtypes of DOR, DOR1 and DOR2, *in vivo*. Importantly, we have found that DOR1- and DOR2-selective ligands have opposing effects on ethanol consumption. Specifically, DOR1 agonists and DOR2 antagonists decrease drinking while DOR2 agonists increase drinking and non-selective ligands produce no effect. If the DOR subtypes have opposing effects on anxiety and pain as well, targeting the “wrong” DOR subtype may be ineffective or may actually exacerbate withdrawal and relapse. Another key observation regarding the DOR is the dynamic regulation of its location in the cell. In naïve animals, many DORs are stored in large dense core vesicles beneath the plasma membrane. Importantly, functional DORs are translocated from intracellular compartments to the cell surface in response to multiple external stimuli, including chronic stress, inflammatory pain, morphine treatment and, as we and others have recently shown, after chronic alcohol exposure as well. However, the functional relevance of these “unmasked” DORs to anxiety, pain and ethanol consumption remains unknown. Here we will report the changes in responsiveness to DOR subtype-selective drugs that occur during chronic voluntary ethanol consumption. Supported by Department of Defense Grant DAMD62-10-5-071 (JLW), NIAAA Center Grant AA017072-01, NIDA Grants DA015232, DA019958 (JLW), and the State of California funds for medical research on alcohol and substance abuse through the UCSF.

**Inhibition of human multiple myeloma cell proliferation by naltrindole**


The antiproliferative activity of naltrindole (Nti), a delta opioid receptor (DOR) antagonist, toward human multiple myeloma (MM) cells was evaluated. Nti inhibits the mixed lymphocyte reaction in vitro, and blocks graft rejection in vivo. Based on its immunosuppressive properties we tested Nti’s effect on proliferation of MM cells. MM is an invasive plasma cell neoplasm responsible for 10% of all hematological malignancies. Nti inhibited the proliferation of human MM cell lines with an EC50 of 20 μM, whereas other human cells lines were substantially less sensitive. To mimic the bone marrow environment localization of MM cells, co-culture of MM cells with bone
marrow stromal cells did not affect the antiproliferative activity of Nti. [3H]-Nti exhibits saturable, low affinity binding to intact MM cells and the pharmacological properties of the Nti binding site differ significantly from those of the DOR, suggesting that Nti inhibits proliferation of MM cells through a non-opioid receptor mechanism. RT-PCR assays confirmed the lack of delta, kappa and mu receptor mRNA in MM cells. The identity of the naltrindole binding site is currently under investigation. Nti does not induce apoptosis in MM cells, based on FACS analysis and caspase cleavage assays, but decreases the rate of cell division. While investigating the mechanism of action of Nti, we found that it increases intracellular calcium levels in MM cells, and the calcium appears to be released from the endoplasmic reticulum, based on inhibition of the response following thapsigargin treatment. This effect is specific to Nti as other opioids such as naltrexone and morphine do not affect the levels of calcium in MM cells, nor do they block the activity of Nti. Based on the anti-proliferative activity of Nti toward MM cell lines, an in vivo study was conducted. Nti injected IP daily at 30mg/kg significantly decreased tumor volumes in a murine SCID/human RPMI 8226 xenograft model over a 39-day period compared with saline injected controls. Further studies on Nti as a potential therapeutic agent for the treatment of human MM are warranted.

**Delta agonist glycopeptides: CNS active drugs from endogenous neuropeptides**

Y. Li¹, D. Giuvelis², J. Lowery², C. M. Kirkmire³, L. Z. Szabô¹, B. Anglin¹, M. Lefever¹, L. Yeomans-Maldonado¹, C. M. Keyari¹, D. Muthu¹, E. J. Bilsky³, J. M. Bidlack², R. Polt¹, ¹Univ. Arizona, Tucson AZ, ²Univ. of Rochester Medical Center, ³Univ. of New England, USA

Glycosylation methods developed in the Polt lab have led to a number of stable and systemically available glycopeptide drug candidates have been synthesized and purified on large scale. Key to greater stability, increased bioavailability and enhanced penetration of the blood-brain barrier (BBB) is the *biousian* activity of the glycopeptides. Essential to this concept is the notion that the glycopeptides can adopt two different conformational ensembles: a water-soluble random coil ensemble with a diverse range of backbone conformations, and a more restrictive membrane-bound ensemble of conformations that allows the glycopeptide to participate in membrane transport processes that ultimately lead to BBB penetration. Short enkephalin-derived glycopeptide drugs have been studied as analgesics. Three distinct classes of the enkephalins have been developed: mu-selective opiate agonists, delta-selective opiate agonists, and mixed mu/delta agonists. All of these morphine substitutes have a high potential for translation to the clinic, and a company has been formed to commercialize their application. Endorphin/Dynorphin-derived helical glycopeptides have been explored. While these glycopeptides have a much higher M.W. than the shorter enkephalins (~2500 vs ~1000), their apparent penetration of the BBB is much better. Amphipathic helices are used to achieve *biousian* behavior. Circular dichroism (CD), NMR and computational methods have been used to provide important biophysical information to aid in the design of these drugs. While we are still working on a more complete understanding of this new class of drugs, it seems clear that we can obtain analgesics that are potent at 600 μg/kilo, and recent studies show that the *biousian* approach is not limited to opioid peptides. Support: Office of Naval Research (N00014-05-1-0807 & N00014-02-1-0471), the
National Science Foundation (CHE-607917) and the National Institute of Neurological Disorders and Stroke (R01-NS52727).

**Delta opioid receptor agonists in Parkinson’s disease: a reappraisal**


The delta opioid peptide (DOP) receptor has been considered a target in Parkinson’s disease (PD) based on evidence of plasticity of DOP transmission in the parkinsonian brain, and symptomatic efficacy of DOP receptor ligands in models of parkinsonism and levodopa-induced dyskinesia. In contrast to the commonly belief that DOP receptor agonists act by reinforcing enkephalinergic transmission in globus pallidus, we proved that the site of their antiparkinsonian action is the substantia nigra reticulata (SNr) where they overinhibit the nigro-thalamic pathway at doses effective in attenuating parkinsonian-like symptoms (Mabrouk et al., 2008, 2009). Since nociceptin/orphanin FQ peptide (NOP) receptor antagonists also act in SNr (Marti et al., 2007), we investigated whether both drug classes synergize in attenuating parkinsonism. Combined administration of subthreshold doses of the DOP agonist SNC-80 and the NOP antagonist J-113397 synergistically attenuated motor deficits in 6-OHDA hemilesioned rats. Microdialysis coupled to behavioral testing revealed that the synergism took place in SNr and was associated with synergistic overinhibition of the nigro-thalamic projection. SNC-80 and J-113397 also synergistically reversed MPTP-induced motor impairment in mice. This effect was maintained over a subacute course of administration, and was not accompanied by sparing of dopaminergic terminals in striatum (i.e. neuroprotection). To finally prove the cross-talk between DOP and NOP receptor signaling in vivo, SNC-80 promoted motor behavior more potently in NOP receptor knockout than wild-type mice. These data add to previous evidence of antiparkinsonian efficacy of DOP receptor agonists, suggesting that the combination of low doses of a DOP agonist and a NOP antagonist may provide sustained therapeutic benefit to PD patients. Mabrouk OS, et al. (2008) J Neurochem 107, 1647-1659; Mabrouk OS, et al. (2009) Neuroscience 164, 360-369; Marti M, et al. (2007) J Neurosci 27, 1297-1307. Supported by a FIRB Internazionalizzazione grant n. RBIN047W33.

**KAPPA**

**Natural product derived KOP ligands as novel treatments for drug abuse**

T. E. Prisinzano Dept. of Med. Chem., Sch. of Pharmacy, Univ. of Kansas, Lawrence, KS, USA

Natural products have played an important role in the development of medications for a number of diseases. However, the search for natural products with utility in the treatment of drug abuse is an area much less developed than the search for anticancer or anti-infective agents. Investigation of psychoactive natural products, such as salvinorin A, provides an opportunity to identify novel scaffolds and selective agents to better characterize known receptor types and study their role in drug abuse. It is relatively rare for natural products to have sufficiently attractive ADME/Tox (Absorption, Disposition, Metabolism, Excretion, and Toxicity) properties to be marketable, despite their excellent potency and selectivity. Thus, the ability to improve these properties by semi- or total synthetic chemistry is important in drug seeking campaigns. A growing amount of
evidence suggests that kappa opioid (KOP) receptors are involved in the abuse related effects of CNS stimulants. KOP receptor agonists have been shown to modulate the activity of dopamine neurons and decrease self-administration of cocaine in non-human primates, while KOP receptor antagonists have the potential to be utilized as opioid abuse therapies and in the treatment of stress-induced reinstatement (a model of drug relapse). As part of our continuing efforts toward developing effective natural product based drug abuse therapies, we report the synthesis and biological characterization of unique semisynthetic analogues of salvinorin A. These agents provide a better understanding of the structure-activity relationships of this unique KOP agonist. This information can then be used to aid in the development of KOP based drug abuse therapeutics with enhanced pharmacological properties. Supported by DA018151 and DA018151S1.

High throughput in vivo screening for the identification of novel analgesics
R. A. Houghten, C. T. Dooley, M. Giulianotti and J. P. McLaughlin, Torrey Pines Institute for Molecular Studies, USA
Typical compound screening used to identify potential drug candidates typically yields compounds that do not have desired drug like properties. Thus identified compounds found in this traditional manner have a high inherent rate of attrition in the later stages of drug development as evidenced by poor in vivo activity. One approach to circumvent this high attrition rate would be to directly use phenotypic in vivo models in the discovery phase to identify enhanced hits with desired biological profiles. Our working hypothesis is that the direct use of mixture-based combinatorial libraries for in vivo testing offers a unique opportunity to carry out successful preliminary studies in which 10s to 100s of thousands of compounds can be used in translational in vivo assays. Two studies will be presented involving the mouse tail flick test (8 animals per time point; times tested were 30 minutes, 1.0 hours, 2.0 hours, 3.5 hours, 5.0 hours, 8.0 hours and 24.0 hours; differences in mixture results were carried out by summing the area under the curve) of a tetra-peptide library which contains Dmt-DALDA as an internal control (the library in total is made up of 17,850,625 peptides with each mixture composed of 274,625 peptides—these were successfully tested at 25 and 5 mgs/kg). Additionally, a classic small molecule library was tested in the same tail flick assay (this library is made up of a total of 738,192 compounds; the single position defined mixtures were made up of 17-28,000 compounds each and were tested by IP administration at 5mgs/kg). The initial results of these studies were published in the AAPS Journal, 8 (2) E371-382, 2006 and AAPS Journal, 12 (3), p. 318-329. These results lead us to conclude that the direct in vivo screening of mixture-based libraries can yield highly active individual compounds having enhanced desired activity. These approaches can be utilized to identify mu, delta and kappa specific analgesics. The breadth and implication of these approaches will be discussed. Funded in part by NIDA R21DA 019620 (to RAH).

Kappa opioid receptor ligands and development of antipruritic agents
A. Cowan and S. Inan, Department of Pharmacology and Center for Substance Abuse Research, Temple University School of Medicine, Philadelphia, PA 19140, USA
Itch, for so long an orphan symptom of several systemic diseases, is in the news. It is a unique sensory modality that is closely related to, yet distinct from, pain. Recently, two high profile papers from Dr. Chen’s lab at Washington University in St. Louis have
raised the possibility of spinal gastrin-releasing peptide serving as a common itch neurotransmitter by relaying information to the somatosensory cortex in response to an array of pruritic stimuli, at least in mice. Chemicals selected to precipitate the particular behavior measured – compulsive scratching of the neck with hindlegs–included chloroquine and compound 48/80. We have found that 5′-guanidinonaltrindole (GNTI), a standard kappa opioid receptor antagonist, also provokes the same frenzied, repetitive scratching when injected s.c. behind the neck in male Swiss Webster mice. Might this be a useful animal model in developing structure-activity data on potential antipruritic agents? What are the alternatives? GNTI-induced scratching is dose-related (0.03-1 mg/kg), stable across at least 30 minutes, and mimicked by the less potent and less efficacious norbinaltorphimine. Critically, either s.c. pre-treatment (0.001-0.03 mg/kg) or post-treatment (0.01-0.03 mg/kg) with nalfurafine, a kappa agonist, attenuates the scratching caused by a standard dose of GNTI (0.3 mg/kg, s.c.). This is an important link to clinical pharmacology since nalfurafine is the first kappa opioid agonist to survive in the commercial arena (against pruritus in hemodialysis patients, in Japan). Our current research is focusing on the relationship between peripherally restricted kappa agonists and the suppression of scratch in mice. We call attention to the anti-scratch properties of asimadoline, an arylacetamide kappa agonist with limited CNS penetration, which is being developed by Tioga/Ono against diarrhea-predominant irritable bowel syndrome. This agent possesses dose-related anti-scratch activity against compound 48/80 and GNTI models of itch in mice. These promising results may hasten the formulation of asimadoline, or like compounds, as skin-directed antipruritics. (DA013429)

Disruption of kappa-opioid receptor function attenuates behavioral effects of stress in rodents

W. A. Carlezon Jr., Psychiatry, Harvard Medical School, McLean Hospital, Belmont MA, USA

Stress can induce profound changes in the brain that have immediate and long-lasting effects on behavior. We have shown that various stressors activate the transcription factor CREB in the nucleus accumbens (NAS). Using viral vectors, we have shown that elevated CREB activity in the NAS causes signs characteristic of depression (anhedonia) and anxiety (resistance to extinction of fear), producing a phenotype similar to that seen in people with post-traumatic stress disorder (PTSD). In contrast, disruption of CREB activity in the NAS has antidepressant-like effects. The mechanism of these effects is unknown, but may involve multiple factors. As one example, CREB may produce these effects by regulating the firing rate of NAS neurons that provide feedback inhibition of mesolimbic dopamine neurons, which in turn send projections to areas more classically implicated in stress responsiveness (amygdala, prefrontal cortex). CREB regulation of dynorphin, an endogenous ligand at KOR receptors, may play a key role in this process. CREB-induced elevation of dynorphin tone leads to increases in the stimulation of KORs located on mesolimbic dopamine neurons, thereby decreasing activity of this system. In support of this model, we now have considerable data indicating that blockade of KORs can prevent, attenuate, and reverse stress effects on behavior. KOR antagonists produce antidepressant-like effects in the forced swim test, regardless of whether they are given before or after exposure to stress. Likewise, KOR antagonists have acute anxiolytic-like effects in the elevated plus maze, and administration of these drugs before fear
conditioning can prevent the development of PTSD-like changes in behavior. We have new data indicating that KOR antagonists reduce the disruptive effects of stress on attention in rats, as reflected by performance in the 5-choice serial reaction time task. Collectively, these data suggest that KOR antagonists might be particularly useful for producing protective effects in cases where it is possible to predict when stress will occur. Support: MH063266

**Discovery and development of selective kappa opioid receptor antagonists**
F. Ivy Carroll, Center for Organic and Medicinal Chemistry, Research Triangle Institute, Research Triangle Park, NC 27709, USA

Stress can induce despair and increase the risk of clinical depression and drug abuse. Dynorphin, the endogenous ligand for the kappa-opioid receptor, is a stress-related neuropeptide in the brain that may mediate these responses. Activation of the kappa-opioid receptor causes place aversion in rodents and dysphoria in humans. The dynorphin/kappa-opioid receptor system is thought to be critical for stress-induced depression-like behaviors and reinstatement to drug-seeking behavior. Since kappa-opioid receptor activation contributes to stress-induced behavior, there is considerable interest in selective kappa-opioid receptor antagonists that possess drug-like properties. Studies from our laboratory led to the identification of JDTic as a potent, selective, orally active kappa-opioid receptor antagonist as a potential pharmacotherapy for treatment of depression, anxiety, and addiction (cocaine, alcohol, nicotine, and heroin). Several JDTic analogs have been identified that have in vitro efficacy similar to that of JDTic. The in vitro efficacy, pharmacokinetic properties, and potencies as an antagonist of U50,488-induced diuresis in rats will be presented. This research was supported by NIDA grant DA09045.

**MOR PROTEINS**

**RGS9-2 actions in the Nucleus Accumbens modulate opiate addiction and analgesia**
D. Terzi, A Varidaki, M. Papachatzaki, K. Psifogeorgou and V. Zachariou, University of Crete, Greece

The signaling modulator RGS9-2 plays a potent role in dopaminergic and opioidergic transmission in the striatum via actions as a GTPase accelerating protein or as effector antagonist for the G protein alpha subunit. Evidence so far points to RGS9-2 as a potent modulator of antiparkinsonian, antipsychotic, psychostimulant and opiate drug actions. In this study we use genetically modified mice to further understand the role of RGS9-2 in addiction, analgesia and depression like behaviors associated with chronic pain or with long term exposure to opiates. Our results suggest that increased activity of RGS9-2 in the nucleus accumbens (NAc) following stereotaxic infection with an adeno associated virus-RGS9-2 construct blocks the rewarding and locomotor sensitizing actions of morphine and leads to a milder opiate withdrawal syndrome. Interestingly, manipulation of RGS9-2 levels in the NAc also affects analgesic tolerance to morphine. We examined changes in RGS9-2 complexes in the NAc following acute and chronic exposure to morphine and we identified changes in the composition of these complexes associated with morphine tolerance. We also examined the way RGS9-2 affects the actions of agents used to alleviate chronic pain symptoms. Using a neuropathic pain model (spared nerve injury) we show that mice lacking the Rgs9 gene develop tolerance to the
antiallodynic actions of morphine much later than their wild type controls, and that they are more sensitive to the antiallodynic actions of tricyclic antidepressants. Tricyclic antidepressants may also improve depression like behaviors associated with chronic pain in the mutant mice at lower doses than those required for their wild type controls. This phenotype is related to RGS9-2 actions in the NAc as it can be rescued by local overexpression of the protein. Our findings provide new insights into the cellular mechanisms of opiate and antidepressant drug actions and suggest that interventions in the formation of RGS9-2 complexes may be used to improve treatment efficiency. Funding was provided by the Greek Secretariat for Research and Technology (PENED03/860)

In vivo evidence for the role of PKC and other intracellular molecules in opioid tolerance  W. L. Dewey¹, H. Akbarali¹, and G. Henderson², ¹Dept. of Pharm. and Tox. Virginia Commonwealth University, Richmond, Virginia, USA, ²Dept. Pharm. Univ. Bristol, U. K.
We hypothesize that the differences in the rate and level of tolerance development might well be due to differences in the effects of chronic mu receptor stimulation on intracellular signaling mechanisms. Recent history has shown that receptor phosphorylation which causes a desensitization and encapsulation of the receptor are both seen after chronic administration of mu opioid receptor agonists and have considerable acceptance as important properties of chronic opioid exposure that leads to tolerance. We have found in whole animal experiments that inhibitors of PKC and inhibitors of PKA both reverse but do not inhibit the development of tolerance to moderately efficacious opioids such as morphine. Neither of these specific kinase inhibitors reversed the tolerance produced by the highly efficacious opioid DAMGO. A combination of the doses of each inhibitor that reversed morphine tolerance when given together did not reverse the tolerance to DAMGO. Further studies with specific inhibitors showed that the gamma, alpha and to a lesser extend the epsilon isomer of PKC are involved in this effect. The studies with the PKC inhibitors were confirmed in electrophysiological experiments in isolate LC neurons. On the other hand GRK inhibitors were found not to alter tolerance to these moderately efficacious opioids but completely reversed tolerance to the highly efficacious opioid DAMGO. We conclude from these and related studies that opioid agonists induce tolerance by different mechanisms, that receptor desensitization plays a major role in both cellular and in vivo tolerance and high efficacy agonists induce tolerance independent of PKC but involve G protein-coupled receptor kinases. In addition we will present recently obtained evidence to suggest that the differentiation in the rate of the development and level of tolerance achieved depends on the role of other intracellular molecules.  This work was supported by grants from NIDA.

CaMKII in opioid tolerance and opioid-induced hyperalgesia
Zaijie Jim Wang, Department of Biopharmaceutical Sciences, Cancer Center, & Program for Collaborative Research in the Pharmaceutical Sciences, University of Illinois, Chicago, IL, USA
Ca²⁺/calmodulin dependent protein kinase II (CaMKII) is a multifunctional, Ca²⁺/calmodulin-activated protein kinase. CaMKII is co-localized with the mu opioids receptor (MOR) in the spinal cord and dorsal root ganglion neurons. Not only does MOR
contain predicted sequence that can be phosphorylated by CaMKII, desensitization of MOR was modulated by CaMKII in cellular models. In several rodent models of opioids tolerance, inhibition of CaMKII by chemical inhibitors, siRNA, or gene-mutation effectively prevented the development of, or reversed the established, tolerance to morphine. These effects correlated well with the biochemical evidence that tracked CaMKII activity. Taken together, these data strongly implicate a critical role of CaMKII in opioids tolerance. Similarly, we found that CaMKII appeared to be essential for the development of opioid-induced hyperalgesia, a phenomenon that is highly relevant for opioids tolerance. The talk will further present evidence for potential mechanisms that may synchronize the action of CaMKII and other kinases in opioid tolerance. Supported by NIH grants DA000505, HL098141, & AT003647

**Mu opioid regulation by beta-arrestins and implications for drug development.**  
L. M. Bohn, K. M. Raehal, C. E. Groer, J. M. Streicher, and C. L. Schmid, Departments of Molecular Therapeutics and Neuroscience. The Scripps Research Institute, Jupiter, FL, USA.

The mu opioid receptor (MOR), like most G protein-coupled receptors, interacts with beta-arrestins (Barrestins) upon agonist stimulation. Barrestins (Barrestins 1 and 2) are intracellular scaffolding proteins that can serve to disrupt receptor-protein signaling scaffolds or facilitate such interactions. The degree of interaction between these two proteins can be influenced by the chemical composition of the ligand. Using Barrestin-2 KO mice, our laboratory has studied this protein’s contributions to MOR-mediated biological responses. We have found that in the absence of Barrestin2, morphine analgesia is enhanced and tolerance is attenuated suggesting that Barrestin2 plays a role in dampening signaling transduction events leading to antinociception. Other morphine-mediated behavioral responses, including dependence (as assessed by antagonist-induced withdrawal), respiratory suppression and constipation are attenuated in this animal model suggesting that Barrestin2 may play a facilitatory role in the signaling underlying these responses. The work presented here further examines the role of individual Barrestins in the regulation of the mOR, including the contribution to ubiquitination and resensitization, of the MOR. Early developments in our drug discovery efforts to generate MOR agonists that are biased against Barrestin recruitment will also be introduced. According to extensive studies in the Barrestin2 mouse models, such a strategy may allow for the treatment of pain with fewer side-effects than seen with traditional opioid therapies. Funding for this work has been sponsored in part by R01DA14600, R01DA18860, R03DA025158 to LMB and F31DA021952 to KMR.

**NEURAL CIRCUITS**

**Stress regulation of kappa opioid receptor signaling in the extended amygdala**  
T.L. Kash, K.E. Pleil, C.J. Li, Department of Pharmacology, Bowles Center for Alcohol Studies, University of North Carolina Chapel Hill, School of Medicine. Chapel Hill, NC, USA

Strong evidence exists for endogenous stress and anti-stress systems in mammalian organisms. Chronic exposure to stress is hypothesized to modulate the relative balance of activities of these systems within key circuitry in the brain, leading to dysregulated emotional behavior. The kappa opioid receptor (KOR) and its endogenous agonist, the
neuropeptide dynorphin, are one such ‘stress’ system. Dynorphin is expressed in the cell bodies and terminals of the bed nucleus of the stria terminalis (BNST), a brain region associated with anxiety and stress, suggesting that KOR activation in this region may play a role in the regulation of emotional behavior. However, the cellular actions of KOR in this region have not been characterized. Using whole-cell voltage clamp recordings in an \textit{ex vivo} mouse brain slice preparation, we investigated the effect of KOR activation on inhibitory transmission in the BNST. We found that activation of KOR reduced GABAergic transmission via a presynaptic mechanism. We next examined the interactions between corticotrophin releasing factor (CRF) and KOR systems. Surprisingly, we found that CRF produced a KOR dependent inhibition of GABAergic signaling, suggesting that CRF can induce dynorphin release in the BNST. We next evaluated the impact of stress exposure on KOR systems. We found that the inhibitory effect of KOR activation on synaptic inhibition was significantly greater in DBA/2J mice compared to C57BL/6J mice. Further, we found that chronic, but not acute restraint, altered KOR modulation in C57BL/6J mice; while both acute and chronic restraint altered KOR modulation in DBA/2J mice. The results from this study add to a growing body of evidence suggesting that the KOR system is involved in the regulation of stress disorders. Supported by an ABMRF Young Investigator Award, a NARSAD Young Investigator Award, an INIA-Stress Pilot Project, R01AA01954 and R00AA17668 from the NIH, and PT090344 from the DoD.

\textbf{Opioid enhancement of GABA$_A$ receptor function in VTA dopamine neurons: A novel non-G protein mediated signaling mechanism induced by stress}

Elyssa B. Margolis, Ernest Gallo Clinic & Research Center, University of California, San Francisco, Emeryville, CA, USA; Dept. of Neurology University of California, San Francisco, CA, USA

Opioid receptors are G-protein coupled receptors that typically signal through activation of inhibitory Gi/o proteins. However, recent themes in GPCR research, including ligand-directed signaling and G protein independent signaling pathways, suggest that a variety of conditions determine the \textit{in vivo} signaling pathway activated when a ligand binds to an opioid receptor. We have discovered that novel postsynaptic delta opioid receptor signaling emerges in VTA neurons following acute footshock stress. This novel signaling pathway causes rapid insertion of postsynaptic GABA$_A$ receptors into the synapse, increasing the ability of synaptically released GABA to inhibit VTA neurons. This effect is PI3K/AKT dependent, but G protein independent. This effect is in the opposite direction to the small DOR-mediated inhibition of GABA$_A$ signaling in naïve rats. Therefore, not only does the magnitude of opioid effects depend upon the state of the animal, but the signaling pathway utilized by opioid receptors is also state-dependent. This novel change in DOR signaling provides a potential mechanism for endogenous opioid release to selectively amplify the inhibition produced by GABA release in a subset of VTA neurons while reducing such inhibition in other VTA neurons. Supported by P50 AA017072, DA-016782-06, DA-030529-01, sponsored by the Army under award numbers W81XWH-08-1-0017 and W81XWH-07-1-043, and funds from the State of California for medical research on alcohol and substance abuse through the University of California, San Francisco.
Dopamine mediated synaptic transmission in the VTA
C. P. Ford, Department of Physiology and Biophysics, Case Western Reserve University, Cleveland, OH, USA
Opioids alter the activity and excitability of midbrain dopamine neurons, the net effect being an alteration dopamine release and signaling at downstream targets. In order to understand the consequences of downstream dopamine signaling we have been investigating the mechanisms that regulate how dopamine mediates synaptic transmission. In the VTA and SNc, dopamine neurons make dendro-dendritic synapses with adjacent dopamine neurons. The dendritic release of dopamine activates postsynaptic D2-type autoreceptors on adjacent dopamine neurons and induces a GPCR-mediated inhibitory synaptic current. This talk will outline recent work characterizing the time course and concentration of dopamine that results from the phasic release of dopamine in the VTA that underlies the generation of this inhibitory synaptic current. This aims to understand the dynamics of temporal profile of dopamine during synaptic transmission. Dopamine is often believed to signal at low concentrations over extended periods at D2-receptors due to the high affinity of the D2-receptor. However, using the combination of whole-cell synaptic recordings, electrochemistry and the rapid application of dopamine to excised patches, we have found that post-synaptic D2-receptors are exposed to a relatively high concentration of dopamine (~10 μM) for a brief period of time (maximum duration ~100 ms) during the peak of phasic transmission. By altering the duration of dopamine that was applied to excised patches we conclude that post-synaptic signaling mechanisms (D2-receptor/G-protein) not the duration of dopamine defines the timecourse of dopamine mediated synaptic transmission. This work suggests that despite being a GPCR agonist, dopamine may signal in a relatively localized manner. Support: NIH/NIDA DA026417 and NARSAD

Context-dependent sensitization to morphine alters hippocampal neuroplasticity
J. A. Moron Concepcion. Dept. of Anesthesiology, College of Physicians and Surgeons, Columbia University Medical Center, New York, NY, USA
Evidence suggests that long-term adaptations to the neural substrates of learning and memory after repeated drug treatment may play an important role in drug addiction. For instance, alterations of hippocampus-dependent contextual learning by drugs of abuse may lead to context-evoked cravings or drug seeking behavior. Glutamatergic systems, including α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptors (AMPARs), are thought to be involved in opiate-induced neuronal and behavioral plasticity, although the mechanisms underlying these effects are only beginning to be understood. The present study examines the effects of repeated morphine administration, using a paradigm that results in context-dependent behavioral sensitization, on the expression of AMPARs and the functional ramifications in the hippocampus. The learned association between morphine and the drug administration environment following context-dependent locomotor sensitization to morphine leads to persistent changes in the expression and synaptic redistribution of AMPARs. More specifically we find that following context-dependent sensitization we observe a persistent increased expression of AMPARs lacking the glutamate receptor 2 (GluR2) subunit in hippocampal synaptic fractions. In addition, we provide electrophysiological evidence that this effect is associated with an increase in excitatory synaptic transmission. Interestingly, we also find that the expression of
context-dependent sensitization is associated with an impairment in long-term potentiation (LTP). However, these alterations are reduced when morphine injections are received in a non-paired environment. We propose that the learned association between environment and morphine effects is mediated by changes in excitatory transmission and plasticity in the hippocampus. Overall, these data suggest that glutamatergic synaptic transmission in the hippocampus may play an important role in drug-induced behavioral sensitization and addictive processes in general. Supported by NIH grant R01 DA025036 to JMC.

Drug-induced GABA transporter currents enhance GABA release and produce opioid withdrawal behaviours

E.E. Bagley1, J. Hacker1, V.I. Chefer2, C. Mallet1, G.P. McNally3, B.C.H Chieng1, T.S. Shippenberg2, M.J. Christie1, 1Brain & Mind Research Institute, University of Sydney, Australia. 2National Institute on Drug Abuse, Baltimore, USA. 3School of Psychology, University of NSW, Australia.

Neurotransmitter transporters can affect neuronal excitability indirectly via modulation of neurotransmitter concentrations or directly through transporter currents. A physiological/pathophysiological role for transporter currents has not previously been described. Here we show both in vivo and in vitro that GABA transporter 1 (GAT-1) cation currents directly increase GABAergic neuronal excitability and increase synaptic GABA release in the periaqueductal gray (PAG) during opioid withdrawal. By contrast, GAT-1 did not indirectly alter GABA receptor responses via modulation of extracellular GABA concentrations. Importantly, we found evidence that this GAT-1-induced increase in GABAergic activity induced many of the PAG-mediated signs associated with opioid withdrawal. Together these data support the hypothesis that GAT-1 activity directly produces opioid withdrawal signs through direct hyperexcitation of GABAergic PAG neurons and nerve terminals, which presumably enhances GABAergic inhibition of PAG output neurons. These data provide the first evidence that neurotransmitter transporter currents can play a pathophysiological role. Supported by the National Health & Medical Research Council of Australia (project 512390, Fellowship to MJC 511914) and the Intramural Research Program of the National Institutes of Health, National Institute on Drug Abuse.
The following organizations have generously supported the work of the
College on Problems of Drug Dependence during the past year:

Catalyst Pharmaceutical Partners, Inc
Grunenthal USA, Inc
NIDA (National Institute on Drug Abuse)
Sanofi Aventis
SAMHSA (Substance Abuse and Mental Health Services Administration)/
CSAT (Center for Substance Abuse Treatment)

The following organizations have generously supported the work of the
International Narcotics Research Conference during the past year:

Alkermes, Inc
NIDA (National Institute on Drug Abuse)

Funding for this conference was made possible (in part) by
Grant Agreement # R13 DA 013192-08
and
Grant Agreement # R13 DA 029354-02
from NIDA

The views expressed in written conference materials or publications and by
speakers and moderators do not necessarily reflect the official policies of the
Department of Health and Human Services; nor does mention of trade names,
commercial practices, or organizations imply endorsement by the U.S.
Government
PROGRAM

73rd Annual Scientific Meeting

The College on Problems of Drug Dependence

June 18-23, 2011

The Westin Diplomat
Hollywood, Florida

International Narcotics Research Conference

June 21-25, 2011

INRC
INRC ABSTRACT INDEX

Special Lectures

Plenary – Eric Nestler 2
Founders – Charles Chavkin 2

Symposia

EPIGENETICS OF DRUG ABUSE GENES 2
HUMAN BRAIN IMAGING OF OPIOID RECEPTORS 4
NEW PERSPECTIVES ON BUPRENORPHINE 5
THERAPEUTIC POTENTIAL OF NOCICEPTIN RECEPTOR LIGANDS 7
SEX DIFFERENCES IN PAIN AND OPIOID ANALGESIA 9
GENETIC MOUSE MODELS FOR THE OPIOID SYSTEM 10
DELTA OPIOID RECEPTORS – NOVEL COMPOUNDS AND USES 12
NOVEL THERAPEUTIC APPLICATIONS OF KAPPA OPIOID RECEPTOR LIGANDS 14
MOR REGULATORY PROTEINS 16
YOUNG INVESTIGATOR SYMPOSIUM: OPIOID MODULATION OF NEURAL CIRCUITS 18

ORAL SESSION THURSDAY, JUNE 23 20

POSTERS (ALPHABETICAL ORDER) 23
PLENARY FRIDAY, JUNE 24
Transcriptional and Epigenetic Mechanisms of Drug Addiction
Eric J. Nestler, M.D., Ph.D. Director, Brain Institute; Mount Sinai School of Medicine, New York, NY USA
Synopsis:
Eric Nestler will discuss the role played by changes in gene expression, and related changes in chromatin remodeling, in the brain’s reward circuits in mediating the long-lasting alterations induced by chronic exposure to drugs of abuse that underlie aspects of drug addiction. Particular attention will be given to two transcription factors of interest, CREB and DeltaFosB, and to their numerous target genes and downstream functional consequences, as important mediators of drug action.
Abstract:
Drug addiction can be viewed as a stable form of drug-induced neural plasticity, whereby long-lasting changes in gene expression mediate some of the stable behavioral abnormalities that define an addicted state. Our laboratory has focused on two main transcriptional pathways in addiction. Chronic exposure to cocaine or opiates causes the prolonged activation of the transcription factor CREB within the brain’s reward circuits and several other brain regions, and this adaptation mediates aspects of drug tolerance and dependence. In contrast, induction of another transcription factor, DeltaFosB, in brain reward regions by virtually all drugs of abuse exerts the opposite effect and contributes to sensitized responses to drug exposure. Studies are underway to explore the detailed molecular mechanisms by which CREB and DeltaFosB regulate target genes and thereby contribute to the complex state of addiction. One way to approach such molecular mechanisms of drug action in vivo is through the study of chromatin remodeling, that is, changes in the acetylation or methylation of histones that bind to certain drug-regulated gene promoters, or changes in methylation of the promoters themselves, as revealed by chromatin immunoprecipitation (ChIP). We are utilizing ChIP to examine chromatin changes at specific candidate genes for CREB and DeltaFosB, as well as genome-wide measures to gain a more global view of target genes for these transcription factors. Prominent among these targets are those that regulate synaptic function and plasticity as well as the morphology of drug-regulated neurons. We have also demonstrated drug regulation of some of the enzymes that catalyze chromatin modifications, which indicates that chromatin remodeling mechanisms are themselves important targets of drug action. These findings establish chromatin remodeling as an important regulatory mechanism underlying drug-induced neural and behavioral plasticity, and provide fundamentally new insight into how CREB and DeltaFosB, and several other drug-regulated transcription factors, contribute to addiction by regulating the expression of specific target genes in the brain’s reward circuitry. These advances can now be mined to develop improved diagnostic tests and treatments for addictive disorders.

FOUNDERS LECTURE SATURDAY, JUNE 25
Dynorphins and the Kappa Opioid Receptor System – Past and Future
Charles Chavkin, Ph.D., Department of Pharmacology, University of Washington School of Medicine, Seattle, WA 98195-7280, USA
I am grateful to the INRC Executive Committee for selecting me as the Founders’ lecturer for the 2011 conference. This is a tremendous honor for me because the INRC has been my scientific home since I first attended this conference while a graduate student in 1979. Looking over the list of previous lecturers, I am proud to be included in this distinguished group of scientists. The charge to the speaker is to answer the question, “how did we get here and where should we be going next?” Having participated in many of the important debates over the years within the INRC, I will be happy to present my personal views on the events leading to our current understandings of opioid receptor signaling, receptor desensitization and tolerance mechanisms, and dynorphins’ structure and function. Each of us have individual views on where we should be going next, and mine is that we need to use our growing understanding of the opioid peptide system’s cellular and molecular actions to better understand complex motivated behaviors. The opioid peptide systems have a central role in the stress response, and I believe that we need to better understand their roles in both healthy and pathological responses to stress. Hopefully these insights will yield novel therapeutics for the treatment of the adverse effects of stress that include the mood disorders of anxiety and depression and also include stress-induced increases in drug addiction risk. The rational design of novel therapeutics based on basic molecular pharmacological insights has been a long-standing goal of the opioid field, and this goal seems increasingly to be within our grasp.

SYMPOSIA
EPIGENETICS OF DRUG ABUSE GENES
DNA methylation: a dynamic and stable regulator of memory
C.A. Miller, Department of Metabolism & Aging, Department of Neuroscience, The Scripps Research Institute, Jupiter, FL, USA
A new line of neuroscience research suggests that epigenetics may be the site of nature and nurture integration by providing the environment with a
mechanism to directly influence the read-out of our genome. Epigenetic mechanisms in the brain are a series of post-translational chromatin and DNA modifications driven by external input. Given the critical hub of epigenetics, neuroscientists have come to suspect its fundamental influence on how our minds change in response to our unique environment and, in turn, how these changes can then impact our future interactions with the environment. We are particularly interested in the role that associative memory plays in driving relapse to drug use, as well as the epigenetic influences on the long-term maintenance of this behavior. Because neuroepigenetics was such a young field at the time we began, we first investigated the mechanisms of simple associative fear memories. Our approach was particularly focused on an epigenetic transcriptional silencing mechanism that has been studied extensively as a lifelong molecular information storage mechanism put in place during development, DNA methylation. We found that learning is associated with hippocampal upregulation of the enzymes responsible for methylation (DNA methyltransferase; DNMT), as well as a rapid increase in the methylation of memory-associated genes. Specifically, a memory suppressing phosphatase, PP1, is transcriptionally silenced through methylation, while a memory promoting gene, reelin, is activated. Further, formation of the associative memory is blocked by intra-hippocampal administration of a DNMT inhibitor. Interestingly, these hippocampal changes return to baseline less than a day after learning. This shifted our focus to the cortex, where many types of memories are thought to reside in the long-term. We found that persistent, gene-specific hypermethylation is induced in the cortex by a single, hippocampus-dependent associative learning experience. Further, pharmacologic inhibition of methylation one month after learning disrupts long-term memory maintenance. We are currently taking this new knowledge of neuronal DNA methylation’s roles in memory and applying it to animal models of relapse to drug-seeking. Funding provided by NIDA (4R00DA024761-03).

