



**2nd Annual Drug Abuse Research
Symposium at Drew:**

“Drug Addiction is a Brain Disease”

**Charles R. Drew University of
Medicine and Science**

W.M. Keck Lecture Hall

August 10, 2006

**2nd Annual Drug Abuse Research Symposium at Drew:
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Charles R. Drew University of Medicine and Science, August 10, 2006**

Objectives

Upon completion of this program, participants will be able to:

1. Discuss the prevalence and epidemiologic indication of drug abuse in the underserved community.
2. Identify current drug abuse research in the underserved community.
3. Provide efficient and effective services to drug abuse patients in the underserved community.
4. Discuss prevention and management of drug abuse in the clinical setting.
5. Discuss the mechanisms of opiates as agents giving pain relief.

Agenda

- 7:30-8:30 am Registration/Pre-Conference Evaluation and Breakfast
- 8:30-9:00 am Welcome and Background on MIDARP at Drew
Ted Friedman, MD, PhD
MIDARP Program Director, Charles R. Drew University
Email: tefriedm@cdrewu.edu
- 9:00-9:40 am Keynote Speech
“Methamphetamine and the Brain: A Problem of Inhibitory Control”
Edythe D. London, PhD
Professor, Department of Psychiatry and Biobehavioral Sciences and
Department of Molecular and Medical Pharmacology
- 9:40-10:20 am Keynote Speech
“Substance Abuse in Los Angeles County”
Jonathan E. Fielding, MD, MPH, MBA
Director of Public Health and Health Officer
Los Angeles County Department of Health Sciences
- 10:20-10:35 am Morning Break

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Agenda

- 10:35-10:55 am “Research Training and Funding Opportunities at National Institute on Drug Abuse (NIDA)/NIH”
Pushpa V. Thadani, PhD
Pharmacologist/Program Director
Division of Basic Neuroscience and Behavioral Research
National Institute on Drug Abuse
Email: pthadani@nida.nih.gov
- 10:55-11:15 am “A Pilot Test of an Environmental Intervention to Reduce Young People’s Access to Drug Paraphernalia in Liquor Outlets”
Didra BrownTaylor, PhD
Visiting Research Psychologist
UCLA-Integrated Substance Abuse Programs
Email: Xdidrax@aol.com
- 11:15-11:35 am “Nicotine Use, Inflammation and Arterial Diseases”
Tripathi B. Rajavashisth, PhD
Professor of Medicine
Charles R. Drew University of Medicine and Science
Email: tripathime@yahoo.com
- 11:35-11:55 am “Final Report of the California Syringe Exchange Program Study (CalSEP): Policy findings, risk assessments, and program improvement results”
Ricky Bluthenthal, PhD
Senior Social Scientist at RAND
Professor, Department of Sociology and
Director, Urban Community Research Center, CSUDH
Email: rickyb@rand.org
- 11:55-12:15 pm “Updates on Intervention For Methamphetamine Abuse”
Steve Shoptaw, PhD
Professor, Center for Health Promotion and Disease Prevention
David Geffen School of Medicine at UCLA
Department of Family Medicine
Email: SShoptaw@mednet.ucla.edu

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Agenda

12:15-1:45 pm Lunch Break/ **Poster Presentations**

Poster Presentations:

Otaren Aimuwu: “Stress’ Ability To Alter Chronic Nicotine’s Effect On The HPA Axis”

Shahrzad Bazargan-Hejazi, PhD: “The Prevalence Of Depression Among A Sample Of Inner-City Ed Patients Engaging In Harmful Drinking”

Victor V. Chaban, Ph.D.: “Estrogen decreases opioid anti-nociception”

Namiko Nerio, MS: “The Effects of CRH Antagonism on Nicotine’s Activation of the HPA Axis ”

1:45-2:45 pm **Trainee Oral Presentations:**

Adrian Anghel, MD: “Regulation Of Mice Hypothalamus And Pituitary Genes By Morphine: A Microarray Study”

Kevin C. Heslin, PhD: “New evidence on acculturation and the Latino Paradox: A comparison of sexual risk behavior among U.S. males”

Paul V. Marquez: “Buprenorphine-induced antinociception was unaltered in mice lacking the pro-orphanin FQ/nociceptin gene”

Xiuhai Ren, PhD: “Acute GHB administration affects the intracellular signal transductions in the brain”

2:45-3:00 pm “Tobacco Control and the African American Community”