The role of chromatin modifying enzymes in the acquisition and extinction of context-drug associated memory

M. Malvaez, S.C. McQuown, G.A. Rogge, M.A. Wood, Dept. of Neurobiology and Behavior, Center for the Neurobiology of Learning & Memory, Univ. of California Irvine, CA, USA

Repeated use of drugs of abuse causes persistent alterations in gene expression responsible for the long-term behavioral and structural changes in central reward pathways. Recently, it has been suggested that epigenetic mechanisms are responsible, in part, for these drug-induced changes in gene expression. Epigenetic regulation of gene expression may provide transient and potentially stable conditions, which in turn may ultimately participate in the molecular mechanisms required for neuronal changes subserving long-lasting changes in drug-seeking behavior. Our research is focused on understanding the role of chromatin modifying enzymes in the acquisition and extinction of context-drug associated memory formation. In particular, we examine how the histone acetyltransferase CREB-binding protein (CBP) and the histone deacetylase 3 (HDAC3) are pivotally involved in regulating histone acetylation required for transcription underlying context-cocaine associated memory formation using the conditioned place preference (CPP) paradigm. One exciting result of this research is that HDAC inhibition after establishing a CPP significantly facilitates extinction of drug-seeking behavior in a manner that is refractive to reinstatement. Thus, understanding chromatin modifying mechanisms that establish and maintain drug-dependent plasticity changes may lead to a better understanding of substance abuse disorders as well as novel approaches for treatment. Supported by NIDA (DA025992) and NIMH (MH081004) grants to M.A.W., an NRSA fellowship (DA029368) to M.M., and Repligen Corporation.

Epigenetics of opioid receptor genes – nutrients, drugs and behavior

L.-N.Wei, Department of Pharmacology, University of Minnesota Medical School, Minneapolis, MN 55455, USA

The three opioid receptor genes, MOR, DOR and KOR, are differentially regulated but share a highly conserved genomic structure and promoter feature. Classical studies established various combinations of transcription factors in regulating these genes in different cellular contexts. Recent studies uncovered fundamentally important roles for chromatin remodeling in the manifestation of these genes’ plasticity, which underlines distinct behavior of the three opioid receptor genes in response to different transcription factors’ action and in various biological contexts. Diets, drugs and behavior all can potentially modulate these genes’ chromatin remodeling processes, thereby altering their chromatin conformation that is principally responsible for the gene’s activity. This paper will present findings supporting epigenetic regulation of opioid receptor genes by various environmental factors, and discuss studies that have begun to examine the molecular mechanisms. Acknowledgment: This work is supported by NIH grants DA11190, DA11806, DK54733, DK60521 and K02-DA13926, and the Distinguished McKnight University Professorship to LNW.
Chromatin plasticity in addicted brain: prodynorphin upregulation in human alcoholics


Genetic, epigenetic and environmental factors may influence the risk for neuropsychiatric disease through their effects on gene transcription. We hypothesize that these effects may be integrated through changes in chromatin states involving methylation of CpG dinucleotides that overlap with single-nucleotide polymorphisms (SNPs) associated with a disorder. We addressed this hypothesis by analyzing methylation of prodynorphin (PDYN) CpG-SNPs, reported to be associated with alcohol dependence, in the brain of human alcoholics. Analysis of postmortem human brain specimens demonstrated that PDYN expression is activated in discrete brain loci including the dl-PFC in alcoholics. This activation may contribute to cognitive dysfunctions relevant for “preoccupation / anticipation” stages of addiction and disrupted inhibitory control. Three of five PDYN SNPs associated with alcohol dependence were found to overlap with CpG dinucleotides. Methylation of these CpG-SNPs was analyzed by pyrosequencing in the dl-PFC and motor cortex (MC; no expression changes) from 14 alcohol dependent and 14 control subjects. In the dl-PFC but not in the MC of alcoholics, methylation levels of one of these three CpG-SNPs, the C, non-risk variant of 3’-untranslated region (3´-UTR) SNP (rs2235749; C>T) were increased (P < 0.001). This methylation positively correlated with PDYN mRNA and dynorphins (P < 0.05). A DNA-binding factor that differentially targeted the T, risk allele and methylated and unmethylated C allele of this SNP was identified. This factor may be involved in PDYN transcription through binding to the methylated 3’-UTR SNP C or T allele. The findings suggest a causal link between alcoholism-associated PDYN 3’-UTR CpG-SNP methylation, activation of PDYN transcription, and vulnerability to develop alcohol dependence in subjects with the non-risk SNP variant. Methylation of CpG-SNPs associated with a disease under environmental influences may be a general phenomenon affecting gene expression and contributing to disease susceptibility. Supported by the Swedish Council for Working Life and Social Research, and the Swedish Science Research Council.

HUMAN BRAIN IMAGING OF OPIOID RECEPTORS

Imaging opioid effects on brain systems

Lino Becerra, Center for Pain and the Brain, Harvard Medical School, Boston, USA

Imaging has provided opportunities to evaluate drug effects on brain function and structure. Opioids, classically used as analgesics are also drugs of abuse. In this session we will discuss two aspects of opioid actions on brain function. The first will discuss different opioid agonist and antagonist phMRI results, showing that specific features of opioid subtypes may be evaluated using functional and phMRI. The second will discuss potential long-term effects of opioids on brain structure and function. Acknowledgements: Louis Herlands Fund for Pain. Imaging Consortium for Drug Development.

Mu-opioid receptors and cocaine addiction

D.A. Gorelick, Intramural Research Program, National Institute on Drug Abuse, National Institutes of Health, Baltimore, MD, USA

Mu-opioid receptors (mOR) are expressed on neurons in several brain regions considered to play a role in cocaine use and craving, and are up-regulated by binge administration of cocaine to rodents. We conducted a series of studies, in collaboration with the Johns Hopkins PET Center, evaluating regional brain mOR binding potential (BP) in healthy adults with current cocaine abuse or dependence, no other current psychiatric disorder (except nicotine dependence), and minimal recent use of other drugs (except cigarettes). The PET radioligand was [11C]carfentanil, a selective mOR agonist. The initial study of 10 men found significantly increased (10-50%) mOR BP, compared to 7 non-addicted controls, in frontal, temporal, and anterior cingulate cortex and striatum after 1-4 days of abstinence. Increased BP in most regions was positively correlated with cocaine craving, and declined towards normal in most subjects after 28 days of abstinence. A second study in 17 non-treatment-seeking cocaine users and 16 healthy controls found increased mOR BP in frontal, anterior cingulate, and lateral temporal cortex after 1 days of abstinence, which correlated with cocaine craving and amount of cocaine use in the 2 weeks prior to admission. Binding remained elevated after 1 week in the frontal cortex, and after 12 weeks in the anterior cingulate and anterior frontal cortex. A shorter interval before relapse to cocaine use (after discharge from the secure research ward) was associated with increased mOR BP in frontal and temporal cortex and with lesser decrease in BP between 1 and 12 weeks. A third study in 25 outpatients receiving psychosocial treatment for cocaine addiction found significant associations between increased mOR BP in medial and middle frontal gyri and greater cocaine use and shorter duration of cocaine abstinence during the 12 weeks
of treatment. These findings suggest that brain mOR play an important role in human cocaine addiction and may offer a therapeutic target for developing new treatments. Supported by the IRP, NIH, NIDA and NIH grants R01-DA 09479, DA-11774, & DA-12274.

Development and clinical use of a PET radioligand for the kappa receptor
D. Martinez, F. Liu, Y. Huang, D.R. Hwang, R. Narendran, R. Carson and M. Slifstein, 1Division on Substance Abuse, Columbia University/New York State Psychiatric Institute; 2Positron Emission Tomography Center; Yale University School of Medicine; 3Department of Radiology, University of Pittsburgh, USA

Both pre-clinical and postmortem human studies investigating kappa receptor binding in cocaine abuse shown that the kappa receptor plays an important role in addiction. Thus, we developed a radiotracer to image this receptor in humans. The initial work performed in baboons showed that this radiotracer was able to cross the blood brain barrier, and had a good ratio of specific to non-specific binding. In addition, the uptake kinetics showed that significant washout occurred within the time frame of the PET experiment. PET blocking studies with naltrexone showed that the cerebellum could be used as a reference region. Subsequent to this, biodistribution studies were performed in human volunteers, in order to measure the organ exposure, which showed that the radiotracer could be used in clinical studies that required multiple scans. Based on these findings, brain imaging studies were performed in human volunteers. To date, studies in control subjects show that kinetics of the radiotracer vary significantly from the baboon studies, such that long scan times are required. In addition, there is no observable reference region in human subjects, such that scans with naltrexone are needed to obtain the non-specific distribution volume. Thus, while clinical studies performed with this radiotracer remain feasible, these issues must be taken into consideration when developing a PET imaging study with this radiotracer. Supported by the National Institute on Drug Abuse.

Endogenous opioid system modulation of motivation circuitry
J.K. Zubiaeta, T.F. Love, M. Peciña, C.S. Stohler, 1Department of Psychiatry and 2Molecular and Behavioral Neuroscience Institute, University of Michigan, and 3School of Dentistry, University of Maryland, USA

The endogenous opioid system, together with dopaminergic circuits, is emerging as a principal site of action of most drugs of abuse, including alcohol, opiates, psychostimulants and marihuana. Within the 3 receptor types involved in opioid neurotransmission, the µ-opioid receptor has been the best studied in humans. Using external imaging with positron emission tomography and selective radiotracers, studies in healthy humans have shown that there is substantial interindividual variation in the function of this neurotransmitter system, both in the in vivo availability of the receptors, as well as in the release of opioid peptides (e.g., β-endorphin, enkephalins, endomorphins) interacting with the µ receptor. In response to a stressful challenge, variations in the concentration of receptors and in the magnitude of neurotransmitter release have been linked to the capacity to regulate the stressful experience. These variations have been linked to specific genetic polymorphisms (e.g., COMT val158met) enriched in substance abusing samples, suggesting that they may underlie variations in the propensity to use drugs and the development of addictions. For example, and in healthy subjects, trait impulsiveness was highly associated with resting and stress-induced µ-opioid system functional measures in the medial and orbitofrontal cortex, anterior cingulate, thalamus, nucleus accumbens and amygdala, accounting for up to 50% of the variance in that personality trait. Patient groups that present high levels of comorbidity with the addictions, such as borderline personality disorder, also present similar alterations in the function of this neurotransmitter system even in the absence of a frank diagnosis of drug dependence. Last, variations in the function of µ-opioid receptors also appear to impact on other neurotransmitter systems, such as the dopaminergic. A common genetic polymorphism in the µ-opioid receptor gene was associated with greater dopaminergic responses to nicotine in tobacco smokers. These data suggest that variation in this neurotransmitter system is implicated in both risk for the addictions and variation in the neural effects to substances of abuse. Supported by grants R01 DA016423, R01 DA027494, R21 DA027066, and R21 MH 069612

NEW PERSPECTIVES ON BUPRENORPHINE
The unique pharmacology of buprenorphine
J. Traynor, Department of Pharmacology and Substance Abuse Research Center, University of Michigan, Ann Arbor, MI 48109, USA

Since its introduction into clinical medicine in the 1970’s in the U.K., buprenorphine has been much studied for its unique pharmacology; properties that have lead to its successful introduction into the opiate abuse medication armamentarium, but properties that still remain to be fully explained. Important assets of buprenorphine include its low rate of dissociation from the mu-opioid (MOP) receptor and its profile as a MOP receptor agonist and kappa opioid receptor antagonist; it also has very low delta opioid receptor

The unique pharmacology of buprenorphine
J. Traynor, Department of Pharmacology and Substance Abuse Research Center, University of Michigan, Ann Arbor, MI 48109, USA

Since its introduction into clinical medicine in the 1970’s in the U.K., buprenorphine has been much studied for its unique pharmacology; properties that have lead to its successful introduction into the opiate abuse medication armamentarium, but properties that still remain to be fully explained. Important assets of buprenorphine include its low rate of dissociation from the mu-opioid (MOP) receptor and its profile as a MOP receptor agonist and kappa opioid receptor antagonist; it also has very low delta opioid receptor
New ligands from an old friend

S.M. Husbands, Department of Pharmacy and Pharmacology, University of Bath, Bath, UK

The use of buprenorphine in the treatment of opiate abuse and dependence by detoxification, substitution and maintenance, is the most noteworthy recent addition to the repertoire of methods available for the treatment of substance abuse disorders. In addition to its activity as a mu opioid (MOP) receptor partial agonist, buprenorphine is a kappa/delta (KOP/DOP) receptor antagonist and more recently profiled as a partial agonist at the nociceptin/orphanin FQ (NOP) receptor. It has been postulated that buprenorphine-like ligands with higher NOP receptor activity might have efficacy as non-addicting analgesics and potential drug abuse medications, while buprenorphine-like compounds with lower, or no, MOP receptor efficacy may have utility as relapse prevention agents in the treatment of drug abuse.

Control over efficacy at four different receptors is difficult to manage, but notable successes have been achieved within the orvinol series. In the search for MOP/NOP receptor partial agonists, ligands with affinities from 8 nM – 133 nM at NOP receptors were generated (buprenorphine K_iNOP 77 nM). Of the compounds with appreciable NOP receptor affinity, efficacy at this receptor ranged from very low (5% of nociceptin) to moderate (58% of nociceptin) with buprenorphine being intermediate in this range (21% of nociceptin). One compound, BU08028, was found to have comparable affinity at opioid and NOP receptors (all between 1.6 – 8.5 nM) and very similar activity to buprenorphine in the [35S]GTPgammaS assay, but with higher efficacy (48% of nociceptin) at NOP receptors. In the search for NOP partial agonists with antagonist activity at MOP and KOP receptors, ligands have been developed with the desired profile in vitro. The further evaluation of these ligands, including initial in vivo evaluations, will be presented and the recent developments in our understanding of structure-activity relationships in this remarkable series discussed. This work was supported by NIDA grants DA020469 & DA007315 (SMH) and DA023281 (L. Toll).

Buprenorphine: a novel receptor target and mechanism of action

S. Grinnell, S. Majumdar, Y.-X. Pan and G.W. Pasternak, Molecular Pharmacology and Chemistry Program and the Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Buprenorphine is a potent analgesic whose use is becoming increasingly widespread, due in part to a number of advantages over traditional mu opioids. However, a number of features of this agent have raised questions regarding its mechanism of action. It is often considered a partial mu agonist. Yet, it also has high affinity for other classes as well. Interestingly, it has a methyl-c-propyl substituent on the nitrogen, similar to naltrexone, but still remains an analgesic. Furthermore, many investigators have suggested that its actions are less easily reversed by the potent opioid antagonist naloxone. These observations led us to examine its mechanism of action. In our hands, buprenorphine is a potent analgesic. However, in a MOR-1 knockout model in which exon 11 and its associated splice variants are eliminated, buprenorphine shows no analgesic actions at doses many fold higher than its normal ED_{50}. This contrasts with morphine and methadone which retain full analgesic activity in these same exon 11 knockout mice. Although there are several exon 11-associated variants of the mu opioid receptor Oprm1 that predict full length, 7 transmembrane receptors, most predict truncated variants containing only 6 TM domains. Evidence from our group suggests that these truncated variants offer a unique target in the design of opioid analgesics and our current results suggest that much of the analgesic actions of buprenorphine can be attributed to these new targets, explaining much of the overall pharmacology. Supported by grants from the National Institute on Drug Abuse (DA02615,
Abuse liability of buprenorphine in humans under various states of opioid physical dependence
S.D. Comer, M.A. Sullivan, S.K. Vosburg, J.M. Manubay, Z.D. Cooper, and J.D. Jones, NYSPI and Columbia University, New York, NY, USA

The abuse potential of buprenorphine (bup) as well as buprenorphine/naloxone (bup/nx) is unclear given the unique pharmacology of bup. Therefore, we conducted a series of studies to assess the abuse potential of bup and bup/nx under various states of opioid physical dependence. Heroin-dependent volunteers, who lived in the hospital for the duration of the studies, were given the opportunity to work for either drug or money using a progressive ratio self-administration procedure. None of the participants were interested in treatment for their drug use and were paid for their participation. The volunteers were detoxified from heroin, maintained on morphine, or maintained on sublingual bup. During a sample session, participants received $20 and a dose of the test drug. During a subsequent choice session, participants could work for the test drug or money they had sampled by making finger press responses. In recently detoxified individuals, bup was self-administered as much as methadone and ratings of drug liking were similar for bup and methadone. When bup was compared to bup/nx in recently detoxified individuals, both drugs were self-administered at the same levels. However, ratings of liking for bup/nx were not different from saline. Instead, participants reported that they self-administered bup/nx because it alleviated mild withdrawal. In morphine-maintained participants, bup alone increased both positive and negative subjective effects, but it was not self-administered at any dose that was tested. In bup-maintained individuals, self-administration of bup/nx was lower than bup alone and heroin. Drug liking and desire to take the drug again also were lower for bup/nx. Consistent with its partial agonist profile, the abuse liability of bup varied depending on the state of opioid physical dependence. The addition of naloxone further reduced the abuse liability of bup under the various experimental conditions. Supported by NIDA (DA90236, DA10909), Schering-Plough, and Reckitt Benckiser.

Therapeutic potential of NOP ligands as spinal analgesics
M.C. Ko, Department of Pharmacology, University of Michigan Medical School, Ann Arbor, MI, USA

Itch/pruritus is the most common side effect derived from spinal administration of mu opioid receptor (MOP) agonists. Given that intrathecal administration of morphine dose-dependently produces antinociception with simultaneous itch/scratching responses in monkeys, this non-human primate model provides a valuable tool to identify a viable target as spinal analgesics. The nociceptin/orphanin FQ (N/OFQ) receptor (NOP) is defined as the 4th member within the opioid receptor family. Although the actions of N/OFQ have much in common with those of classical opioids at the cellular level, the in

C. Olsen 2, F. Jiang 2, 1Astraea 2SRI International, Menlo Park, CA, USA
N.T. Zaveri1, L. Toll 2, T.V Khroyan2, W.E. Polgar2, C. Olsen2, F. Jiang2, 1Astraea 2SRI International, Menlo Park, CA, USA

The abuse potential of buprenorphine (bup) as well as buprenorphine/naloxone (bup/nx) is unclear given the unique pharmacology of bup. Therefore, we conducted a series of studies to assess the abuse potential of bup and bup/nx under various states of opioid physical dependence. Heroin-dependent volunteers, who lived in the hospital for the duration of the studies, were given the opportunity to work for either drug or money using a progressive ratio self-administration procedure. None of the participants were interested in treatment for their drug use and were paid for their participation. The volunteers were detoxified from heroin, maintained on morphine, or maintained on sublingual bup. During a sample session, participants received $20 and a dose of the test drug. During a subsequent choice session, participants could work for the test drug or money they had sampled by making finger press responses. In recently detoxified individuals, bup was self-administered as much as methadone and ratings of drug liking were similar for bup and methadone. When bup was compared to bup/nx in recently detoxified individuals, both drugs were self-administered at the same levels. However, ratings of liking for bup/nx were not different from saline. Instead, participants reported that they self-administered bup/nx because it alleviated mild withdrawal. In morphine-maintained participants, bup alone increased both positive and negative subjective effects, but it was not self-administered at any dose that was tested. In bup-maintained individuals, self-administration of bup/nx was lower than bup alone and heroin. Drug liking and desire to take the drug again also were lower for bup/nx. Consistent with its partial agonist profile, the abuse liability of bup varied depending on the state of opioid physical dependence. The addition of naloxone further reduced the abuse liability of bup under the various experimental conditions. Supported by NIDA (DA90236, DA10909), Schering-Plough, and Reckitt Benckiser.

Therapeutic potential of NOP ligands as spinal analgesics
M.C. Ko, Department of Pharmacology, University of Michigan Medical School, Ann Arbor, MI, USA

Itch/pruritus is the most common side effect derived from spinal administration of mu opioid receptor (MOP) agonists. Given that intrathecal administration of morphine dose-dependently produces antinociception with simultaneous itch/scratching responses in monkeys, this non-human primate model provides a valuable tool to identify a viable target as spinal analgesics. The nociceptin/orphanin FQ (N/OFQ) receptor (NOP) is defined as the 4th member within the opioid receptor family. Although the actions of N/OFQ have much in common with those of classical opioids at the cellular level, the in...
vivo pharmacological profiles of N/OFQ and NOP-related ligands are not fully known in primates. This presentation provides an overview of recent studies of NOP- and MOP-related ligands in rhesus monkeys. First, intrathecal N/OFQ over a wide dose range produced antinociception without hyperalgesia, scratching, sedation, and muscle relaxation. In contrast, intrathecal MOP agonists such as morphine and DAMGO produced antinociception with profound scratching. When N/OFQ was combined with morphine intrathecally, this combination produced greater antinociceptive effect. Second, Ro 64-6198, a nonpeptidic NOP agonist, produced antinociceptive effects that are independent of MOP. Unlike the NOP agonist alfentanil, systemic Ro 64-6198 produced morphine-comparable antinociception. Unlike alfentanil, Ro 64-6198 did not produce reinforcing, respiratory depressant, or pruritic effects. Intrathecal Ro 64-6198 also produced NOP-mediated antinociception. Third, intrathecal UFP-112, a chemical modification of N/OFQ, produced long-lasting antinociception against acute noxious stimulus and capsaicin-induced allodynia. Antinociceptive effects of UFP-112 were antagonized by the NOP antagonist, J-113397, but not by the MOP antagonist, naltrexone. In addition, intrathecal combination of inactive doses of UFP-112 and morphine significantly produced antinociception. Taken together, these findings strongly support the therapeutic potential of NOP agonists as spinal analgesics. Supported by U.S. Dept of Defense, Grant W81XWH-07-1-0162.

The Nociceptin/Orphanin FQ system, as a treatment target for addiction.

R. Ciccocioppo, School of Pharmacy, Pharmacology Unit, University of Camerino, Italy.

Nociceptin/orphanin FQ (N/OFQ), the endogenous ligand of the NOP receptor, previously referred to as opioid receptor-like1 (ORL1) receptor, is a 17 aminoacid neuropeptide structurally related to the opioid peptide dynorphin A. From a functional point of view, N/OFQ possesses antipodioid properties and, acting as a presynaptic neuron inhibitor, it is able to control dopaminergic, noradrenergic and glutamatergic neurotransmission in different brain sites. In addition, it has been shown that N/OFQ possesses marked anxiolytic and anti-stress properties presumably mediated by its ability to blunt extrahypotalamic corticotropin releasing factor (CRF) activity. Altogether, these findings point at the N/OFQ–NOP receptor as a system potentially involved in the regulation of reward and drug abuse processes. Indeed, several studies demonstrate that activation of this system results in reduction of the rewarding properties of ethanol, morphine and cocaine. Recent rodent data suggest also that central administration of N/OFQ reduces reinstatement of alcohol-seeking behavior elicited by stress and by environmental conditioning factors. Buprenorphine has long been in clinical use for treatment of moderate-to-severe pain and its use for maintenance treatment of heroin dependence has been approved in several countries. This drug has long been known to be a partial agonist at µ-opioid receptors but has also antagonistic or agonistic properties at κ and δ opioid receptors. In an unexpected development, it has recently been realized that buprenorphine also is agonist/partial agonist at the NOP receptors. Consistent with these findings we found that in rats this drug reduces excessive alcohol drinking via activation of NOP receptors. Based on these data we suggest that NOP receptors may represent a suitable target for addiction treatment development. Support: NIH/NIAAA grant AA014351.

Discovery and development of nociceptin receptor agonists in alcohol dependence

S.P. Brothers1,2,3, Y.T. Chen1, H. Salah-Uddin1,2,3, M. Cameron1, A. Thorsell1, M. Roberto1, T. Bannister1, M. Heilig1, C. Wahlestedt1,2,3, 1Molecular Therapeutics, The Scripps Research Institute - Scripps Florida, Jupiter, FL, USA, 2Department of Neuroscience, The Scripps Research Institute - Scripps Florida, Jupiter, FL, USA, 3Department of Psychiatry and Behavioral Sciences and the Hussman Institute for Human Genomics, University of Miami, Miami, FL, USA (current affiliation), 4National Institute on Alcohol Abuse and Alcoholism, National Institutes of Health, Bethesda MD, USA, 5Committee on the Neurobiology of Addictive Disorders, The Scripps Research Institute, La Jolla, CA, USA

Alcohol dependence and abuse represents a considerable health and economic burden on society with available pharmacotherapies demonstrating insufficient efficacy. We designed novel, potent, and selective NOP agonists as tools for research on alcohol dependence with potential as clinically effective therapeutic agents. Currently available NOP small molecule agonists all have some mu or kappa opioid receptor activity, limiting their usefulness as research tools. Our unpublished data show several promising novel molecules that are selective for the nociceptin receptor over the mu and kappa opioid receptors. Our molecules have been tested for in vitro activity and pharmacokinetic parameters. While our compounds are not orally bioavailable, they do show a high brain penetrance, and long half life in vivo. Our compounds also act in the central amygdala to reduce an ethanol dependant increase in GABA transmission. Finally, in animal models of hangover anxiety, our compounds show promising results that suggest some potential for future clinical translation. These studies were supported by NIH/NIAAA grant 5R01AA017943-02.
SEX DIFFERENCES IN PAIN AND OPIOID ANALGESIA

Gender differences in pain
L. LeResche, Dept. of Oral Medicine, University of Washington, Seattle, WA, USA

Although age- and sex-specific prevalence patterns differ for different pain conditions, prevalence rates of most common chronic pain conditions are higher in women than in men. For example, in population-based studies of adults, female: male ratios for headache, neck, shoulder, knee and back pain average around 1.5:1; for orofacial pains, ratios are about 2:1; for migraine headache, 2.5:1; and for fibromyalgia the ratio is over 4:1. Women are also more likely than men to experience multiple pains simultaneously. Having multiple pain problems (as opposed to a single pain condition) is associated with higher levels of disability and psychological distress, as well as higher risk of onset for new pain conditions. Differences in pain prevalence in men and women could be due to biological sex differences in nociceptive or perceptual mechanisms or to gender differences in pain appraisal, pain behavior or social roles. The gonadal hormone estrogen clearly plays a role in some pain conditions in women (migraine headache, temporomandibular pain). For other pain problems, evidence of hormonal involvement is less clear. However, rates of many pain conditions increase as girls pass through puberty, whereas rates for adolescent boys are stable or rise less steeply than for girls. Pain-related behavior differs by gender; women are more likely than men to seek health care for pain, resulting in a high proportion of women in many pain treatment settings. The higher rate of treatment seeking may in part be due to the fact that pain is more often severe for women than for men. Women’s higher pain intensity also seems to be a major factor influencing clinicians’ treatment decisions, especially prescription of medications for acute pain – although evidence suggests that clinicians’ gender stereotypes also play a role in these decisions, independent of the patient’s pain level. Women, particularly elderly women, are more likely than men to be prescribed opioid medications for pain and to use opioids long term. Understanding both biological and social contributions to gender differences in pain may help optimize treatment for people of both sexes. Supported by R01AG034181.

Opioid analgesia and sex differences: An overview
E. Sarton, Department of Anesthesiology, Leiden University Medical Center, 2300 RC Leiden, The Netherlands

Although a contribution of sex in opioid efficacy has garnered much attention, the confirmation and direction of any such difference remain elusive. We performed a systematic review of the available literature on sex differences in μ and mixed μ/κ opioid effect on acute and experimental pain. Fifty unique studies (including three unpublished studies) were included in the analyses. Across the 25 clinical studies on μ-opioids there was no significant sex-analgesia association. Restricting the analysis to patient-controlled analgesia (PCA) studies (irrespective of the opioid) yielded greater analgesia in women (n=15, effect size 0.22, 95% c.i. 0.02-0.42, P=0.028). Further restricting the analysis to PCA morphine studies yielded an even greater effect in women (n=11, effect size=0.36, 95% c.i. 0.17-0.56, P=0.003). Meta-regression indicated that the longer the duration of PCA, the difference in effect between the sexes further increased. Across experimental pain studies on μ-opioids women had greater antinociception from opioids (n=11, effect size=0.35; 95% c.i. 0.01-0.69, P=0.047), which was predominantly due to 6 morphine studies. Female patients had greater μ/κ opioid analgesia (n=7, effect size 0.84; 95% c.i. 0.25-1.43, P=0.005), but no sex-analgesia association was present in experimental studies (n=7). Sex differences exist in morphine-induced analgesia in both experimental pain studies and clinical PCA studies, with greater morphine efficacy in women. The data on non-morphine μ and mixed μ/κ-opioids are less convincing and require further study.

Impact of age and sex in the antihyperalgesic actions of morphine: Role of periaqueductal gray
A. Z. Murphy, Neuroscience Institute, Georgia State University, Atlanta, GA, USA

Opioid-based narcotics are the most widely prescribed therapeutic agent for the alleviation of persistent pain; however, it is becoming increasingly clear that morphine is significantly less potent in females compared to males. Indeed, studies from our lab using a variety of pain assays, including somatic, visceral and orofacial pain, have consistently shown that females require approximately twice the amount of morphine as a male to produce comparable levels of pain relief. The midbrain periaqueductal gray (PAG), via its descending projections to the rostral ventromedial medulla and the dorsal horn of the spinal cord, is considered an essential neural substrate for opioid-based analgesia. The PAG contains a dense population of mu opioid receptor (MOR) expressing neurons, and we hypothesized that MOR expression in the PAG was sexually dimorphic, and that these sex differences in opioid receptor levels contribute to the observed sex differences in morphine potency. Using a variety of techniques, including immunohistochemistry, western binding and autoradiography, we found that males have significantly higher levels of MOR expression in the ventrolateral PAG compared to cycling females. Inflammatory hyperalgesia induced by intraplantar administration of Complete Freund’s Adjuvant (CFA) was significantly reversed in males following direct
administration of morphine into the PAG. By contrast, the antihyperalgesic actions of morphine were significantly attenuated in proestrus and estrus females. Additional studies by our lab have shown that selective lesions of MOR-expressing neurons in the ventrolateral PAG significantly reduces the antihyperalgesic effects of systemic morphine in males only, and this reduction was positively correlated with the level of MOR expression in the ventrolateral PAG. Together, our studies suggest that sex differences in PAG MOR expression may provide the biological bases for the observed sexually dimorphic actions of morphine. Funded by NIH grant DA16272.

The importance of sex in pain; sexual dimorphic expression in spinal cord of mu-opioid and kappa-opioid receptor heterodimers.

AR. Gintzler, State Univ. NY, Downstate Medical Center, Brooklyn, NY, USA

Sexually dimorphic nociception and opioid antinociception has been extensively demonstrated. In particular, the nociceptive vs. antinociceptive consequences of kappa opioid receptor (KOR) activation is sexually dimorphic. Although it has been established for some time that KOR agonists have weaker analgesic activity and produce greater nociception in males vs. females, determinants of the balance between nociceptive and antinociceptive properties of KOR agonists remain largely unknown. My laboratory had demonstrated that the concomitant activation of spinal μ-opioid receptors (MOR) and KOR is necessary for spinal morphine antinociception in females, but not males. This sexual dimorphism can be explained by spinal cord expression of a MOR/KOR heterodimer that is vastly more prevalent in the spinal cord of females vs. males. Cross-linking experiments in combination with in vivo pharmacological analyses indicate that heterodimeric MOR/KOR utilizes spinal dynorphin 1-17 as a substrate and is likely to be the molecular transducer for the female-specific KOR component of spinal morphine antinociception. The existence of heterodimeric MOR/KOR provides a mechanism for activating spinal KOR-mediated antinociception without the concomitant pro-nociceptive functions that monomeric KOR also subserves. The presence of an ovarian sex steroid-dependent functional interaction of KOR with MOR, suggested by the dependence of MOR/KOR expression on stage of cycle, can explain sexually dimorphic analgesic mechanisms solicited by spinal morphine as well as male female differences in the balance between pronociceptive vs. antinociceptive responsiveness to KOR agonists. Supported by R01 DA027663.

**GENETIC MOUSE MODELS FOR THE OPIOID SYSTEM**

**Functional characterization of the OPRM1 A112G SNP in mice**

S. D. Mague1, J. R. Turner1, G. Carlson2, J. A. Blendy1, Departments of 1Pharmacology and 2Psychiatry, University of Pennsylvania, Philadelphia, PA, USA

A single nucleotide polymorphism (SNP) in the human μ-opioid receptor gene (OPRM1 A118G) has been widely studied for its association in a variety of drug addiction and pain sensitivity phenotypes; however, the extent of these adaptations and the mechanisms underlying these associations remain elusive. To clarify the functional mechanisms linking the A118G SNP to altered phenotypes, we derived a mouse model possessing the equivalent nucleotide substitution (A112G), which corresponds to the same amino acid replacement in the Oprml gene. These mice have alterations in basal and morphine-evoked responses in a variety of behavioral tasks, including nociception, behavioral sensitization and conditioned place preference. Some of these behavioral differences may be explained by reductions in MOPR expression levels, however MOPRs are reduced in a sub-set, but not all, brain regions. Specifically, the levels of MOPRs in the hippocampus are not different between genotypes. The hippocampus is an ideal structure to evaluate circuit function. Therefore, to investigate if this SNP impacts a functional response in the absence of reduced receptor levels, we utilized voltage-sensitive dye imaging in hippocampal slices before and after MOPR stimulation with DAMGO. Utilizing several analytical methodologies, we found significant reductions in DAMGO-mediated responses in animals with the G112 allele. These data further support claims that this SNP results in a loss of receptor function. Supported by DA-027066.

The role of OPRM1 variation for alcohol reward examined using a reverse translational approach

M. Heilig, A. Thorsell. Laboratory of Clinical and Translational Studies, NIAAA, Bethesda MD, USA

Purpose: Mu-opioid (OPRM1) receptors are key to rewarding properties of alcohol, and the target for the approved alcoholism medication naltrexone. Based on secondary analyses of clinical trials, A118G variation at the OPRM1 locus has been suggested to moderate therapeutic efficacy of naltrexone, but this notion remains highly controversial. The purpose of the present set of studies was to examine the role of OPRM1 A118G variation for alcohol related behaviors using a reverse-translational approach. Humanized mouse lines carrying the human 118A and 118G variants, respectively, were generated on a C76BL/6 background. Ligand affinity was determined using displacement of [3H]DAMGO in cloned CHO-cells. Distribution, binding density and
signaling were determined using autoradiography. A standard behavioral phenotyping battery was carried out. Alcohol-induced DA-release was examined using microdialysis, and alcohol consumption was assessed using two-bottle free-choice drinking. Both humanized receptor variants showed normal ligand affinity, distribution, binding density, and signaling, with no differences by genotype. In the basic behavioral phenotyping battery, 118GG mice were more bold/exploratory than 118AA mice. Similar to our human 11C-raclopride PET data, alcohol-induced DA-release was greater in male 118GG than male 118AA mice. Male, but not female 118GG mice consumed higher amounts of alcohol than 118AA mice of the corresponding sex, in particular at higher alcohol concentrations. The functional OPRM1 118G variant is sufficient to confer greater alcohol-induced DA-release and consumption. These findings are consistent with a role of this variant to predispose human carriers to endorphin-dependent alcoholism, but also to render patients more responsive to opioid antagonist treatment.

Direct visualization of delta opioid receptor internalization under physiological conditions
D. Massotte1, L. Faget1, E. Erbs1, J. Le Merrer1, G. Scherrer2, A. Mattias3, J.-L. Vonesch3, F. Noble4, B. L. Kieffer1, 1Dept of Neurobiology and Genetics, IGBMC, Illkirch-Graffenstaden, France, 2Dept of Physiology and Cellular Biophysics, Columbia University, New York, NY 10032, USA, 3Imaging Center, IGBMC, Illkirch-Graffenstaden, France, 4Neuropsychopharmacologie des Addictions, Université Paris Descartes, Paris, France.

Drug addiction is a complex disorder involving gradual and long-term adaptations of the brain in response to repeated drug exposure. This entails modifications of neuronal connectivity, signaling and plasticity. In heroin addicts, re-exposure to environmental elements previously associated with heroin abuse induce intense drug craving. Therefore, numerous behavioral studies addressed the impact of environmental cues on drug seeking. We developed a protocol in which morphine was repeatedly administered in a given environment at a dose leading to physical dependence. This paradigm elicited context-induced withdrawal upon re-exposure of drug-free animals and induced activation of the hippocampus. Using knock-in mice expressing a functional fluorescent delta opioid receptor (DOR-eGFP), we then investigated delta receptor activation and subsequent internalization by fluorescence microscopy to address in vivo dynamics of the receptor under physiological conditions. The authors acknowledge NIDA support to the Center for Opioid Receptors and Drugs of Abuse (#DA 005010), ANR, CNRS, INSERM, the University of Strasbourg and the Alsace region.

Opioids induced cellular and behavioral changes in MOPr phosphorylation-deficient (PD) mice
J.B. Wang1, E. Barbier1, Y. Chiu2, and L.Y. Liu-Chen2, 1Dept. of Pharmaceut. Sci. Univ. of Maryland Baltimore, Sch. of Pharmacy, 2Dept. of Pharmacol, Temple Univ Med Sch., Philadelphia, PA, USA

Acute or chronic opioid treatment produces major behavioral responses. Upon exposure to agonists, MOPr undergoes phosphorylation in cultured cells, which is related to desensitization and internalization. To assess contributions of in vivo MOPr phosphorylation to regulation of opioid induced behaviors, we have generated a knockin mouse with the putative key phosphorylation residue T349 in MOPr mutated to alanine. Our study revealed that the MOPr phosphorylation deficient (PD) mice displayed interesting phenotypes at both behavioral and cellular levels. MOPr-PD mice showed attenuated acute tolerance to morphine and etorphine-induced analgesia and different withdrawal responses compared with their wild type littermates. At cellular levels, MOPr internalization in the spinal cord following systemic etorphine was diminished in the MOPr-PD mice. 2D DIGE analysis of the brain tissue from the MOPr-PD mice will provide a further insight regarding the role of receptor phosphorylation for the actions of different opioids. Therefore, the MOPr-PD mice serve as a unique animal model to validate and more importantly extend our understanding of regulation of MOPr functions by opioid drugs from cellular models to whole animals. [supported by NIH grants DA011925 to JBW and DA17302 to LYLC]

Dynorphins regulate the intensity of fear memory: from mice to men
A. Bilkei-Gorzo1, S. Erk2, K. Michel1, B. Schürmann1,2, H. Boecker2, L. Scheef3, H. Walter1, and A. Zimmer1, 1Institute of Molecular Psychiatry, 2Department of Psychiatry and Functional Neuroimaging Group, Department of Radiology, University of Bonn, Sigmund-Freud-Str. 25, 53127 Bonn, Germany

The formation of fear memories and their extinction are necessary for the adaptation to a changing environment. Here with a translational approach we investigated the role of dynorphins in the dynamic change in fear memories in mice and in humans. In mice, genetic deletion of the dynorphin encoding gene Pdyn in mice resulted in enhanced cue-dependent fear conditioning, as well as delayed extinction in contextual and cue conditioning/extinction paradigms. The pharmacological blockade of kappa opioid receptors produced a similar effect on fear extinction as the dynorphin deletion. The behavioral data are supported by the analysis of the induction of the immediate early gene c-fos, which demonstrated that
the absence of dynorphin results in reduced neuronal activity in key limbic structures during extinction. Translating these findings into the human domain, we could demonstrate that a polymorphism in the dynorphin encoding gene Pdyn impacts the activity of the amygdala, functional coupling between amygdala and the prefrontal cortex and the intensity of stress responses during extinction. Our findings establish a role of Pdyn/KOR signaling in fear extinction and suggest a biological mechanism for the success of trauma exposure therapy.

**DELTA OPIOID RECEPTORS – NOVEL COMPOUNDS AND USES**

**Dual efficacy of DOR subtype selective ligands for ethanol consumption and its side effects of withdrawal-induced anxiety and hyperalgesia**

J. L. Whistler and R. van Rijn, Ernest Gallo Clinic and Research Center at the University of California San Francisco, USA

A strong co-morbidity exists between alcoholism and anxiety disorders. Indeed, alcohol withdrawal-induced anxiety is a primary contributing factor for relapse, and anxiolytics are a common adjuvant therapy prescribed for treatment-seeking alcoholics. Treatment for anxiety disorders and alcoholism exist but are not universally effective. The delta opioid receptor (DOR) has been shown to play a role in both alcohol consumption and anxiety in preclinical animal models making it a very interesting clinical target. Although, there is only one gene that encodes the DOR, there are two distinct pharmacologically-defined subtypes of DOR, DOR1 and DOR2, in vivo. Importantly, we have found that DOR1- and DOR2-selective ligands have opposing effects on ethanol consumption. Specifically, DOR1 agonists and DOR2 antagonists decrease drinking while DOR2 agonists increase drinking and non-selective ligands produce no effect. If the DOR subtypes have opposing effects on anxiety and pain as well, targeting the “wrong” DOR subtype may be ineffective or may actually exacerbate withdrawal and relapse. Another key observation regarding the DOR is the dynamic regulation of its location in the cell. In naïve animals, many DORs are stored in large dense core vesicles beneath the plasma membrane. Importantly, functional DORs are translocated from intracellular compartments to the cell surface in response to multiple external stimuli, including chronic stress, inflammatory pain, morphine treatment and, as we and others have recently shown, after chronic alcohol exposure as well. However, the functional relevance of these “unmasked” DORs to anxiety, pain and ethanol consumption remains unknown. Here we will report the changes in responsiveness to DOR subtype-selective drugs that occur during chronic voluntary ethanol consumption. Supported by Department of Defense Grant DAMD62-10-5-071 (JLW), NIAAA Center Grant AA017072-01, NIDA Grants DA015232, DA019958 (JLW), and the State of California funds for medical research on alcohol and substance abuse through the UCSF.

**Inhibition of human multiple myeloma cell proliferation by naltrindole**


The antiproliferative activity of naltrindole (Nti), a delta opioid receptor (DOR) antagonist, toward human multiple myeloma (MM) cells was evaluated. Nti inhibits the mixed lymphocyte reaction in vitro, and blocks graft rejection in vivo. Based on its immunosuppressive properties we tested Nti’s effect on proliferation of MM cells. MM is an invasive plasma cell neoplasm responsible for 10% of all hematological malignancies. Nti inhibited the proliferation of human MM cell lines with an EC50 of 20 μM, whereas other human cells lines were substantially less sensitive. To mimic the bone marrow environment localization of MM cells, co-culture of MM cells with bone marrow stromal cells did not affect the antiproliferative activity of Nti. [3H]-Nti exhibits saturable, low affinity binding to intact MM cells and the pharmacological properties of the Nti binding site differ significantly from those of the DOR, suggesting that Nti inhibits proliferation of MM cells through a non-opioid receptor mechanism. RT-PCR assays confirmed the lack of delta, kappa and mu receptor mRNA in MM cells. The identity of the naltrindole binding site is currently under investigation. Nti does not induce apoptosis in MM cells, based on FACS analysis and caspase cleavage assays, but decreases the rate of cell division. While investigating the mechanism of action of Nti, we found that it increases intracellular calcium levels in MM cells, and the calcium appears to be released from the endoplasmic reticulum, based on inhibition of the response following thapsigargin treatment. This effect is specific to Nti as other opioids such as naltrexone and morphine do not affect the levels of calcium in MM cells, nor do they block the activity of Nti. Based on the antiproliferative activity of Nti toward MM cell lines, an in vivo study was conducted. Nti injected IP daily at 30mg/kg significantly decreased tumor volumes in a murine SCID/human RPMI 8226 xenograft model over a 39-day period compared with saline injected controls. Further studies on Nti as a potential therapeutic agent for the treatment of human MM are warranted.
Delta agonist glycopeptides: CNS active drugs from endogenous neuropeptides

Y. Li1, D. Giuvelis2, J. Lowery2, C. M. Kirkmire3, L. Z. Szabó1, B. Anglin1, M. Lefever1, L. Yeomans-Maldonado1, C. M. Keyari1, D. Muthu1, E. J. Bilsky4, J. M. Bidlack2, R. Polt1, 1Univ. Arizona, Tucson AZ, 2Univ. of Rochester Medical Center, 3Univ. of New England, USA

Glycosylation methods developed in the Polt lab have led to a number of stable and systemically available glycopeptide drug candidates have been synthesized and purified on large scale. Key to greater stability, increased bioavailability and enhanced penetration of the blood-brain barrier (BBB) is the bioiusian activity of the glycopeptides. Essential to this concept is the notion that the glycopeptides can adopt two different conformational ensembles: a water-soluble random coil ensemble with a diverse range of backbone conformations, and a more restrictive membrane-bound ensemble of conformations that allows the glycopeptide to participate in membrane transport processes that ultimately lead to BBB penetration. Short enkephalin-derived glycopeptide drugs have been studied as analgesics. Three distinct classes of the enkephalins have been developed: mu-selective opiate agonists, delta-selective opiate agonists, and mixed mu/delta agonists. All of these morphine substitutes have a high potential for translation to the clinic, and a company has been formed to commercialize their application. Endorphin/Dynorphin-derived helical glycopeptides have been explored. While these glycopeptides have a much higher M.W. than the shorter enkephalins (~2500 vs ~1000), their apparent penetration of the BBB is much better. Amphipathic helices are used to achieve bioiusian behavior. Circular dichroism (CD), NMR and computational methods have been used to provide important biophysical information to aid in the design of these drugs. While we are still working on a more complete understanding of this new class of drugs, it seems clear that we can obtain analgesics that are potent at 600 µg/kilo, and recent studies show that the bioiusian approach is not limited to opioid peptides. Support: Office of Naval Research (N00014-05-1-0807 & N00014-02-1-0471), the National Science Foundation (CHE-607917) and the National Institute of Neurological Disorders and Stroke (R01-NS52727).

Identity of dorsal root ganglion and spinal neurons mediating delta opioid receptor analgesia

G. Scherrer (1), B.L. Kieffer (2), A.I. Basbaum (3), A.B. MacDermott (1), (1) Columbia University, USA, (2) IGBMC, France, (3) UCSF, USA

Opioid analgesics targeting the mu opioid receptor (MOR) have limited utility for the management of nerve injury-induced mechanical hypersensitivity (mechanical allodynia/touch-evoked neuropathic pain). While the mechanisms underlying neuropathic pain start to be elucidated our limited understanding of the neuronal circuits on which opioids act prevents us from developing more efficient opioid therapeutics against touch-evoked pain. We recently showed that the delta opioid receptor (DOR), in contrast to MOR, is predominantly expressed by sensory neurons with myelinated axons, and that DOR agonists reduce mechanical hypersensitivity in a mouse model of neuropathic pain. Here we used in situ hybridization,
Natural product derived KOP ligands as novel treatments for drug abuse

T. E. Prisinzano Dept. of Med. Chem., Sch. of Pharmacy, Univ. of Kansas, Lawrence, KS, USA

Natural products have played an important role in the development of medications for a number of diseases. However, the search for natural products with utility in the treatment of drug abuse is an area much less developed than the search for anticancer or anti-infective agents. Investigation of psychoactive natural products, such as salvinorin A, provides an opportunity to identify novel scaffolds and selective agents to better characterize known receptor types and study their role in drug abuse. It is relatively rare for natural products to have sufficiently attractive ADME/Tox (Absorption, Disposition, Metabolism, Excretion, and Toxicity) properties to be marketable, despite their excellent potency and selectivity. Thus, the ability to improve these properties by semi- or total synthetic chemistry is important in drug seeking campaigns. A growing amount of evidence suggests that kappa opioid (KOP) receptors are involved in the abuse related effects of CNS stimulants. KOP receptor agonists have been shown to modulate the activity of dopamine neurons and decrease self-administration of cocaine in non-human primates, while KOP receptor antagonists have the potential to be utilized as opioid abuse therapies and in the treatment of stress-induced reinstatement (a model of drug relapse). As part of our continuing efforts toward developing effective natural product based drug abuse therapies, we report the synthesis and biological characterization of unique semisynthetic analogues of salvinorin A. These agents provide a better understanding of the structure-activity relationships of this unique KOP agonist. This information can then be used to aid in the development of KOP based drug abuse therapeutics with enhanced pharmacological properties. Supported by DA018151 and DA018151S1.

High throughput in vivo screening for the identification of novel analgesics

R. A. Houghten, C. T. Dooley, M. Giulianotti and J. P. McLaughlin, Torrey Pines Institute for Molecular Studies, USA

Typical compound screening used to identify potential drug candidates typically yields compounds that do not have desired drug like properties. Thus identified compounds found in this traditional manner have a high inherent rate of attrition in the later stages of drug development as evidenced by poor in vivo activity. One approach to circumvent this high attrition rate would be to directly use phenotypic in vivo models in the discovery phase to identify enhanced hits with desired biological profiles. Our working hypothesis is that the direct use of mixture-based combinatorial libraries for in vivo testing offers a unique opportunity to carry out successful preliminary studies in which 10s to 100s of thousands of compounds can be used in translational in vivo assays. Two studies will be presented involving the mouse tail flick test (8 animals per time point; times tested were 30 minutes, 1.0 hours, 2.0 hours, 3.5 hours, 5.0 hours, 8.0 hours and 24.0 hours; differences in mixture results were carried out by summing the area under the curve) of a tetra-peptide library which contains Dmt-DALDA as an internal control (the library in total is made up of 17,850,625 peptides with each mixture composed of 274,625 peptides—these were successfully tested at 25 and 5 mg/kg). Additionally, a classic small molecule library was tested in the same tail flick assay (this library is made up of a total of 738,192 compounds; the single position defined mixtures were made up of 17-28,000 compounds each and were tested by IP administration at 5mg/kg). The initial results of these studies were published in the AAPS Journal, 8 (2) E371-382, 2006 and AAPS Journal, 12 (3), p. 318-329. These results lead us to conclude that the direct in vivo screening of mixture-based libraries can yield highly active individual compounds having enhanced desired activity. These approaches can be utilized to identify mu, delta and kappa specific analgesics. The breadth and implication of these...
approaches will be discussed. Funded in part by NIDA R21DA 019620 (to RAH).

**Kappa opioid receptor ligands and development of antipruritic agents**

A. Cowan and S. Inan, Department of Pharmacology and Center for Substance Abuse Research, Temple University School of Medicine, Philadelphia, PA 19140, USA

Itch, for so long an orphan symptom of several systemic diseases, is in the news. It is a unique sensory modality that is closely related to, yet distinct from, pain. Recently, two high profile papers from Dr. Chen’s lab at Washington University in St. Louis have raised the possibility of spinal gastrin-releasing peptide serving as a common itch neurotransmitter by relaying information to the somatosensory cortex in response to an array of pruritic stimuli, at least in mice. Chemicals selected to precipitate the particular behavior measured – compulsive scratching of the neck with hindlegs–included chloroquine and compound 48/80. We have found that 5′-guanidinonaltrindole (GNTI), a standard kappa opioid receptor antagonist, also provokes the same frenzied, repetitive scratching when injected s.c. behind the neck in male Swiss Webster mice. Might this be a useful animal model in developing structure-activity data on potential antipruritic agents? What are the alternatives? GNTI-induced scratching is dose-related (0.03-1 mg/kg), stable across at least 30 minutes, and mimicked by the less potent and less efficacious norbinaltorphimine. Critically, either s.c. pre-treatment (0.001-0.03 mg/kg) or post-treatment (0.01-0.03 mg/kg) with nalfurafine, a kappa agonist, attenuates the scratching caused by a standard dose of GNTI (0.3 mg/kg, s.c.). This is an important link to clinical pharmacology since nalfurafine is the first kappa opioid agonist to survive in the commercial arena (against pruritus in hemodialysis patients, in Japan). Our current research is focusing on the relationship between peripherally restricted kappa agonists and the suppression of scratch in mice. We call attention to the anti-scratch properties of asimadoline, an arylacetamide kappa agonist with limited CNS penetration, which is being developed by Tioga/Ono against diarrhea-predominant irritable bowel syndrome. This agent possesses dose-related anti-scratch activity against compound 48/80 and GNTI models of itch in mice. These promising results may hasten the formulation of asimadoline, or like compounds, as skin-directed antipruritics. (DA013429)

**Disruption of kappa-opioid receptor function attenuates behavioral effects of stress in rodents**

W. A. Carlezon Jr., Psychiatry, Harvard Medical School, McLean Hospital, Belmont MA, USA

Stress can induce profound changes in the brain that have immediate and long-lasting effects on behavior. We have shown that various stressors activate the transcription factor CREB in the nucleus accumbens (NAS). Using viral vectors, we have shown that elevated CREB activity in the NAS causes signs characteristic of depression (anhedonia) and anxiety (resistance to extinction of fear), producing a phenotype similar to that seen in people with post-traumatic stress disorder (PTSD). In contrast, disruption of CREB activity in the NAS has antidepressant-like effects. The mechanism of these effects is unknown, but may involve multiple factors. As one example, CREB may produce these effects by regulating the firing rate of NAS neurons that provide feedback inhibition of mesolimbic dopamine neurons, which in turn send projections to areas more classically implicated in stress responsiveness (amygdala, prefrontal cortex). CREB regulation of dynorphin, an endogenous ligand at KOR receptors, may play a key role in this process. CREB-induced elevation of dynorphin tone leads to increases in the stimulation of KORs located on mesolimbic dopamine neurons, thereby decreasing activity of this system. In support of this model, we now have considerable data indicating that blockade of KORs can prevent, attenuate, and reverse stress effects on behavior. KOR antagonists produce antidepressant-like effects in the forced swim test, regardless of whether they are given before or after exposure to stress. Likewise, KOR antagonists have acute anxiolytic-like effects in the elevated plus maze, and administration of these drugs before fear conditioning can prevent the development of PTSD-like changes in behavior. We have new data indicating that KOR antagonists reduce the disruptive effects of stress on attention in rats, as reflected by performance in the 5-choice serial reaction time task. Collectively, these data suggest that KOR antagonists might be particularly useful for producing protective effects in cases where it is possible to predict when stress will occur. Support: MH063266

**Discovery and development of selective kappa opioid receptor antagonists**

F. Ivy Carroll, Center for Organic and Medicinal Chemistry, Research Triangle Institute, Research Triangle Park, NC 27709, USA

Stress can induce despair and increase the risk of clinical depression and drug abuse. Dynorphin, the endogenous ligand for the kappa-opioid receptor, is a stress-related neuropeptide in the brain that may mediate these responses. Activation of the kappa-opioid receptor causes place aversion in rodents and
dysphoria in humans. The dynorphin/kappa-opioid receptor system is thought to be critical for stress-induced depression-like behaviors and reinstatement to drug-seeking behavior. Since kappa-opioid receptor activation contributes to stress-induced behavior, there is considerable interest in selective kappa-opioid receptor antagonists that possess drug-like properties. Studies from our laboratory led to the identification of JDTic as a potent, selective, orally active kappa-opioid receptor antagonist as a potential pharmacotherapy for treatment of depression, anxiety, and addiction (cocaine, alcohol, nicotine, and heroin). Several JDTic analogs have been identified that have in vitro efficacy similar to that of JDTic. The in vitro efficacy, pharmacokinetic properties, and potencies as an antagonist of U50,488-induced diuresis in rats will be presented. This research was supported by NIDA grant DA09045.

**MOR REGULATORY PROTEINS**

**RGS9-2 actions in the Nucleus Accumbens modulate opiate addiction and analgesia**

D. Terzi, A. Varidaki, M. Papachatzaki, K. Psifogeorgou and V. Zachariou, University of Crete, Greece

The signaling modulator RGS9-2 plays a potent role in dopaminergic and opioidergic transmission in the striatum via actions as a GTPase accelerating protein or as effector antagonist for the G protein alpha subunit. Evidence so far points to RGS9-2 as a potent modulator of antiparkinsonian, antipsychotic, psychostimulant and opiate drug actions. In this study we use genetically modified mice to further understand the role of RGS9-2 in addiction, analgesia and depression like behaviors associated with chronic pain or with long term exposure to opiates. Our results suggest that increased activity of RGS9-2 in the nucleus accumbens (NAc) following stereotaxic infection with an adeno associated virus-RGS9-2 construct blocks the rewarding and locomotor sensitizing actions of morphine and leads to a milder opiate withdrawal syndrome. Interestingly, manipulation of RGS9-2 levels in the NAc also affects analgesic tolerance to morphine. We examined changes in RGS9-2 complexes in the NAc following acute and chronic exposure to morphine and we identified changes in the composition of these complexes associated with morphine tolerance. We also examined the way RGS9-2 affects the actions of agents used to alleviate chronic pain symptoms. Using a neuropathic pain model (spared nerve injury) we show that mice lacking the Rgs9 gene develop tolerance to the antiallodynic actions of morphine much later than their wild type controls, and that they are more sensitive to the antiallodynic actions of tricyclic antidepressants. Tricyclic antidepressants may also improve depression like behaviors associated with chronic pain in the mutant mice at lower doses than those required for their wild type controls. This phenotype is related to RGS9-2 actions in the NAc as it can be rescued by local overexpression of the protein. Our findings provide new insights into the cellular mechanisms of opiate and antidepressant drug actions and suggest that interventions in the formation of RGS9-2 complexes may be used to improve treatment efficiency. Funding was provided by the Greek Secretariat for Research and Technology (PENED03/860)

**In vivo evidence for the role of PKC and other intracellular molecules in opioid tolerance**

W. L. Dewey¹, H. Akbarali¹, and G. Henderson², ¹Dept. of Pharm. and Tox. Virginia Commonwealth University, Richmond, Virginia, USA, ²Dept. Pharm. Univ. Bristol, U. K.

We hypothesize that the differences in the rate and level of tolerance development might well be due to differences in the effects of chronic mu receptor stimulation on intracellular signaling mechanisms. Recent history has shown that receptor phosphorylation which causes a desensitization and encapsulation of the receptor are both seen after chronic administration of mu opioid receptor agonists and have considerable acceptance as important properties of chronic opioid exposure that leads to tolerance. We have found in whole animal experiments that inhibitors of PKC and inhibitors of PKA both reverse but do not inhibit the development of tolerance to moderately efficacious opioids such as morphine. Neither of these specific kinase inhibitors reversed the tolerance produced by the highly efficacious opioid DAMGO. A combination of the doses of each inhibitor that reversed morphine tolerance when given together did not reverse the tolerance to DAMGO. Further studies with specific inhibitors showed that the gamma, alpha and to a lesser extend the epsilon isomer of PKC are involved in this effect. The studies with the PKC inhibitors were confirmed in electrophysiological experiments in isolate LC neurons. On the other hand GRK inhibitors were found not to alter tolerance to these moderately efficacious opioids but completely reversed tolerance to the highly efficacious opioid DAMGO. We conclude from these and related studies that opioid agonists induce tolerance by different mechanisms, that receptor desensitization plays a major role in both cellular and in vivo tolerance and high efficacy agonists induce tolerance independent of PKC but involve G protein-coupled receptor kinases. In addition we will present recently obtained evidence to suggest that the differentiation in the rate of the development and level of tolerance achieved depends on the role of other intracellular molecules. This work was supported by grants from NIDA.
CaMKII in opioid tolerance and opioid-induced hyperalgesia

Z. Jim Wang, Department of Biopharmaceutical Sciences, Cancer Center, & Program for Collaborative Research in the Pharmaceutical Sciences, University of Illinois, Chicago, IL, USA

CaMKII in opioid tolerance and opioid-induced hyperalgesia

CaMKII in opioid tolerance and opioid-induced hyperalgesia

L. M. Bohn, K. M. Raehal, C. E. Groer, J. M. Streicher, and C. L. Schmid, Departments of Molecular Therapeutics and Neuroscience. The Scripps Research Institute, Jupiter, FL, USA.

The mu opioid receptor (MOR), like most G protein-coupled receptors, interacts with beta-arrestins (Barrestins) upon agonist stimulation. Barrestins are intracellular scaffolding proteins that can serve to disrupt receptor-protein signaling scaffolds or facilitate such interactions. The degree of interaction between these two proteins can be influenced by the chemical composition of the ligand. Using Barrestin-2 KO mice, our laboratory has studied this protein’s contributions to MOR-mediated biological responses. We have found that in the absence of Barrestin2, morphine analgesia is enhanced and tolerance is attenuated suggesting that Barrestin2 plays a role in dampening signaling transduction events leading to antinociception. Other morphine-mediated behavioral responses, including dependence (as assessed by antagonist-induced withdrawal), respiratory suppression and constipation are attenuated in this animal model suggesting that Barrestin2 may play a facilitatory role in the signaling underlying these responses. The work presented here further examines the role of individual Barrestins in the regulation of the mOR, including the contribution to ubiquitination and resensitization, of the MOR. Early developments in our drug discovery efforts to generate MOR agonists that are biased against Barrestin recruitment will also be introduced. According to extensive studies in the Barrestin2 mouse models, such a strategy may allow for the treatment of pain with fewer side-effects than seen with traditional opioid therapies. Funding for this work has been sponsored in part by R01DA14600, R01DA18860, R03DA025158 to LMB and F31DA021952 to KMR.

Desensitization and trafficking of mu-opioid receptors in locus coeruleus neurons: Modulation by kinases

S. Arttamangkul, H. W. Lu and J. T. Williams, Vollum Institute, Oregon Health & Science University, Portland, Oregon, USA

Mu opioid receptor (MOR) desensitization and internalization induced by many opioid agonists is thought to result from receptor phosphorylation by G-protein receptor kinases (GRKs) and an increase in affinity of arrestins to the phosphorylated receptor. Morphine is different from other agonists in that it is inefficient at recruiting GRKs and arrestins and thus results in little receptor desensitization and internalization. Nevertheless, morphine-induced desensitization can be facilitated by activation of protein kinase C. It is unclear if the activation of PKC also facilitates morphine-induced internalization. This study uses the combination of intracellular recordings and live cell imaging of Flag-tagged-MORs from rat and mouse locus coeruleus neurons to examine the role of PKC in acute desensitization and receptor trafficking. In addition several kinase inhibitors were studied to understand the effects of phosphorylation on MOR desensitization. Blocking GRK2 via a specific inhibitor (NaPP1) in the LC neurons from GRK2-mutant mice showed no effects on MOR desensitization. SB203580 and SP600125, drugs known to inhibit p38 MAPKs and JNKs did not prevent MOR desensitization, internalization or alter the recovery from desensitization. Interestingly, MOR desensitization still occurred but the trafficking of the receptors was altered from normal following pretreatment with staurosporine, at high concentrations. The modified trafficking of receptors was also observed in Flag-tagged-MOR mice lacking arrestin-3. The results suggest that agonist-selective desensitization may take place at an early step following agonist binding that is modulated by, but not dependent on kinase activity. The work was supported by NIH Grants DA08163, DA026617.
**YOUNG INVESTIGATOR SYMPOSIUM: OPIOID MODULATION OF NEURAL CIRCUITS**

**Stress regulation of kappa opioid receptor signaling in the extended amygdala**

T.L. Kash, K.E. Pleil, C.J. Li, Department of Pharmacology, Bowles Center for Alcohol Studies, University of North Carolina Chapel Hill, School of Medicine. Chapel Hill, NC, USA

Strong evidence exists for endogenous stress and anti-stress systems in mammalian organisms. Chronic exposure to stress is hypothesized to modulate the relative balance of activities of these systems within key circuitry in the brain, leading to dysregulated emotional behavior. The kappa opioid receptor (KOR) and its endogenous agonist, the neuropeptide dynorphin, are one such 'stress' system. Dynorphin is expressed in the cell bodies and terminals of the bed nucleus of the stria terminalis (BNST), a brain region associated with anxiety and stress, suggesting that KOR activation in this region may play a role in the regulation of emotional behavior. However, the cellular actions of KOR in this region have not been characterized. Using whole-cell voltage clamp recordings in an *ex vivo* mouse brain slice preparation, we investigated the effect of KOR activation on inhibitory transmission in the BNST. We found that activation of KOR reduced GABAergic transmission via a presynaptic mechanism. We next examined the interactions between corticotrophin releasing factor (CRF) and KOR systems. Surprisingly, we found that CRF produced a KOR dependent inhibition of GABAergic signaling, suggesting that CRF can induce dynorphin release in the BNST. We next evaluated the impact of stress exposure on KOR systems. We found that the inhibitory effect of KOR activation on synaptic inhibition was significantly greater in DBA/2J mice compared to C57BL/6J mice. Further, we found that chronic, but not acute restraint, altered KOR modulation in C57BL/6J mice; while both acute and chronic restraint altered KOR modulation in DBA/2J mice. The results from this study add to a growing body of evidence suggesting that the KOR system is involved in the regulation of stress disorders. Supported by an ABMRF Young Investigator Award, a NARSAD Young Investigator Award, an INIA-Stress Pilot Project, R01AA01954 and R00AA17668 from the NIH, and PT090344 from the DoD.

**Opioid enhancement of GABA<sub>A</sub> receptor function in VTA dopamine neurons: A novel non-G protein mediated signaling mechanism induced by stress**

Elyssa B. Margolis, Ernest Gallo Clinic & Research Center, University of California, San Francisco, Emeryville, CA, USA; Dept. of Neurology University of California, San Francisco, CA, USA

Opioid receptors are G-protein coupled receptors that typically signal through activation of inhibitory Gi/o proteins. However, recent themes in GPCR research, including ligand-directed signaling and G protein independent signaling pathways, suggest that a variety of conditions determine the *in vivo* signaling pathway activated when a ligand binds to an opioid receptor. We have discovered that novel postsynaptic delta opioid receptor signaling emerges in VTA neurons following acute footshock stress. This novel signaling pathway causes rapid insertion of postsynaptic GABA<sub>A</sub> receptors into the synapse, increasing the ability of synaptically released GABA to inhibit VTA neurons. This effect is PI3K/AKT dependent, but G protein independent. This effect is in the opposite direction to the small DOR-mediated inhibition of GABA<sub>A</sub> signaling in naïve rats. Therefore, not only does the magnitude of opioid effects depend upon the state of the animal, but the signaling pathway utilized by opioid receptors is also state-dependent. This novel change in DOR signaling provides a potential mechanism for endogenous opioid release to selectively amplify the inhibition produced by GABA release in a subset of VTA neurons while reducing such inhibition in other VTA neurons. Supported by P50 AA017072, DA-016782-06, DA-030529-01, sponsored by the Army under award numbers W81XWH-08-1-0017 and W81XWH-07-1-043, and funds from the State of California for medical research on alcohol and substance abuse through the University of California, San Francisco.

**Dopamine mediated synaptic transmission in the VTA**

C. P. Ford, Department of Physiology and Biophysics, Case Western Reserve University, Cleveland, OH, USA

Opioids alter the activity and excitability of midbrain dopamine neurons, the net effect being an alteration dopamine release and signaling at downstream targets. In order to understand the consequences of downstream dopamine signaling we have been investigating the mechanisms that regulate how dopamine mediates synaptic transmission. In the VTA and SNc, dopamine neurons make dendro-dendritic synapses with adjacent dopamine neurons. The dendritic release of dopamine activates postsynaptic D2-type autoreceptors on adjacent dopamine neurons and induces a GPCR-mediated inhibitory
synaptic current. This talk will outline recent work characterizing the time course and concentration of dopamine that results from the phasic release of dopamine in the VTA that underlies the generation of this inhibitory synaptic current. This aims to understand the dynamics of temporal profile of dopamine during synaptic transmission. Dopamine is often believed to signal at low concentrations over extended periods at D2-receptors due to the high affinity of the D2-receptor. However, using the combination of whole-cell synaptic recordings, electrochemistry and the rapid application of dopamine to excised patches, we have found that post-synaptic D2-receptors are exposed to a relatively high concentration of dopamine (~10 μM) for a brief period of time (maximum duration ~100 ms) during the peak of phasic transmission. By altering the duration of dopamine that was applied to excised patches we conclude that post-synaptic signaling mechanisms (D2-receptor/G-protein) not the duration of dopamine defines the timecourse of dopamine mediated synaptic transmission. This work suggests that despite being a GPCR agonist, dopamine may signal in a relatively localized manner. Support: NIH/NIDA DA026417 and NARSAD

Context-dependent sensitization to morphine alters hippocampal neuroplasticity

J. A. Moron Concepcion. Dept. of Anesthesiology, College of Physicians and Surgeons, Columbia University Medical Center, New York, NY, USA

Evidence suggests that long-term adaptations to the neural substrates of learning and memory after repeated drug treatment may play an important role in drug addiction. For instance, alterations of hippocampus-dependent contextual learning by drugs of abuse may lead to context-evoked cravings or drug seeking behavior. Glutamatergic systems, including α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptors (AMPARs), are thought to be involved in opiate-induced neuronal and behavioral plasticity, although the mechanisms underlying these effects are only beginning to be understood. The present study examines the effects of repeated morphine administration, using a paradigm that results in context-dependent behavioral sensitization, on the expression of AMPARs and the functional ramifications in the hippocampus. The learned association between morphine and the drug administration environment following context-dependent locomotor sensitization to morphine leads to persistent changes in the expression and synaptic redistribution of AMPARs. More specifically we find that following context-dependent sensitization we observe a persistent increased expression of AMPARs lacking the glutamate receptor 2 (GluR2) subunit in hippocampal synaptic fractions. In addition, we provide electrophysiological evidence that this effect is associated with an increase in excitatory synaptic transmission. Interestingly, we also find that the expression of context-dependent sensitization is associated with an impairment in long-term potentiation (LTP). However, these alterations are reduced when morphine injections are received in a non-paired environment. We propose that the learned association between environment and morphine effects is mediated by changes in excitatory transmission and plasticity in the hippocampus. Overall, these data suggest that glutamatergic synaptic transmission in the hippocampus may play an important role in drug-induced behavioral sensitization and addictive processes in general. Supported by NIH grant R01 DA025036 to JMC.

Drug-induced GABA transporter currents enhance GABA release and produce opioid withdrawal behaviours

E.E. Bagley¹, J. Hacker¹, V.I. Chefer², C. Mallet¹, G.P. McNally³, B.C.H Chieng¹, T.S. Shippenberg², M.J. Christie¹, ¹Brain & Mind Research Institute, University of Sydney, Australia. ²National Institute on Drug Abuse, Baltimore, USA. ³School of Psychology, University of NSW, Australia.

Neurotransmitter transporters can affect neuronal excitability indirectly via modulation of neurotransmitter concentrations or directly through transporter currents. A physiological/pathophysiological role for transporter currents has not previously been described. Here we show both in vivo and in vitro that GABA transporter 1 (GAT-1) cation currents directly increase GABAergic neuronal excitability and increase synaptic GABA release in the periaqueductal gray (PAG) during opioid withdrawal. By contrast, GAT-1 did not indirectly alter GABA receptor responses via modulation of extracellular GABA concentrations. Importantly, we found evidence that this GAT-1-induced increase in GABAergic activity induced many of the PAG-mediated signs associated with opioid withdrawal. Together these data support the hypothesis that GAT-1 activity directly produces opioid withdrawal signs through direct hyperexcitation of GABAergic PAG neurons and nerve terminals, which presumably enhances GABAergic inhibition of PAG output neurons. These data provide the first evidence that neurotransmitter transporter currents can play a pathophysiological role. Supported by the National Health & Medical Research Council of Australia (project 512390, Fellowship to MJC 511914) and the Intramural Research Program of the National Institutes of Health, National Institute on Drug Abuse.
Regulation of opioid dependence by let-7 microRNAs

Y. He and Z. Wang, Department of Biopharmaceutical Sciences, Cancer Center, & Program for Collaborative Research in the Pharmaceutical Sciences, University of Illinois, Chicago, USA

MicroRNA (miRNA) has emerged as a critical regulator of neuronal functions. We previously reported that let-7 family miRNAs can post-transcriptionally regulate the μ opioid receptor (MOR) and opioid tolerance. The aim of this study was to test the hypothesis that let-7 family miRNAs can regulate the development of opioid dependence. We found that expression of let-7 was significantly increased in SH-SY5Y cells that were treated with morphine (1 μM, for 48 h). LNA-modified antisense oligonucleotides (LNA-anti-let-7) not only inhibited endogenous expression of let-7 in SH-SY5Y cells, but also abolished morphine-induced cAMP overshoot. In agreement with the in vitro findings, let-7 levels were up-regulated by morphine in mice. Real-time PCR analysis further demonstrated a temporal correlation between let-7 up-regulation and the development of opioid dependence (one 75 mg morphine pellet/mouse, s.c.). Moreover, treatment with LNA-anti-let-7 decreased the supraspinal level of let-7 and attenuated naloxone-induced withdrawal in mice dependent on morphine. Morphine conditioned place preference (CPP) was also blocked by LNA-anti-let-7. Taken together, these data suggest let-7 plays an integral role in the development of opioid addiction. (Supported in part by NIH grants RO1HL098141 and KO7AT003647)

Mu opioid receptor biased ligands: delivering powerful analgesia and minimizing side effects

S. M. DeWire, D. Yamashita, C. J. LaBuda, M. W. Lark, and J. D. Violin, Trevena Inc., King of Prussia, PA

Many classical mu-opioid receptor (MOR) agonists are established analgesics, but all possess a number of limiting side effects, notably respiratory depression and constipation. Unlike “off target” side effects which can be eliminated by improving receptor selectivity, these “on target” side effects act directly through the MOR. Building on the findings that beta-arrestin2 knock-out mice exhibit increased analgesic responses to morphine, yet show reduced respiratory depression, tolerance, and constipation (Bohn LM et al, Science 1999, Raehal KM, JPET, 2005), we sought to discover and develop a biased MOR agonist that would recapitulate the genetic findings, i.e. a ligand which engages Gi signaling with similar potency and efficacy to morphine, but with significantly less beta-arrestin recruitment. After performing a high throughput screen and iterative chemistry campaign, we have identified a collection of MOR G-biased ligands. These compounds are potent and fully analgesic in the mouse 56 degree hot plate model, and when compared to morphine, display an enhanced therapeutic window between analgesia and two models of constipation: glass bead colonic motility and fecal bolus accumulation. Additionally, MOR G biased ligands exhibit less respiratory depression at equianalgesic doses, implying a greater safety margin. Taken together, these data indicate that MOR G biased ligands may offer improved safety and tolerability, potentially enabling a better risk/benefit profile for pain management.

Deciphering mu-opioid receptor phosphorylation and dephosphorylation

C. Doll(1), F. Pöll(1) and S. Schulz(1), (1)Institute of Pharmacology and Toxicology, University Hospital, Friedrich Schiller University Jena, Germany

The molecular basis of agonist-selective signaling at the mu-opioid receptor is poorly understood. We have recently shown that full agonists such as [D-Ala²-MePhe⁴-Gly-ol]enkephalin (DAMGO) stimulate the phosphorylation of a number of carboxyl-terminal phosphate acceptor sites including threonine 370 (T370) and serine 375 (S375) that is followed by a robust receptor endocytosis. In contrast, morphine promotes a selective phosphorylation of S375 without causing rapid receptor internalization. Here, we identify kinases and phosphatases that mediate agonist-dependent phosphorylation and dephosphorylation of the mu-opioid receptor using siRNA knock down screening. We found that DAMGO-driven phosphorylation of T370 and S375 was catalyzed by G protein-coupled receptor kinases (GRK) 2 and 3 whereas morphine-driven S375 phosphorylation was catalyzed by GRK5. As a functional consequence, siRNA knock down of GRK5 abrogated morphine-induced but not DAMGO-induced ERK activation. We also identified protein phosphatase 1gamma (PP1gamma) as mu-opioid receptor phosphatase that catalyzed T370 and S375 dephosphorylation at or near the plasma membrane within minutes after agonist removal. Together, the morphine-activated mu-opioid receptor is an efficient substrate for phosphorylation by GRK5 but a poor substrate for GRK2/3. GRK5 phosphorylates mu receptors selectively on S375, which is sufficient to stimulate ERK signaling but not sufficient to drive receptor sequestration. This study was supported by the Deutsche Forschungsgemeinschaft.

Differential binding of non-visual arrestins to the intracellular domains of the mu-opioid receptor

School of Physiology and Pharmacology, University of Bristol, Bristol, UK, "Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, Tennessee, USA, b Department of Biochemistry and Molecular Biology, Thomas Jefferson University, Philadelphia, Pennsylvania, USA.

Upon agonist binding the µ-opioid receptor (MOPr) is phosphorylated and can recruit arrestin-2 and arrestin-3. Apart from promoting the desensitization and internalization, the binding of arrestins can also lead to the triggering of alternative signalling pathways. We have shown that kinases including GRK2, PKC and CaMKII can regulate MOPr. Here we used GST-fusion constructs of the intracellular regions of MOPr to investigate whether arrestin-2 and -3 can bind to these sequences in vitro, and secondly to determine whether phosphorylation of these sequences can alter their ability to bind arrestins. GST-fusion constructs of the intracellular loop2 (ICL2), loop3 (ICL3) and the COOH-terminus (CT) of MOPr coupled to GST beads were incubated with purified arrestin-2 or -3 before being subjected to SDS-PAGE and Western blotting. The degree of arrestin-2 or -3 binding was determined with specific antibodies. Our results indicate that arrestin-3 binds to the unphosphorylated MOPr-ICL2, ICL3 and the CT whereas arrestin-2 shows preferential binding to the GST-MOPr-CT over the intracellular loops. Phosphorylation of the GST-MOPr-CT by GRK2 increased the binding of arrestin-2 and -3. Phosphorylation of the GST-MOPr-CT by PKC and CAMKII increased arrestin-2 and -3 binding but to a lesser extent than GRK2. Non-visual arrestins can bind to intracellular regions of MOPr in vitro, with GRK2 phosphorylation increasing the ability of the CT to bind arrestins. These interactions may well be important for the association of arrestins with the intact, agonist-activated MOPr. Supported by Rusan Pharma Pvt. Ltd. (Mumbai, India)

Bivalent ligand MDAN-21 blocks receptor endocytosis by bridging mu-delta opioid heteromers

A.S. Yekkirala (1,2), A.E. Kalyuzhny (3), and P.S. Portoghese (1,2,3), (1) Dept. of Medicinal Chemistry, College of Pharmacy, (2) Dept. of Pharmacology, (3) Dept. of Neuroscience, Medical School., University of Minnesota, Minneapolis, Minnesota, USA

The regulation of opioid receptors by endocytosis has been suggested to play a significant role in the development of antinociceptive tolerance. Studies have indicated that the endocytosis of mu opioid receptors has an inverse relationship to tolerance, whereas the endocytosis of delta receptors correlates with increased tolerance. With focus on the role of opioid receptor heteromers in antinociception and the physiological relevance of heteromer trafficking, we have employed MDAN-21, a bivalent ligand that contains mu agonist and delta antagonist pharmacophores linked through a 21-atom spacer, as a pharmacological tool to investigate this relationship. MDAN-21 has been reported to produce potent antinociception via mu-delta heteromers without tolerance, dependence, or place preference in mice. Here we show that MDAN-21 did not produce any internalization of mu-delta heteromers in HEK-293 cells. In contrast, both the corresponding mu monovalent ligand (MA-19) and a bivalent ligand MDAN-16 with a short spacer, produced robust internalization of mu opioid receptors. As it is known that a 16-atom spacer does not permit efficient bridging of heteromers, it is likely that MDAN-16, like MA-19, interacts univalently with mu-delta heteromers. These results suggest that MDAN-21 prevents endocytosis by bridging neighboring mu and delta protomers in these heteromers, whereas univalent interaction leads to internalization of mu.

Changes in ligand-biased signaling are associated with opioid tolerance

E. N. Bobeck (1), T. A. Macey (2), K. L. Suchland (1), M. M. Morgan (1) and S. L. Ingram (1), (1) Department of Psychology, WSU Vancouver, Vancouver WA, (2) VA Hospital, Oregon Health & Science University, Portland OR, USA.