Bruce Allen, Jr. DrPH

Assistant Professor

Charles R. Drew University of Medicine and Science

Email: brallen@cdrewu.edu

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Agenda

- 3:00-3:15 pm “Showing Up is the Goal: Perspectives on Achieving Best Outcomes
for Substance Abuse Treatment”
Brenda Wiewel, LCSW
Executive Director
Los Angeles Centers for Alcohol and Drug Abuse (CADA)
Email: bwfranken@socal.rr.com
- 3:15-3:30 pm “Nicotine Induces Insulin Resistance and Glucose Intolerance in Mice”
Yanjun Liu, MD, PhD
Assistant Professor
Charles R. Drew University of Medicine and Science
Email: dryanjunliu@hotmail.com
- 3:30-3:45 pm “Beta-Endorphin Plays a Significant Role in Cocaine-Induced Reward”
Kabirullah Lutfy, PhD
Associate Professor, Department of Pharmaceutical Science
College of Pharmacy, Western University of Health Sciences
Email: klutfy@westernu.edu
- 3:45-4:00 pm Closing Remarks/Post-Conference Evaluation/Awards
Ted Friedman, MD, PhD
- 4:00 pm Adjourn

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Sponsor

MINORITY INSTITUTIONS' DRUG ABUSE RESEARCH DEVELOPMENT PROGRAM (MIDARP)

Charles R. Drew University is a site of the **MIDARP**. Dr. Theodore Friedman is the Program Director. The overall goals of the MIDARP are to: (1) develop the drug abuse research at Drew; (2) provide research development support and experiences to faculty and staff to facilitate independent drug abuse research careers, (3) foster interest in drug abuse research for students and residents and provide them research experiences, and 4) provide for continued drug abuse research funded by NIDA or other agencies. We will specifically encourage the development of minority faculty and students.

The theme of the training and education program will be “Addiction is a brain disease and it matters” and will incorporate expertise at Drew in both the basic and clinical aspects of substance abuse. We have elected not to limit the area of substance growth at Drew; all projects related to the theme of substance abuse as a disease of the brain will be encouraged. Although the primary projects are both basic science projects related to mechanisms of opiate addiction, the aims of this grant will be to increase all aspects of substance abuse research (basic science, translation, clinical and survey research), based on the interests of the faculty.

Technical Assistance

UCLA Integrated Substance Abuse Program

The UCLA Integrated Substance Abuse Programs (ISAP) coordinates substance abuse research and treatment within the Department of Psychiatry and Biobehavioral Sciences, David Geffen School of Medicine at UCLA. As one of the largest substance abuse research groups in the United States, ISAP works to: develop and evaluate new approaches for the treatment of substance abuse disorders; move empirically supported treatments into mainstream application; advance the empirical understanding of substance abuse and support efforts to ameliorate related problems; and investigate the epidemiology, neurobiology, consequences, treatment, and prevention of substance abuse. With more than 300 researchers, clinicians, and support personnel, ISAP is led by Walter Ling, M.D. (Director), M. Douglas Anglin, Ph.D. (Associate Director), Douglas Longshore, Ph.D. (Associate Director), and Richard Rawson, Ph.D. (Associate Director). ISAP's network of activities extends from highly sophisticated and specialized laboratory research (including molecular genetics, brain imaging, and medication testing), to pharmacological and behavioral clinical research, to community-based research, research on public health policy, and substance abuse treatment services. For more information, visit www.uclaisap.org.

Pacific Southwest Addiction Technology Transfer Center (PSATTC)

Funded by the Substance Abuse and Mental Health Services Administration (SAMHSA) as one of 14 regional centers, the Pacific Southwest Addiction Technology Transfer Center (PSATTC) is jointly operated by the UCLA Integrated Substance Abuse Program and the University of Arizona Applied Behavioral Health Policy Division. The PSATTC's vision is that all individuals with alcohol and drug problems receive the most up-to-date, clinically effective, and culturally competent substance abuse treatments to help them overcome addiction, and, as a result, lead productive and meaningful lives. The PSATTC's mission is to establish an infrastructure among key stakeholders in Arizona, California, and New Mexico to facilitate the transfer of addiction technology based on sound science through knowledge dissemination, training, and enhanced professional standards and practices that will improve the delivery of effective treatment for substance abuse disorders. Guiding principles include: inclusion, collaboration, sound science, information sharing, quality standards and programs, cultural competency, and informing public policy. For more information, visit www.psattc.org.