Opioids, such as morphine, are the most effective treatment for pain, but their use is diminished with the development of tolerance following repeated administration. Recent data from our laboratory demonstrated that morphine activates extracellular signal-related kinase (ERK1/2) phosphorylation selectively in tolerant compared to opioid naïve rats. These results suggest that morphine activation of mu-opioid receptor (MOPr)-coupled effectors is altered following repeated morphine administration and the development of tolerance. The current studies tested MOPr coupling to multiple effectors in the ventrolateral periaqueductal gray (vPAG) following acute administration of multiple opioid agonists in opioid-naïve or opioid-tolerant rats. We also tested the hypothesis that MOPr activation of ERK1/2 in the vPAG is dependent on dynamin, a GTPase essential for vesicle endocytosis. A single microinjection of morphine did not activate ERK1/2 levels over background, even though it initiated antinociception that can be inhibited by alpha-dendrotoxin, an inhibitor of presynaptic Kv channels. However, in morphine tolerant rats, a single microinjection of morphine induced ERK1/2 activation that was blocked with microinjections of myristoylated dynamin dominant-negative peptide (Dyn-DN)
compared to rats given a myristoylated scrambled peptide (Dyn-scr) 20 min prior to the morphine microinjection. These results suggest that MOPr activation of ERK1/2 signaling occurs via a dynamin-dependent mechanism in tolerant rats and that repeated morphine administration increases MOPr recruitment of endocytic proteins in response to morphine. Funding by NIH grant DA 015498. Morphine sulfate was a gift from NIDA.

**RGS9 knockout enhances MOR-mediated inhibition of adenylyl cyclase in a CNS region dependent manner**

D.E. Selley (1), V. Zachariou (3), M.P. Cassidy (1), C.K. Chen (2), E.J. Nestler (4) and L.J. Sim-
Selley (1), (1) Dept. of Pharmacology & Toxicology and (2) Biochemistry and Molecular Biology, Virginia Commonwealth University, Richmond, VA, USA; (3) Dept. of Pharmacology, University of Crete, Faculty of Medicine, Heraklion, Crete, Greece; (4) Fishberg Department of Neuroscience, Mount Sinai School of Medicine, New York, NY, USA

Regulator of G-protein signaling (RGS) type 9-2 is a CNS-expressed splice variant of retinal RGS9. RGS9-2 is highly expressed in the striatum (caudate-putamen and nucleus accumbens), with lower levels expressed in hippocampus, periaqueductal gray (PAG) and spinal cord. Our previous work showed that antinociceptive and conditioned rewarding effects of morphine were enhanced in RGS9 knockout (KO) mice, without any difference in striatal mu opioid receptor (MOR) levels. In the present study, the effect of RGS9 knockout on MOR-mediated inhibition of forskolin-stimulated adenylyl cyclase activity was examined in various CNS regions. Results in nucleus accumbens showed that adenylyl cyclase inhibition by the MOR-selective full agonist DAMGO was unaffected by RGS9 genotype, however inhibition by the high efficacy partial agonist morphine was significantly enhanced in RGS9 KO mice. In contrast, DOR-mediated inhibition of adenylyl cyclase was unaffected by RGS9 KO. Interestingly, in caudate-putamen, neither DAMGO nor morphine-mediated inhibition of adenylyl cyclase differed between genotypes. DAMGO-mediated inhibition of adenylyl cyclase in hippocampus was also not different between genotypes, whereas this response was significantly enhanced in the PAG and spinal cord of RGS9 KO mice. These results indicate that RGS9-2 negatively regulates inhibitory signaling of the MOR to adenylyl cyclase in CNS regions that control motivational and antinociceptive effects of mu opioids, but not regions that mediate motor and memory effects of these drugs. Supported by grants DA014277 (LJS), DA10770 (DES) and DA08227 (EJN) from the National Institute on Drug Abuse

---

**Mouse strain-specific analgesic responses in MOR-1 and DOR-1 KO mice**


Initial analysis of MOR-1 and DOR-1 KO mice produced in our laboratory revealed unexpected analgesic responses when these mutant alleles were initially analyzed while being maintained on mixed 129S6/C57Bl6 backgrounds. Specifically we found retention on M6G analgesia in MOR-1 KO mice and a dramatic increase in BW363U86 analgesia in DOR-1 KO mice. To better understand these analgesic responses, both mutant alleles were backcrossed onto both C57Bl6 and 129S6 stains and analgesic responses assayed. Both the retained M6G analgesia and the dramatically increased BW363U86 analgesia were present in MOR-1 and DOR-1 KOs on the 129S6 background, respectively, but were completely absent in the MOR-1 and DOR-1 strains maintained on C57Bl6. BW363U86 responses were also present in 129S6 triple KO mice, indicating the presence of MOR-1 did not account for this activity. To begin to understand the modifier genes regulating these strain-specific effects of mutation, MOR-1 C57 x MOR-1 129S6, DOR-1 C57 KO x DOR-1 129, and TKO 129S6 x TKO C57Bl6 mice were crossed to produce F1 and F2 generations. While F1 DOR-1 KO mice completely lack BW363U86 analgesia, this analgesia re-appeared at cut-off levels in ~1/4 of F2 offspring suggesting that at most a few genes regulate this response. Similarly, while F1 MOR-1 KO mice completely lacked M6G analgesia, this analgesia also re-appeared in F2 KO mice. QTL analysis has begun to identify loci with significant associations with these analgesic phenotypes. In addition, analysis of TKO mice is currently in progress to determine whether the MOR-1 and DOR-1 analgesic responses coordinately reappear in F2 mice. We conclude that strain-specific modifier genes can regulate phenotypes of both MOR-1 and DOR-1 KO mice and may reveal novel analgesic pathways. Supported by DA-18592, NJTBI, and the NJ Governor Council.
POSTERS (ALPHABETICAL ORDER)

L-theanine suppresses abstinence signs in morphine-dependent rhesus monkeys and has anxiolytic-like activity in the mouse elevated plus maze
M.D. Aceto, L.S. Harris, L.D. Hughes, I.D. Premaratne, L.E. Wise and A.H. Lichtman, Department of Pharmacology, School of Medicine, Virginia Commonwealth University, Richmond, Virginia, USA
L-theanine, 2-Amino-4-(ethylcarbamoyl) butyric acid, is an amino acid that found in green tea (Camellia sinensis) and is sold in the United States as a dietary supplement. L-theanine blocked caffeine-induced convulsions (Kimura and Murata 1971) and spontaneous motor activity (Kimura and Murata, 1980) in the mouse and inhibited caffeine’s EEG stimulatory effect in the rat (Kakuda et al., 2000). These reports suggested that it might be a caffeine antagonist. In addition, Collier (1974) noted that xanthones mimicked opioid withdrawal signs in rats. We found that caffeine (4.0-32.0 mg/kg, s.c.) elicited many opioid withdrawal signs in normal rhesus monkeys (Aceto et al., 1978). Thus, we speculated that L-theanine might attenuate opioid withdrawal signs and have anxiolytic properties. In morphine-dependent rhesus monkeys in withdrawal, L-theanine dose-dependently (1, 4 and 8 mg/kg, s.c) attenuated the number of withdrawal signs designated slowing, fighting, rigid abdominal muscles, vocalizing on palpation of abdomen, pacing, tremors, coughing, retching, vomiting and wet-dog shakes (Kruskal-Wallis ANOVA and Mann-Whitney comparisons, P < 0.05). It had a quick onset and its duration of action was at least 2½ hours. In the mouse, L-theanine dose-dependently produced anxiolytic-like effects in the elevated plus maze (One-way ANOVA, p = 0.004). Mice treated with 16 mg/kg, i.p. of L-theanine 60 min before testing in a 5 min session spent more time in the open arms (p < 0.01) than mice treated with vehicle. Additionally, mice traveled the same distance in the closed arm (p < 0.05) regardless of treatment indicating that changes in motor behavior did not account for the anxiolytic-like actions. L-theanine may be of use in the pharmacotherapy of opioid drug abuse and anxiety. These studies were approved by the University IACUC Committee and supported by NIH (NINDA) 7-8859, DA017259 and DA009789.

Down-regulation of beta-arrestin2 contributes to morphine tolerance in the gastrointestinal tract
H. I. Akbarali, M. Kang, H. Maguma, T.H. Smith, G.R. Ross and W.L. Dewey. Dept. of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA 23298, USA
Inhibition of gastrointestinal peristalsis is a major side-effect of chronic morphine that significantly limits its clinical utility. Morphine and other mu-receptor opioids reduce neurotransmitter release by presynaptic inhibition of excitatory and inhibitory enteric neurons. We have previously reported that repeated administration of morphine results in tolerance development in the ileum but not the colon, reflecting the lack of morphine-induced tolerance to constipation (Ross et al., JPET, 2008: 327, 561-72). In this study we examined the role of beta-arrestin2 in morphine-induced tolerance development in the ileum and colon. The longitudinal muscle-myenteric plexus (LMMP) preparations from guinea-pig ilea and colon were subject to electrical field stimulation (EFS). beta-arrestin2 and ERK 1/2 expression was determined by Western blots in LMMP and isolated enteric ganglia. Tolerance to morphine-induced inhibition of EFS was observed following 2 hour incubation (10 μM) in isolated ileum but not the colon in guinea-pig LMMP. The IC50 (LogM) significantly shifted to the right from 5.7 ± 0.08 to 5.45 ± 0.09 (n=9) (p<0.0001) in the ileum but not in the colon (5.43 ± 0.14 to 5.48 ± 0.17). A corresponding time-dependent down-regulation of beta-arrestin2 occurred in the ileum but not the colon LMMP and isolated enteric ganglia. Pretreatment with naloxone prevented the down-regulation of beta-arrestin2 in the ileum. In beta-arrestin2 knock-out mice, repeated administration of morphine resulted in tolerance to muscle contraction in both ileum and colon. These findings suggest that down-regulation of beta-arrestin2 by chronic administration of morphine is associated with development of tolerance in the ileum whereas genetic deletion of beta-arrestin2 is required to induce morphine tolerance in the colon. Supported by NIH DA024009.

Unexpected opioid activity profiles of analogs of the novel peptide kappa opioid receptor ligand CJ-15,208
The cyclic tetrapeptide natural product CJ-15,208 (cyclo[Phe-D-Pro-Phe-Trp]) is a novel kappa opioid receptor (KOR) antagonist (Saito et al., J. Antibiot.
An alanine scan was performed on CJ-15,208 to determine which residues contribute to the potent in vivo agonist activity observed for the parent peptide. These cyclic tetrapeptides were synthesized by a combination of solid phase peptide synthesis of the linear precursors, followed by cyclization in solution. One alanine substituted analog exhibited higher KOR affinity than the parent peptide in binding assays, while the other analogs had much lower KOR affinities. Also like the parent peptide, each of the analogs exhibited agonist activity and KOR antagonist activity in the 55 degree C warm-water tail-withdrawal assay in vivo after intracerebroventricular (i.c.v.) administration. Unlike the parent peptide, the agonist activity of these analogs was predominantly mediated by mu opioid receptors, with agonist potency (ED50 (95% confidence intervals)) varying from 0.1 (0.03-0.35) to 7.0 (1.0-47.4) nmol compared to 1.7 (0.6-4.8) nmol for the parent peptide. The two analogs in which one of the phenylalanine residues was replaced by alanine exhibited both potent agonist activity and KOR antagonist activity in vivo. These peptides represent novel lead compounds for the development of peptide-based opioid analgesics. Research supported by grants R01 DA018832 and R01 DA023924.

Using an operant orofacial assay to measure the analgesic effects of morphine and the hyperalgesic effects of withdrawal

E. M. Anderson (2) and R. M. Caudle (1,2). (1) Department of Oral Surgery, University of Florida, Gainesville, FL, USA (2) Department of Neuroscience University of Florida College of Medicine, Gainesville, FL, USA

A divergence exists between methods of measuring the effects of opioids in animals and in humans. In rodents, morphine analgesia and tolerance are generally measured with reflex-based procedures. Humans on the other hand are simply asked how much pain they feel. We present a procedure that allows an animal to report how opioids affect its pain. This is a reward/conflict assay which forces an animal to endure an aversive stimulus in order to receive a reward. A rat’s adjustment of its behavior in this assay gives us a measure of their response to opioids.

Fasted hairless rats were trained to press their faces into two heated aluminum tubes in order to be able to receive a reward of diluted sweetened condensed milk. Sensors were attached to the tubes and feeding bottle so that each time a rat made contact with either a recording was made. After training at a non-aversive 37°C the temperature was changed to an aversive 46°C and rats were tested for a baseline reading. Rats were then injected twice daily with 10mg/kg of morphine and tested every 2-3 days at 46°C. After 10 days injections were ceased and rats were tested through withdrawal. Data was analyzed by taking the number of licks and dividing it by the amount of facial contact time. Aversive temperatures of 46°C caused the ratio of licks per contact to decrease from the values taken at 37°C. Morphine reversed this effect and caused the ratio to increase significantly, demonstrating analgesia. This ratio decreased over the 10 days of injections due to tolerance. The ratio then dropped below baseline during withdrawal, demonstrating hyperalgesia. This assay may allow a more accurate measure of the effects of opioids in rodents than reflexive measures of pain as the animal is essentially reporting to us the amount of pain it can withstand. Funding for this project was provided by the NIDA. DA030044

Acute Tolerance to Etorphine and Morphine Dependence in MOPr Phosphorylation Deficient Mice

E. Barbier, J.B. Wang. Dept. of Pharmaceutical Sciences, Univ. of Maryland-Sch. of Pharmacy, Baltimore, USA.

Mu opioid receptor (MOPr) phosphorylation is a key event in the receptor internalization and desensitization in vitro, which underlie the development of tolerance and dependence induced by opioid treatment in vivo. Using the MOPr – T394A phosphorylation deficient (PD) knockin mice we previously reported that compared with their wild type (WT) littermate controls the MOPr-PD mice did not develop tolerance to the analgesic effect of acute morphine treatment, this was paralleled with reduced etorphine-induced internalization at the spinal cord level. In the present study we assessed the contribution of the T394 phosphorylation site in the development of acute tolerance to etorphine analgesia and in the development of naloxone-precipitated morphine withdrawal. We describe the development of acute tolerance to etorphine analgesia in WT mice submitted to the hot plate test in a paradigm of two administrations of etorphine separated by a three hours interval. Under the same conditions MOPr-PD mice did not display any tolerance. The preliminary study of cumulative dose-response effect of naloxone in chronically morphine treated mice revealed a higher frequency of physical signs of withdrawal in MOPr-PD mice compared with their WT littermates. These behavioral studies suggest that phosphorylation of the MOPr at the T394 site is a crucial mechanism in the development of acute tolerance to the analgesic effect of opioid and a key point in the development of morphine dependence. Supported by NIH grant DA011925 to JBW.
Activation of spinal Mu and Delta opioid receptors potently inhibits substance P release induced by peripheral noxious stimuli

H. Beaudry, D. Dubois and L. Gendron, Université de Sherbrooke, Canada

Over the past few years, delta (DOPR) and mu (MOPR) opioid receptors were shown to interact with each other. We have previously observed that expression of MOPR was essential for morphine and inflammation to potentiate the analgesic properties of selective DOPR agonists. In vivo, it is not clear if MOPR and DOPR are expressed in the same neurons. Indeed, it was recently proposed that these receptors are segregated in different populations of nociceptors, with MOPR and DOPR being respectively expressed by peptidergic and non-peptidergic fibers. In the present study, the role and the effects of DOPR and MOPR selective agonists in two different pain models were compared. Using PPTA-/- mice, we first confirmed that substance P partly mediates intraplantar formalin- and capsaicin-induced pain behaviors. In these mice, we found a significant reduction in pain behaviors when compared to PPTA+/- mice. We then measured the effects of intrathecal deltorphin II (DOPR agonist) and DAMGO (MOPR agonist) on pain-like behaviors, neuronal activation and substance P release following formalin and capsaicin injection. We found that both agonists were able to decrease formalin- and capsaicin-induced pain, an effect that was correlated with a reduction in the number of c-fos positive neurons in the superficial laminae of the lumbar spinal cord. Finally, visualization of NK1 internalization revealed that DOPR and MOPR activation strongly reduced formalin- and capsaicin-induced substance P release via a direct action on primary afferent fibers. Taken together, our results indicate that functional MOPR and DOPR are both expressed by peptidergic nociceptors. Supported by CIHR, NSERC and FRSQ

The superoxide-generating enzyme NADPH oxidase is required for the normal expression of opioid addictive behaviors

M. A. Beckerman (1), M. J. Glass (1, 2), (1) Department of Neurology and Neuroscience, and (2) Graduate Program in Neuroscience, Weill Cornell Medical College, New York, NY 10065, USA

Identifying novel signaling pathways that contribute to the development and persistence of drug-related neural plasticity is critical for elucidating the mechanisms of opioid addiction. Although reactive oxygen species (ROS) like superoxide have traditionally been viewed as deleterious byproducts of cellular metabolism, they have more recently been established to be important signaling molecules generated by specific and highly regulated enzymes in a variety of cell-types. There is also emerging evidence that ROS play important roles in neural processes critical to addiction, including the modulation of dopamine, glutamate, and G-protein-coupled receptor signaling, in addition to synaptic plasticity, learning, and memory. However, there is little direct evidence that specific ROS-generating enzymes are involved in opioid addiction. We provide evidence that the superoxide-producing enzyme NADPH oxidase (NOX) plays a role in the normal expression of opioid addictive behaviors. Mice with a constitutive knockout of the catalytic Nox2 NOX subunit show alterations in opioid dependence and reward behaviors, as well as patterns of neural activity associated with opioid use. These findings demonstrate that a specific ROS-producing enzyme plays a critical role in opioid addictive behaviors; this information may enhance our understanding of opioid addiction by identifying novel free radical-mediated intracellular signaling pathways involved in opioid plasticity and provide new targets for the development of future addiction treatments. Supported by: DA-016735, DA-024030 (MJG)

Kinetics of fluorescent opioid ligand binding to the mu opioid receptor

W. Birdsong (1), S. Arttamangkul (1), K. Rice (2), J. Williams (1), (1) Vollum Institute, Oregon Health & Science University, Portland, OR, USA, (2) National Institute on Drug Abuse, Bethesda, MD, USA

In intact cells, opioid receptor function is often inferred from the activity of downstream effectors. Fluorescent ligands provide a tool for examining opioid receptor function at the receptor level directly. Here we use confocal microscopy and rapid solution exchange to characterize the binding kinetics of a previously described opioid peptide as well as novel fluorescent derivatives of an alkaloid agonist and antagonist. We have found that fluorescent conjugates of the opioid peptide dermorphin bind to FLAG tagged mu opioid receptors in a specific and reversible manner with affinity ranging from 20 to 100 nM in intact cells under physiological conditions. The affinity of dermorphin conjugated to alexa488 measured using kinetic binding in intact cells is at least 10 fold lower than that previously measured using competition radioligand binding assays of solubilized membranes. Fluorescent conjugates of the alkaloid agonist oxymorphone display variable affinity and potency depending on the identity of the attached fluorophore. Fluorescent naltrexamine maintains antagonist activity and binds with an affinity of approximately 50nM. Interestingly, naltrexamine derivatives unbind with a time constant of 1-3 minutes while dermorphin and oxymorphine unbind much more rapidly with time constants ranging from 5-30 seconds. Interestingly, the rate of unbinding of all ligands was dependent on...
the length of agonist application suggesting that binding is not a simple first order process. In summary, we present data examining the kinetics of binding of functional fluorescent derivatives of an opioid peptide—dermorphin, a morphine-like agonist—oxymorphine, and an antagonist—naltrexamine. Supported by DA08163, DA026617 (JT) and DA007262-18 (WT).

**Csnk1e is a genetic regulator of sensitivity to psychostimulants and opioids**


1Department of Human Genetics, University of Chicago, Chicago, IL USA, 2Department of Psychiatry and Behavioral Neuroscience, University of Chicago, Chicago, IL USA, 3Center for Sleep and Circadian Biology, Northwestern University, Evanston, IL USA, 4Department of Neurobiology and Physiology, Northwestern University, Evanston, IL USA

Recent evidence suggests that Csnk1e, the gene encoding casein kinase 1-epsilon, modulates sensitivity to amphetamines in mice and humans. Additionally, a CSNK1E genetic variant is associated with heroin addiction, suggesting that it may also regulate opioid sensitivity. In this study, we used both a forward and reverse genetics strategy to test the hypothesis that Csnk1e is a genetic regulator of sensitivity to psychostimulants and opioids. Reciprocal congenic lines of C57BL/6J (B6) and DBA/2J (D2) origin capturing Csnk1e were phenotyped for methamphetamine (MA) and opioid sensitivity. We also tested the phenotypic consequence of a Csnk1e-null or tau mutation. B6.D2Csnk1e mice carrying a 4.63 cM introgressed region of D2 origin (78-86.8 Mb) on a B6 background showed an increase in MA sensitivity whereas D2.B6Csnk1e mice carrying a 0.55 cM introgressed region of B6 origin (78.7-81.6 Mb, Csnk1e = 79.2 Mb) on a D2 background showed a decrease. Interestingly, B6.D2Csnk1e mice were also more sensitive to the locomotor stimulant of fentanyl. Mice harboring a null Csnk1e mutation showed an increase in MA sensitivity whereas mice harboring the tau mutation showed a decrease in MA sensitivity. Mirroring the knockout results, the new selective Csnk1e inhibitor PF-4800567 increased the locomotor response to both MA and fentanyl. These results provide selective genetic and pharmacological evidence that Csnk1e regulates sensitivity to two distinct classes of abused drugs. We are currently testing the effect of PF-4800567 in Csnk1e knockout mice in order to demonstrate pharmacological specificity and examining Csnk1e gene expression differences in the congenic lines.

**Interactions between cortical cannabinoid and opioid receptors during neuropathic pain**

I. Bushlin, A. Gupta, L. K. Miller, S. D. Stockton Jr., and L. A. Devi, Dept. of Pharmacology and Systems Therapeutics, Mount Sinai School of Medicine, New York, New York, USA

The expression and function of opioid and cannabinoid receptors are altered during neuropathic pain. Most studies thus far have examined changes in these receptors in peripheral sensory neurons (primary afferents and DRGs) and in spinal cord, as peripheral sensory signals are initiated through these circuits. However, neuropathic pain is also associated with neuroplastic changes in supraspinal brain regions, leading to enhanced anxiety, altered impulse control, and activation of descending analgesia. Exogenous activation of supraspinal opioid and cannabinoid receptors is known to lead to reduced anxiety and antinociception, however alterations in the expression and function of these receptors during a neuropathic pain state have not been well explored. We examined changes in the expression, function and interaction of these receptors in the cerebral cortex of rats experiencing neuropathic pain. We find that the expression of cannabinoid type 1 receptor (CB1R) and delta opioid receptor (DOR) are increased in the cortex of lesioned animals; however, while CB1R activity is increased, DOR activity is decreased. We hypothesized that this decrease could be due to interactions between these two receptors; this is based on previous in vitro experiments that had shown inhibitory interactions between CB1R and DOR. We tested this by examining allosteric modulation of DOR activity by CB1R ligands and determining if alterations in DOR activity could be blocked by a CB1R-DOR heteromer-specific antibody. We find that in cortical membranes from neuropathic animals, low, non-signaling doses of CB1R ligands significantly enhance DOR activity and this is selectively blocked by the heteromer-specific antibody. Together, these studies support a role for CB1R-DOR heteromers in altered cortical function of DOR during neuropathic pain. Supported by NIH grants DA08863 and DA19521 to L.A.D.

**In vivo modulation the behavioral effects of the kappa-opioid hallucinogen salvinorin A by p-glycoprotein ligands**

E.R. Butelman, S. Rus, K. Lovell, T.E. Prisinzano, and M.J. Kreek

1The Rockefeller University; New York NY USA, 2Dept. of Medicinal Chemistry, University of Kansas, Lawrence KS USA

Salvinorin A is a kappa-agonist hallucinogen from the plant Salvia divinorum. Salvinorin A – based products are widely available in shops and on the internet. While there is little population-based data,
there appear to be variable responses to self-administration of salvinorin A-based products in humans. A recent in vitro study reported that salvinorin A was a potential substrate for the multidrug resistance blood-brain barrier efflux transporter, p-glycoprotein (Teksin et al., 2009; Eur J Pharm Biopharm 72:471-477). It may thus be hypothesized that the functional status of the p-glycoprotein transporter influences the effects of salvinorin A in vivo. Unconditioned behavioral effects (ptosis and facial relaxation) of i.v. salvinorin A (0.01 mg/kg) were studied in rhesus monkeys (n=4). Salvinorin A alone (0.01 mg/kg; n=4) produced moderate, time-dependent, ptosis (eye closure) and facial relaxation, similar to other centrally penetrating kappa-opioid agonists. Pretreatment with the clinically available p-glycoprotein substrate loperamide, which is a peripherally-selective mu-opioid agonist (0.032-0.32 mg/kg, i.v. 5 min pretreatment), resulted in a dose-and time-dependent enhancement in the effects of salvinorin A on ptosis, but not on facial relaxation. In a second experiment, the p-glycoprotein blocker tariquidar (0.32-3.2 mg/kg; 30 min pretreatment) also enhanced the effects of salvinorin A on ptosis, but less so on facial relaxation. Overall, these studies are consistent with the hypothesis that centrally mediated effects of salvinorin A are modulated by functional status of the p-glycoprotein transporter. These studies suggest that variability in the incidence and severity of salvinorin A effects may thus differ in individuals due to pre-existing (e.g., genetic) variation in p-glycoprotein function, or due to concurrent medications. We gratefully acknowledge funding by NIH-NIDA grants DA017369 (ERB), DA018151, and DA05130 (MJK).

Morphine-induced hyperalgesia is associated with AMPAR trafficking in the dorsal horn of the spinal cord

D. Cabañero1, Y. Xia1, A. Baker2, S. Zhou2, S. M. Carlton2, J. Morón-Concepción1. 1Anesthesiol. Dept., Columbia Univ. Med. Center, New York, USA, 2Dept. of Neurosci. and Cell Bio., UTMB, Galveston, USA

Repeated morphine administration promotes the insertion of calcium permeable, GluR2-lacking AMPAR in hippocampal synapses (Billa SK et al, 2010). We find that the same treatment elicits cold and mechanical sensitivity (lasting 12 hrs and one week, respectively), which could be mediated by an increase in GluR2-lacking AMPAR in the spinal cord. In this work, we examine the effects of morphine on AMPAR subunit expression in the dorsal horns of the spinal cord. C57BL/6 mice received saline or four escalating doses of morphine (5, 8, 10 and 15 mg/kg i.p.) administered at 12 hrs intervals, and were sacrificed 12 hrs or one week after the last injection. Using western blotting, expression levels of GluR1/2/3/4 and phosphorylation levels of GluR1/2/4 were determined in the homogenate (H) or in a fraction enriched in the postsynaptic density (PSD) from spinal cord dorsal horns. In order to examine changes in AMPAR subunit composition, GluR4 was co-immunoprecipitated (co-IP) with GluR2 and GluR3 in PSD samples. Twelve hours after morphine, GluR4, pGluR1 and pGluR2 levels significantly increased in the H; GluR4 and pGluR4 levels were also increased at the PSD. One week after treatment GluR4 and pGluR4 returned to normal levels, but pGluR1 and pGluR2 were still increased in the H of morphine-treated mice. The co-IP study showed a significant decrease in the proportion of GluR4-GluR2 heteromers 12 hrs after morphine. Our results suggest that morphine exposure induces a postsynaptic increase in GluR4 homomers, which could trigger an early enhancement in the excitability of projection neurons of the dorsal horn. Interestingly, cold and mechanical sensitivity correlate respectively with the increases in GluR4 and GluR1/2 phosphorylation. This is the first report describing morphine-induced changes in AMPAR trafficking at the spinal cord dorsal horn, a mechanism that could participate in morphine-induced hyperalgesia.

Supported by NIH DA027460 to JMC

The effect of mastitis and milk congestion on the levels of beta-casomorphin-8 in milk and plasma samples from puerperal women

A. Carlsson (1), L. Righard (2), F. Nyberg (1), (1)Department of Pharmaceutical Biosciences, Uppsala University, Uppsala, Sweden, (2)Department of Paediatrics, University hospital, Malmö, Lund University, Lund, Sweden

In addition to the classical opioids, which are mainly produced in the CNS, the so-called atypical opioid peptides have been identified and characterized. One of these is β-casomorphin, derived by partial hydrolysis of the milk protein β-casein. β-casomorphin was originally detected in bovine milk, and in subsequent studies β-casomorphin-8 (H-Tyr-Pro-Phe-Val-Glu-Pro-Ile-Pro-OH) – like immunoreactivity has been measured in human plasma, CSF and milk. Atypical opioid peptides share many effects typical for the classical opioids. In addition, the β-casomorphins have been suggested to be involved in the interplay between mother and child during lactation but also in the etiology of some psychiatric diseases. Studies have implicated increased levels of β-casomorphin-like peptides in postpartum psychosis, a rare but serious condition following birth. It has also been postulated that an underlying reason for postpartum psychosis is milk congestion. In this study we examined whether milk congestion may induce increased levels of β-
casomorphin-8 in milk and in plasma from puerperal women. Milk and blood samples from fourteen women with mastitis were collected during the acute phase and after 2-3 weeks, when the symptoms had disappeared. Samples from ten women without problems served as controls. The samples were purified and analyzed for β-casomorphin-8-like immunoreactivity using radioimmunoassay. The results demonstrate a significant increase in β-casomorphin-8-like immunoreactivity in milk samples from women with mastitis in the acute phase compared to controls. After recovery from the mastitis, the β-casomorphin-8-like immunoreactivity was restored to levels of control subjects. No significant difference, although a tendency, was seen in the plasma samples. This result suggests that β-casomorphin may be of importance in the development of mastitis. This study was supported by the Swedish Medical Research Council (Grant 9459).

Antinociceptive effects of NOP receptor agonists, nociceptin, Ro 64-6198 and (+)-5a Compound, given by intra-periaqueductal gray injection

L.-C. Chiou (1, 2, 3, 4), H.-J. Lee (1, 3) and Y.-Y. Liao (2), (1) Dept. Pharmacology, Coll. Medicine, (2) Grad. Inst. Pharmacology and (3) Zoology, National Taiwan University, Taipei, Taiwan

We previously showed that the functional heterogeneity of nociceptin/orphanin FQ (N/OFQ) peptide (NOP) receptors in ventrolateral periaqueductal gray (vlPAG) slices can be revealed by two non-peptide agonists of NOP receptors, Ro 64-6198 (Ro) (Chiou et al., J. Pharmacol. Exp. Ther. 2004) and (+)-5a Compound (5a) (Liao et al., Int. J. Neuropsychopharmacol. 2010). Both compounds activated K+ channels via one, and the same, subset of NOP receptors in vlPAG neurons while N/OFQ was effective in those Ro/5a-insensitive NOP receptors. Interestingly, most of 5a-sensitive neurons are GABAergic. The vlPAG is enriched with intrinsic GABAergic tone and inhibition of this tone via K+ channel activation can lead to analgesia. We, therefore, examined if Ro and 5a given by intravlPAG (i.vlPAG) injection would be antinociceptive in the mouse hot-plate test. Indeed, i.vlPAG injection of 5a (30-100 nmol) and Ro (30 nmol) increased paw withdrawal latency in the hot-plate test. These antinociceptive effects of 5a and Ro were markedly antagonized by i.vlPAG UFP-101 (10 nmol), a NOP receptor antagonist, but was also partially reversed by i.vlPAG naloxone (5 nmol). Surprisingly, i.vlPAG N/OFQ (1 nmol) was also antinociceptive. Its antinociceptive effect was effectively blocked by i.vlPAG UFP-101, and also partially reversed by i.vlPAG naloxone. UFP-101 and naloxone had not effect per se. Biphasic effects of i.c.v. N/OFQ have been reported in regulating pain, motor activity and learning memory. However, i.vlPAG N/OFQ only produced antinociceptive, but no pronociceptive, effect at the dose ranged from 0.01 to 3 nmol. These results suggest that activation of NOP receptors in the vlPAG, instead of hyperalgesia, results in analgesia via a mechanism partly mediated by endogenous opioids. (Supported by grants NHRI-EX99-9506NI, NSC-98-2320-B-002-011-MY3, NSC-98-2323-B002-012 and NTU-99R81855).

Prolonged stimulation of μ-opioid receptors in locus coeruleus neurons induces β-arrestin-2-dependent heterologous desensitization of α2-adrenoceptors

M.J. Christie(1), B.Chieng(1), V.C. Dang(2), (1)Brain & Mind Research Inst. U. Sydney Australia. (2) Dept Psychiat UCSF, CA 94158, USA

Profound desensitization of μ-receptors (MOR) develops during exposure of locus coeruleus (LC) neurons to high concentrations of met-enkephalin or DAMGO for up to 5 min. At this time the efficacy of coupling of other GPCRs such as the α2-adrenoceptor (α2-AR) to activation of GIRK is little affected, ie. MOR desensitization is largely homologous. More prolonged activation of MOR produced greater heterologous desensitization of α2-ARs in mouse LC. Heterologous desensitization also reversed more slowly than homologous desensitization. Although homologous desensitization of MOR persisted in LC neurons from β-arrestin-2 (βarr2) k.o. mice (Dang et al. 2009, J Neurosci. 29:3322-7), heterologous desensitization of α2-AR was ablated. In wild type mice, heterologous desensitization of the α2-AR was blocked by intracellular application of GRK2 but not dynamin inhibitors, suggesting that βarr2 binding to MOR is required but endocytosis is not necessary. Heterologous desensitization was also blocked in wild types by ERK (U0126) and cSRC (PP2) inhibition, suggesting a βarr2-ERK1/2-cSRC-mediated mechanism. This mechanism may be physiologically significant because the adrenergic inhibitory post-synaptic current in LC neurons was also heterologously depressed after met-enkephalin exposure in wild type but not βarr2 knockout mice. Together, these findings demonstrate a novel mechanism by which βarr2 regulates neuronal responsiveness to endogenous neurotransmitter release after exposure to high concentrations of opioids that mobilize βarr2. Supported by the National Health & Medical Research Council of Australia
ALKS 33, a novel opioid receptor modulator, attenuates cocaine-induced increases in extracellular DA concentrations and cocaine self-administration in rats

J.I. Cunningham$^1$, M.S. Todtenkopf$^1$, R.L. Dean$^1$, M.R. Azar$^2$, G. Koob$^3$, D.R. Deaver$^1$, D.J. Eyerman$^1$

$^1$Alkermes, Inc., Waltham, MA, $^2$Behavioral Pharma, Inc., La Jolla, CA, $^3$The Scripps Research Institute, La Jolla, CA, USA

Cocaine increases extracellular concentrations of dopamine (DA$_{ext}$) in the nucleus accumbens shell (NAc-sh). In addition, opioid receptor agonists and antagonists have been found to alter cellular and behavioral responses to cocaine. We had two objectives: 1) to compare the ability of ALKS 33, a mu receptor antagonist with partial agonist/antagonist activity at delta and kappa receptors, and naltrexone (NTX) to inhibit cocaine-induced elevations in NAc-sh DA$_{ext}$ when given by the subcutaneous (SC) and oral (PO) routes; and 2) to determine if ALKS 33 would inhibit cocaine self-administration in a fixed ratio 1 (FR1) or progressive ratio (PR) schedule of reinforcement. In the first experiment, in-vivo microdialysis was performed in rats (n=5-6 per group) with probes inserted into the NAc-sh. Dialysate samples were collected during baseline and for 3 hrs post-drug administration. Cocaine (5 mg/kg, IP) caused an approx. 300-350% increase from baseline in NAc-sh DA$_{ext}$. SC administration (1 mg/kg) of NTX 30 minutes prior to cocaine significantly (P<0.05) attenuated increases in DA$_{ext}$, but no reduction was observed when NTX was given orally (10 mg/kg). Importantly, regardless of the route of administration, ALKS 33 significantly (P<0.05) attenuated cocaine-induced increases in NAc-sh DA$_{ext}$ (1 mg/kg, SC or 10 mg/kg, PO). In the second experiment, treatment with ALKS 33 (1 mg/kg, SC) did not significantly alter self-administration in the FR1 paradigm in rats (n=9-10 per group) trained to self-administer cocaine (0.5 mg/kg/inf, IV). However, in the PR paradigm, ALKS 33 had a marked effect on cocaine self-administration; rats in the control group reached a break point of 62, whereas in rats treated with ALKS 33 the break point was 18 (p<0.005). The combined neurochemistry and self-administration results suggest that ALKS 33 might be an effective treatment for cocaine dependency. All work funded by Alkermes, Inc.

Using the transitive inference task to study the relational memory deficits associated with withdrawal from chronic nicotine in the C57BL/6 mouse

K.A. Cordero, R. C. Cassells, T. J. Gould, Dept. of Psychology, Neuroscience Program, Temple University, Philadelphia, PA, USA

Nicotine and opioid abuse show high comorbidity. This is the first in a series of experiments to investigate this relationship. The present study explored the effects of withdrawal from chronic nicotine on relational learning and memory by utilizing the transitive inference task (TI). TI is a form of relational memory characterized by the ability to infer that B is more likely to be rewarded than D after directly learning the following hierarchy: (A>B), (B>C), (C>D), and (D>E). Preference is also calculated for a novel control pair (A vs. E) which does not entail inference because (A) is always rewarded and (E) is never rewarded. During chronic administration of nicotine or saline, administered via osmotic minipumps implanted subcutaneously (SC), mice were tested on days 14 and 15 for their initial preference for the novel TI pair (B vs. D) and the novel control (A vs. E). Preliminary data indicate C57L/6 mice exhibit an enhanced preference for B over D during chronic nicotine administration (12mg/kg/day). To determine the effect of withdrawal from chronic nicotine on this task osmotic minipumps were removed to terminate nicotine treatment and the same animals were tested again at 24 and 48 hours for TI pair preference (B vs. D) and the control pair (A vs. E). Preliminary data indicate withdrawal produces cognitive deficits as exemplified by a decreased preference for the TI pair (B vs. D), but not the control pair (A vs. E). This study is the first to demonstrate that withdrawal from chronic nicotine impairs relational memory, whereas chronic nicotine enhances inferential memory in the same animal. Follow up experiments involving transitivity in mice can further explore the relationship between nicotine and opioid dependence. It has previously been demonstrated that smoking rates are positively correlated with heroin abuse. These findings could help in developing better substance abuse treatment programs for individuals suffering from multiple addictions. Supported by NIDA Grants DA024687 and DA017949
Investigation on DNA methylation status of opioid peptides promoters in PBMCs of subjects with bipolar disorder

C. D’Addario,1,3 M. Di Benedetto1, B. Dell’Ossò2, S. Bastias Candia1, F. Cortini1, D. Galimberti1, E. Scarpini1, S. Candeletti1, M. Maccarrone1, A.C. Altamura2 and P. Romualdi1, 1Dept of Pharmacology, University of Bologna, Bologna, 2Dept of Psychiatry, University of Milan and 3Dept of Neurological Sciences, University of Milan, Milano, Italy

The pathophysiology of Bipolar Disorder (BD) has not been clearly established. Many evidences support the hypothesis, in addition to dopamine and serotonin, of a role for the endogenous opioid peptides, in particular dynorphin and nociceptin, whose levels have already been found to be affected in psychotic illness. It has been already proposed that altered expression of multiple mRNAs in psychotic subjects may be due to epigenetic mechanisms, thus we investigated dysregulation of DNA methylation in peripheral blood samples of subjects with BD. DNA was isolated from PBMCs of patients diagnosed with BD either type I or II (according to DSM-IV criteria), and from healthy control. Peripheral blood samples are easily accessible and an useful peripheral marker and model of epigenetic gene regulation in the brain. Following bisulfite conversion of DNA samples, Real-Time Methylation Specific PCR was used for the quantification of the methylated promotors. The percentage of methylation was calculated by the 2-\(\Delta\Delta C_t\) method, where \(\Delta C_t = (C_{t,\text{Target}} - C_{t,\text{Myod}})_{\text{sample}} - (C_{t,\text{Target}} - C_{t,\text{Myod}})_{\text{reference}}\) fully methylated DNA and multiplying by 100 where Myod is the internal reference gene to control for input DNA. A selective increase in DNA methylation of dynorphin promoter region was observed in BD II patients (23 %; n = 26, p<0.05), but not in BD I (15 %; n = 35) compared to controls (16 %; n = 32). No significant differences were found in DNA methylation status of nociceptin promoter of both BD I and BD II subjects. Our preliminary findings, showing selective changes in dynorphin regulation by epigenetic mechanisms, provide new insight in the possible involvement of dynorphin in mediating susceptibility to neuropsychiatric diseases. Grants from PRIN (SC) and RFÖ (PR).