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Presenter’s Biographical Paragraphs

Keynote Speaker:

Jonathan E. Fielding, MD, MPH, MBA

Director of Public Health and Health Officer

Jonathan E. Fielding, M.D., M.P.H., M.B.A., is the Director of Public Health for the Los Angeles County Department of Health Services. Dr. Fielding is responsible for all Public Health programs and planning, evaluation, and policy development. With an annual budget of over \$430 million and 3,600 full-time positions, Public Health provides programs for the largest county in the United States including: disease control, family health, community health services, alcohol and drug programs, health facility inspections, policy and program development, and epidemiology and data analysis.

Dr. Fielding works with a wide range of community, state, and national organizations to promote public health. He conducts interviews and meetings with the news media and community groups addressing public health policy and programs. He has authored over 150 original scientific publications and chapters on disease prevention and health promotion, health care financing, economic analysis, regulation, and health risk assessment. He currently authors a column on health issues in the Los Angeles Times.

Dr. Fielding also has an extensive foundation and corporate background. He is Vice Chairman of the Partnership for Prevention, a national public-private membership organization whose mission is to increase the importance of prevention issues in national and state health policy. He has also served as Chairman and Board Member of the California Wellness Foundation, was founder and CEO of U.S. Corporate Health Management, and Vice President and Health Director for Johnson & Johnson Health Management, Inc.

Currently, Dr. Fielding is Vice Chair of the U.S. Community Preventive Services Task Force. He is also Professor of Health Services and Pediatrics at UCLA’s Schools of Public Health and Medicine and is Co-Director of the UCLA Center for Healthier Children, Families, and Communities. He was formerly the founding Co-Director of the UCLA Center for Health Enhancement Education and Research.

Previously, Dr. Fielding served as Commissioner of Public Health for the Commonwealth of Massachusetts. He received his M.D. and M.P.H. degrees from Harvard University and his M.B.A. in finance from Wharton School of Business. He is a Fellow and the immediate past president of the American College of Preventive Medicine, is a Fellow of the Association for Health Services Research and the American Academy of Pediatrics, and is a member of the National Academy of Sciences Institute of Medicine.

Keynote Speaker:

Edythe D. London, PhD

Edythe London, PhD is a neuropharmacologist, whose primary research contributions are in the application of brain imaging methods to the study of substance abuse. She has authored 231 original research articles and 68 reviews, mostly on drug action in the brain. She also has edited several books, including one entitled "Imaging Drug Action in the Brain."

Beyond the area of substance abuse, she has contributed to the development of new approaches and probes for studies of brain function. Such technical advances are applicable to a variety of neuropsychiatric disorders. Dr. Edythe London's research has advanced the study of substance abuse and the development of new approaches and probes for studies of brain function. Her most recognized accomplishments involve PET scanning of human subjects who suffer from addictions. Dr. London's group was the first to show a relationship between drug craving and activity of brain regions that link memory with emotion. She also showed that drug abusers have structural abnormalities in prefrontal cortex and deficits in decision-making tasks that depend on prefrontal cortex function.

Her work influenced other researchers to look toward the frontal lobe for an understanding of the compulsive self-administration of drugs despite detrimental effects, which characterizes drug addiction. Most recently, she and her colleagues have developed new probes for external imaging of those receptors in the brain where nicotine binds to produce its behavioral actions.

Presenters in alphabetical order:

Bruce Allen Jr., DrPH

Dr. Bruce Allen, Jr., is an assistant professor in the Department of Obstetrics and Gynecology at the King/Drew Medical Center in Los Angeles who has successfully completed several federal, state and locally-funded research and education projects. Notably, Dr. Allen served as the principal investigator of a breast cancer research project designed to increase the rate of screening mammography among inner city residents and served as a consultant to a NIH-funded colorectal cancer study.

Additionally, he has served as the principal investigator of a: (1) California Department of Health Services Perinatal Smoking Intervention project; (2) University of California Tobacco-Related Disease Research study of African Americans and their preference for mentholated cigarettes; (3) National Cancer Institute study to evaluate the effectiveness of a brief physician-delivered (4As currently 5As) anti-smoking message; (4) peer-led tobacco use prevention project; and (5) clinic-based smoking cessation project.

Dr. Allen is an advocate for tobacco control and prevention having served on the advisory board of the California African American Tobacco Education Network that spearheaded the recall of X brand cigarettes; served on a Los Angeles County Tobacco Control Coalition that won a share of the Master Settlement Agreement fund for tobacco use prevention and control activities; and is currently a Governor's appointee to the California Tobacco Education and Research Oversight Committee (TEROC). Dr. Allen also serves as a reviewer for the National Registry of Effective Programs.

Ricky Bluthenthal, PhD

Ricky N. Bluthenthal, Ph.D. is a Senior Social Scientist at the RAND Corporation and a Professor of Sociology and Director of the Urban Community Research Center at California State University Dominguez Hills. Dr. Bluthenthal's major research contributions have been in the areas of HIV epidemiology and prevention for drug injectors, racial/ethnic differences in alcohol consumption, consequences, and treatment outcomes, and community approaches to health promotion, prevention and care. Dr. Bluthenthal received his doctoral degree in Sociology from the University of California, Berkeley in 1998.

Didra BrownTaylor, PhD

Dr. Didra BrownTaylor is a visiting Research Psychologist at the Integrated Substance Abuse Programs-UCLA. She received a Ph.D. in Clinical Psychology at California School of Professional Psychology, Los Angeles, California. She also earned a B.A. degree in Black Studies at University of the Pacific, Stockton, California. Dr. BrownTaylor is currently a Research Scholar at National Institutes of Health (NIH) Office of Minority Health & Health Disparities. Dr. BrownTaylor has received several research grants as principal investigator and well published in peer-reviewed journals.

Theodore C. Friedman, MD, PhD

Dr. Theodore Friedman is an Associate Professor of Medicine-UCLA School of Medicine, Charles R. Drew University of Medicine & Science; Chief, Division of Endocrinology, Molecular Medicine and Metabolism; Director, Body Composition Core of the Drew Center of Excellence for Metabolic Research, Director of the Minority Institutes Drug Abuse Research Program (MIDARP) and Director of the Minority Biomedical Research Support (MBRS) Program. Dr. Friedman is board certified in Internal Medicine and Endocrinology, Diabetes and Metabolism. He received his undergraduate degree from Stanford University in Chemistry and Biological Sciences and his MD-PhD from Mount Sinai School of Medicine, with his PhD from City University of New York in Pharmacology. He completed his Internal Medicine residency from University of Michigan and his fellowship in Endocrinology at the National Institutes of Health, National Institute of Child, Health and Human Development. He held a faculty appointment in the Endocrinology Division at Cedars-Sinai Medical Center prior to coming to Charles R. Drew University. His basic science research interests are in pro-hormone processing as related to drug addiction, diabetes, thyroid disease and obesity. He is also studying the effects of nicotine on the hypothalamic, pituitary, adrenal axis and the effects of opiates on genes and proteins. His clinical interests are adrenal, pituitary, thyroid and fatigue disorders.

Yanjun Liu, MD, PhD

Yanjun Liu, M.D., Ph.D. Postdoctoral fellow at Division of Endocrinology, Charles R. Drew University of Medicine & Science – UCLA School of Medicine under the direction of Dr. Theodore C. Friedman. He received his MD in medical science, with his Master Degree of Medicine from Jilin University in China. He received his Ph.D. in Biochemistry and Molecular Endocrinology from Hamamatsu University School of Medicine in Japan. He held visiting professor and Pediatrician appointments in Pediatrician Department of Pediatrics, 1st Teaching Hospital, Jilin University in China. His basic science research interests are in pro-hormone processing and to study the regulation of the enzymes 11 β -hydroxysteroid dehydrogenase (type 1 and type 2) and how they regulate glucocorticoid occupancy of tissue mineralocorticoid

(MR) and glucocorticoid receptors (GR) relation to insulin resistance, obesity, diabetes, hypertension. He is also studying the interaction of nuclear hormone receptors between oxysterol liver x receptors (LXR) and GR-mediated local glucocorticoid action in the pathogenesis of type 2 diabetes with obesity.

Kabirullah Lutfy, PhD

Dr. Kabirullah Lutfy is an Associate Professor in the Department of Pharmaceutical Sciences, College of Pharmacy, Western University of Health Sciences (Pomona, CA). He also holds an adjunct assistant professor position at Charles R. Drew University of Medicine and Science (Los Angeles, CA). Dr. Lutfy has received his degree in pharmacy from the Faculty of Pharmacy, Kabul University (Kabul, Afghanistan). He received his master's degree in Pharmaceutical Sciences from St. John's University (Queens, NY) and his Ph.D. in Pharmacology & Toxicology from the University of California, Irvine (UCI). He has completed his post-doctoral training at the laboratory of Dr. Nigel T. Maidment at the University of California, Los Angeles (Los Angeles, CA) and became an assistant research pharmacologist at UCLA before joining Western University in 2003. His area of research deals with understanding the neurobiological mechanisms of Pain and Drug Addiction.