Orphanin FQ/Nociceptin activates Oct-2 in SH-SY5Y human neuroblastoma cells

C. L. Donica (1) and K. M. Standifer (2). (1) OK Center for Neuroscience, (2) Dept of Pharmaceutical Sciences, OUHSC, OKC, OK, USA

A natural reward pathway exists in the brain that provides an incentive to obtain different factors needed for survival, including food, water and reproduction. Activation of this pathway leads to increased dopamine transmission and positive reinforcement of these behaviors. Several abused substances, such as cocaine, ethanol, heroin and morphine hijack this pathway to produce positive reinforcement. These abused substances function, in part, by increasing tyrosine hydroxylase (TH) expression. TH is the rate-limiting enzyme in dopamine synthesis. Endogenous neuropeptide orphanin FQ/nociceptin (OFQ/N) modulates the
effects of abused substances, including a reduction in ethanol consumption as well as inhibition of alcohol-seeking behavior and inhibition of the rewarding properties of cocaine, yet it does not affect heroin-seeking behavior. We previously reported that OFQ/N inhibits chronic morphine-induced TH expression, with a simultaneous up-regulation of the transcription factor, Oct-2. Studies have shown that an Oct-2 binding site is located upstream of the TH promoter. To determine if OFQ/N modulates morphine-induced TH expression through Oct-2, SH-SY5Y human neuroblastoma cells were treated with OFQ/N in the presence and absence of morphine and assessed for changes in Oct-2 protein expression, nuclear accumulation and DNA binding. SiRNA is currently being used to confirm the effect of Oct-2 in this process. For the first time, we show that OFQ/N increases the protein expression, nuclear accumulation and the DNA binding of Oct-2 in a time-dependent manner, as determined by immunoblotting and electromobility shift assay. These studies are consistent with the hypothesis that OFQ/N inhibits morphine-induced TH expression in an Oct-2-dependent manner and will help elucidate the cellular mechanism(s) by which OFQ/N modulates the reward pathway. These studies were supported by DAO17380 and OCAST HR08-152.

Correlating MOR ligand induced receptor internalization with acute antinociceptive tolerance
C. Dooley, J. Mislerr, L. Li, K. Reilley, S. Eans and J. McLaughlin. Torrey Pines Institute for Molecular Studies, Port St. Lucie, Florida, USA
While many studies have been carried out in vitro on the relative propensity of MOR ligands to internalize, fewer have been carried out comparing internalization efficacy with induction of antinociceptive tolerance. To test the hypothesis that the inverse relationship between efficacy at internalization and induction of antinociceptive tolerance in vivo holds for diverse opioid structures (1), we examined three compounds with strong and three with poor MOR internalization efficacy in a mouse model of acute antinociceptive tolerance. We chose an acute model of opioid antinociceptive tolerance (2) as a starting point as it is less likely to be confounded by competing pathways and utilizes less material. Internalization efficacy was measured as fold increase in average particle number internalized (P.I.) using GFP-tagged mu-opioid receptors stably expressed in HEK293 cells. Antinociceptive tolerance was assessed by comparing dose response curves and ED50 values of tested compounds administered i.c.v with a second ED50 value generated from doses administered 8 hours later. Compounds with high efficacy for internalization did not produce the rightward shifts observed for the compounds lacking ability to internalize receptors. In conclusion the inverse correlation of efficacy at internalization and induction of tolerance in vivo seems a valid predictor of agonist-induced acute tolerance in this model.

<table>
<thead>
<tr>
<th></th>
<th>1st LD</th>
<th>2nd LD</th>
<th>+8h inj.</th>
</tr>
</thead>
<tbody>
<tr>
<td>P.I.</td>
<td></td>
<td></td>
<td>(+8h)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAMG</td>
<td>3.0</td>
<td>4.29</td>
<td>(2.02-7.30)</td>
</tr>
<tr>
<td>O</td>
<td>4.0</td>
<td>4.29</td>
<td>(0.69-9.30)</td>
</tr>
<tr>
<td>YmFG-</td>
<td>2.8</td>
<td>1.76</td>
<td>(0.87-3.56)</td>
</tr>
<tr>
<td>NH2</td>
<td>7.5</td>
<td>1.76</td>
<td>(10.4-3.56)</td>
</tr>
<tr>
<td>TPIMS6</td>
<td>2.0</td>
<td>0.68</td>
<td>(0.17-1.30)</td>
</tr>
<tr>
<td>32-4</td>
<td>9.0</td>
<td>0.68</td>
<td>(0.49-1.30)</td>
</tr>
<tr>
<td>Morphin</td>
<td>1.2</td>
<td>22.5</td>
<td>(1.13-61.9)</td>
</tr>
<tr>
<td>Ac-</td>
<td>1.0</td>
<td>15.7</td>
<td>(1.85-82.5)</td>
</tr>
<tr>
<td>Arf</td>
<td>4.8</td>
<td>3.0</td>
<td>(6.56-30.0)</td>
</tr>
<tr>
<td>Herkinor</td>
<td>1.0</td>
<td>23.6</td>
<td>(3.07-39.0)</td>
</tr>
<tr>
<td></td>
<td>0.9</td>
<td>23.6</td>
<td>(9.83-39.0)</td>
</tr>
</tbody>
</table>


Effects of A118G polymorphism and personality factors on HPA-axis response to metyrapone in normal volunteers
E. Ducat, B. Ray, M. Randesi, A. Ho and M.J.K. Kreek, Laboratory of the Biology of Addictive Disease, The Rockefeller University, New York, NY USA
We recently reported on our finding that the 118G variant of the mu-opioid receptor blunts the HPA-axis ACTH stress response to metyrapone challenge (Ducat et al, in press, Addiction Biology). This current study investigates the relationship between personality traits and stress hormone response differences. Healthy, normal subjects were recruited in our ongoing genetics studies at Rockefeller University. Subjects received medical and psychiatric evaluations during outpatient clinic visits. A subset of the subjects reported above completed the NEO-PI-R, a 240-item measure of the five factors of personality, the evening of admission to the Rockefeller University Hospital inpatient unit. On the test day, blood was sampled prior to administration of a standard dose of oral metyrapone,
2.25gm, up to 8 hrs afterward; plasma levels of ACTH and cortisol were assayed. Three time points were used in analyses of the ACTH response to metyrapone: time 0, 4hr and 8 hrs after administration. The data from 33 subjects who completed both the NEO-PI-R and metyrapone testing were analyzed; 22 with 118A genotype and 11 with 118G genotype. Subjects with the 118G genotype were found to score significantly higher (p<0.05) on the Agreeableness factor of the NEO-PI-R than subjects with the 118A prototype. While we found no significant correlation between A118G genotype and the factor of neuroticism, subjects with the 118G variant showed an inverse relationship of Neuroticism score with ACTH plasma levels 8 hrs following metyrapone stress challenge (r=0.617, p<0.05). This was not seen in subjects with the 118A prototype. This result provides preliminary evidence that discrete personality factors such as neuroticism, may interact with specific genetic variants to affect HPA-axis stress responsivity. NIH-NIDA P60-DA005130 (M.J.K.), RR ULIRR024143 (B.C.) and The Adelson Medical Research Foundation.


S.O. Eans (1), M.L. Ganno (1), J.V. Aldrich (2), J.P. McLaughlin (1), (1)Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL; (2)Dept. of Med. Chem., Univ. of Kansas, Lawrence, KS

Cyclic peptides are resistant to proteolytic cleavage, potentially preserving activity after systemic administration. When administered centrally, by the intracerebroventricular (i.c.v.) route, the cyclic tetrapeptide JVA-2802 produced a dose-dependent, KOR-selective antagonism that lasted less than 18 h. We hypothesized that the cyclic structure of JVA-2802 would reduce proteolytic cleavage, facilitating retention of KOR antagonist activity after systemic administration by the subcutaneous (s.c.) or per os (p.o., or oral) routes. Pretreatment with JVA-2802 by either route (1-10 mg/kg, s.c. or p.o.) dose-dependently antagonized the antinociception induced by the selective KOR agonist U50,488 (10 mg/kg, i.p.) in C57Bl/6j mice tested in the 55 degC warm water tail withdrawal assay. KOR antagonism lasted less than 6 and 18 h after p.o. or s.c. administration, respectively, of a maximally-effective (10 mg/kg) dose. Furthermore, mice pretreated orally for 3 h with JVA-2802 demonstrated a dose-dependent (10-60 mg/kg p.o.) antagonism of U50,488 administered centrally (100 nmol, i.c.v.), strongly suggesting orally administered JVA-2802 crosses the blood-brain barrier to antagonize KOR in the central nervous system. From this, we further hypothesized that oral administration of JVA-2802 would prevent reinstatement of cocaine-seeking behavior. Mice demonstrating cocaine-conditioned place preference (CPP) and subsequent extinction were pretreated daily with vehicle or JVA-2802 (60 mg/kg, p.o.), and exposed to repeated forced-swim stress or a single additional session of cocaine place conditioning. JVA-2802 prevented the stress-induced, but not cocaine-induced, reinstatement of cocaine-CPP, consistent with previous demonstrations with KOR antagonists. These data validate the use of modified, systemically active peptides such as JVA-2802 as potentially useful therapeutics. (Supported by the State of Florida and DA018832 & DA023924 from NIDA).

Social influences on morphine sensitivity in adolescent rodents

S. Eitan (1), S. R. Hofford (1), S. L. Cole (1), D. J. Evert (1), P.J. Wellman (1), (1) Behavioral and Cellular Neuroscience Program, Dept. of Psychology, Texas A&M University, College Station, Texas, USA

Social/peer influences are among the strongest predictors of adolescents’ drug use. Hence, we recently examined whether this phenomenon can also be modeled in rodents. Specifically, we examined how housing rodents with different social partners affected the subsequent activating (i.e. locomotion) and rewarding (i.e. conditioned place preference) properties of morphine. Both mice and rats were used in these studies. All animals were group-housed four per cage in one of two conditions. In the mixed treatment condition, morphine- and saline-treated animals were housed together (i.e. 2 rodents receiving morphine and 2 rodents receiving saline per cage). In the separated treatment conditions, all 4 animals in the cage received either morphine or saline, and cages were visually separated from each other. Animals were then individually examined for their responses to morphine. Our results demonstrate that housing with different social partners altered both the activating and rewarding properties of morphine (i.e. significant differences were found between animals treated identically but housed in the mixed versus separated conditions). Notably, in both mice and rats, the social effects on morphine sensitivity were prevalent among adolescents but were not observed in adults. Also, although the effects were observed in both species, the nature of the effect differed between mice and rats. This species-dependant difference seems to be due to the different effects of opioids on social contact and play in mice and rats. Thus, our results suggest that the quantity and quality of juvenile social contact and play (i.e. the nature of the ‘social network’ of adolescents) have an effect on both the activating and rewarding properties of morphine, and possibly of other drugs of abuse. Supported by NIH (DA022402 to SE and DA013188-07 to PJW).
Opioids block the effects of the HIV entry inhibitors Maraviroc and AMD-3100 in CNS glia
N. El-Hage, S. M. Dever, T. Ahmed, Y. Zhang, K. F. Hauser, Department of Pharmacology and Toxicology, Virginia Commonwealth University, Richmond, VA 23298, USA
There are currently 27 HIV medications used in various combinations to treat HIV and AIDS, including inhibitors of viral entry. Maraviroc is a CCR5 inhibitor used with other HIV medications to treat CCR5 (R5)-tropic HIV and AMD-3100, a CXCR4 antagonist, is used to reduce CXCR4 (X4)-tropic HIV levels. Since these two inhibitors have the ability to inhibit HIV entry in target cells and opioid abusers are more susceptible to the neurodegenerative effects of HIV in the CNS, the goal of this study was to investigate the impact of opioids such as morphine, widely abused drugs among people infected with HIV as well as DAMGO, on the inhibitory effects of Maraviroc and AMD-3100 on HIV entry in human microglia and astrocytes. We first confirmed that astrocytes and microglia express CCR5 and CXCR4 using flow cytometry. HIV binding and entry were directly visualized by confocal microscopy using GFP-labeled R5 (BaL) and X4 (NL4-3) virions and infection was further confirmed using a HIV Tat-activated luciferase reporter assay. As expected, we found that Maraviroc inhibited R5 HIV entry and reduced HIV infection levels by 95% in astrocytes and microglia. However, morphine and DAMGO treatment compromised the anti-HIV entry effects of Maraviroc leading to increased HIV levels in these cells. Similar results were found with opioids and AMD-3100 using X4 HIV. Our data suggest that opioids impair the effects of HIV entry inhibitors and may contribute to increased susceptibility of HIV entry in opioid abusers which could lead to accelerated CNS neuropathogenesis in these individuals.

Streptozotocin-induced type 1 diabetes impairs learning abilities in Barnes Maze and alters growth hormone receptor (GHR) but not prodynorphin (PDYN) mRNA expression in the prefrontal cortex of male mice
E. Enhamre, A. Carlsson, A. Grönladh, H. Watanabe, B.-M. Johansson, M. Hallberg, F. Nyberg, Department of Pharmaceutical Biosciences, Division of Biological Research on Drug Dependence, Uppsala University, Uppsala, Sweden
It is well known that chronic treatment with opiates and other drugs is associated with impaired cognitive abilities in humans as well as in rodents. By establishing a pathophysiological status of an impaired cognitive function, we here intend to simulate the negative effects of long-term opioid treatment in the brain. Previous studies report that experimental diabetes in rodents, induced by streptozotocin (STZ), is associated with a reduced neurogenesis in combination with an increased neuronal apoptosis in the hippocampus. These animals also display cognitive impairments in several learning and memory tasks. Male C57BL/6J mice were injected with STZ 150 mg/kg i.v. and the control group received saline in the same volume. On day 21 the learning and memory function of the animals were tested in the Barnes Maze (BM) for 5 consecutive days including a probe trial. The day after the probe trial the animals were decapitated and brain tissue dissected and frozen for further analysis.
RNA-preparation, cDNA synthesis and Taqman® real time PCR were conducted in order to measure the mRNA levels of prodynorphin (PDYN) and growth hormone receptor (GHR), both entities involved in cognition, in the prefrontal cortex of the animals. The results demonstrate a significant difference between diabetic animals and controls in their ability to locate the target hole in the BM. No significant differences were seen between the two groups in the probe trial. However, alterations in mRNA expression of GHR but not PDYN were seen in the prefrontal cortex of the diabetic mice. This study was supported by grants from the Swedish Medical Research Council (Grant 9459) and from Swedish Council for Working Life and Social Research.

Role of dynorphin/kappa opioid receptor in forced swim test behavior in rats
N.Z. Fang, Y. Zhou, S. Chen, B. Mayer-Blackwell, B. Reed, M.J. Kreek, Lab of the Biology of Addictive Diseases, Rockefeller University, NY, NY, USA
Antagonism of the kappa opioid receptor (KOR) has been reported to have anti-depressant-like properties. The dynorphin/KOR system is a crucial neurochemical substrate underlying the pathologies of addictive diseases and other disease states. However, the molecular underpinnings of the dysregulation of this system are not yet well understood. The aims of this study were: (1) to confirm if the selective KOR antagonist nor-binaltorphimine (nor-BNI) can have antidepressant-like effects in the forced swim test (FST); (2) to determine the extent of alteration of preprodynorphin (ppDyn) mRNA levels induced by FST; and (3) to elucidate other molecular mechanisms. Young adult male Sprague-Dawley rats were placed in a cylinder of water for 15 minute intervals. Immediately after the initial exposure, they were treated with vehicle or nor-BNI (5 or 10 mg/kg). One day after treatment, the rats were placed in the FST for five minutes and scored for immobility, swimming, and climbing. Nor-BNI increased climbing time (5 and 10 mg/kg both) and significantly reduced immobility (10 mg/kg only) in the FST, measures indicative of anti-depressant
activity. Rats were sacrificed under stress minimized conditions thirty minutes after the FST. Their brains were subsequently dissected. Several brain regions were analyzed, including: caudate-putamen, nucleus accumbens, hypothalamus, and amygdala. The regions were homogenized and the mRNA was isolated using Trizol. ppDyn mRNA levels were measured with real-time optical PCR and normalized to GAPDH mRNA. In comparison to control animals not exposed to FST, we observed a significant elevation in ppDyn mRNA levels following FST in the caudate-putamen but not in the nucleus accumbens, hypothalamus, and amygdala. In animals exposed to FST, nor-BNI treatment did not alter ppDyn mRNA levels in comparison to animals that received vehicle. Future studies will look at additional brain regions, additional gene expression levels, hormonal levels, and potential epigenetic mechanisms. Support: NIH-NIDA Grants P60-DA05130 (M.J.K.)

Interactions of gonadal steroids and acute stress on levels of phosphorylated mu opioid receptors in the rat hippocampus

K. L. Gonzales1, J. D. Chapleau1, D. Kelter1, J. P. Pierce1, T. J. Williams1, A. Torres-Reveron1,2, B. S. McEwen1, E. M. Waters1, T. A. Milner1, 1Dept. of Neurology/Neurosci. Weill Cornell Medical Col., NY, NY, USA, 2Lab of Neuroendocrin., Rockefeller Univ., NY, NY, USA, 3Col. of Pharm., Nova Southeastern University, Ponce Puerto Rico

Opioids play a critical role in hippocampally dependent behaviors and plasticity. In the hippocampal formation (HF), mu opioid receptors (MOR) are prominent in parvalbumin (PARV) containing interneurons. Previously we found that the trafficking of MORs in PARV interneurons is modulated by gonadal hormones (GH). Although sex differences in response to stress are well documented, the point at which opioids, sex and stress interact to influence HF function remains elusive. Thus, we used quantitative light and electron microscopic immunocytochemistry for the phosphorylated MOR (pMOR) in rats to assess these interactions. In both sexes, pMOR-immunoreactivity (ir) was prominent in axons and terminals in dentate gyrus (DG) hilus and CA3 stratum lucidum and in a few neurons, some of which contained PARV, in DG hilus. In unstressed rats, the levels of pMOR-ir in the DG or CA3 were not different between the sexes nor between females at any point in the estrous cycle. However, the levels of pMOR-ir following acute immobilization stress (AIS; 30 minute) were affected by sex and estrous cycle stage. In particular, males had higher levels of pMOR-ir following AIS whereas females at proestrus had lower levels of pMOR-ir within the DG. In contrast, the number and types of neuronal profiles with pMOR-ir were not altered by AIS in either sex. These data suggest that although GH do not alter levels of pMOR-ir in non-stressed animals, GH may alter the expression of pMOR, and ultimately the effects of opioids following AIS. These interactions may be the foundation for reported sex differences in hippocampally dependent behaviors in acutely stressed animals. NIH grants DA08259 & HL096571 (TAM), T32 DA007274(JDC), DK07313 (EMW), NS007080(BSM), MSTP grant GM07739(TJW)

Analgesic tolerance to high efficacy agonists but not to morphine is reversed in phosphorylation-deficient S375A mu-opioid receptor knockin mice

G. Grecsksch(1), A.-K. Imhof(2), C. Pierstorff(1), S. Just(2), C. Doll(2), A. Lupp(2), A. Becker(1), T. Koch(1), R. Stumm(2), V. Höllt(1) and S. Schulz(2)

(1)Institute of Pharmacology and Toxicology, University Hospital, Otto-von-Güericke-University Magdeburg, Germany (2)Institute of Pharmacology and Toxicology, University Hospital, Friedrich Schiller University Jena, Germany

Morphine is one of the most potent analgesic drugs. However, the utility of morphine in the management of chronic pain is limited by its rapid development of tolerance. Morphine exerts all of its pharmacological effects via the mu-opioid receptor. We have recently shown that mu-opioid receptor phosphorylation occurs in an agonist-selective manner. High efficacy agonists such as [D-Ala2-MePhe4-Gly-ol]enkephalin (DAMGO) or etonitazene stimulate the phosphorylation of both carboxyl-terminal threonine 370 (T370) and serine 375 (S375) with S375 being the primary site of phosphorylation. In contrast, morphine promotes the phosphorylation of S375 but fails to stimulate T370 phosphorylation. Here, we have assessed the contribution of S375 phosphorylation to the development of antinociceptive tolerance to mu-opioid receptor agonists with different efficacy. We show that S375 phosphorylation of the mu-opioid receptor occurs in vivo in intact mouse brain shortly and transiently after administration of both morphine and etonitazene. In knockin mice expressing the phosphorylation-deficient S375A mutant of the mu receptor, antinociceptive tolerance after repeated subcutaneous application of etonitazene or repeated intracerebroventricular application of DAMGO was strongly reduced. In contrast, tolerance to the antinociceptive effect of morphine was retained. Thus, tolerance to high- and low-efficacy agonists develops through two distinct pathways. Whereas tolerance induced by DAMGO or etonitazene requires agonist-driven phosphorylation of S375, the development of antinociceptive tolerance to morphine occurs independent of S375 phosphorylation. This study was supported by the Deutsche Forschungsgemeinschaft.
Prodynorphin gene expression in rats treated with ethanol and growth hormone
A. Grönbladh, J. Johansson, E. Enhams, B-M. Johansson, M. Hallberg, F. Nyberg. Division of Biological Research on Drug Dependence, Department of Pharmaceutical Biosciences, Uppsala University, Uppsala, Sweden

Alcohol dependence is a neuropsychiatric disorder that may lead to severe consequences, cognitive impairment being one of them. Connections between alcohol dependence and the endogenous opioid system have been confirmed in several studies and ethanol has, in addition, been demonstrated to induce changes in the prodynorphin system. The prodynorphin system has been implicated in deficits in learning and memory and it has previously been demonstrated that dynorphins may impair spatial learning in rats. Growth hormone (GH), on the contrary, has been demonstrated to induce beneficial effects on memory and learning. Thus, GH might have an ability to counteract cognitive impairments that may occur in humans and other mammals in connection to alcohol dependence. In the present study, we investigated the effects on the prodynorphin gene expression and spatial learning and memory in rats after treatment with ethanol and GH. Male Wistar rats were treated once daily with ethanol (3.2 mg/kg) i.g and/or GH (1 IU/kg) s.c for six days. Controls were treated with water and saline. The Barnes maze, a circular platform with 18 holes, was used to test spatial learning and memory. Training sessions were performed with three trials per day for three days and a probe trial was conducted one day after the last training session. Three trials of reverse learning were performed one hour after the probe trial. The rats were then decapitated, brain tissues were dissected and immediately frozen. After RNA preparation and cDNA synthesis, quantitative real time PCR of prodynorphin was performed using a TaqMan® gene expression assay. Comparisons between ethanol and GH treated animals demonstrate a tendency of increased prodynorphin gene expression in the hippocampus after treatment with ethanol, a trend that seemed to be reduced in the presence of GH. Support: Swedish Medical Research Council (Grant 9459).

Antinociception of perineurally applied drugs via modulation of tight junction proteins in the perineurium
D. Hackel 1,2, S. Amasheh 4, S. Krug 4, S.A. Mousa 3, E.J. Wrede 1, M. Fromm 4, A. Brack 2, H.L. Rittner 2, 1Dept of Anaesthesiology, CBF, Charité–Berlin, Germany, 2Dept of Anaesthesiology, University hospital of Würzburg, Germany, 3Dept of Anaesthesiology, CCV, Charité – Berlin, Germany, 4Institute of Clinical Physiology, CBF, Charité – Berlin, Germany

During postoperative pain treatment regional anesthesia aims at specifically blocking the transmission of signals in nociceptors to prevent pain. Most widely used substances in clinical use are local anesthetics blocking sodium channels in all neurons with the effect of numbness from touch receptors and paralysis from block of motor neurons. Nav 1.7 blockers or hydrophilic opioids which target only nociceptors could not be used in vivo because they do not penetrate into the peripheral nerve. The peripheral nerve is surrounded by the perineurium composed of perineurial cells, special membrane proteins for active transport and tight junction proteins to limit paracellular permeability. Previously we showed that hypertonic solutions applied in the subcutaneous tissue increase permeability and facilitate peripheral opioid analgesia. We examined the possibility to facilitate nociceptor specific analgesia using perisciatic injection of hypertonic saline. This allowed for an increase in the mechanical pain threshold after injection of ProToxin II (Nav 1.7 blocker) or DAMGO or DPDPDE in rats. Furthermore we explored the downstream events to ultimately open tight junctions in the perineurium. We showed in rats a reversible and directed opening of the perineurial barrier via reduced expression of claudin-1 and under influence of metalloproteinase and its inhibitors. This presents a first step of the analysis of the molecular events following the perisciatic application of hypertonic saline to facilitate nociceptor specific analgesia. Our findings also put forward new targets for the specific and regulated opening of the perineurium for targeted drug delivery. This work was supported by the DFG (German Research Foundation) FOR 721.

Bivalent ligands for the characterization of opioid receptor heterodimers
J. Harvey (1, 2), R. van Rijn (1), P. England (2), J. L. Whistler (1, 2), 1Ernest Gallo Clinic and Research Center, Emeryville, CA, USA, (2) University of California, San Francisco, San Francisco, CA, USA

Several recent studies have suggested that a heteromer of the mu (MOR) and delta (DOR) opioid receptors could be a relevant target for the treatment of several indications including pain, anxiety and alcoholism. However, elucidating the functional role
of the MOR/DOR heteromer *in vivo* has been hindered by the lack of pharmacological agents that selectively activate or inactivate the MOR/DOR heteromer without affecting activity at the MOR and DOR homomers. We have designed and synthesized a series of novel “tuned-affinity” bivalent ligands to selectively target opioid receptor heteromers. Here we report the characteristics of these ligands *in vitro* and how we have used them to probe the role of receptor heteromers *in vivo*. J.H. is supported by the AP Gianini Foundation and a PBBR Fellowship. This work was supported by NIH grant 1R21DA031574 and funds provided by the State of California for medical research through the University of California San Francisco both to JLW and PE.

**Analysis of antinociceptive efficacy following microinjection of mu-opioid receptor agonists into the periaqueductal gray of the rat**

R.A. Haseman, E.N. Bobeck, S.L. Ingram, M.M. Morgan, Washington State University Vancouver, Vancouver WA, USA

The antinociceptive efficacy of mu-opioid receptor (MOPr) agonists is important in predicting receptor signaling. High efficacy agonists, such as fentanyl, produce limited tolerance, whereas low efficacy agonists such as morphine produce rapid tolerance. However, tolerance develops to repeated microinjections of fentanyl or DAMGO into the ventrolateral periaqueductal gray (vPAG) suggesting that fentanyl and DAMGO are not high efficacy MOPr agonists in the vPAG or that the inverse relationship between efficacy and tolerance does not hold true in the vPAG. To test these hypotheses, antinociceptive efficacy of morphine and fentanyl was determined using the irreversible MOPr antagonist, beta-funaltrexamine hydrochloride (Beta-FNA). Six hours after Beta-FNA (0, 0.1, 0.5, 5, or 10 microgram per 0.5 microliters) administration, cumulative doses of morphine or fentanyl were microinjected into the vPAG. Nociception was assessed after each MOPr agonist injection. Increasing doses of Beta-FNA caused a graded decrease in antinociception for both agonists. However, the decrease in fentanyl was enhanced compared to morphine using % maximum possible effect (%MPE), demonstrating that morphine has higher efficacy than fentanyl when injected into the vPAG. The comparison of morphine and fentanyl using % of analgesic animals, instead of %MPE, the agonists showed equal efficacy. These data are in contradiction with differences in efficacy following systemic administration. This study was supported by NIH grant DA 015498. Morphine sulfate was a gift from NIDA.

**Pharmacological functional magnetic resonance imaging analysis for pain research with understanding the mechanisms within the brain that provoke pain**


Functional magnetic resonance imaging analysis (fMRI) has been introduced to detect spatial as well as temporal brain activation following experimental pain induced by various stimuli. This technique allows us to characterize a network in the brain that forms a pain matrix. Pharmacological MRI (phMRI) is the combination of fMRI with drug administration. phMRI is a promising tool that may greatly contribute to our understanding of the mechanisms within the brain that provoke pain. Furthermore, it appears that this technology may be useful for identifying molecules and developing drugs for the modulation of pain in clinical practice. We are currently attempting to image pain processing, based on molecular mechanisms in animal models using phMRI. The inflammatory pain stimuli induced by intraplantar injection of complete Freund’s adjuvant caused robust positive signal activity in the cingulate cortex and somatosensory cortex. In contrast, these activations were diminished in prodynorphin knockout mice, indicating that the dynorphin A is responsible for the activation of these pain-related regions in the acute phase of inflammatory pain. The neuopathic pain-like stimuli induced by intrathecal injection of protein kinase C activator, phorbol 12,13-dibutyrate, caused a remarkable increase in the activity of the cingulate cortex and somatosensory cortex. Those activations were abolished in mice that lacked the PKCγ gene, suggesting that the activation of spinal PKCγ plays a role in direct acceleration of the ascending nociceptive pathway. There results suggest that phMRI is a powerful tool with a potential for high sensitivity and specificity for evaluating analgesics in early drug development and clinical studies.

**Opioid & alcohol pharmacodynamics:** Contributions of innate immune signaling to drug response

M.R. Hutchinson (1,2), Y. Wu (2), E.J. Jaehne (2), L. Liu (2), K.R. Diener (3), J.D. Hayball (3), K.C. Rice (4), L.R. Watkins (5), A.A. Somogyi (2), (1) Physiology, Univ of Adelaide, Adelaide, Australia; (2) Pharmacology, Univ of Adelaide, Adelaide, Australia; (3) School of Pharmacy & Medical Sciences, Univ of SA, Adelaide, Australia; (4) Chem
Bio Res Branch, NIDA & NIAAA, Rockville, MD, USA (5) Dept Psychology & the Center Neuroscience, Univ Colorado at Boulder, Boulder, Colorado, USA

Opioid & alcohol behavioral actions have classically been categorized as solely neuronal events. Recent discoveries have demonstrated that both opioid & alcohol activation of innate immune Toll Like Receptor 4 (TLR4) signaling also plays a critical role. However, the functional involvement of other TLRs & their signaling pathways remains to be determined. Given that both opioids & alcohol have TLR actions, this raises the possibility of a novel site of drug interaction that may contribute to their established synergistic interactions. The aim is to examine the impact of TLR signaling on opioid & alcohol action in mice. Acute (analgesia dose response) and chronic (analogic tolerance & withdrawal) morphine actions in male wild-type (WT) Balb/c mice, and mice with knockouts (KO) of TLR4, TLR2, TLR2/4, MYD88, TRIF or TIR8 were quantified. Acute alcohol actions (loss of righting reflex [LRR] & rotorod performance), & morphine & alcohol drug interaction (LRR) were examined in the first 4 KO mice strains. Acute morphine analgesia was potentiated by KO of TLR2 &/or TLR4 signaling compared to WT. Tolerance did not develop in TLR4 or TLR2/4 mice. Withdrawal was not significantly influenced by TLR signaling. Acute alcohol action was reduced by KO of TLR2 &/or TLR4 signaling. Interestingly, alcohol & morphine synergism was dependent on TLR2 & MyD88 signaling, but not TLR4. Opioid radioligand binding data from the KO mice will also be presented. These data highlight an important role that TLR signaling has in a broad range of opioid & alcohol actions individually & on their drug interactions. Supported by NIH DA015642, DA023132, DA024044, DE017782; NHMRC ID465423; ARC DP110100297

Novel analogs of endorphins provide antinociception without spatial and recognition memory deficits produced by morphine

J.N. Jernberg (1), X. Zhang (2), J.E. Zadina (1,2,3,4)
(1) Graduate Neuroscience Program, Dept. of (2) Medicine & (3) Pharmacology, Tulane Univ. Sch. of Med., (4) SE LA Veterans HCS, New Orleans, LA, USA

Currently opioids that activate the mu opioid receptor are considered the gold standard treatment for moderate to severe pain. Due to a variety of side effects, such as reward/addictive potential, motor impairment, respiratory depression, and cognitive dysfunction, physicians are often reluctant to implement opioid therapy. Endorphins and their analogs, however, have shown promise for producing potent antinociception with fewer adverse side-effects. The focus of this study is on cognitive effects of endorphin analogs relative to those of morphine in rats. Doses of the analogs were optimized to produce antinociception equal to or greater than that of morphine throughout the timeframe of the behavioral tests. The effects on spatial and recognition memory were examined using standard Morris water maze (MWM) and novel object recognition paradigms. Preliminary data demonstrates that an antinociceptive dose of morphine significantly impairs both spatial and recognition memory using measures that control for motor impairment. By contrast, novel endorphin analogs at doses producing equal or greater antinociception produce no significant cognitive impairments. In the MWM, morphine, but not endorphin analogs, impaired average swim speed as well as average distance from the platform, an index of spatial memory unaffected by swim speed. Morphine, but not the analogs, also impaired exploration of novel objects, an index of recognition memory. Studies of potential mechanisms of the differential antinociceptive/side effect profile are underway, and future studies will use similar methods to examine effects of acute and chronic opioids in an aging model. Since some side effects of opioid therapy are particularly serious in older adulthood, the results are anticipated to provide evidence that these novel endorphin analogs have reduced side effects that may translate to safer pain medications for older adults. Supported by the VA, ONR, and DOD.

Opioid withdrawal induced hyperalgesia is mediated in the peripheral nervous system via Transient Receptor Potential Vanilloid 1 (TRPV1)

J.A. Jira (1), V. Spahn (2), O. Fischer (2), C. Zöllner (1), (1) University Hospital Hamburg Eppendorf, Center for Anaesthesiology and Intensive Care Medicine, Hamburg, Germany, (2) Charité Berlin, CBF, Department of Anaesthesiology and Operative Intensive Care Medicine, Berlin, Germany

Vanilloid receptor type 1 (TRPV1) is a ligand-gated ion channel expressed in sensory neurons that responds to noxious heat, protons, and chemical stimuli such as capsaicin. TRPV1 plays a critical role in the development of pain after tissue injury, inflammation or nerve lesions and can be sensitized by phosphorylation. Opioid withdrawal following chronic activation of the mu-opiod receptor induces AC superactivation and subsequently an increase in cAMP and protein kinase A (PKA) activity. In the current project we investigated whether opioid withdrawal can increase TRPV1 activity in cells, animals and humans. Opioid withdrawal induces an increase of intracellular cAMP, resulting in phosphorylation and sensitization of TRPV1. In whole cell patch clamp and calcium imaging experiments opioid withdrawal significantly...
increased capsaicin-induced TRPV1 activity in a nalaxone and pertussis toxin sensitive manner. A decrease in paw withdrawal latency after peripheral opioid treatment was detected in male Wistar rats, indicating opioid induced hyperalgesia. Volunteers were enrolled in a randomized, double-blind, placebo-controlled study. Capsaicin stimulation induced acute pain and stable areas of mechanical hyperalgesia to pinprick stimuli and touch (allodynia). The magnitude of pain and area of hyperalgesia were assessed before, during, and after opioid infusion. Opioid treatment reduced pain and areas of mechanical hyperalgesia during infusion. In contrast, postinfusion pain and hyperalgesia were significantly higher than control. In summary, our results demonstrate that opioid withdrawal increases the activity of TRPV1. This mechanism is mediated via the PKA/cAMP pathway and delineates a new mechanism underlying hyperalgesia during opioid withdrawal. These projects are funded by the DFG (German Research Foundation).

The impact of long term GHB treatment on spatial learning in male rats
J. Johansson, A. Grönladh, F. Nyberg, M. Hallberg.
Dept Pharm Biosciences, Uppsala University, Sweden.
The illicit "club drug" gamma-hydroxy butyric acid (GHB), is usually abused for its euphoric and sedative effects, but it is also commonly used by body builders for its ability to increase lean muscle weight. In humans, GHB is known to induce short-term amnesia and disruption of memory and learning has been reported in animal studies. In this present study, we investigated the effects of repeated treatment with GHB on spatial learning and memory using the Morris water maze (MWM), and related neurochemical changes in the brain, including the endogenous opioids. Thus, the expression of the opioid receptors in brain areas related to cognition, such as hippocampus and frontal cortex is being considered. Adolescent male Sprague Dawley rats were orally administrated with 100 mg/kg and 300 mg/kg GHB or saline, daily during 16 consecutive days. Behavioral tests in the MWM were performed on day 10-15, one hour after administration. Data collected from biochemical analysis of opioid receptors using receptor autoradiography are compared with behavioral performance. Although, no significant difference in swim speed or percentage of time spent in the four different quadrants were detected, rats treated with the high dose of GHB required a significant longer time to find the hidden platform during acquisition. In the probe trial, the high-dose treatment group shows a tendency to spend shorter percentage time in the target quadrant and a longer latency in visiting target zone. This study was supported by SMRC, grant 9459.

Exploring bifunctional activity of 3-substituted piperidin-4-y1,3-dihydroindol-2-one class of NOP ligands at the mu-opioid receptor (MOP)
V. Journigan (1), W. Polgar (2), L. Toll (2), N. T. Zaveri (1), (1) Astraea Therapeutics, LLC, Mountain View, CA; (2) SRI International, Menlo Park, CA.
The nociceptin receptor (NOP/ORL-1) and its endogenous peptide N/OFQ play a significant role in the reward process and morphine abuse. N/OFQ administered i.c.v. decreases basal and morphine-stimulated dopamine release in the nucleus accumbens; moreover, this endogenous peptide blocks morphine-induced conditioned place preference (CPP). These results point to an “anti-opioid” role for N/OFQ agonism in reward. We hypothesize that bifunctional compounds with NOP full agonist activity and MOP partial agonist activity will result in analgesics with reduced dependence liability. In vivo studies of SR16835, a potent NOP agonist/MOP partial agonist developed in our laboratory, show attenuation of morphine-induced CPP when given prior to morphine, an effect that reverses upon treatment with selective NOP antagonist SB612111. In our laboratory, we have developed extensive structure-activity relationships (SAR) of our piperidin-4-y1,3-dihydroindol-2-one scaffold to produce potent NOP agonists. Interestingly, ethyl substitution at the 3-indolinone position of this scaffold resulted in increased MOP affinity while retaining potent NOP agonism. Our SAR also shows that substitution at the piperidine nitrogen with cyclic and aromatic-containing structures allows for modulation of MOP intrinsic activity while retaining the crucial NOP agonism/partial agonist component. The SAR and in vitro activity of these NOP/MOP bifunctional ligands will be presented. This work is supported by grant R01DA027811 (NZ).

Remifentanil exposure produces prolonged hyperalgesia under certain pain conditions but not morphine tolerance in rats
E. M. Jutkiewicz, Y. Sun, J. S. Schimmel, and J. R. Traynor, Department of Pharmacology, University of Michigan Medical School, University of Michigan Substance Abuse Research Center, University of Michigan, USA.
The mu-opioid receptor agonist remifentanil is infused intravenously (i.v.) during surgery and other procedures to promote anesthesia and/or analgesia and has been reported to increase postoperative pain and morphine requirements. The present study investigated the effects of 1 h continuous i.v. remifentanil administration to rats on noxious stimuli thresholds, antinociceptive doses of morphine, and opioid withdrawal signs. Rats were implanted with i.v. catheters and infused with remifentanil (0-320
Nicotine prevents neuropathic pain following peripheral nerve injury through the suppression of neuroinflammation.