Tripathi B. Rajavashisth, PhD

Dr. Rajavashisth is an internationally renowned scientist with Professor of Medicine appointments at Drew University and at the David Geffen School of Medicine at UCLA. Before joining Drew, Dr. Rajavashisth has served UCLA for over twenty years and Harvard University for two years as assistant, associate to full professor. He has earned a reputation as a molecular biologist through his research on aspects of lineage commitment of stem cells to white blood cells and pathological processes leading to their migration, growth and survival inside the vessel wall using a combination of biochemical, molecular and genetic approaches. His seminal observation led the way to establish the prominent role of inflammation in the pathogenesis of atherosclerosis. Over many years, he has focused his research on the role of inflammation in processes that contribute to arterial pathologies. His research programs have been funded by NIH, AHA, Eisner Foundation and Phillip Morris External Research. An account his scholarly activities can be obtained through the World Wide Web using either Google scholar or Pubmed search sites.

Steve Shoptaw, PhD

Steve Shoptaw, PhD is a Professor in the Center for Disease Prevention and Health Promotion at the Department of Family Medicine at the David Geffen School of Medicine at UCLA . He is a Principal Investigator of a NIDA-funded P-50 investigating medication development for stimulant abuse. Dr. Shoptaw is also a professor, Department of Family Medicine, UCLA. His research work involves evaluations of behavioral and pharmacological treatments for substance abuse, particularly as they intersect HIV-relevant populations. Dr. Shoptaw works with his colleague, Dr. Cathy Reback, to evaluate behavioral drug-counseling methods for their value in preventing HIV transmission and reducing drug abuse in gay/bisexual substance users in Los Angeles. He is Director of the Intervention Core of the UCLA Center for HIV Identification, Prevention and Treatment Services and Executive Director for Safe House, a residential facility for persons with HIV/AIDS who have co-occurring mental illness and/or chemical dependency, a project supported by the City of Los Angeles Housing Opportunities for Persons With AIDS program.

Pushpa V. Thadani, PhD

As a Program Director, Dr. Thadani oversees and administers a program in basic research that focuses on the consequences of maternal and paternal drug abuse on the fetal and offspring development. She also directs a national program focused on understanding the pathophysiology of cardiovascular and pulmonary systems associated with cocaine, marijuana and other abused and/or inhaled substances. Dr. Thadani is responsible for direct planning of scientific conferences, workshop, and symposia to exchange information and disseminate new information to the field. She is a pharmacologist with interests in perinatal pharmacology and CNS development. Prior to joining NIDA, Dr. Thadani did research in Fetal Alcohol Syndrome at the Washington, DC VAMC using a rodent animal model that she had developed during her postdoctoral training at Duke University Medical Center.

In her Program Director capacity, she is also involved with the Institute's Special Population office program focused on training Under-represented Minorities in biomedical research.

Brenda Wiewel, LCSW

The Executive Director, Brenda Wiewel, L.C.S.W., is a social worker with 30 years of experience in the field, 15 of those in a leadership capacity with the agency. She is a Past President of the Santa Fe Springs Rotary Club and current board member for the California Association of Drug and Alcohol Program Executives (CAADPE). Her coauthored article on the Family Foundations Program is pending publication with the Journal of Offender Rehabilitation.

Poster Presentation Abstracts:

“Stress’ Ability To Alter Chronic Nicotine’s Effect On The Hpa Axis”

Otaren Aimiuwu¹, Adrian Anghel¹, Namiko Nerio¹, Kabir Lutfy², Theodore Friedman¹.

¹Division of Endocrinology, Metabolism, and Molecular Medicine.
Charles Drew University of Medicine and Science, Los Angeles CA 90059.

²College of Pharmacy, Western University, Pomona, CA 91766.

Nicotine is a well-known addictive drug. Our preliminary data showed that oral intake of nicotine via self-administration activates the hypothalamic-pituitary-adrenal (HPA) axis. We hypothesized that activation of the HPA axis can help sustain nicotine’s stimulatory effects on the stress response. The subjects were C57B/L6 male mice, 8 weeks old, weighing approximately 22-25g. They were exposed to chronic oral self-administration for 14 days (experiment 1) or 7 days (experiment 2). In Experiment 1, one group of mice was exposed to 0.012% nicotine plus 10% sucrose while the other group was exposed to 0.006% sodium tartrate plus 10% sucrose for the first 7 days. During the next 7 days, they were given a choice between 0.006% sodium tartrate and 0.012% nicotine. In Experiment II, 2 groups of 12 mice each were subjected to 0.006% sodium tartrate plus 10% sucrose or 0.024% nicotine plus 10% sucrose instead of drinking water for 7 days. 6 mice from each group underwent swim stress for 3 minutes at 15°C. Mice were decapitated 15 minutes thereafter and blood was collected in tubes containing 7% EDTA. Plasma was extracted and stored at -80°C until analyzed by RIA for ACTH and corticosterone. In experiment I, mice exposed to nicotine during the first week consumed more nicotine than the group exposed to sodium tartrate. In experiment II, HPA axis activation was observed in the groups that underwent the swim stress. Nicotine increased ACTH ($p < 0.05$) and corticosterone ($p < 0.001$) levels. Experiment I shows that subjects pretreated with nicotine tend to prefer it over those that were not pre-exposed with it. Experiment II showed that stress plus nicotine induces activation of the HPA axis, more than each exposure separately. These results may explain some of the addictive properties of nicotine and why smokers consume more cigarettes in the time of stress.

This research was supported by a Grant from NIH: R24DA017298, R21DA016867

“The Prevalence Of Depression Among A Sample Of Inner-City Ed Patients Engaging In Harmful Drinking”

Shahrzad Bazargan-Hejazi PhD, Mike Jimenez MD, Ameet Shah MD, Chizobam Ani MD, MPH, and Mohsen Bazargan PhD

Charles R. Drew University of Medicine and Science, Los Angeles, CA 90059

Objective: With Emergency Department patients sample we aimed to 1) estimate the prevalence of depression and 2) identify the relationship between depression and alcohol use. *Methods:* Cross-sectional analysis of 412 surveys conducted at King Drew Medical Center Emergency Department (KDMC-ED) over a 5-week period. Instruments included depression (Center for Epidemiological Studies on Depression and various measures of alcohol (AUDIT, RAPS4, DSM-IV Abuse, DSM-IV Dependence, Binge Drinking). Other measures included: sociodemographics, drug use, impulsivity, and stress. *Results:* Of the sample, 37% were female

with a mean age of 38 years. African-Americans comprised 48% and Latinos 52%. Nearly 51% (n=208) of the sample scored positive for depression (≥ 16). 88% reported lifetime alcohol use with the prevalence of disorder as followed: AUDIT 26% (n=96), RAPS4 29% (n=104), DSM-IV abuse 26% (n=93), DSM-IV dependence 11% (n=40), and binge drinking 28% (n=101). Depression was significantly associated with alcohol dependency (OR 14.3; CI 3.8 -53.9; $p < 0.001$). Confounders, female gender (OR 3.3) younger age (OR 2.2), and impulsivity (OR 5.2). Conclusion: High prevalence of depression and a significant relationship between depression and alcohol dependency exists in Ed's. ED clinicians and social services should consider routine screening of alcohol dependency and depression among these patients.

“Estrogen decreases opioid anti-nociception”

Victor V. Chaban

Department of Biomedical Sciences, Charles R. Drew University of Medicine and Science

While several actions of estrogen (E_2) have been demonstrated in the nervous system, the mechanism of E_2 pain modulation is unclear and the question whether E_2 is pro- or anti-nociceptive remains unresolved. Within the context of our hypothesis E_2 modulation of nociceptive response depends on the type of pain, its durations and the involvement of other anti-nociceptive mechanisms. Response of primary afferent neurons located in the dorsal root ganglion (DRG) to pro-nociceptive stimuli has been modeled by exposure to prostaglandin E_2 (PGE_2) and ATP *in vitro*. DRG neurons were grown on coverslips and then microinjected with FICRHR (2 μ M) to monitor $[cAMP]_i$ or loaded with Fura-2AM (5 μ M) to study intracellular calcium ($[Ca^{2+}]_i$) levels using digital fluorescent videomicroscopy. PGE_2 rapidly increased $[cAMP]_i$ levels, which did not return to baseline for the duration of the experiments. The time course of the PGE_2 -stimulated $[cAMP]_i$ was decreased by the MOP agonist 3H -D-Ala², N-Me-Phe⁴, glycinol⁵-enkephalin (DAMGO, 10 nM) but E_2 alone neither increased $[cAMP]_i$ levels nor augmented PGE_2 stimulated $[cAMP]_i$. E_2 (100 nM for 5 min) prevented DAMGO attenuation of the PGE_2 effect which is consistent with an E_2 blockade of MOP action. In another set of experiments, E_2 actions on DAMGO inhibition of ATP-induced $[Ca^{2+}]_i$ flux were tested in DRG neurons. As expected, E_2 (100 nM) blocked the DAMGO attenuation of ATP-induced $[Ca^{2+}]_i$.