S. Kishioka, N. Kiguchi, Y. Kobayashi, S. Tominaga, J. Nakamura, T. Maeda, Department of Pharmacology, Wakayama Medical University, Japan

Neuropathic pain is caused by peripheral nerve damage and is characterized by allodynia and hyperalgesia. Although growing evidence indicates that up-regulation of inflammatory mediators plays a crucial role in the pathogenesis of neuropathic pain, the detailed mechanisms are still unclear. It was reported that activation of nicotinic acetylcholine receptor (nAChR) on inflammatory cells improves inflammatory disease through the suppression of neuroinflammation. Therefore, we examined the role of nAChR in the nerve injury-induced neuropathic pain. Mice were given partial sciatic nerve ligation (PSL) under the pentobarbital anesthesia. PSL-induced tactile allodynia and thermal hyperalgesia were evaluated by von Frey test and Hargreaves test, respectively. Drugs were perineurally injected once a day for 4 days in a volume of 10 microliter under the pentobarbital anesthesia. PSL-operated mice showed long-lasting tactile allodynia and thermal hyperalgesia on the ipsilateral but not contralateral paws. By RT-PCR, up-regulation of pro-inflammatory cytokines (e.g., IL-1beta and TNFalpha) and chemokines (e.g., MIP-1alpha and MIP-1beta) were observed in the injured sciatic nerve (SCN) following PSL. By western blotting and immunohistochemistry, nAChR subunit alpha4 were increased in the injured SCN. PSL-induced tactile allodynia and thermal hyperalgesia were prevented by the early phase injection of nicotine (1-20 nmol, day0-3) in a dose-dependent manner. The preventive effects of nicotine were inhibited by the co-injection of dihydro-beta-erythroidine, a selective antagonist for alpha4. PSL-induced up-regulation of inflammatory mediators (IL-1beta, TNF-alpha, MIP-1alpha, and MIP-1beta) in the injured SCN on day7 was suppressed by nicotine. In conclusion, activation of nAChR in the peripheral nerves prevents the pathogenesis of neuropathic pain through the suppression of neuroinflammation. This work was supported by a grant from the Smoking Research Foundation.

Stimulation of the brain reward system attenuates the analgesic effects of the NMDA antagonist LY235959

C. M. Knapp (1), L. Tozier (1,2), S. Tapan (1), C. Kornetsky (1,2), (1) Division of Psychiatry and (2) Dept of Pharmacology, Boston University School of Medicine, Boston MA, USA

Morphine elevates the threshold for escape from noxious stimulation delivered to the mesencephalic reticular formation (MRF). This antinociceptive action is attenuated by the simultaneous delivery of low intensity stimulation to the medial forebrain (MFB). Stimulation of the MFB with moderate current intensities results in rewarding effects. MFB stimulation has also been found to potentiate the nociceptive effects of MRF stimulation. These effects of combined MRF –MFB stimulation resemble those of an opioid antagonist. In order to determine if these observed phenomena reflect the presence of an endogenous opioid antagonist our previous experiment was repeated substituting the putative analgesic agent LY235959 for morphine. LY235959 is a competitive N-methyl-D-aspartate (NMDA) receptor antagonist. In the present experiment two electrodes were implanted into each rat, one in the MFB and one in the MRF. After establishing that MFB stimulation resulted in rewarding effects, MRF thresholds were determined using a modification of the rate independent psychophysics method of limits. The administration of LY235959 (0.5, 1, and 2 mg/kg s.c.) produced a significant dose dependent elevation of the MRF-escape thresholds in the absence of MFB stimulation. In contrast, delivery of 5 or 10 µA’s of MFB stimulation concurrently with MRF stimulation produced a lowering of the escape-threshold significantly below control levels in animals treated with LY235959. These results indicate that LY
235959 may have anti-nociceptive effects at the supra-spinal level. They suggest that the anti-analgesic effects of combined MRF-MFB stimulation may not restricted to opioid analgesics and point to the possible presence of an endogenous anti-analgesic system. Supported in part by NIDA Grant 5R21DA-025586 to CK.

Selective interaction of G-protein coupled receptors with isoforms of ADP-ribosylation factor (ARF)

T. Koch, M. Rankovic, J. Konietzko, E. Kahl, and Volker Höllt, Dept. of Pharmacology and Toxicology, Otto-von-Guericke-University, Magdeburg, Germany

ARF1 and ARF6 are distinct members of the ADP-ribosylation factor (ARF) small-G-protein subfamily. ARF1 is mostly cytosolic, with minor locations at the Golgi and plasma membrane, whereas ARF6 is restricted to the plasma membrane. In previous studies we have demonstrated that the opioid-mediated and ADP-ribosylation factor (ARF)-dependent activation of phospholipase D2 (PLD2) is a prerequisite for MOPr endocytosis. By coexpressing the MOPr and dominant negative or constitutively active ARF mutants in human embryonic kidney (HEK) 293 cells and primary cultured cortical neurons as well as with the use of siRNA-technology, we identified the ARF6 protein to be involved in PLD2 activation and regulation of MOPr endocytosis. Remarkably, ARF6 is involved in the endocytosis and PLD2 activation of several but not all GPCRs. We demonstrate here, that the activation of PLD2 and the induction of the 5-HT$_{2A}$ receptor endocytosis is mediated via interaction with ARF1. A specific conserved motif, NPxxY, which is found at the junction of the tm7 and ct domains of many GPCRs, has been implicated as a determinant of ARF-receptor interactions and specificity. Therefore, in the present study we investigated the effect of the N332D, N332A, and Y336A mutations in the conserved NPxxY motif within the C-tail of the MOPr on the ARF-selectivity, PLD2 activation and endocytosis of the MOPr. This work was supported by Deutsche Forschungsgemeinschaft (KR1740/10-1) and by the Land Saxony-Anhalt from the "Europäischen Fond für regionale Entwicklung (EFRE 2007-2013).

Morphine-induced motor stimulation after repeated administration: age-related differences in mice

W. Koek, Departments of Psychiatry and Pharmacology, University of Texas Health Science Center at San Antonio, TX, USA

Given evidence for age-related differences in the effects of drugs of abuse, surprisingly few preclinical studies have explored effects of opioids in adolescents (versus adults). The present study compared the motor stimulating effects of morphine in adolescent and adult mice, 2 days and 5 weeks after its repeated administration. Morphine (3.2 – 56 mg/kg, i.p.) increased locomotion along an inverted U-shaped dose-response curve in adolescent, late adolescent, and adult male C57BL/6J mice treated with saline once per day for 4 days. The maximum effect of morphine, assessed 2 days after the last injection of saline, was higher in adolescents than in adults. Repeated treatment with morphine (10-100 mg/kg) shifted the dose-response curve of morphine upward, and 17.8 mg/kg was the lowest dose to do so in each of the age groups. The maximum extent to which the dose-response curve shifted upward was similar in each age group (i.e., 1.6 – 1.9 fold). The enhancing effects of repeatedly administered morphine were still evident 5 weeks later, when the adolescents had become adult, but consisted of a smaller upward shift (i.e., 1.4-fold) that occurred only at a higher dose (i.e., 56 mg/kg). In animals treated repeatedly with morphine as adults, its enhancing effects were no longer evident 5 weeks later. Repeated administration of morphine produced similar short-term enhancement of its motor stimulating effects in all age groups, but evidence for long-term enhancement was obtained only in adolescents. These findings suggest that compared with adults, adolescents are more sensitive not only to the acute locomotor stimulating effects of morphine, but also to its long-lasting locomotor sensitizing effects. Supported by DA23261

µ-opioid control of P2X3 receptors in DRG sensory neurons of rat is crucially dependent on the experimental in vitro conditions

O. Krihtal, (1), I. Chizhmakov (1), V. Kulyk,(1), D. Simone (2) and G. Bakalkin (3), (1) Dept. of Cell. Membranol., Bogomoletz Institute of Physiol., Kiev, Ukraine, (2) School of Dentistry, Univ. Minnesota, Minneapolis, USA, (3) Dept. of Pharm. Biosci., Uppsala University, Uppsala, Sweden

P2X receptors in nodose sensory neurons of rat are under opioid control: µ-opioid agonists powerfully inhibit the currents generated by nodose neurons isolated from rat and kept in primary culture (Chizhmakov et al., 2005). This evidence has been obtained on the “slow” responses to ATP generated by P2X2 and P2X2/3 receptors. According to existing paradigm, homomeric P2X3 receptors (expressed almost exclusively in the sensory neurons) play especially important role in the nociception. In this study we have examined the effect of µ-opioids on the currents generated by P2X3 receptors in the neurons from DRG of rat. In acutely isolated cells, inward currents generated by P2X3 receptors were effectively blocked by µ-opioid agonists (endorphin1 or leu-enkephalin, in concentrations
10-100 nM). However, the experiments on the neurons kept in primary culture demonstrated complete loss of sensitivity of P2X3 receptor-mediated currents to opioids after only 24 hours of culturing. Histochemical evidence indicates that chronic treatment with opioid receptor antagonists increases the density of µ-opioid receptors in cell culture and in the intact animal (Patel et al., 2002). Such increase in receptor density is possibly due to a reduction in internalization of opioid receptors. We have tested whether opioid effect on P2X3 receptors can be preserved when opioid antagonist is added to the culture medium. Addition of naloxone (1 µM) for 24 hours completely restored the effect of opioids on P2X3 receptor. This simple procedure allows to achieve experimental conditions when histochemical and electrophysiological evidence successfully merge. Our data indicate at the necessary caution in the compiling in vivo and in vitro data when studying volatile mechanisms of opioid signaling. FIRCA grant R03TW008228-01A1 (1,2) and Visby grant 00697/200 (1,3)

**Suppression of malignancy of gefitinib-resistant human non-small-cell lung cancer (NSCLC) cells by activation of δ-opioidergic system**


The δ-opioidergic system has been recognized as a neurotransmitter system that could be directly involved in emotionality, immunity and the development of cells including neurogenesis. In this study, we found that H1975 cells, which are human non-small-cell lung cancer (NSCLC) cells and that are resistant to an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor gefitinib, expressed δ-opioid receptors (DORs). Addition of the DOR agonist SNC80 produced a concentration-dependent decrease in H1975 cell growth. Under these conditions, the addition of SNC80 to H1975 cells produced a significant decrease in phosphorylated-signal transducers and activator of transcription 3 (p-STAT3). It has been reported that expression of the key pluripotent genes of embryonic stem (ES) and induced pluripotent stem (iPS) cells has been found in cancer stem cells. In the present study, the pluripotency genes were absent in normal human lung fibroblasts cells, whereas these were found in H1975 cells. The addition of SNC80 to H1975 cells produced a significant and concentration-dependent decrease in pluripotency gene expression. These results suggest that the stimulation of DOR by agonist may help to reset the pluripotent state by inhibiting STAT3 activity. Furthermore, the present findings constitute promising support for the notion that DORs may be prime candidates for EGFR-TKI-resistant NSCLC therapy.

**Role of Galphao protein in opioid agonist-dependent signaling and behavior**

J. Lamberts (1), E. Jutkiewicz (1, 2) and J. Traynor (1, 2), (1) Department of Pharmacology and (2) Substance Abuse Research Center, University of Michigan, Ann Arbor, MI

Mu-opioid receptor (MOR) agonists elicit analgesia via activation of the Galphao subunit of heterotrimeric G proteins—most notably Galphao. Signal termination is accelerated by the family of regulator of G protein signaling (RGS) proteins. To evaluate Galphao signaling and determine whether RGS proteins modulate Galphao activity in vivo, we have measured both biochemical and behavioral endpoints of MOR agonist action in heterozygous mice from two different 129S6 strains, in comparison with their respective wild type littermates: (1) a Galphao knockout strain (Galphao (+/−)), constituting a “loss-of-function” system and (2) a “knock-in” mutant strain expressing an RGS-insensitive (RGSi) Galphao protein (Galphao (+/GS)), constituting a “gain-of-function” system. In Galphao (+/−) mice, there was a 4-fold reduction in the potency of morphine to elicit antinociception, as measured in the hot plate test. In contrast, the potency of morphine was enhanced 3-fold in Galphao (+/GS) mice. In whole brain homogenates from Galphao (+/−) mice, the loss of Galphao protein was confirmed, and resulted in a reduction in both high-affinity MOR binding (28.2 ± 8.6%) and maximal MOR agonist-stimulated [35S]GTPγS incorporation (DAMGO, 14.4 ± 6.4%; morphine, 39.2 ± 9.4%), supporting the findings in vivo. Despite the observed enhancement in morphine antinociception in Galphao (+/−) mice, whole brain homogenates from these mice showed a paradoxical reduction of Galphao protein (39.3 ± 2.8%), high-affinity MOR binding (24.8 ± 7.9%) and MOR-dependent G protein activation (DAMGO, 40.5 ± 10.5%; morphine, 53.3 ± 12.8%), presumably due to developmental compensation caused by the Galphao “gain-of-function” mutation. Differences in the development of tolerance and dependence between the mouse strains will also be presented. Together, these results highlight the importance of Galphao for MOR-mediated signaling and behavior. Supported by GM077667, DA007267 (JL) and DA04087 (JT).
Morphine tolerance, desensitization and recovery in locus coeruleus neurons from morphine-treated rats

E. Levitt and J. Williams, Vollum Institute, Oregon Health & Science University, Portland, OR, USA

Cellular tolerance can be observed following long-term morphine treatment either in vivo or in vitro. Tolerance to morphine-mediated G protein-coupled inwardly rectifying potassium conductance is observed in locus coeruleus neurons from rats treated with morphine (50 mg/kg/day) for 6 or 7 days. This tolerance is long-lasting since brain slices were washed in morphine-free buffer for several hours prior to testing. However, part of the tolerance induced in vivo reversed within a relatively short (< 2 h) wash, which was revealed by comparison to slices continuously incubated in morphine and is consistent with previous findings (Bailey et al., 2009). The rapidly recovering portion of tolerance was dependent on the time spent in morphine-free buffer and the concentration of morphine used to maintain desensitization. In the presence of the Ser/Thr phosphatase inhibitor okadaic acid, desensitization was still able recover to the same extent as control after a long-term (> 2 h) wash. Cellular tolerance can also be induced by incubating brain slices from naïve rats in morphine for 4-6 hours. Okadaic acid enhanced the onset of morphine tolerance in slices, with significant effects observed following just 1-3 hours of morphine incubation. These results indicate that phosphorylation/dephosphorylation cycles are ongoing during the development of tolerance, in line with reports that PKC activity is required to maintain morphine tolerance. Together, these results identify two forms of tolerance induced in vivo distinguished by the time-course of recovery, and implicate phosphatase activity during the development of morphine tolerance. Supported by T32NS007381 and DA08163.

Pharmacogenetics of methadone dose requirement in opioid addiction treatment

O. Randesi (1), M. J. Kreek (1)(1)Laboratory of the Biology of Addictive Diseases, The Rockefeller University, New York, NY, USA, (2)Dr. Miriam and Sheldon G. Adelson Clinic for Drug Abuse, Treatment and Research, Elias Sourasky Medical Center, Tel Aviv, Israel

The inter-individual differences in the efficacy and toxicity of methadone may be affected in part by gene variants in genes encoding proteins involved in pharmacokinetic processes and pharmacodynamic effects. We have recently shown that homozygosity to SNP 1236T allele in the ABCB1 transporter gene is associated with high methadone dose requirement (>150 mg). Other studies suggested a role of OPRM1, DRD2, BDNF, and KCNJ6 variants in MMT response. To explore the role of additional genes in methadone dose requirement, we have genotyped variants in genes encoding the major methadone metabolizing enzymes CYP3A4, CYP2D6 and CYP2B6, as well as genes encoding the neurotrophins, BDNF and NGFB, that mediate synaptic plasticity. Our sample includes well-characterized Israeli former heroin addicts in MMT (n=74), with a stabilizing daily methadone dose range of 12.5 mg -260 mg (mean 140±52 mg) and no major co-medication that may affect methadone metabolism. The sample was shown to be primarily of Middle Eastern/European ancestry based on ancestry informative markers. Out of the 45 informative SNPs analyzed, homozygosity for the variant alleles of three SNPs showed significant association with a relatively low methadone dose requirement: NGFB intronic SNP rs2239622 (P = 0.0002), and CYP2B6 SNPs 785A>G and 516G>T (P = 0.01, 0.04, respectively). Repeated analysis controlling for the ABCB1 1236 TT genotype (that showed an opposite effect on methadone dose) substantiated the result (P = 0.0036, 0.019, respectively). CYP2B6 SNPs are in high LD and constitute the CYP2B6*6 allele that was previously shown to be associated with slow methadone metabolism. No significant differences in trough plasma (R/S) methadone levels were identified between subjects with different genotypes of these SNPs. Support: NIDA-P60-05130 (M.J.K.) and the Adelson Medical Research Foundation.

Pharmacokinetic interaction and safety of naltrexone hydrochloride co-administered with oral opioids

N. Levy-Cooperman1, B. Setnik2, N.L. Chen1, B. Chakraborthy1, K. Schoedel1, M.K. Romach1, E.M. Sellers1, Sommerville, K², V. Goli1, 3, 1Kendle Early Stage-Toronto, Canada, 2King Pharmaceuticals Inc., Cary, NC, USA, 3Duke University Medical Center, Durham, NC, USA

The effect of naltrexone hydrochloride on the pharmacokinetics of 120 mg morphine, 60 mg oxycodone, and 60 mg hydrocodone in healthy recreational drug users was investigated in 4 randomized blinded crossover studies (N= 98). Co-administration of increasing doses of naltrexone with 120 mg morphine dose dependently increased Cmax, AUCL-0-8 hr and AUCL-0-inf. Compared to morphine alone, percentage increase in peak and extent of exposure ranged between 7.9 - 35% for naltrexone doses ranging from 2.4 mg to 38.4 mg. Naltrexone also delayed Tmax (up to 16%) and decreased clearance (5-21%). Similarly, co-administration of 2.4 to 14.4 mg naltrexone with 60 mg oxycodone resulted in a 16-32% increase in Cmax, a 17-26% increase in AUCL-0-8hr, and a 6-19% increase in AUCL-0-inf. The pattern of increase in Cmax was also noted to be a lesser extent (8-
17%) following administration of 60 mg hydrocodone with 2.4 to 7.2 mg naltrexone. Naltrexone did not substantially affect other pharmacokinetic parameters in these studies. In general, the incidence and severity of adverse events for all 3 opioids decreased with increasing doses of naltrexone. Naltrexone has previously been shown to increase the bioavailability of morphine but this has not yet been reported with other opioids. Despite the increase in plasma concentration, administration of naltrexone was associated with a reduction of opioid-induced subjective reports of drug-liking and high. The current studies found modest increases in the bioavailability of morphine, oxycodeone, and hydrocodone suggesting a weak interaction. This finding may be the result of naltrexone displacing protein-bound opioids and saturating binding sites or possibly a result of accelerated gastric emptying. Changes in opioid bioavailability should be considered when planning bioavailability or bioequivalence studies of opioids in healthy volunteers where naltrexone blockade is often used.

**Endorphin peptide & glycopeptide analogues with helix address domains provide potent antinociception in mice**

Y. Li¹, M. Lefever¹, D. Muthu¹, C. M. Kirkmire³, D. Giuvelis, J. M. Bidlack², E. J. Bilsky³, and R. Polt¹, ¹Univ. Arizona, Tucson AZ, USA ²Univ. of Rochester Medical Center, ³Univ. of New England, USA

Opioid SAR of peptides related to endorphin or dynorphin has provided a rational & powerful approach toward the design of peptide therapeutics. Analogues had modified address domains with altered intrinsic helix stabilities. Unglycosylated peptides & glycopeptides bearing mono- & disaccharides were studied. The endorphin analogue Tyr-D-Thr-Gly-Phe-Leu-Pro(Linker)-Asn-Leu-Aib-Glu-Lys-Ala-Leu-Lys-Ser[beta-O-Glc]-Leu-NH₂ was modified at the indicated positions and binding affinities Ki measured using human receptors expressed in CHO cells. All the peptides and glycopeptides were pan-agonists, showing low nanomolar affinity for all 3 opioid receptors. Helix stability was altered by substituting Aib, Ala, and Gly, which alters membrane affinity which is correlated with helix stability. Charges on the address side chains were altered by substituting Asn, Glu, and Lys. The Ser residue bore either a lactoside, a glucoside or was unglycosylated. Peptides were studied by CD and by NMR in H₂O (pH = 5.5), in TFE/H₂O, or SDS micelles as a membrane model. In H₂O the glycosylated analogues showed nascent helix behavior and random coil conformations. Chemical Shift Indices and NOE confirmed helical structures in the presence of membrane mimics. Detailed backbone conformations were determined using distance constraints provided by NOE volumes. Based on the CD experiments, most of the endorphin glycosides showed substantial helicity in the presence of micelles. Several glycopeptides demonstrated BBB penetration and produced potent antinociceptive effects in mice after i.v. injection. The amphipathic address played a major role in BBB penetration, as reflected by the i.v. activities. Acknowledgement: We thank the Office of Naval Research (N00014-05-1-0807 & N00014-02-1-0471), the National Science Foundation (CHE-607917) and the National Institute of Neurological Disorders and Stroke (R01-NS52772).

**Fluorescent opioid peptides from a cyclic peptide combinatorial library**

Y. Li, M. Cazares, J. Thompson, J. Misler, R. Houghten and C. Dooley, Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL, USA

A positional scanning library of 30,420 cyclic peptides was prepared using a pentapeptide thioester scaffold on mercaptomethylphenyl-functionalized silica gel. Positions R₁ and R₃ were fixed with glycine and Dap (diaminopropionic acid; for subsequent addition of 2-amino benzoic acid). Positions R₂ and R₄ contained 36 L and D- amino acids and position R₅ contained 19 L- amino acids. Cyclization was performed in a mixture of acetonitrile and 1.5 M aqueous imidazole solution at room temperature for 5 days. The library was screened in binding assays for all three opioid receptors. Activity was greatest in mu and delta receptors. Combinations of amino acids found at each position yielded active cyclic peptides (Ki = 16 nM). Screening profiles of the cyclic peptide library, the individual sequences identified, selectivity and signaling behavior of these fluorescent peptides will be presented.

This work was funded in part by: NIH RO3 DA025850, NSF funding (CHE0455072) and the State of Florida, Executive Office of the Governor’s Office of Tourism, Trade, and Economic Development.
Morphine-induced mu-opioid receptor mediated desensitization of GIRK conductance in locus coeruleus neurons of RMOR mice.

A. Madhavan, J. L. Whistler, Ernest Gallo Clinic & Research Center, Emeryville, California 94608, USA

Recently, we generated a novel knock-in mouse that expresses a mutant form of the mu opioid receptor (MOR) that undergoes endocytosis and recycling in response to activation by morphine (RMOR). Here, we examined receptor activation, desensitization and resensitization following activation of the MOR and RMOR receptors with, met-enkephalin and morphine, in neurons of the locus coeruleus (LC). We find that the potency and efficacy of morphine and met-enkephalin are indistinguishable in wild type (WT) and RMOR LC neurons. However, while application of a saturating dose of morphine (30 µM) induces little desensitization in WT LC neurons, the same dose induces significant desensitization of the GIRK conductance in RMOR neurons. We then assessed recovery from desensitization (resensitization) of the GIRK conductance in WT and RMOR mice. To examine resensitization, 30 µM of either the endogenous ligand met-enkephalin or morphine, was applied for 10 minutes. Next slices were treated with 300 nM β-FNA, a membrane impermeant irreversible MOR antagonist to silence all remaining surface receptors. Resensitization of MOR was then tested 5 and 30 minutes later with application of 30 µM of met-enkephalin. Both WT and RMOR showed resensitization following treatment with met-enkephalin and β-FNA, suggesting that a pool of receptors is endocytosed and recycled in response to met-enkephalin in both genotypes. However, only RMOR showed resensitization following treatment with morphine and β-FNA. Together, these data suggest that endocytosis in response to morphine produces a protected pool of receptors in the RMOR mouse that are recycled and resensitized in the LC. This work was supported by funds from the state of California for research on alcohol and substance abuse and NIDA grants DA019958 to J.L.W. A.M. is supported by an individual NRSA F32DA027286.

Truncated MOR-1 splice variants: targets for potent opioid analgesics lacking side-effects

S. Majumdar1, S. G. Grinnell1, V. Le Rouzic1, M. Burgman1, L. Polikar1, M. Ansonoff1, Y. Xiang Pan1, J. E. Pintar2 and G. W. Pasternak1, 1Laboratory of Molecular Pharmacology and Chemistry, Memorial Sloan-Kettering Cancer Center, NY, NY 10065, USA, 2Department of Cell Biology and Neuroscience, University of Medicine and Dentistry of New Jersey, Piscataway, NJ 08854, USA

We have been particularly interested in the vast array of splice variants of mu opioid receptors (MOR-1) gene (Oprm1). There are two primary classes of MOR-1 splice variants generated by different promoters. The primary promoter is associated with exon 1 and generates a large number of traditional 7 transmembrane domain receptors. The second promoter, associated with exon 11 generates a number of truncated, 6 transmembrane domains. We have previously shown that, heroin and M6G analgesia is present in exon 1 KO animals while it is markedly diminished in the exon 11 KO animals, indicating a role of truncated MOR-1 splice variants...
in the analgesic response of these drugs. We now report another novel exon 11-associated binding site remaining in the exon 1 KO mice, but lost in the exon 11 KO mice using a novel radioligand $^{125}$I-BNtxA synthesized in our laboratories. IBNtxA is an effective analgesic. This analgesia persists in the exon 1 KO mice, but is lost in the exon 11 KO mice. The selectivity of this site is quite unique, with morphinans and benzomorphans showing very high affinity while drugs like morphine and the antagonist naloxone bind very poorly. This selectivity is supported by antagonist studies in vivo. Preliminary studies indicate that IBNtxA lacks respiratory depression, significant constipation, physical dependence or reward. It shows no cross tolerance to morphine and can be given to morphine-dependent mice without a decrease in its analgesic actions or the precipitation of withdrawal. Thus, this ligand comes close to the ideal opioid analgesic through a novel receptor target comprising truncated 6 transmembrane domain splice variants of the mu opioid receptor MOR-1 and can be used as a lead compound to design a library of opioid analgesics. Supported by DA0641, DA02615 and DA00220.

**Opioid-sensitive GABA inputs from RMTg neurons synapse on midbrain dopamine neurons**

A. Matsui and J. T. Williams, Vollum Institute, Oregon Health and Science University, Portland, OR, USA

All drugs of abuse increase the activity of midbrain dopamine neurons. Opioids increase dopamine neuron activity through disinhibition mediated by a hyperpolarization of GABAergic neurons. However, the specific GABAergic neurons projecting to dopamine neurons are still not clear. Increasing evidence suggests that GABAergic neurons in Rostromedial Tegmental Nucleus (RMTg) also known as tail of VTA project to midbrain dopamine neurons and these neurons express mu-opioid receptor. RMTg neurons projecting to the ventral tegmental area (VTA) were identified using retrograde tracers injected into the VTA. The labeled RMTg neurons were characterized by whole-cell current clamp recordings. RMTg neurons were hyperpolarized by DAMGO and Met-Enkephalin. In addition, electrical and channelrhodopsin2 stimulation in RMTg evoked GABA IPSCs in dopamine neurons. The amplitude of GABA IPSCs was reduced upon DAMGO application. Thus, the GABAergic neurons in RMTg project to dopamine neurons in the VTA and are sensitive to opioids. Supported by DA08163

**DOR-KOR heteromer signaling in peripheral sensory neurons**

B. A. McGuire, W. P. Clarke, and K. A. Berg, Department of Pharmacology, University of Texas Health Science Center, San Antonio, TX, USA

Several studies have demonstrated that delta opioid (DOR) and kappa opioid receptors (KOR) can form heteromers. 6'-guanidinonaltrindole (6’GNTI) has been reported to be a selective DOR/KOR heteromer agonist which produces analgesia when administered into spinal cord, but not brain, supporting the notion that heteromer-selective ligands will provide improved specificity. In this study, we sought to determine if, in peripheral sensory neurons, DOR and KOR form heteromers. We also compared the signaling characteristics of the heteromer agonist, 6’GNTI, to those of selective agonists for the individual protomers, DPDPE (DOR) and U50488 (KOR). Co-immunoprecipitation and signaling experiments were done in primary cultures of adult rat sensory neurons. Following cell surface crosslinking and immunoprecipitation with KOR antibody, a single, 120kd immunoreactive band for DOR was visualized with western blot. The signaling characteristics were determined for inhibition of adenylyl cyclase (AC) activity and activation of Extracellular Signal-Regulated Kinase (ERK). All three agonists produced an inhibition of AC in a pertussis toxin (PTx, 24h, 400ng/ml) sensitive manner. The DPDPE AC response was blocked by the DOR antagonist, naltrindole (20 nM), but not the KOR antagonist, nor-BNI (3nM). The U50488 AC response was blocked by nor-BNI but not naltrindole. The 6’GNTI AC response was blocked in the presence of either naltrindole or nor-BNI. All three agonists elicited ERK activation in a sustained manner (2.5 – 30 min incubation). Whereas DPDPE and U50488-mediated ERK activity was PTx sensitive, 6’GNTI-mediated ERK activity was PTx insensitive. These data indicate that, in peripheral sensory neurons, DOR and KOR form heteromers with different signaling mechanisms in comparison to the individual receptor protomers. Targeting opioid heteromers on peripheral sensory neurons may provide new approaches for the pharmacological treatment of pain. Supported by DA026619 and DA024865
Differential KOR agonist-induced activation of ERK1/2 MAP kinase mediates paradoxical potentiation of cocaine-conditioned place preference (CPP)

J.P. McLaughlin(1,2), M.R. Hoot(2) and K. Rasakhaham(1,3), (1)Northeastern University, Dept. of Psychology, Boston, MA USA, (2)Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL, USA 34987 (3)Temple University, Dept. of Pharmacology, Philadelphia, PA, USA

Acute administration of kappa opioid receptor (KOR) agonists suppresses drug reward, but prolonged exposure has been observed to paradoxically potentiate drug reward. We hypothesized that while two structurally distinct KOR agonists (U50,488 and salvinorin A) would acutely suppress cocaine-CPP, the differential ability of these agonists to activate ERK1/2 MAP kinase would correlate with their respective ability to potentiate cocaine-CPP. Initial place conditioning with equianalgesic doses of the KOR agonists alone produced conditioned place aversion, and a 30-min pretreatment with each agonist suppressed cocaine-CPP in a nor-BNI-sensitive manner. However, when the agonist pretreatment interval matched antinociceptive abatement (90 min), U50,488-pretreatment paradoxically produced a 2.5-fold potentiation of cocaine-CPP, whereas salvinorin A-pretreated mice demonstrated normal cocaine-CPP responses. Western Blot analysis of mouse brain revealed that U50,488 increased ERK1/2 MAP kinase activity only after a 90-min treatment, whereas salvinorin A did not at any time. We then examined the effects of agonists on pERK1/2 in KOR-GFP/HEK293 cells. Immunolabeling (Western blot and ELISA) experiments after timed incubations and graded doses (0.1-10 uM) of each agonist demonstrated that both increased pERK1/2 labeling after a brief (5 min) incubation, whereas only U50,488 (not salvinorin A) increased late-phase (>15-90 min) pERK1/2 labeling in a mechanism mediated by KOR internalization. Notably, and supporting the hypothesis, pretreatment of mice with either the KOR antagonist nor-BNI or the ERK1/2 MAP kinase inhibitor SL-327 prevented the U50,488-induced potentiation of cocaine-CPP. Overall, these results suggest differential KOR agonist-induced activation of MAP kinase may mediate potentiation of cocaine-CPP. (Supported by NIH grant DA015232-07 and funds provided by the State of California for medical research through the University of California San Francisco both to JLW)

Kappa opioid tetrapeptides from expanded deconvolution of a positional scanning library

J. Misler, M. Cazares, T. LaVoi, T. Gibbins, A. Morales, L. Maida, M. Giulianotti and C. Dooley, Torrey Pines Institute for Molecular Studies, Port St. Lucie, Florida, USA

We have previously identified novel tetrapeptides for the three opioid receptors from a single tetra-peptide positional scanning combinatorial library (1). The library contained over 13 million peptides from which we synthesized only 24 peptides to identify novel KOR ligands. The active sequences identified were all D amino acid peptides lacking an N-terminal tyrosine (D-Phe-D-Nal-D-Nle-D-Arg-NH2). With the knowledge that the library contained additional active sequences not identified in the first screen we have used a similar tetrapeptide library (63 amino acids versus 60 in the first library) and employed a new mixture linking analysis to assist in the library deconvolution. Positional scanning deconvolution can be prohibitive when combination of all active amino acids requires the synthesis of a large number of peptides. Mixture linking analysis allowed the

Mu and delta opioid receptor heteromerization: the importance of being trafficked.

L. Milan-Lobo, J. Enquist & J.L. Whistler, Ernest Gallo Clinic and Research Center, Department of Neurology, University of California San Francisco, UCSF, Emeryville, CA, USA

Heteromerization of mu (MOR) and delta (DOR) opioid receptors has been shown to alter opioid receptor pharmacology and receptor trafficking. The observation that heteromerization may affect receptor trafficking is of particular relevance for heteromers of the MOR and DOR, since the MOR is primarily recycled after endocytosis and the DOR is degraded in the lysosome. We examined the endocytic and post-endocytic fate of MORs, DORs and DOR/MOR heteromers in HEK293 stably expressing each receptor alone or co-expressing both receptors. We found that the clinically relevant MOR agonist methadone promotes endocytosis of MOR but also of the DOR/MOR heteromer. Furthermore, we show that DOR/MOR heteromers that are endocytosed in response to methadone are targeted for degradation, while MORs in the same cell are significantly more stable. Importantly, we found that the DOR-selective antagonist naltrexone (NTB) could block both methadone- and DAMGO-induced endocytosis of the DOR/MOR heteromers but did not block signaling from this heteromer. Together, our results suggest that the MOR adopts novel trafficking properties in the context of the DOR/MOR heteromer. In addition, they suggest that the heteromer shows “biased antagonism”, whereby DOR antagonist can inhibit trafficking but not signaling of the DOR/MOR heteromer. Here we describe how we have used this biased antagonism for trafficking versus signaling to assess the role of the DOR/MOR heteromer in nociception. LML was supported by a Schrödinger fellowship from the Austrian Science Fund (FWF) (J2967-B09). This study was also supported by NIH grant DA015232-07 and funds provided by the State of California for medical research through the University of California San Francisco both to JLW.
Enkephalinergic system is involved in cocaine induced behavioral sensitization and the associated increase in AMPA receptor surface expression in nucleus accumbens and caudate putamen

B. Mongi Bragato1, M. A. Assis1, M. Bartos1, A. Zimmer2, L. M. Cancela1, 1IFEC-CONICET, Departamento de Farmacología, Facultad de Ciencias Químicas, Universidad Nacional de Córdoba. 5000 Córdoba, Argentina, 2 Institute of Molecular Psychiatry, University of Bonn. 53105 Bonn, Germany

Opioid receptors and endogenous opioid peptides, mainly enkephalin, are largely distributed in the mesolimbic system. However, their contribution to cocaine-induced sensitization on behavioral and associated molecular parameters has been poorly studied. Male C57B/6J wild type (WT) and preproenkephalin knockout (KO pENK) mice were daily treated with cocaine (15mg/Kg i.p.) and vehicle for 9 days followed by a cocaine challenge (7.5mg/Kg) on days 15 and 21 of the treatment. The locomotor activity was measured on days 15 and 21. In another set of experiments, male C57B/6J WT mice received the same treatment but 30 min. before each cocaine injection, the animals were administered with a naloxone injection (1mg/Kg s.c.). The locomotor activity was measured on days 1, 15 and 21. On this day, mice were killed for biochemical analysis. The nucleus accumbens, striatum, hippocampus and prefrontal cortex were dissected and GluR1, dopamine transporter, ERK and CREB levels were measured by western blot. Penk KO mice did not show sensitization to the behavioral effects induced by cocaine and failed to show the cocaine-induced increases in ERK activation and AMPA cell surface expression evidenced in the WT mice. However, the locomotor activity in response to an acute injection of the drug and the levels of dopamine transporter were similar in both KO and WT mice. Wild type mice pretreated with naloxone did not show the cocaine-induced increased in ERK and CREB phosphorylation. These results indicate that preproenkephalin-derived opioid peptides, possibly through the activation of opioid receptors in mesolimbic areas, are strongly involved in the long-term plasticity underlying behavioral sensitization to cocaine. Financial Support: FONCYT, Ministerio de Ciencia y Tecnología, CONICET

Morphine resistance and its underlying mechanisms in an experimental mouse model of fibromyalgia

T. Mukae, M. Nishiyori, K. Araki, H. Ueda, Division of Molecular Pharmacology and Neuroscience, Nagasaki University Graduate School of Biomedical Sciences, Japan

Fibromyalgia (FM) is a common condition with generalized or widespread allodynia that affects at least 2% of the US, European and Japanese populations. Although the etiology of this disease remains to be fully understood, physical and psychological stressors have been assumed to play a role in the development of FM. Previously, we have established a novel mouse model of FM, using intermittent cold stress (ICS) exposure (Mol Pain, 2008, 4, 52). This model was found to show long-lasting mechanical allodynia and thermal hyperalgesia in a female-predominant manner, as often observed in FM patients. In contrast, constant cold stress (CCS) produced a transient allodynia. Importantly, we found that anticonvulsant agent gabapentin, especially when injected intracerebroventricularly, produces potent anti-allodynic and anti-hyperalgesic effects in the ICS-exposed mice. Furthermore, we have recently found that ICS model mice show morphine resistance (Neurosci Lett, 2010, 472, 184-187), as often observed in FM patients. In this study, systemic or intracerebroventricular, but not intrathecal or intraplantar, injection of morphine causes no significant analgesia in the ICS-exposed mice. In addition, we found that intracerebroventricularly administrated morphine increases the 5-hydroxytryptamine turnover ratio in the dorsal half of the spinal cord of control mice, but not in the ICS-exposed mice. Taken together, these results indicate that ICS model well reflects pathological and pharmacotherapeutic features of FM patients, and the loss of descending serotonergic activation seems to be a key mechanism underlying the absence of morphine-induced analgesia in the ICS model.

Involvement of long-chain fatty acid receptors, GPR40 and GPR120, in the induction of antinociception of docosahexaenoic acid

K. Nakamoto1, T. Nishinaka1, K. Matsumoto1, M. Mankura2, S. Tokuyama1, 1Department of Clinical Pharmacy, School of Pharmaceutical Sciences, Kobe Gakuin University, Japan 2Ikeda Tohka Industries Co., Ltd.

We have previously demonstrated that the n-3 polyunsaturated fatty acid docosahexaenoic acid (DHA) has an antinociceptive effect on various pain stimuli in a naloxone-reversible manner. Recently, it is reported that G-protein receptor (GPR) 40 and GPR120 can be activated by polyunsaturated fatty
Different μ-opioid receptor activation profiles of oxycodone and morphine at specific brain regions in mouse femur bone cancer pain model


Oxycodone, an opioid analgesic, is prescribed to control moderate to severe pain related to cancer or neuropathy. Pervious study showed that the efficacy profile of oxycodone in the mouse femur bone cancer (FBC) model does not overlap those of morphine and fentanyl. Here, mechanism of the analgesic effect of oxycodone was investigated in the FBC model. The anti-hyperalgesic effect of oxycodone was more effective compared with that of morphine in the FBC model. The anti-hyperalgesic effects of both opioids were antagonized by a μ-opioid receptor (MOR) antagonist, but not by a κ-opioid receptor antagonist, suggesting an involvement of the MOR in the anti-hyperalgesic effect. In the FBC model mice, maximal efficacy and potency of MOR activation by oxycodone and morphine were attenuated at the several brain regions compared with the sham control mice. Interestingly, the degree of attenuation differed between the two opioids, and the MOR activation by morphine was more affected at the mediodorsal thalamus, periaqueductal gray matter (PAG) and region ventral to PAG compared with those by oxycodone. No significant difference was observed in the levels of the total MOR mRNA at those brain regions between the FBC model mice and the control mice. Our results showed that in the FBC model the activation of MOR by oxycodone is relatively unaffected compared with that by morphine at several brain regions related to the pain transmission, and suggested that this agonist dependent MOR function may be responsible for the unique analgesic effect of oxycodone.

Possible change in microRNAs associated with mesolimbic motivation/valuation circuitry under neuropathic pain


Neuropathic pain is the most difficult type of pain to control, and patients lose their motivation with a decrease in their quality of life. Using a functional magnetic resonance imaging analysis, we demonstrated that blood oxygenation level-dependent signal intensity was increased in the ipsilateral nucleus accumbens (N.Acc.) in nerve-ligated mice, indicating that neuropathic pain induces neuronal plasticity in the mesolimbic dopaminergic system. microRNAs (miRNAs) are small, noncoding RNA molecules that direct the post-transcriptional suppression of gene expression, and play an important role in regulating synaptic plasticity. In this study, we found that sciatic nerve ligation induced a drastic decrease in the expression of miR200b and miR429 in N.Acc. neurons. The expression of DNA methyltransferase 3a (DNMT3a), which is the one of the predicted targets of miR200b/429, was significantly increased in the N.Acc. at 7 days after sciatic nerve ligation. Double-immunolabeling with antibodies specific to DNMT3a and NR1 showed that DNMT3a-immunoreactivity in the N.Acc. was dominantly located in NR1-labeled neurons, indicating that increased DNMT3a proteins were predominantly expressed in post-synaptic neurons in the N.Acc. area under a neuropathic pain-like state. The results of these analyses provide new insight into epigenetic modification that is accompanied by a dramatic decrease in miR200b and miR429 along with the dysfunction of “mesolimbic motivation/valuation circuitry” under a neuropathic pain-like state. These phenomena may result in an increase in DNMT3a in neurons of the N.Acc. under neuropathic pain, which leads to the long-term transcription-silencing of several genes.
Effects of morphine on acetic acid-induced suppression of appetitive and reward related behaviors in mice

H. Neelakantan (1), S.J. Ward (1), E.A. Walker (1), (1) Department of Pharmaceutical Sciences, Temple University, Philadelphia, USA

Pain, an affective state, is known to depress behaviors and the reversal of these behaviors is an important marker for the efficacy of pain medications. In preclinical rodent models, pain states can depress behaviors such as locomotion, feeding and operant responding for positive reinforcers. In the present study, we hypothesized that while acetic acid-induced acute nociception will suppress the rate of responding for food and the rewarding effects of drugs, morphine will reverse the acetic acid-induced effects. To study the effects of exposure to acetic-acid nociception on food reward, mice were trained to respond for a 50% Ensure solution under a fixed ratio 10 schedule of reinforcement. Response rates were measured following IP injection of saline, acetic acid (0.2-0.4%), morphine (3.2-10 mg/kg) and a combination of 0.4% acetic acid and 3.2 mg/kg morphine. Results demonstrated that: a) acetic acid produced concentration-dependent suppression of appetitive responding in mice; b) low to intermediate doses of morphine alone maintained intermediate to high response rates; and, c) pretreatment with morphine reversed the acetic acid-induced attenuation of response rates for food reward. Morphine and cocaine reward were measured under the influence of chemical nociception using the condition place preference (CPP) procedure. Following pretreatment with either water, acetic acid, or a combination of morphine and acetic acid, the mice were conditioned for 6 days with saline and drug on alternative sides of the CPP chambers. Results demonstrated that while acetic acid significantly and selectively attenuated conditioned morphine but not cocaine reward, pretreatment with morphine showed a trend towards reversing the depressive effects of acetic acid on contextual reward. In conclusion, assessment of pain-depressed behaviors in mice may be a useful measure for determining the role of pain as a subjective state on various behaviors including the propensity for future drug reward. (Supported by Peter F. McManus Charitable Trust)

Effects on proopiomelanocortin (POMC) expression and conditioned place aversion during protracted spontaneous withdrawal from chronic intermittent escalating-dose heroin in POMC-EGFP promoter transgenic mice

K. Niikura, Y. Zhou, A. Ho, M. J. Kreek, Laboratory of the Biology of Addictive Diseases, The Rockefeller University, New York, NY, USA

In opiate-dependent individuals, heroin “highs” are inexorably followed by a severe negative emotional state (e.g. dysphoria, anxiety, irritability, aversion) when access to the drug is prevented (withdrawal state). In this study, we examined both POMC expression in hypothalamic and extra-hypothalamic regions, using POMC-EGFP bacterial artificial chromosome (BAC) transgenic mice, and heroin withdrawal-induced aversion (using conditioned place aversion, CPA) during withdrawal from chronic escalating-dose heroin administration (3x2.5 mg/kg/day on day 1 up to 3x30 mg/kg/day on day 14). The CPA pre-test was conducted before the drug exposure. In conditioning sessions, mice were confined for 30 min to the conditioning chamber following 12 h withdrawal from the last heroin injection across days 11–14. The CPA post-tests were conducted in three separate groups of POMC-EGFP (+) and (-) mice at 12-hour, 7-day or 14-day of withdrawal from chronic heroin exposure. Immunohistochemistry for ACTH- or beta-endorphin-immunoreactivity demonstrated ~90% colocalization with the EGFP-expressing neurons in the arcuate nucleus of hypothalamus (ARC). The POMC-EGFP neurons were visualized in the basomedial amygdala (BMA), nucleus accumbens and caudate-putamen, in addition to those in the ARC and dentate gyrus of the hippocampus. In 12-h acute withdrawal, both POMC-EGFP (+) and (-) mice displayed significant CPA, an effect persistent into chronic 14-day withdrawal. Chronic 14-day withdrawal from 14-day escalating-dose heroin resulted in an increased number of POMC-EGFP cells in the BMA, but not ARC. Our results suggest that increased POMC expression in BMA in withdrawal after 14-day chronic heroin is associated with negative emotional behavior. 3, 6 diacetyl-morphine HCl (heroin) was generously provided by NIH-NIDA Division of Drug Supply and Analytical Services. NIH-NIDA P60-DA05130 (MJK)
Differences in opioid peptide levels in Wistar rats from five different suppliers
S. Palm, E. Roman, I. Nylander, Dept Pharmaceutical Biosciences, Uppsala University, Uppsala, Sweden
The opioid system is involved in ethanol-induced reward and in the development of addiction but there is a gap in our knowledge of effects on opioids after long-term voluntary ethanol intake. We have previously shown that there are profound differences in voluntary ethanol intake within the Wistar strain depending on supplier. Therefore, it was of great interest to examine endogenous opioid peptides in rats from these suppliers. Dynorphin B and met-enkephalin-Arg^6^Phe^7^ were measured in naïve animals and in ethanol-drinking animals. Voluntary ethanol consumption over six weeks in outbred Wistar rats from BK Universal UK, Charles River Germany, Harlan Laboratories US, Harlan Laboratories the Netherlands and Taconic Denmark was measured using an intermittent access paradigm. Age-matched water drinking controls from each supplier were also included. Different brain structures and the pituitary gland were dissected and the levels of opioid peptides were analyzed using radioimmunoassay. Similar ethanol induced effects were found in brain areas related to reward pathways in most groups. The group that had the lowest ethanol intake generally showed little or no ethanol-induced effects. Basal differences were found in for example the hypothalamus, the pituitary and the hippocampus, indicating differences in the hypothalamic-pituitary-adrenal axis. In the hypothalamus, the ethanol-induced effects differed between groups. The results show that although all rats are of Wistar origin, the levels of opioid peptides are different in certain areas, both basally and after voluntary ethanol consumption. The choice of Wistar can therefore have implications for the outcome and make comparisons between studies difficult. The present findings highlight an important parameter to consider when planning and performing preclinical animal studies in the field of addiction research. Funded by the Alcohol Research Council of the Swedish Alcohol Retailing Monopoly (SRA 07-21:3; E.R.) and the Swedish Medical Research Council (K2008-62X-12588-11-3; I.N.).

Detection of nor-BNI in mouse brain weeks after administration using LC-MS/MS
K. A. Patkar, M. L. Ganno, H. D. Singh, N. C. Ross and J. P. McLaughlin, Torrey Pines Institute for Molecular Studies, Port St. Lucie, FL, USA
Therapeutic development of the kappa opioid receptor (KOR) selective antagonist nor-BNI has been hampered by prolonged pharmacological activity (days to weeks), the mechanisms of which are currently being investigated. We evaluated the potential accumulation of nor-BNI in brain tissue following direct intracerebroventricular (i.c.v., 1-100 nmol) or systemic intraperitoneal (i.p., 1-10 mg/kg) administration to C57Bl/6j mice, determining if the chronic presence of this compound in brain matched the prolonged duration of KOR antagonist activity in vivo. Additional mice were administered saline or the short acting, non-selective opioid antagonist naloxone (100 nmol i.c.v.). In the mouse warm-water tail-withdrawal assay, a single administration of nor-BNI (30 nmol i.c.v., 10 mg/kg i.p. or greater) significantly antagonized U50,488-induced antinociception at least 7 d, whereas naloxone- (100 nmol i.c.v. or 10 mg/kg i.p.) mediated antagonism lasted less than 24 h. The mice were euthanized at various time points ranging from 30 min to 21 days post administration, and brain extracts prepared from isolated tissues using a simple organic extraction for LCMS/MS analysis. Nor-BNI was detected in brain up to 21 days after a single i.c.v. injection of 30 or 100 nmol, and up to 24 h following administration of a 10 nmol dose. Likewise, nor-BNI was detected in brain 6 h after an i.p. administration of 10 (but not 1) mg/kg. In contrast, naloxone was not detected in brain after 6 h. Additional data will discuss comparison of mouse brain and plasma from same animal for the presence of nor-BNI and naloxone post administration. However, to the best of our knowledge, this is the first direct physical determination of nor-BNI in brain after pretreatment. The continued presence of nor-BNI (but not naloxone) in mouse brain days after a single injection correlates with the prolonged antagonism of U50,488, and may offer insight into the long duration of KOR antagonism mediated by nor-BNI. (Supported by the State of Florida.)

Clinically insignificant QTc changes among former opiate addicts during first years of Methadone Maintenance Treatment (MMT)
E. Peles¹, S. Linzy² M.J. Kreek³, M. Adelson¹²³, ¹Dr. Miriam and Sheldon G. Adelson Clinics for Drug Abuse Treatment and Research, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, and ²La Vegas, NV, USA, ³The Rockefeller University, New York, NY, USA
Because of the suspected but unproven risk for TdP due to QTc prolongation in MMT patients, we prospectively studied QTc changes during MMT from admission. Between Oct/2007- Dec/2010, 435 new patients were admitted to the two Adelson clinics - Tel Aviv (TA) and Las Vegas (LV) (TA-101, LV-334). Of them 345 were included, excluding 64 admitted from other MMT, and 26 with no ECG, or ECG >28 days in MMT. The study included 3 groups: (A) 215 addicts who underwent an ECG for QTc before 1st dose; (B) 46 patients whose ECG was done following 1-28 days in MMT; and (C) 84 addicts who had used illicit methadone prior to their admission. QTc values were restudied before the first
Differential desensitization of pre- and postsynaptic mu opioid receptors regulating POMC neurons

R. L. Pennock and S. T. Hentges, Department of Biomedical Sciences, Colorado State University, Fort Collins, CO, USA

Mu opioid receptors located on terminals presynaptic to proopiomelanocortin (POMC) neurons are not desensitized by acute application of opioid agonists. In the present study, whole-cell voltage clamp recordings were made in POMC neurons of the arcuate nucleus to closely examine pre- and postsynaptic desensitization in response to the application of opioid agonists. Application of a high dose of [Met5]-enkephalin (ME) induced an outward current in the postsynaptic cell as well as a robust inhibition of the amplitude of evoked inhibitory postsynaptic currents (eIPSCs). After ten minutes of continuous superfusion of ME the outward current had desensitized to near control levels, however the presynaptic inhibition of eIPSC amplitude showed no such desensitization. Similar effects were observed with the partial mu agonist morphine. As has been shown in previous studies, the lack of presynaptic desensitization also persisted after 5 days of chronic treatment with morphine and after reduction of receptor number through beta-chlormaltrexamine treatment in POMC neurons. Together these data suggest that neither rapid receptor recycling or large receptor reserve are likely to explain the lack of acute desensitization of presynaptic receptors. Similar to the mu receptor, kappa opioid receptors presynaptic to POMC neurons also show no acute desensitization.

Altogether these findings suggest that pre- and postsynaptic opioid receptors may play differing roles in the development of tolerance and withdrawal from chronic opioid treatment. Interestingly, differences in pre- and postsynaptic desensitization extend to other Gi coupled GPCRs regulating POMC neurons, including GABAA and ORL1 receptors. Exploring the similarities between these receptors may provide a means for determining whether differential coupling or covalent modifications may underlie differences in desensitization of Gi coupled GPCRs found in distinct cellular compartments. NIH Grant R01DK0798749

Hypothalamic KOP-r and MOP-r expression in Fischer and Lewis rats after dose escalation preference paradigm of heroin self-administration

R. Picetti, A. Ho, and M. J. Kreek, The Rockefeller University, New York, NY, USA

During the withdrawal from drugs of abuse, dysregulation of HPA axis occurs in humans and rodent models. Rats that self-administer drugs of abuse over extended periods of time increase the number of infusions over time. Recently, we published a new self-administration paradigm whereby rats choose between different doses of a drug and escalate dose as well as number of infusions. Using this model, we measured the mRNA levels of MOPr and KOPr in the hypothalamus of Fischer and Lewis self-administering heroin. Rats were trained to self-administer heroin (50 ug/kg/injection) in two-hour daily sessions (10-14 d). After acquisition, rats were exposed to extended (18h) self-administration sessions for 14 days. Rats had access to two active levers associated with two doses of heroin. If a rat preferred the lever associated with the higher dose for two consecutive days, then a higher dose was available. During escalation, four heroin doses were used ranging between 20 to 250 ug/kg/infusion. Total RNA was isolated from each hypothalamus, and gene expression was assessed by RT qPCR. After 14 days, Lewis rats escalated the total amount of heroin infused per day, whereas Fischer rats minimally escalated the unit dose and, in general, self-administered very low quantities of heroin. Lewis and Fisher rats self-administered an average of 5.2±0.9 mg/kg/session and 1.3±0.2 mg/kg/session of heroin, respectively. MOPr and KOPr mRNA levels in controls and in rats preferring to self-administer 50 ug/kg/infusion were lower in Lewis than in Fischer rats. Two-way ANOVA (strain x drug) shows a significant main effect of strain for both genes, with MOPr and KOPr mRNA levels being lower in Lewis than Fischer rats in both heroin self-administering rats and controls. In conclusion, Lewis rats have lower levels of MOPr and KOPr mRNA than Fischer rats and self-administered more heroin. This work was supported by a NIH-NIDA...
P60-DA05130 grant and the Carson Family Charitable Trust. Heroin was generously provided by NIH-NIDA Division of Drug Supply and Analytical Services.

**Regulation of Tat-mediated neurotoxicity and glial inflammatory signaling by CCR5 and the mu-opioid receptor**


The CCR5 receptor is critical to HIV-1 infection through interaction with HIV-1 gp120, but may also be an important mediator of HIV-1 Tat signaling, which elevates the CCR5 ligand, RANTES in glia. Additionally, mu-opioid receptor and CCR5 interactions could influence the exacerbation of neurotoxicity seen with combined morphine and Tat treatments. We hypothesized that inhibition of CCR5 would suppress Tat-mediated neurotoxicity by interfering with glial inflammatory signaling and may modify the response of opioid convergent effects. To address this hypothesis, co-cultures of neurons and glia were subjected to morphine (500 nM) and Tat + morphine treatments, illuminating the importance of CCR5 to Tat’s effects. To elucidate the underlying mechanism(s), NF-kappaB p65 nuclear translocation was assessed due to its importance in astrocyte-mediated inflammatory signaling. Maraviroc suppressed Tat-induced p65 translocation at 6 and 12 h time points. Additionally, while morphine did not affect p65 activation by Tat, full internalizing and non-internalizing mu-opioid receptor agonists, DAMGO and herkinorin respectively (1 microM each), suppressed Tat’s response at 12 h but not 6 h. This result infers that mu-opioid receptor signaling converges with Tat to modulate the maintenance of Tat-mediated inflammation, but not response induction. Herkinorin had divergent effects on chemokine release by Tat, suppressing MCP-1 production, while elevating RANTES release, suggesting alternative transcriptional regulation of inflammatory signaling. Ongoing studies are aimed at examining interactions between mu-opioid signaling and Tat’s actions through CCR5. Support: NIH P01 DA019398 & T32 DA007027

Repetitive morphine administration alters contextual learning, synaptic plasticity, and requires phosphorylation of GluR1-containing AMPA receptors in the hippocampus

G.S. Portugal, Y. Xia, J. Liu, and J.A. Morón Concepcion. Dept. of Anesthesiology, College of Physicians and Surgeons, Columbia University Medical Center, New York

The effects of drugs of abuse on the neural substrates of learning and memory plays an important role in drug addiction, and numerous studies have demonstrated that alterations of hippocampus-dependent learning by drugs of abuse can lead to context-evoked cravings, drug seeking behavior and relapse. The trafficking of α-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptors (AMPARs) towards and away from the synapse plays an important role in NMDAR-dependent long-term potentiation (LTP) in the hippocampus. Thus, changes in synaptic AMPAR expression by drugs of abuse may lead to maladaptive changes of both learning and memory and synaptic plasticity. In this study, we investigated the effects of context-dependent sensitization to morphine on synaptic plasticity and AMPAR expression. We find that the association between morphine administration and the drug administration environment leads to persistent changes in behavior, neuroplasticity, and AMPAR expression. Specifically, the results demonstrate that context-dependent psychomotor sensitization to morphine increases synaptic GluR1 subunit expression, increases basal synaptic transmission, and severely disrupts hippocampal LTP. Importantly, these changes in behavior, AMPA receptor expression, and synaptic plasticity were not observed or were less robust when morphine administration was not paired with the drug administration environment. Furthermore, the infusion of a viral vector that blocks GluR1 phosphorylation in the hippocampus impairs the acquisition and expression of context-dependent behavioral sensitization. These data suggest that glutamatergic synaptic transmission in the hippocampus may play an important role in drug-induced changes to associative learning. This work was supported by NIH grant R01 DA025036 to JMC.

**Variants of mu opioid receptor influence HIV viral load change in individuals before initiating HAART**


52
The mu opioid receptor (OPRM1) is involved in a number of important physiological functions including modulation of HPA axis by tonic inhibition. Ligands of OPRM1 may alter the expression of chemokines and chemokine receptors that are involved in the mechanisms of penetration of HIV-1 into the cell. We suggest that the variants of OPRM1 may affect the pathophysiology of HIV infection. Using DNA samples of HIV positive subjects of African American, Hispanic and Caucasian ethnicities recruited for the Women Interagency HIV Study (WIHS) from 1994 to 2002 and who survived as of April 2006 (704 subjects total), we performed regression analysis of 18 genetic variants of OPRM1 with change of viral load (VL) between two study points: admission to WIHS and start of HAART. During this interval subjects were on no-therapy, mono-therapy or combination therapy. The duration of this time interval was 30.3±1.6 months in African Americans, 26.8±2.2 months Hispanics and 34.9±3.3 months in Caucasians. Overall, we found significant decrease of the VL in individuals of all ethnicities between admission to WIHS and start of HAART. A significant effect of genotype on decrease of VL was found in Caucasians for variants rs1799971 (118A>G), rs510769, rs524731 and rs9479757 (0.01<p<0.04). The decline of VL was greater in individuals with at least one allele A of functional variant 118A>G. These findings may provide new insights in functionality of OPRM1. Supported by NIH-NIDA P60-DA05130 (MJK), NIH-NIMH MH79880 (MJK), NIH-NIMH MH076537 (HC) and NSFC from the Chinese Government 30730057 (JO). We also acknowledge NIH-NIAID supported Women Interagency HIV Study for specimens and limited clinical data.

**Differential role for beta-arrestin2 in the development of antinociceptive tolerance and physical dependence in response to distinct opioid analgesics**

K. M. Raehal, L. M. Bohn, Departments of Molecular Therapeutics and Neuroscience, The Scripps Research Institute, Jupiter, FL, USA

Morphine and other clinically relevant opiates effectively treat pain but also produce several undesirable side effects including analgesic tolerance and physical dependence via activation of the mu opioid receptor, a G protein-coupled receptor (GPCR). We have previously shown that mice lacking beta-arrestin2, an important GPCR receptor regulatory protein, display enhanced analgesia in response to morphine whereas other opiate agonists like methadone and fentanyl do not produce different antinociceptive responses in these animals. Therefore, we investigated whether the loss of beta-arrestin2 would also affect the development of antinociceptive tolerance and physical dependence in an agonist-dependent manner. Beta-arrestin2 knockout mice and their wild-type littermates were chronically infused with morphine, methadone, fentanyl or oxycodone as equi-efficacious doses using subcutaneously implanted osmotic pumps, and tolerance was evaluated by measuring antinociceptive responses using a hot plate test. Physical dependence was assessed by measuring naloxone-precipitated withdrawal responses following chronic infusion with all four drugs. While beta-arrestin2 knockout mice develop very little antinociceptive tolerance in response to chronic morphine administration, tolerance develops at the same rate and to the same degree in both genotypes with methadone, fentanyl, or oxycodone treatment. Similarly, the beta-arrestin2 mice develop physical dependence to a lesser degree than wild-type mice following chronic infusion with morphine, but not methadone, fentanyl, or oxycodone at several doses tested. Collectively, these studies lend further support to the idea that the nature of the agonist can differentially promote beta-arrestin2 regulation of the mu opioid receptor. Work Supported by NIDA grants RO1 DA18860 (LMB) and F31 DA021952 (KMR)

**Variants of kappa opioid receptor influence viral load of HIV positive females on HAART**

M. Randesi (1), D. Proudnikov (1), M. Dorn (2), V. Yuferov (1), H. Crystal (3), A. Ho (1), J. Ott (4, 2), and MJ Kreek (1), (1) Lab. of Biology of Addictive Diseases, The Rockefeller Univ., New York, USA, (2) Institute of Psychology, CAS, Beijing, China, (3) Dept. of Pathol., SUNY Downstate Medical Center, Brooklyn, USA, (4) Lab. of Statistical Genetics, The Rockefeller Univ., New York, USA

Many studies have found cross-desensitization interactions between opioid and chemokine receptors both in vivo and in vitro. Opioids selectively promote pro- or anti-inflammatory effects depending on the involvement of mu and kappa opioid agonists, which previously were found to be acting in opposition to each other. In this study, we tested whether genetic variants of the kappa opioid receptor (OPRK1) may influence the outcome of HAART. The study was conducted using DNA isolated from HIV positive subjects of African American, Hispanic and Caucasian ethnicities, who were recruited by the Women’s Interagency HIV Study (WIHS) from 1994 through 2002 and who survived through April 2006 (N = 704). We performed a regression analysis of 16 genetic variants of OPRK1 with change of viral load between two clinical measurement points: start of HAART and the most recently available visit from which we received biological specimens. The duration of this interval was 95.4±1.7 months in African Americans, 106.5±3.5 months in Caucasians, and 108.7±2.7 months in Hispanics. In Caucasians, the decline in viral load was significantly affected by
Microdialysis-mass spectrometry quantification of vasopressin in the hypothalamus and amygdala of freely moving rats

B. Reed1,2, B. T. Chait2, M. J. Kreek1, 1The Laboratory of the Biology of Addictive Diseases, 2The Laboratory of Mass Spectrometry and Gaseous Ion Chemistry. The Rockefeller University, New York, NY, USA

Stress responsivity plays a crucial role in the development of addiction to all drugs of abuse, with our understanding of this role especially prominent for heroin, cocaine, and alcohol. Rodent models of drug abuse and addiction, in both our and others’ laboratories, have recently demonstrated important changes in the vasopressinergic systems in crucial stress-responsive brain regions such as the amygdala and hypothalamus. Our understanding of the roles of vasopressin, the opioid peptides, and other neuropeptides in the development of drug addiction stands to be considerably advanced with the development of robust methodology for the quantification of these molecular entities in vivo. We have developed innovative targeted mass spectrometry methodology combined with microdialysis for the measurement of vasopressin in select brain regions of awake, freely moving animals, with the goal of investigating the timecourse of the extracellular peptide level response to exposure to drugs of abuse. In these initial studies, we have characterized the levels of vasopressin in microdialysis experiments with probes targeting the basolateral amygdala and the paraventricular region of the hypothalamus of Fischer rats, demonstrating that the peptides are, as expected, responsive to 1 M NaCl (>10-fold increase). In preparation for future drug exposure studies, we performed mock injections of the rats in the microdialysis chambers, a procedure which is inherently stressful, and observed an increase in vasopressin levels in the hypothalamus, ranging from 150-2200%, with more modest and variable responses observed in the amygdala. These observations of vasopressin increases in response to a mock injection (with no actual injection) will serve as an important guide in interpreting any observed increases in response to drugs of abuse in future studies. Support: NIH-NIDA Grant P60-DA05130 (M.J.K.) and NCRR Grant RR00862 (B.T.C.).

Oral availability of CJ-15,208, an opioid mixed agonist/antagonist analgesic with fewer liabilities in vivo

N.C. Ross (1), S. Kulkarni (2), J. V. Aldrich (2) and J. P. McLaughlin (1), (1) TPIMS, Port St. Lucie, FL, USA, (2) Dept. of Med. Chem., Univ., of Kansas, Lawrence, KS, USA

Opioid analgesics with a mixed agonist/antagonist activity profile such as pentazocine and nalbuphine are thought to produce antinociception with fewer liabilities such as reduced tolerance, psychostimulation and drug abuse. Recently, the cyclic tetrapeptide CJ-15,208 was characterized in vivo as a mixed mu-opioid receptor (MOR) and kappa-opioid receptor (KOR) agonist and short-acting (>24 h) KOR-selective antagonist using C57Bl/6J mice in the 55°C warm-water tail withdrawal assay. We hypothesized that CJ-15,208 would be orally active and that the dual opioid receptor activity of CJ-15,208 would produce antinociception with fewer liabilities of use, specifically a lack of antinociceptive tolerance, locomotor activity and reinforcing properties. Oral administration of CJ-15,208 produced dose-dependent antinociception. Liability potential was then assessed, starting with acute antinociceptive tolerance to repeated i.c.v. administration of morphine or CJ-15,208. Morphine pretreatment (3 nmol, i.c.v) produced a 9.6-fold rightward shift in the D50 value of morphine administered a second time 8 h later (22.5 (8.48-61.9) nmol vs 2.35 (1.13-5.03) nmol initially), a demonstration of acute antinociceptive tolerance. In contrast, pretreatment with CJ-15,208 (3 nmol, i.c.v.) did not significantly change the dose response of subsequently administered CJ-15,208 8 h later (5.23 (2.76-9.93) nmol vs an initial D50 value of 1.82 (0.58-5.77) nmol). CJ-15,208 produced a smaller dose-dependent bidirectional effect on spontaneous locomotor activity than morphine or U50,488. Moreover, whereas morphine (10 nmol i.c.v.) produced conditioned place preference (CPP), and U50,488 (100 nmol, i.c.v.) produced conditioned place aversion, CJ-15,208 (3, 10 or 30 nmol, i.c.v.) did not produce significant place preference or aversion. This data suggests the potential utility of CJ-15,208 as a clinically relevant, orally available low liability analgesic (Supported by NIDA grants R01 DA018832 and DA023924).
Opioid and gp120 interactive neuropathogenesis in HIV-1

K. L. Samano (1, †), P. E. Knapp (2), K. F. Hauser (1), (1) Depts. of Pharmacology and Toxicology, (2) Anatomy and Neurobiology, Virginia Commonwealth University, Richmond, VA, 23298, USA

Opioid use and HIV-1 are globally linked epidemics and some clinical studies have demonstrated that opioid abusers show an accelerated development towards neuroAIDS. The HIV-1 coat glycoprotein, gp120, is neurotoxic alone and it is suggested that the presence of glia, especially microglia, are instrumental in this damage. While our lab has shown co-morbidity of opioids with HIV Tat through effects on glia, few studies have addressed interactive effects of morphine and HIV-1 gp120. We hypothesize that morphine will potentiate the reactive gliosis caused by the viral protein gp120. To test this in vivo, C57BL/J6 mice were treated with systemic pellets of morphine (5 mg/day) ± naltrexone (12 mg/day) and were stereotaxically injected with gp120 (100 ng) into the striatum since it has high levels of the mu-opioid receptor (MOR) and is a preferential target of HIV. At 48-h, immunohistochemical studies co-localizing Iba-1 (a microglial marker) and 3-nitrotyrosine (a marker of nitrosative stress) revealed increases in activated microglia with morphine + gp120 treatment, but not in animals receiving morphine + vehicle injection. Additionally, the proportion of GFAP immunopositive astrocytes in which MOR was co-detected increased after morphine + gp120 treatment, but not in morphine + vehicle injected animals. This suggests that HIV-1 gp120 may alter the CNS response to opioids. Future in vitro studies will explore how neuron-glia signaling pathways involved in glial activation and inflammation modulate HIV infection in the presence of opioids. Collectively, the above findings suggest opioids and gp120 interact through novel mechanisms to influence the neuropathogenesis of HIV. Support: NIH DA019398 & DA007027

Modulation of behavioral responses to stress by opioid receptor systems


Recently, an increasing number of findings have suggested that stress responses are modulated by opioid receptor systems. In response to physiological stressors transgenic μ-opioid receptor knockout (MOR-KO) mice displayed significantly decreased responses compared with wild-type (WT) mice. Similarly, chronic social defeat stress induced aversion to social contact in WT mice, but this consequence of psychosocial stress was decreased in MOR-KO mice. These results suggest that the μ-opioid receptor (MOR) at least partially mediates these behavioral sequelae of exposure to stressful stimuli. In addition, the selective non-peptide δ-opioid agonist SNC80 has recently been demonstrated to reduce stress responses in the forced swim test. We report here an investigation of the interactions between μ-opioid receptor and δ-opioid receptor systems in response to forced swim stress. In forced swim stress procedure, MOR-KO mice exhibited decreased immobility time compared with WT mice. Administrations of the δ-opioid receptor agonist to WT mice decreased immobility time compared to saline-treated control mice. Administration of KNT-127 to MOR-KO mice before the forced swim stress procedure enhanced the reduction of immobility time compared with saline-treated MOR-KO mice and produced a greater reduction that in KNT-127 treated control mice. These findings may suggest that activation of the δ opioid receptor has synergistic effects on the reduction of stress responses produced by the absence of μ-opioid receptors in MOR-KO mice. Supported by Grants-in-Aid from MECSST and Health Sciences Research Grants from MHLW, Japan and intramural funding from the NIDA-IRP, NIH/DHHS (GRU/FSH).

The kinetics of priming-induced functional competence of delta opioid receptors

L. Scarlota, M. Rowan, K. Berg, W. Clarke, Dept. of Pharm., Univ. of Texas Health Sci. Center, San Antonio, TX, USA

Unreliable opioid receptor analgesia in the periphery represents a major challenge in pain management; however, analgesic effects of opioids are enhanced in inflamed tissues, providing insight into how efficacy may be improved via ancillary pathways. Consistent with these findings, our lab has shown that prior administration of the inflammatory mediator, bradykinin (BK), promotes delta opioid receptor (DOR)-mediated responses in a primary culture of trigeminal ganglion (TG) neurons and a behavioral model of pain. To further characterize the kinetics of this interaction, we measured the ability of a DOR agonist, DPDPE, to reduce prostaglandin E(2) (PGE2)-mediated responses following multiple BK pretreatment times (0-90min). In rats that received hindpaw injections of BK prior to co-administration of DPDPE and PGE2, DPDPE attenuated PGE2-induced thermal allodynia, but only following 15-
30 min of BK pretreatment. Parallel studies in TG cultures mimicked the in vivo effects, with DPDPE producing a significant reduction in PGE2-stimulated cAMP accumulation when primed for 10–30 min, but not 60 min. Considering the relatively short time frame of the priming effect, we next examined if functional competence to DPDPE could be reinduced with an additional application of BK. In rats, a second injection of BK (60 min after initial BK) reestablished DPDPE-mediated thermal analgesia. Similarly, reapplication of BK in TG cultures (60 min after initial BK) promoted DPDPE-mediated inhibition of PGE2-stimulated cAMP accumulation. The time-dependent reduction in DOR competence following longer BK pretreatments could reflect desensitization of the BK system or BK metabolism; however, the ability of a second application of BK to re-induce DOR activity suggests the system is not refractory to the induction of functional competence and may be amenable to more prolonged maintenance. Future studies will address the mechanisms underlying priming-induced competence to identify potential adjuvants to promote persistent peripheral opioid receptor analgesia. Supported by DE14318 (COSTAR) and DA24865

**Novel peptide and non-peptide opioid agonists lacking a positively charged nitrogen**

P.W. Schiller, G. Weltrowska, I. Berezowska, T.M.-D. Nguyen, B.C. Wilkes, C. Lemieux, N.N. Chung, Laboratory of Chemical Biology and Peptide Research, Clinical Research Institute of Montreal, Montreal, Que., Canada

All classical peptide and non-peptide opioid agonists contain a positively charged nitrogen, the ionic interaction of which with the Asp residue in the third transmembrane helix of opioid receptors has been thought to be indispensable for receptor binding and activation. Here we describe novel opioid receptor ligands derived from endogenous opioid peptides or from classical non-peptide opiates that lack a protonatable nitrogen. While substitution of novel non-nitrogenous Tyr or Phe analogues for Tyr1 in opioid peptides produced neutral high-affinity antagonists with various opioid receptor selectivities, the first known examples of delta opioid agonists lacking a positively charged nitrogen were also obtained. In particular, the negatively charged DTLET analogue Bcpp-D-Thr-Gly-Phe-Leu-Thr-OH (Bcpp = 4-[N-((4'-phenyl)-phenethyl)-carboxamido]-3-phenylpropanoic acid) turned out to be a delta-selective opioid agonist with potency comparable to that of leu-enkephalin. Elimination of the positive charge of normorphine through formylation of its nitrogen resulted in a moderately potent mu and kappa opioid antagonist. On the other hand, analogues of fentanyl and carfentanyl in which the nitrogen was replaced with a carbon (“carba”-analogues) showed full or partial mu agonist activity with potencies that were reduced as compared to their nitrogen-containing parents, but were still significant (Ki[mu] = 85 – 225 nM). These results indicate that elimination of the positively charged nitrogen in opioid agonists may have a divergent effect on the efficacy (agonism, partial agonism or antagonism), depending on the receptor binding interactions of other moieties present in the molecule. Finally, the inability of these compounds to engage in a salt bridge may result in the stabilization of distinct receptor conformations, leading to functional selectivity with regard to receptor signaling and internalization. Supported by grants from the NIH (DA-004443) and CIHR (MOP-89716)

**Regional mRNA expression of the endogenous opioid and dopaminergic systems in brains of C57BL/6J and 129P3/J mice: Strain and heroin effects**

S.D. Schlussman, J. Cassin, Y. Zhang, O. Levran, A. Ho and M.J. Kreek, The Laboratory of the Biology of Addictive Diseases, The Rockefeller University, New York NY, USA

We have previously shown strain and dose differences in heroin-induced behavior, reward and regional expression of Sstr mRNAs in C57BL/6J and 129P3/J mice. Using Real Time PCR we examined the effects of five doses of heroin on the levels of the transcripts of endogenous opioid peptides and their receptors and dopaminergic receptors in the mesocorticolimbic and nigrostriatal pathways in these same mice. Compared to C57BL/6J animals, 129P3/J mice had higher mRNA levels of Oprk1 in the nucleus accumbens and of Oprd1 in the nucleus accumbens and a region containing both the substantia nigra and ventral tegmental area (SN/VTA). In the frontal cortex of 129P3/J mice, lower levels of both Oprk1 and Oprd1 mRNAs were observed. Pdyn mRNA was also lower in the caudate putamen of 129P3/J mice. Strain differences were not found in the levels of Oprm1, Penk or Pomp mRNAs in any region examined. Within strains, complex patterns of heroin dose-dependent changes in the levels of Oprm1, Oprk1 and Oprd1 mRNAs were observed in the SN/VTA. Additionally, Oprd1 mRNA was dose-dependently elevated in the hypothalamus. Also in the hypothalamus, we found lower levels of Drd1a mRNA in 129P3/J mice than in C57BL/6J animals and lower levels of DAT (Sle6a3) mRNA in the caudate putamen of 129P3/J animals than in C57BL/6J counterparts. Heroin had dose-related effects on Drd1a mRNA in the hypothalamus and on Drd2 mRNA in the caudate putamen. Significant strain- and region-specific correlations were found between Oprk1 mRNA levels and heroin-induced locomotion and between both Pdyn and Penk mRNA levels and heroin-
induced conditioned place preference. Acknowledgements: 3, 6 diacetyl-morphine HCl was generously provided by NIH-NIDA Division of Drug Supply and Analytical Services. This work was supported by grants from NIH-NIDA (DA05130), the Arcadia Charitable Trust and The Carson Family Charitable Trust to MJK.

Dynorphin gene expression in the amygdala after stress exposure
J. T. Silveira, S. Gouty, G. Bull, and B. M. Cox, Dept of Pharmacology, Uniformed Services University, Bethesda MD 29814, USA.

The role of dynorphin (DYN) in the aversive response to severe stress is unclear, although it has long been known that there is significant expression of the DYN gene in the amygdala, a brain structure intimately involved in the elicitation of fear-induced behaviors. Dynorphin is expressed in discrete groups of neurons within the amygdala of rats, with most concentrated expression in parts of the central amygdala (CeA). The CeA is a critical output nucleus sending information from the amygdala to the peri-aqueductal gray area, a brain region regulating the expression of fear, pain, and autonomic reactions to aversive stimuli. Exposure of rats to a sustained severe stress (restraint with random mild tail-shocks for 2 hrs per day for 3 days) resulted in a significant increase 24 hr later in expression of the processed product of dynorphin gene expression, DYN A(1-8), in fibers in the lateral division of the anterior CeA, but not in the medial CeA or in more caudal parts of the amygdala. Neurons expressing the mRNA for DYN were found throughout the anterior CeA with noted expression in its lateral division. DYN A(1-8) fibers were also noted to be present in close proximity to the mu-opioid receptor-expressing neurons of the intercalated nuclei of the amygdala that are arrayed around the basolateral amygdala (BLA), although there were few DYN A(1-8) fibers in the BLA itself. The relationship of the expression of DYN to other endogenous opioids in amygdala is being evaluated. Our results suggest that DYN may play a role in the response of the brain to aversive stress. Supported by a grant from USAMRMC, #W81XWH-08-2-0575).