In DRG neurons, E_2 reversed opioid inhibition of PGE_2 -induced cAMP levels and reduced ATP-induced $[Ca^{2+}]_i$ flux suggesting that E_2 has direct actions on opioid-mediated signal transduction. Based on our studies, E_2 under certain conditions, such as those associated with opioid anti-nociception, becomes pro-nociceptive by blocking anti-nociceptive opioid input which is congruent with reports that sex steroids appear to mediate differential responses to opiate analgesics in men and women.

“The Effects of CRH Antagonism on Nicotine’s Activation of the HPA Axis”

N Nerio, A Anghel, Y Liu, K Lutfy, O Aimuwu, TC Friedman.

Division of Endocrinology, Metabolism, and Molecular Medicine, Charles R. Drew University of Medicine and Science, Los Angeles, CA 90059.

Nicotine is a lipophilic, addictive substance; acute administration of the said substance activates the hypothalamic-pituitary-adrenal (HPA) axis. We explored the potential for CRH antagonists antalarmin and astressin to curb nicotine's physiological effects in the hopes that doing so may curb its addictive potential as well. The two distinct antagonists' optimal working conditions were determined via carrying out time course (TC) and dose response curves (DRC) in male C57B/L6 mice. ACTH and corticosterone levels were assessed. Upon determination of optimal parameters, each antagonist was challenging with nicotine. Time course data, collected at 0, 15, 30, 60, 90, 120-minutes post-injection revealed that astressin (0.3-mg/kg, ip), in comparison to its vehicle, optimally suppresses corticosterone release at 15 minutes post-injection (n=4). Astressin's DRC consisted of the following dosages: 0, 0.03, 0.1, 0.3, 1.0, and 3.0-mg/kg (ip) and revealed optimal corticosterone suppression at 0.3-mg/kg (n=7; p<0.05), 1.0-mg/kg (n=7; p<0.01), and 3.0-mg/kg (n=7; p<0.01) when compared to 0-mg/kg (n=7). Antalarmin (20-mg/kg, ip) TC and DRC data are not currently available. Preliminary co-administration data of antagonist with nicotine revealed that both drugs attenuate nicotine's physiological profile as antalarmin decreased ACTH and astressin suppressed corticosterone and ACTH in relation to nicotine alone. Though astressin diminishes nicotine's potential to activate the HPA axis to a greater extent, both antagonists may potentially attenuate nicotine-induced behavioral changes.

Trainee Oral Presentation Abstracts:

“Regulation Of Mice Hypothalamus And Pituitary Genes By Morphine: A Microarray Study”

A. Anghel^{*}, K. Lutfy^{}, Y. Liu^{*}, N. Nerio^{*} and T.C. Friedman^{*}**

^{*}Dept. of Endocrinology, Charles Drew Univ., Los Angeles, CA

^{**}Dept. of Pharm. Sci., Western Univ., Pomona, CA

Morphine dependence is associated with short- and long-term adaptive changes in the brain that involve gene expression. Different behavioral effects of morphine are mediated by different brain regions, for example opioid structures in hypothalamus mediate analgesia whereas in pituitary morphine induce modification in secretion of different hormones. Using DNA microarray analysis in mice, we now characterize gene expression changes that occur in these brain regions with acute and chronic morphine administration. Considering two fold thresholds we found tenths to hundreds of genes which are up- or downregulated in both organs in both condition of treatment. In hypothalamus the most regulated genes belong to obesity pathway (neuropeptide Y, agouti related protein, etc), whereas in pituitary they are more heterogeneous as metalloenzymes (carbonic anhydrase), immunity mediators (CD79B antigen, chemokines), cellular oxidation (cytochrome P450). Furthermore, we identify clusters of genes that are regulated similarly by acute or chronic morphine, as well as clusters that show opposite regulation under these two conditions. This result suggests that gene expression induced by drug addiction is complex and novel pathways may mediate some effects of morphine.