Effects of dextromethorphan/morphine on treatment of neuropathic pain in mice

Neuropathic pain is chronic pain results from primary lesions or dysfunction in the nervous system. Increasing evidences indicate that inflammatory and immune mechanisms play a role in these processes. In clinic, morphine is not very effective in treating neuropathic pain, and chronic morphine alone results in tolerance and dependence. Dextromethorphan (DM) is a well known N-methyl-D-aspartate (NMDA) receptor antagonist and has long history of clinical safety as an antitussive drug for 5 decades. Our previous studies have shown that co-administration of DM and morphine could potentiate the antinociceptive effect of morphine and also attenuated the tolerance and dependence to morphine. In the present study we have used a partial sciatic nerve ligation (PSNL) model to produce neuropathic pain in male ICR mice and investigated the effects of DM by itself or combined with morphine. Treated drug(s) was (were) administered 2 hours after surgery and twice a day for 5 days or longer. We found that: (1) Chronic morphine treatment attenuated PSNL-induced allodynia (measured by von Fey test) at a dose of 10 mg/kg, but not at 5 mg/kg (s.c.); (2) repeated administration of DM (20 mg/kg; i.p., bid) alone significantly reduced allodynia on post-operative day 5; (3) Co-administration of morphine (5 mg/kg; s.c.) and DM (20 mg/kg; i.p.) did not show greater effects than DM alone. (4) Chronic co-administration of morphine (10-20 mg/kg) + DM (20 mg/kg) for long term (more than 10 days) significantly attenuated the PSNL-induced allodynia. We also found that repeated administration of morphine, DM or co-administration of morphine and DM attenuated the PSNL-induced expression of GFAP (astrocyte activation marker), Iba1 (microglial activation marker), inducible nitric oxide synthase (iNOS), at L4-L6 spinal cord (determined by immunoﬂuorescence). Therefore, the beneficial effect of chronic morphine or DM on the development of allodynia may be related to its effect on inhibiting the activation of glia cells. (supported by NSC-97-2320-B-016-005-MY3, Taiwan)

Regulation of prodynorphin expression in human brain: Transcription factors targeting SNPs associated with alcohol dependence

Several PDYN SNPs are associated with alcoholism. Here we analyzed whether three (rs1997794, rs6045819, rs2235749) of them showing high significance of association, may serve as targets for transcription factors (TFs) regulating PDYN in human brain. First, we demonstrated that the T allele of PDYN promoter SNP (rs1997794) resides within noncanonical AP1-binding element, and may be targeted by AP1 TF. The T and C alleles of this SNP differ in AP1 DNA-binding affinity. Analysis of human brain AP1 that interacts with PDYN demonstrated that the complex consists of JUND and FOSB, the dominant AP-1 constituents in this tissue. The C allele of this SNP forms a CpG site that is
methylation at low levels in the human brain. Evaluation of association of the promoter SNP variants with PDYN expression in brain of human alcoholics and controls using the principal component analysis suggested that PDYN expression in the dl-PFC may be related to alcoholism, while in the hippocampus may depend on the genotype. Analysis of the exon 4 SNP (rs6045819) demonstrated that its C allele forms a noncanonical E-box which may be targeted by USF2 TF in human brain. Cpg site formed by this allele was methylated in human brain but a limited number of subjects precluded analysis of its influence on PDYN expression. The T allele of 3’-UTR SNP (rs2235749) forms T-box, an E-box variant and may be targeted by the 63 kDa, T allele specific binding factor which has differential binding affinity for T and C alleles. This SNP also forms a CpG site, which methylation is elevated in dl-PFC of human alcoholics, where it positively correlates with PDYN mRNA and peptides. Thus, PDYN SNPs associated with alcoholism may functions as targets for TFs regulating PDYN transcription, and may be regulated through methylation of their C alleles. These SNPs, their methylation and the identified TFs could mediate effects of long-term alcohol consumption on brain area specific pattern of PDYN expression in human brain. Supported by the Swedish FAS and VR.

Buprenorphine/naltrexone by iontophoresis: a transdermal approach to drug abuse treatment

A. Taverner, S. Cordery, R.H. Guy, M.B. Delgado-Charro, C.P. Bailey, S.M. Husbands, Department of Pharmacy and Pharmacology, University of Bath, Bath, UK

There has long been interest in the ability of buprenorphine to decrease cocaine use, but the clinical utility of this approach has been limited by the obvious problems of giving an opioid to a cocaine user. A combination of buprenorphine and naltrexone, where the naltrexone is present in sufficient quantity to block the mu partial agonist activity of buprenorphine, also appears to have utility in reducing cocaine use, as well as preventing relapse to opioid use. A problem with this treatment strategy arises from the need to administer buprenorphine and naltrexone by different routes. However, both buprenorphine and naltrexone can be delivered transdermally using iontophoresis, and we are currently using this technique to develop a buprenorphine/naltrexone combination therapy. Using conditioned place preference (CPP) in male Sprague-Dawley rats, the rewarding properties of buprenorphine and naltrexone combinations were assessed. The ability of buprenorphine/naltrexone to inhibit drug-primed reinstatement of morphine-induced CPP was then tested. Buprenorphine alone (0.3 mg/kg) was rewarding, whereas a buprenorphine to naltrexone ratio of 1:10 (0.3 and 3 mg/kg) was aversive. However, a ratio of 1:3 (0.3 and 1 mg/kg) was neither rewarding nor aversive. A morphine priming dose of 2.5mg/kg reinstated morphine CPP (animals were trained to demonstrate CPP with 10mg/kg morphine followed by extinction training), an effect that appeared to be inhibited by prior administration of buprenorphine/naltrexone (0.3 and 1 mg/kg respectively). All drugs were administered i.p. We have demonstrated a combination of buprenorphine/naltrexone with no rewarding or aversive effects that appears to inhibit reinstatement in an animal model of drug-seeking behaviour. Our ongoing work will test further the ability of buprenorphine/naltrexone to prevent CPP reinstatement, particularly to cocaine, and to optimise conditions for their transdermal delivery. Acknowledgments: We gratefully acknowledge funding from the Medical Research Council (G0802728).

The novel opioid antagonist, ALKS 37, reduces morphine-induced slowing of gastrointestinal transit in rodents and hydrocodone-induced slowing in dogs

M.S. Todtenkopf¹, R.L. Dean¹, D. Arnelle¹, K.A. Heang¹, K.S. O’Neill¹, J.M. Bidlack², B.I. Knapp², D.R. Deaver¹, ¹Life Sciences and Toxicology Dept, Alkermes, Inc., Waltham, MA, USA, ²Dept of Pharmacology and Physiology, School of Medicine and Dentistry, Univ. of Rochester, Rochester, NY, USA

ALKS 37 is a novel, orally active, peripherally-restricted, gastrointestinal (GI) tract targeted, metabolically stable, mu-opioid receptor antagonist being developed for the treatment opioid-induced bowel dysfunction (OBD), including constipation and associated GI abnormalities resulting from chronic opioid use. Here, we characterize the pharmacodynamic effects of ALKS 37 in rats and dogs. In rats, the ability of ALKS 37 to block morphine-induced delay in GI transit was assessed following oral (PO) administration. Rats were pretreated with ALKS 37 (0–10mg/kg,PO) 30min prior to morphine (14mg/kg,PO). A charcoal suspension was administered (PO) 60min later, and the small intestine was removed 20min following the charcoal meal. Morphine decreased the distance traveled by a charcoal meal by approximately 25%. Oral administration of ALKS 37 dose-dependently attenuated morphine’s effects with the highest dose tested (10mg/kg) returning GI motility to 90.6% of controls. In addition, we utilized a novel method for assessing opioids effects on oro-caecal transit time (OCTT) in dogs and tested the effects of ALKS 37 on hydrocodone-induced increases in OCTT. OCTT was determined by appearance of sulphapyradine in plasma after PO administration of sulphasalazine.
Dogs received ALKS 37 (0 or 20mg,PO) 30 min before hydrocodone (0.33mg/kg,PO). Sulphasalazine (120mg/kg) was administered 30min later and blood samples were collected for 6 hrs. ALKS 37 pretreatment prevented hydrocodone-induced delay in OCTT. In conclusion, ALKS 37 demonstrated efficacy in these models following oral administration, and is currently being investigated in clinical trials for the treatment of ÒBD. All work funded by Alkermes, Inc.

(+)-5a Compound, but not nociceptin, excited projection neurons in rat periaqueductal gray slices
L.-W. Tung (1) and L.-C. Chiou (1, 2). (1) Grad. Inst. and (2) Dept. Pharmacology, Coll. Medicine, National Taiwan University, Taiwan
(+)-5a Compound (5a), ((3aS, 6aR)-1-(cis-4-isopropylcyclohexyl)-5k methyl-2k-phenylhexahydrospiro[piperidine-4,1k-pyrrolo[3, 4-c][pyrrole]], is a non-peptide agonist of nociceptin/orphanin (N/OFQ) peptide (NOP) receptors with the structure backbone similar to Ro 64-6198 (Ro). We have previously shown that both 5a and Ro activated K+ channels via one, and the same, subset of NOP receptors in vlPAG neurons while N/OFQ was effective in those Ro/5a-insensitive NOP receptors, and most of 5a-sensitive neurons are GABAergic. (Liao et al., Int. J. Neuropsychopharmacol. 2010). Here, we further compared effects of 5a and N/OFQ on synaptic transmission and subsequent neuronal activity of the PAG neurons which project to the rostral ventral medulla (RVM). PAG-RVM projection neurons in the PAG of Wistar rats (P7-P11) were retrogradely labeled by stereotaxically injecting retrobeads into the RVM (DV-7.5 mm, AP-1.6 mm, ML-0.0 mm) 3-4 days ahead. Visualized whole cell patch clamp recording was conducted in PAG-RVM projection neurons in 300 mm-thick PAG slices in the current clamp mode. NOF/Q (300 nM) caused membrane hyperpolarization (7.67±0.81 mV, n=11) in 11/12 (92%) recorded neurons, while 5a (10 microM) only hyperpolarized 29% (4/14) of the recorded neurons (6.47±1.86 mV, n=4). Local stimulation-evoked postsynaptic potential (PSP), which is a summation of excitatory and inhibitory PSPs, was depressed by NOF/Q (300 nM) from 9.82±1.95 mV to 5.86±1.9 mV (n=5, p<0.05) after membrane potential correction. However, 5a (10 microM) caused each tested projection neurons firing action potentials when evoked PSPs before drug treatment were at the same level (7.85±1.62 mV, n=6) as that (9.82±1.95 mV) for treating N/OFQ. In the group with smaller PSPs, 5a (10 μM) had no significant effect on PSPs (5.04±1.23 mV vs. 4.85±1.33 mV, n=7, p=0.56). These results suggest 5a, but not N/OFQ, exerts an overall excitatory effect on PAG-RVM projection neuronal activity. (Supported by grants NHRI-EX99-9506NI, NSC-98-2320-B-002-011-MY3, NSC-98-2323-B002-012 and NTU-99R81855).

HDAC inhibitors recover the epigenetically silenced mu-opioid receptor expression in neuropathic pain model
H. Ueda, H. Uchida, K. Araki, Division of Molecular Pharmacology and Neuroscience, Nagasaki University Graduate School of Biomedical Sciences, Japan
Peripheral nerve injury causes chronic neuropathic pain, which is often refractory to treatments with conventional painkillers, including morphine. Previously we have demonstrated that injury down-regulates mu opioid receptor (MOP) expression in the dorsal root ganglion (DRG), thereby causing loss of peripheral morphine analgesia via epigenetic silencing of MOP gene in the DRG (J Neurosci, 30, 4806–4814, 2010). This study has revealed that NRSF is recruited to the NRSE (NRSE, also known as RE-1) site within MOP gene post-injury, and then causes histone hypoacetylation, which is closely related to transcriptional suppression. It has been known that NRSF, when it binds to NRSE, recruits histone deacetylase (HDAC) through its corepressors, mSin3 and CoREST, for generating a repressive chromatin environment. Therefore, we here tested whether HDAC inhibitors, including trichostatin A (TSA), could block NRSF-mediated epigenetic silencing of MOP gene, and then ameliorate the loss of peripheral morphine analgesia. We successfully found that HDAC inhibitors prevent the development of loss of peripheral morphine analgesia as well as ameliorate established morphine resistance in neuropathic pain. Taken together, we provided first evidence that epigenetic therapy with HDAC inhibitors is effective against morphine resistance in neuropathic pain.

A naturally occurring genetic model of human mu-opioid receptor genetic variation
E.J. Vallender, Z. Xie, D.M. Platt, G.M.Miller, Division of Neuroscience, New England Primate Research Center, Harvard Medical School, Southborough, MA, USA
Human variation has long been recognized in the mu-opioid receptor; two variants, A118G (N40D) and T17C (V6A), both occur in the extracellular N-terminal domain and seem to be functionally relevant. Their ethnic distributions, however, are extremely heterogeneous with the A118G polymorphism being most common outside of Africa and the T17C polymorphism almost exclusively seen...
in African populations. Both of these variants have been associated with substance use disorders and pharmaceutical treatment, though the results have been mixed. The aforementioned ethnic genetic heterogeneity may contribute as well as the more common environmental variation that plagues human studies. We have identified a polymorphism in rhesus macaques, C77G (P26R) that occurs at moderate frequencies and appears to functionally parallel the human variation. We and others have also successfully demonstrated that this variant is associated with alcohol preference and consumption in rhesus macaques as well as their response to treatment with naltrexone. G77 homozygote animals demonstrate an ~40% increase alcohol consumption across concentrations (0.5%-4.0% w/v). These animals also respond to naltrexone at 30-fold lower concentrations than C77 homozygotes. In both cases heterozygous animals show intermediate phenotypes indicative of an additive genetic model. This development of an animal model of the genetic variation seen in human has allowed us to further explore the underlying causes for the phenotypic variation in humans. Notably our current work confirms and extends the functional similarities across mu-opioid receptor polymorphisms regardless of species. We have also leveraged the animal model to explore the differential sensitivity to naltrexone conferred by the polymorphisms. Together this allows us to better interpret the human findings and to explore the functional effects of mu-opioid receptor polymorphism in an experimental model system. Supported by NIH grants AA019688 (EJV), AA016828 (DMP), AA016184 (GMM), DA025697 (GMM) and RR000168

Lead optimization studies of n-(2-[1,1'-biphenyl]-4-yethyl)-8-cac
M. A. VanAlstine (1), M. P. Wentland (1), D. J. Cohen (2), J. M. Bidlack (2), (1) Dept. of Chemistry and Chemical Biology, Rensselaer Polytechnic Institute, Troy, NY, USA; (2) Dept. of Pharmacology and Physiology, University of Rochester, Rochester, NY, USA
N-(2-[1,1'-biphenyl]-4-yethyl)-3-(cyclopropylmethyl)-1,2,3,4,5,6-hexahydro-6,11-dimethyl-2,6-methano-3-benzazocine-8-carboxamide has very high affinity for opioid receptors. This lead compound is an analogue of the well-known opioid cyclazocine where its prototypic (of opioids) phenolic-OH is replaced by an N-substituted carboxamido group. We now report analogues of this lead compound where a) the ethylene group linking the carboxamido N to the biphenyl group has been substituted with a mono-methyl or a fused-cyclopropyl group and b) a methylene or oxygen spacer has been inserted between the phenyls of the biphenyl group. Compared to the lead compound, analogues in the first group displayed considerably reduced binding affinity against all receptors while several in the second group displayed comparable or enhanced binding affinity [Ki (mu) as low as 0.059 nM]. (Supported by NIDA grants R01 DA012180 and KO5-DA00360)

Pharmacological profile of delta and kappa opioid receptor subtypes in spinal cord.
R. M. van Rijn, D. I. Brissett, J. L. Whistler
Ernest Gallo Clinic and Research Center, Department of Neurology, University of California San Francisco, CA, USA
The opioid receptor family consists of four types: mu (MOR), delta (DOR), kappa (KOR) and nociceptin. While no functional splice variants have been cloned for the DOR and KOR pharmacological evidence in vivo suggests the existence of multiple opioid receptor subtypes. Opioid receptors play an important role in the perception of pain and are abundantly expressed in brain and spinal cord. Recently, it was shown that MOR and DOR are distinctly located in circuits mediating thermal and tactile pain, respectively. However, the expression of the KOR or opioid receptor subtypes in these circuits is unclear. Therefore, we set out to elucidate the molecular basis of the DOR and KOR subtypes. We injected C57BL/6 mice intrathecally with type and subtype selective drugs and measured thermal pain and tactile antinociception using tail-flick and Von Frey filaments, respectively, in wild-type as well as opioid receptor knockout mice. Our data suggests that in naïve mice KOR and MOR are present in circuits mediating thermal pain and that there are no pharmacological differences between DOR and KOR subtypes. We injected naïve mice KOR and MOR are present in circuits mediating thermal pain and that there are no pharmacological differences between DOR and KOR subtype selective agonist. We find evidence for the existence of opioid receptor homomers as well as DOR-MOR, KOR-DOR and KOR-MOR heteromers in circuits mediating tactile pain. Additionally, we find that mice that have been voluntarily drinking ethanol express functional DOR-MOR heteromers in circuits mediating functional DOR-MOR heteromers in circuits mediating thermal pain. Our data provides a better understanding of the distribution of opioid receptor types and subtypes in the spinal cord which could assist designing more selective and efficacious analgesic drugs, with reduced side effects. This work was funded by the Foundation for Alcohol Research-ABMRF (RvR), the Department of Defense (JW), NIDA (JW) and funds provided by the State of California for medical research on alcohol and substance abuse through the University of California, San Francisco (JW).

Neuropeptides have not been previously identified as causative factors for neurodegenerative disorders. The spinocerebellar ataxias (SCAs) are a genetically heterogeneous group of neurodegenerative disorders characterized by progressive cerebellar ataxia, dysarthria and loss of the Purkinje cells. The SCA23 locus has been previously located on chromosomal region 20p12.3-p13. We here report the identification of four missense mutations in prodynorphin (PDYN) located in this region. SCA23 families and 1100 ataxia patients, and 500 control individuals were screened for PDYN mutations. In cellular experiments, expression and processing of mutant PDYNs and effects of wt- and mutant peptides on striatal neurons were analyzed. Cellular pathways were studied by shotgun proteomic and key-node analyses in autopsy samples. Three mutations were located in Dyn A, a peptide with non-opioid neurodegenerative actions. Two mutations resulted in excessive generation of Dyn A. Two Dyn A mutants induced toxicity above that of wild type peptide. The fourth mutation was located upstream of dynorphins and affected expression of components of the opioid and glutamate system in the cerebellum. PDYN and Dyn A were located in Purkinje cells. Elevated non-opioid actions of Dyn A mutants or impairment of secretory pathways by mutant PDYNs may lead to glutamate neurotoxicity that underlies Purkinje cell degeneration and ataxia. This is the first demonstration of causative link between mutations in neuropeptides and neurodegenerative/neuropsychiatric disorders. Identification of such mutations will also provide further insight into neuropeptide functions.

Acknowledgments: R. Franklin Fellowship, University of Groningen, the Netherlands; the Swedish VR and FAS.

Both JNK and β-arrestin 2 play a role in ligand dependent signaling of the mu opioid receptor

N. Mittal1,2, M. Tan1, O. Egbuta1, N. Desai1, C. Crawford2, T. Xie1, C. Evans1, W. Walwyn1, 1Dept. Psychiatry & Biobehavioral Sciences, Stefan Hatos Ctr Neuropsycharmacol., Semel Institute, UCLA, CA 90095, 2Dept. of Psychology, California State University, San Bernardino, CA 92407

c-Jun N-terminal kinase (JNK), a member of the stress activated map kinase family, is best known for its role in differentiation, apoptosis and neurodegeneration. More recently JNK has also been found to play a role in ligand directed signaling by the mu opioid receptor, particularly desensitization and tolerance induced by the clinically important opioid agonist, morphine. As one of the members of this family, JNK3, binds with β-arrestin 2, this scaffolding and signal transduction molecule may form an important component of JNK- and ligand-dependent opioid receptor signaling. Using mice lacking β-arrestin 2 (β-ar2-/-) we first determined the role of β-arrestin 2 in the nuclear-cytoplasmic shuttling of the major downstream target of JNK, cJun, as a measure of activity within the JNK cascade. We found that morphine, but neither DAMGO nor Fentanyl, increased the nuclear import of the phosphorylated, therefore activated form, of cJun in β-ar2-/- neurons. This enhanced activation of the JNK cascade explained the enhanced thermal analgesia induced by a single dose of morphine in β-ar2-/- mice. By contrast the acute analgesic effect of fentanyl was neither β-arrestin 2 nor JNK dependent. This profile of JNK and β-arrestin 2 dependent signaling can be explained by a morphine-specific confirmational change of the mu receptor affecting the confirmation of the recruited arrestin isoforms. This allows the arrestin associated upstream members of the JNK cascade to align, phosphorylate and activate JNK. (DA-05010)

Mu- and delta-opioid receptor agonists mediate up-regulation of RGS19 protein in SH-SY5Y cells

Q. Wang and J.R. Traynor, Department of Pharmacology and Substance Abuse Research Center, University of Michigan, Ann Arbor, USA

Regulator of G protein signaling protein 19 (RGS19), also known as G alpha-interacting protein (GAIP), was the first mammalian RGS family member identified. RGS19 acts as a GTPase accelerating protein (GAP) for Gα1,3 and Gαs subunits. In addition, interactions with GIPN (GAIP-interacting protein N-terminus), and GIPC (GAIP-interacting protein C-terminus), link RGS19 to a variety of intracellular proteins, ranging from receptors, including opioid receptors, to transporters and scaffolding molecules. Here we show that RGS19 is abundantly expressed in SH-SY5Y cells that endogenously express mu-opioid and delta-opioid receptors (MOR and DOR respectively). Overnight treatment with 10 microM of either MOR (DAMGO) or DOR (DPDPE) agonist increased RGS19 protein by 3-4 fold, but did not change the level of RGS19 mRNA, suggesting an effect on protein stabilization. Up-regulation of the level of RGS19 protein by DAMGO and DPDPE was both time- and dose-dependent. Lentiviral delivery of shRNA against RGS19 reduced RGS19 protein levels by at least 50% in SH-SY5Y cells, compared to cells infected...
with lentivirus encoding shRNA against GFP. This led to an increase in the ability of acute MOR (morphine) and acute DOR (SNC80) agonists to inhibit forskolin-stimulated adenylyl cyclase. These findings indicate a role for RGS19 in modulating acute opioid receptor signaling and suggest that the increase in RGS19 protein level may be implicated in the chronic opioid state. Supported by DA04087

OPRM1 A118G SNP reduces MOPR expression in some, but not all, brain regions in a mouse model

Y-J. Wang¹, P. Huang¹, A. Ung¹, J. Blendy², L-Y. Liu-Chen¹,¹Dept. Pharmacol., Temple Univ, ²Dept. Pharmacol., Univ of Pennsylvania, Philadelphia, PA, USA

OPRM1 A118G, a common single nucleotide polymorphism (SNP) in the human mu opioid receptor gene, is associated with high morphine doses for postoperative pain and better treatment outcome for alcohol addiction. A mouse model possessing the equivalent substitution (A112G) in the Oprml gene was generated. The mutant mice displayed reduced antinociceptive and locomotor responses to morphine and female mice showed attenuated morphine reward. The alteration in MOPR expression in A112G variant may play a role. In this study, [³H]DAMGO binding was examined in mice homozygous for the A allele (A/A) or G allele (G/G) using quantitative in vitro autoradiography. Brain sections (20 μm) were incubated with 5 nM [³H]DAMGO with or without 10 μM naloxone. Sections were exposed to [³H]sensitive screens and the images were quantitated. Data were analyzed with a 2-way ANOVA followed by Bonferroni post-hoc test. There was genotype effect in some brain regions, but no sex effect or genotype x sex interaction. A/A mice exhibited markedly higher [³H]DAMGO binding than G/G in the cingulate, motor, and insular cortices, NAc core and shell, hypothalamus, thalamus, amygdala, PAG, superficial grey of superior colliculus, and VTA. No genotype differences were observed in somatosensory cortex, CPU, and hippocampus. In males A/A mice showed markedly higher [³H]DAMGO binding than G/G in the cingulate, motor, and insular cortices, NAc core and shell, hypothalamus, thalamus, amygdala, PAG, superficial grey of superior colliculus, and VTA. Thus, the A112G SNP reduces MOPR expression in some, but not all, brain regions, and appears to be sex dependent. As this SNP eliminates one N-linked glycosylation site, there may be differences in the components of N-linked glycosylation machinery among brain regions and between sexes, leading to differential effects of the SNP on MOPR expression. (supported by NIDA grants)

Pathogenic activities of dynorphin a mutants that cause human neurodegenerative disorder spinocerebellar ataxia type 23: induction of nociceptive behaviors in mice through non-opioid mechanism


We previously identified four missense mutations in PDYN that cause human SCA23 (Bakalkin et al., Am J Hum Gen 2010). Three mutations were located in Dyn A1-17 substituting Leu5, Arg6, and Arg9 to Ser (L5S), Trp (R6W) and Cys (R9C). R6W and L5S mutations resulted in excessive Dyn A generation, while R6W- and R9C-Dyn A were highly neurotoxic. It had been previously reported that Dyn A administered intrathecally (i.t.) into mice produces a characteristic SBL responses, the hindlimb Scratching along with Biting and Licking of the hindpaw / tail (Tan-No et al., Pain, 2005). We here report that all mutants administered in femtomolar doses also produced SBL responses. Compared to wild type (wt)-peptide, mutant peptides were more potent in these responses 2-3 fold, while for L5S- and R6W-mutants effective doses were lower 10-30 – fold. R6W-mutant was the most potent peptide. The SBL-responses induced by R6W-Dyn A were dose dependently inhibited by morphine (i.p.; 0.1-1 mg/kg) or MK-801, an NMDA ion channel blocker (i.t. co-administration; 5-7.5 nmol). CP-99,994, a tachykinin NK1 receptor antagonist (i.t. co-administration; 2 nmol) and naloxone (i.p.; 5 mg/kg) failed to block effects of R6W-Dyn A. Thus, mutant-Dyn A peptides have elevated potential to produce nociceptive responses. Similarly to wt-Dyn A, these responses or at least those induced by R6W-Dyn A may be mediated through NMDA receptor but not opioid and tachykinin NK1 receptors. Enhanced non-opioid activities of mutant-Dyn A support the hypothesis on pathogenic role of these peptides in neurodegeneration in human brain. Supported by the Swedish Science Council, Uppsala Univ., Swedish Inst., a Rosalind Franklin Fellowship, Univ. Groningen, the Japan Society for the Promotion of Science.
Modulation of full-length mu opioid receptor (MOR-1) expression and function by truncated proteins with single transmembrane domain of the mu opioid receptor gene, OPRM1

J. Xu1, M. Xu1, G.C. Roşşi2, C.E. Inturrisi3, G.W. Pasternak1, Y.-X. Pan1 1 Dept of Neurology, Memorial Sloan-Kettering Cancer Center, New York, NY. 2 Dept of Psychology, CW Post College, Long Island University, Brookville, NY. 3 Dept of Pharmacology, Weill Medical College of Cornell University, New York, NY, USA

Mu opioids, widely used for pain management and also abused, act through mu opioid receptors. Clinical differences in the actions of many of these drugs raised the possibility of mu receptor subtypes, a concept confirmed by the identification of a vast array of both 3’ and 5’ splice variants from the mu opioid receptor (OPRM1) gene. In the present study, we report the isolation of additional splice variants that encode truncated proteins containing single transmembrane domain (TM) from the OPRM1 genes. These single TM variants are conserved from mouse, rat and human. Expression level of these variants’ mRNAs was quite abundant. We explored the function of the single TM variants in modulating full-length MOR-1 expression using stably transfected Tet-off CHO cell lines, in which the MOR-1 expression was constant whereas the expression of the single TM variants were under control of doxycycline. The results showed that the single TM variants can dimerize with MOR-1, which was initiated in endoplasmic reticulum (ER), leading to increased expression of MOR-1 protein determined by [3H] DAMGO binding and Western blot analysis. Furthermore, our studies suggested that the dimerization of the single TM variants with MOR-1 facilitated proper folding or conformation of MOR-1 in ER, promoting its escaping from ER-associated degradation pathway and increasing turnover rate of MOR-1 determined by pulse-chase studies. In vivo antisense studies suggested that the single TM variants play an important role in morphine analgesia. Our studies raise questions regarding the functional significance of truncated proteins from other GPCR families. (Supported by DA13997 & DA029244 (Y.-X.P), DA02615 & DA07242 (G.W.P) and DA01457, DA07274& DA05130 (C.E.I.) from NIDA)

Epigenetic mechanism of prodynorphin upregulation in the brain of human alcoholics: dependence on promoter methylation and USF2 transcription factor

Dept. Pharmaceutical Biosciences, Uppsala University, Sweden.

Changes in the epigenetic landscape with DNA methylation / demethylation and histone modifications in gene regulatory elements have been proposed to underlie human neuropsychiatric diseases including substance addiction. Critical evidence for the hypothesis is still missing. Our study demonstrated that expression of the prodynorphin gene (PDYN) producing opioid peptides dynorphins is elevated in the prefrontal cortex (PFC) of human alcohol-dependent subjects. This upregulation may be a critical molecular event underlying development or maintenance of the addictive state. Molecular mechanisms of PDYN activation in human brain were addressed by analysis of alterations in DNA methylation in PDYN promoter. The 1.7 kB promoter area was analyzed in post-mortem specimens, the PFC (BA9) and motor cortex (MC; BA4) of human alcoholics and controls (n=14 subjects in each group) using bisulfite treatment / DNA pyrosequencing. A short CpG rich domain in the promoter was found to be strongly and significantly demethylated in the PFC in alcoholics. The differentially methylated region (DMR) encompassing approximately 150 nt, was apparently located within a single nucleosome. No differences were evident in the MC, which showed no PDYN activation in alcoholics. Search for transcription factor (TF) binding sites found canonical E-box in the DMR, and then Upstream Stimulatory Factor-2 (USF2) with strong histone-modifying activities was identified as a dominant E-box binding factor in the human PFC by EMSA. In this brain area, USF2 was found i) to be colocalized with PDYN protein using immunostaining; and ii) to be bound to the PDYN DMR using ChIP-qPCR. We hypothesize that the PDYN DMR functions as the brain-area specific “epigenetic switch” affected by alcohol; DMR demethylation may promote USF2-mediated recruitment of histone modifiers to the promoter resulting in PDYN activation in alcoholics. Supported by the Swedish Council for Working Life and Social Research, and the Swedish Science Research Council.
Sleep disturbances in a neuropathic pain-like condition are associated with altered GABAergic transmission in the cingulate cortex
Insomnia is a common problem for people with chronic pain. Cortical GABAergic neurons are part of the neurobiological substrate that underlies homeostatic sleep regulation. In the present study, we confirmed that sciatic nerve ligation caused thermal hyperalgesia and tactile allodynia in mice. Mild noxious heat stimuli caused a significant increase in the release of glutamate in the cingulate cortex of nerve-ligated mice compared to that of sham-operated mice. In this experimental model for neuropathic pain, we found an increase in wakefulness and a decrease in non-rapid eye movement (NREM) sleep under a neuropathic pain-like state. The membrane-bound GABA transporters (GATs) on activated glial fibrillary acidic protein (GFAP)-positive astrocytes were significantly increased in the cingulate cortex of mice with sciatic nerve ligation. In an experiment with primary cultured glial cells from the mouse cortex, treatment with glutamate led to the translocation of GATs from intracellular vesicles to the plasma membrane. Furthermore, extracellular GABA levels in the cingulate cortex after depolarization were rapidly decreased by nerve injury. Under this condition, sleep disturbance induced by sciatic nerve ligation was improved by the intracingulate cortex injection of a GATs inhibitor. These findings provide novel evidence that sciatic nerve ligation decreases extracellular-released GABA along with an increase in membrane-bound GATs on activated astrocytes in the cingulate cortex of mice. These phenomena may, at least in part, explain the insomnia in patients with neuropathic pain.

Non-Medical Use of Prescription Narcotics in the Sequence of Adolescent Drug-Use Initiation and Epidemiology of Narcotic-Use by Indiana Adolescents

Non-medical use of prescription drugs, including narcotics, is the fourth most prevalent type of drug use engaged in adolescents. A habit of non-medical use of prescription drugs has the potential to develop into abuse and dependence on the medication. The objective is to study the epidemiology of using narcotics and other drugs by adolescents and to identify repercussions experienced by adolescents due to the use of narcotics. Data from 1993 to 2009 Annual Surveys of Alcohol, Tobacco, and Other Drug Use by Indiana Children and Adolescents is used for the current study. A closed-ended, self-administered, written, anonymous questionnaire was used to ask adolescents about their use of twenty different types of drugs. Market basket analysis was used to identify sequences of drug use. An index was created to evaluate consequences and risk behavior due to drug-use. Overall drug use among adolescents in Indiana is 45.3%, prescription drug use is 10.9% and annual use of narcotics is 10.9%, although only 0.04% uses narcotics alone. Overall, adolescent drug abuse has decreased in recent years while the use of narcotics has increased. A sequence exists between initial use of gateway drugs and nonmedical use of medications later in life. Combined drug use behavior is more common with increasing age. Rates of combined drug use are also higher among males and whites. Being female or white is associated with increased reporting of negative consequences due to narcotics use. Males and other races are more likely to report to personal-safety issues due to drug use. Combining narcotics with other prescription drugs is associated with increased reporting of negative consequences due to the drug use. Prevention programs should address issues related to gender, racial, and ethnic differences in drug abuse, prescription drug use including narcotics, sequences of drug-use initiation and negative consequences as well as risk behavior that result from adolescent drug use.

Expression of OPRK1, PDYN and CXCR4 in the caudate in postmortem brain of HIV infected and HIV negative subjects
V. Yuferov (1), A. Ho (1), S. Morgello (2), M.J. Kreek (1), (1) Laboratory of Addictive Diseases, The Rockefeller University, New York, NY, USA, (2) Pathology, Mount Sinai Medical Center, New York, NY, USA

Opioid and chemokine receptors are implicated in neuronal functions, immune responses, and co-receptor-dependent HIV-1 infection. Recent studies have demonstrated cross-desensitization between opioid and chemokine receptors, including bi-directional cross-talk between CXCR4 and KOR receptors in both in vitro and in nociceptive tests in rats (Finley et al, 2008). The aims of the study were to examine (1) levels of the CXCR4, OPRK1 and PDYN mRNAs in the caudate of HIV positive and HIV negative subjects; (2) the correlation of the CXCR4, OPRK1, and PDYN mRNA levels with mRNA levels of markers of glial and neuronal cells. Tissues from postmortem brain of 24 HIV+ and 14 HIV- subjects were obtained from the Manhattan HIV Brain Bank (The Mount Sinai Medical Center, New York, NY). Total RNA was isolated from the caudate, and used for synthesis of cDNA.
Quantification of mRNA of OPRK1, PDYN, CXCR4, GFAP, CD163 and CD68 was carried out using SYBR Green RT-PCR. Copy number of cDNA transcripts was expressed normalized to GAPDH cDNA. There was no difference in the OPRK1, CXCR4, or PDYN expression in the caudate between HIV+ and HIV- subjects. There were significantly higher levels of GFAP, CD163 and CD68 mRNAs in HIV+ subjects compared to HIV- (p<0.05). No correlation was found between levels of OPRK1 and CXCR4 mRNA in either HIV+ or HIV- subjects. Regression analyses showed significant correlation in expression of OPRK1 with CD163 in HIV+ subjects, and of PDYN expression with CD68 in both HIV- and HIV+ brains. The increased expression of glial/macrophage markers reflects a pronounced gliosis and inflammation in brain of HIV infected subjects. Our results suggest a relationship of OPRK1 and PDYN with specific markers of immune cells. Support: NIDA-P60-05130 (MJK), NIMH-R01-79880 (MJK), NIMH -U01-MH083501

Duration of withdrawal from chronic escalating-dose binge cocaine: effects on cocaine-induced conditioned place preference and expression of selective components of the opioid system
Y. Zhang, S. D. Schlussman, E. R. Butelman, A. Ho and M. J. Kreek, The Laboratory of the Biology of Addictive Diseases The Rockefeller University New York, NY, USA

Relapse to cocaine is a serious problem in the treatment of cocaine addiction. Understanding cocaine re-exposure-induced behavioral and neurobiological alterations following chronic escalating-dose binge cocaine administration and withdrawal may provide insight into the neurobiological basis of cocaine relapse. To investigate how exposure to chronic escalating-doses of cocaine affects development of cocaine-induced conditioned place preference (CPP) and changes in components of the endogenous opioid system, mice were injected with either escalating-dose binge cocaine (15-30 mg/kg/injection x 3/day) or saline for 14 days. Place preference conditioning with 15 mg/kg of cocaine commenced either 1 or 14 days after the last day of binge cocaine or saline injections. After 1 or 14 days’ withdrawal, CPP was studied in three groups of mice: 1. Mice had received escalating-dose cocaine, then conditioned with cocaine. 2. Mice had received saline, then conditioned with cocaine. 3. Mice had received saline, then conditioned with saline. Cocaine induced CPP in mice previously exposed only to saline following 1 or 14 days’ withdrawal. Mice did not form CPP to cocaine following 1 day withdrawal from escalating-dose binge cocaine, but mice did develop CPP to cocaine following 14 days’ withdrawal from escalating-dose binge cocaine.

Penk mRNA levels in the caudate putamen and nucleus accumbens core were higher whereas MOP-r densities were lower, in mice that developed CPP to cocaine after 14 days’ withdrawal from escalating-dose binge cocaine. Thus, duration of withdrawal plays an important role in the rewarding effect of cocaine. Elevation in Penk mRNA levels may explain, in part, why the longer withdrawal interval induced CPP to cocaine re-exposure. Acknowledgements: Cocaine-HCl was generously provided by NIH-NIDA Division of Drug Supply and Analytical Services. This work was supported by NIH-NIDA DA05130 to MJK

Chronic morphine tolerance upregulated spinal proinflammatory cytokines which are revised by HSV vector expressing interleukin 4 in rats
X. Zheng1,2, J. Sun1 S. Liu1,2, M. Mata1, D. Fink1 and S. Hao1,2, 1Dept. of Neurol, Univ. Michigan, Ann Arbor, MI, USA 2Dept. of Anesthesiology, Univ. Miami Miller Medical School, Miami, FL, USA

Morphine is very effective analgesics used to treat moderate to severe pain in clinic, however, the repeated use of morphine is limited by the off-target effects (e.g., tolerance and dependence). Recent studies show that chronic morphine activates glial cells in the central nervous system to release proinflammatory cytokines during the tolerance. In the current study, we confirmed that chronic morphine (IP, once a day) for 7 days induced antinociceptive tolerance and increased spinal glia marker, TNFα and IL-1β. Then, we examined the neuroimmune response in the rodent model of morphine tolerance using the Herpes Simplex Virus (HSV) vector expressing interleukin 4 (IL-4, one of anti-inflammatory cytokines). Subcutaneous inoculation of HSV expressing IL-4 into the hind paw delayed the development of morphine tolerance behavior response. Inoculation of the HSV vector expressing IL-4 prevented the increases in the spinal TNFα and IL-1β in rats with morphine tolerance. The study suggested that proinflammatory cytokines involved the development of morphine tolerance, and that gene therapy expressing anti-inflammatory cytokine may provide a novel approach to treating morphine tolerance. This study was supported by grants from the NIDA, NINDS.
Chronic voluntary alcohol drinking enhances proopiomelanocotin (POMC) gene expression in nucleus accumbens (NAc) and hypothalamus of alcohol-preferring rats

Y. Zhou¹, G. Columbo², K. Niikura¹, M.A.M. Carai², A. Ho¹, G.L. Gessa², M.J. Kreek¹
¹Lab of Biology of Addictive Diseases, Rockefeller University, New York, USA; ²CNR Neuroscience Institute, Monserrato (CA), Italy

Evidence obtained in humans and rodents indicates that beta-endorphin is critical in the regulation of alcohol-drinking behavior. However, the alcohol effect on POMC gene expression has not been studied in rodent mesolimbic regions, like NAc. In the present study, we first utilized POMC-EGFP promoter transgenic mice to visualize POMC neurons, and found that POMC-EGFP cells were scattered through NAc shell and core, in addition to hypothalamic arcuate nucleus. We then examined whether there are genetically determined differences in basal mRNA levels of POMC and mu opioid receptor (MOP-r) between selectively bred Sardinian alcohol-preferring (sP) and non-preferring (sNP) rats, and if mRNA levels are altered by chronic alcohol drinking in sP rats. Rats of both lines were offered either water or a free choice of 10% (v/v) alcohol and water with unlimited access for 17 days. POMC and MOP-r mRNA levels were measured in NAc core and shell, caudate-putamen (CPu), medial/basolateral amygdala (MeBLA) and hypothalamus. sP rats had higher basal POMC mRNA levels only in hypothalamus compared with sNP rats, indicating genetically determined differences between these two lines. Alcohol drinking increased POMC mRNA levels in both hypothalamus and NAc shell of sP rats. sP rats had lower basal MOP-r mRNA levels in NAc shell, MeBLA and CPu than sNP rats, and alcohol had no effect on MOP-r mRNA levels in these regions. Our results for the first time show the POMC-expressing neuron distribution in NAc of POMC-EGFP mice, and suggest that increased POMC gene expression at basal levels in hypothalamus (genetically determined) and after alcohol drinking in both hypothalamus and NAc (drug-induced) are associated with high alcohol preference and consumption in sP rats. NIH-DA-P60-05130 (MJK); CNR grant (GC).