“New evidence on acculturation and the Latino Paradox: A comparison of sexual risk behavior among U.S. males”

Kevin C. Heslin, PhD

Charles R. Drew University of Medicine and Science

Acculturation presumably causes the health of Latino immigrants to decline as their time in the U.S. increases. We analyzed data on 3,185 men to assess the role of acculturation in racial/ethnic differences in reports of having sex under the influence (SUI) of alcohol or drugs in the previous year. Binary logistic regression was used to estimate the odds of ever (versus never) having SUI among all men. Ordered logistic regression was used analyze increasingly frequent SUI (sometimes-to-always) among those who ever had SUI (n=1,619). Results from the binary model showed that Latinos had lower odds of ever having SUI than non-Latino white (NLW) men. This difference between Latinos and NLWs was eliminated after accounting for country of birth, which showed that non-U.S.-born men had lower odds of SUI than U.S.-born men. Further, the difference between non-U.S and U.S.-born men was eliminated after accounting for percentage of life in the U.S. In the ordinal model, odds of SUI frequency did not differ between Latinos and NLWs. Evidence of the “Latino paradox” depended on the form of the outcome variable. Acculturation is a risk for ever having SUI, and it explained Latino males’ advantage over NLWs for the “ever vs. never” outcome.

“Buprenorphine-induced antinociception was unaltered in mice lacking the pro-orphanin FQ/nociceptin gene”

Paul Marquez and Kabirullah Lutfy.

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Previously, we have shown that the antinociceptive effect of buprenorphine was enhanced in mice lacking the opioid receptor-like (ORL-1) receptor (Lutfy et al., 2003). In the current study, we tested the hypothesis that this enhancement could be due to the release of orphanin FQ/nociceptin (OFQ/N), the endogenous agonist ligand of the ORL-1 receptor. In Experiment 1, we confirmed our previous findings by conducting a dose-response study for buprenorphine-induced antinociception in wild type and ORL-1 knockout mice. Mice were tested for baseline tail flick latency, injected with buprenorphine (0.3 mg/kg, s.c.) and tested for antinociception 15 min later. Immediately thereafter, mice were injected with the next dose of buprenorphine (1 mg/kg, s.c.) and tested 15 min later. Finally, mice received another injection of buprenorphine (3 mg/kg, s.c.) and tested 15 min later. Wild type mice displayed a sub-maximal antinociceptive effect following cumulative doses of buprenorphine. In contrast, ORL-1 receptor knockout mice displayed maximal antinociception after this treatment. In Experiment 2, we tested whether the enhanced antinociception observed in ORL-1 knockout mice was due to the release of endogenous OFQ/N. Mice lacking the pro-OFQ/N gene (OFQ/N deficient mice) and their wild type littermates were tested for baseline tail flick latency and injected with buprenorphine (0.3, 1 and 3 mg/kg, s.c.) and tested as described above. Both wild type and pro-OFQ/N knockout mice displayed similar antinociception following buprenorphine administration. Taken together, the present results suggest that the enhanced antinociception induced by buprenorphine in mice lacking the ORL-1 receptor is not due to the release of OFQ/N since the antinociceptive effect of buprenorphine was not altered in OFQ/N deficient mice (supported by R01 DA016682 to KL).

“Acute GHB administration affects the intracellular signal transductions in the brain”

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γ -Hydroxybutyrate (GHB) is a natural constituent of mammalian brain derived from GABA. Recently GHB has emerged as a major recreational drug of abuse. GHB abuse has been associated with acute intoxication, cognitive impairments and development of addiction. However, the intracellular signaling mechanisms underlying these effects remain unclear. We have examined the effects of acute GHB exposure on the phosphorylation of two important signaling proteins, extracellular signal-regulated kinase 1 and 2 (ERK1/2) of mitogen-activated protein kinases (MAP kinases) and the prototype nuclear gene transcription factor cyclic AMP-responsive element-binding protein (CREB), in mouse brain. It was found that acute administration of GHB (500 mg/kg, i.p.) significantly increased CREB phosphorylation in all the major brain regions including frontal cortex, hippocampus, striatum and hypothalamus, whereas GHB caused a fast and long-lasting inhibition of the MAP kinase phosphorylation in these brain

regions. Moreover, we found that a pretreatment with the specific GABA_B receptor antagonist CGP56999A (20 mg/kg, i.p.) prevented the actions of GHB on the phosphorylation of MAP kinase and CREB, indicating that GHB acts through a GABA_B receptor-mediated mechanism. These findings may provide new insights into the intracellular mechanisms underlying the various effects of GHB on the central nervous system.