



# CNRA Connections

Center for Neurobehavioral Research on Addiction

Department of Psychiatry

## Role of the Orexin Receptor System at the Nexus of Stress, Sleep and Drug Abuse



**Scott Lane, Ph.D.**

Stimulant dependence continues to be a significant public health problem, and there are currently no FDA-approved medication options to facilitate abstinence or prevent relapse. Of the stimulants, cocaine presents the largest burden to the healthcare and criminal justice systems in terms of mortality, morbidity, violent crime, and un-

employment – and this trend has not declined significantly for decades. Prevalence rates in North America approach 6.5 million users. Cocaine abuse leads to cognitive deficits, compulsive drug use, loss of control over drug-taking, and repeated relapses despite the desire to quit. Even current treatments are marked by high relapse rates, prompting a need for innovative and novel neurobiological research, and eventually new treatment options.

addiction relapse. The use of drugs to reduce physical and psychological stressors has been well documented. Lifetime stress is significantly associated with cocaine use severity.

### **Sleep**

Sleep patterns are disrupted in chronic drug use (including cocaine), including both slow-wave and REM sleep. These disruptions produce deficits in total sleep, and are associated with exacerbation of psychiatric symptoms and declined cognitive function. And there is a reciprocal relationship between cocaine use severity and sleep quality and duration, creating a viscous cycle of impaired sleep, increased stress, and increased risk for cocaine use. Previous studies suggest that medications that improve sleep quality can aid in reducing substance use, and sleep enhancement is a documented treatment

### **Stress and Anxiety**

Complicating the burden of addiction is stress and anxiety, which contribute substantially to all phases in addiction: from risk for binge use, to the onset of dependence, to triggering relapse. Importantly, stress and anxiety increase the magnitude of drug-cue reactivity, and serve as risk factors for both the initiation of substance use and

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Newsletter layout and design by Kathryn Tipton

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## CNRA: About us

### MISSION:

*To develop evidence-based treatment for substance use disorders (SUDs) using decisions informed by behavioral neurosciences.*

### AIMS:

*In pursuit of this mission the CNRA aims to:*

- Map out the neurological, behavioral, and clinical mechanisms that contribute to drug addiction
- Target key mechanistic processes in the development of SUD treatment
- Evaluate treatment efficacy using innovative clinical trial designs and statistical methods

### Core Faculty:

*Charles Green, Ph.D.*

*Angela Heads, Ph.D.*

*Scott Lane, Ph.D.*

*Joy Schmitz, Ph.D.*

*Anka Vujanovic, Ph.D.*

*Margaret Wardle, Ph.D.*

*Michael Weaver, M.D.*

*Jin Yoon, Ph.D.*

### Interested in research?

## Contact us!

# (713) 486-2823

Rolanda Johnson  
CNRA Program Manager

# Director's Message



### Joy Schmitz, Ph.D.

2016 marks the start of several new initiatives at the CNRA.

**On the research front:** The Peter F. McManus Charitable Trust Foundation recently honored Dr. Scott Lane with a grant to investigate the role of stress, sleep dysregulation, and drug craving – critical functions that increase addiction vulnerability. Building upon evidence

that the orexin system regulates these functions, the next question Dr. Lane hopes to answer is whether pharmacotherapies targeting the orexinergic system have potential for addiction treatment and relapse prevention.

**On the clinical front:** The INNOVATIONS Clinic at the CNRA recently opened a new behavioral counseling program for addiction treatment. Leading clinician, Dr. Angela Heads, is a licensed Counseling Psychologist with years of experience working with adolescents and adults with substance use disorders and co-occurring behavioral and emotional conditions. She joins Dr. Michael Weaver, addiction medicine physician for INNOVATIONS, in offering patients a clinically effective combination of behavioral counseling with medication-assisted treatment for addiction. For more information or to schedule an appointment, please call (713) 486-2700 (INNOVATIONS is part of the UT Physicians Psychiatry Outpatient clinic practice of the John P. and Kathrine G. McGovern Medical School.)

### On the dissemination and outreach fronts:

Find CNRA on Facebook! Our goal is to use social media as another way to reach the community with the latest news and information from the CNRA and from research centers nationwide. Make sure to visit and “like” us at [www.facebook.com/UTHealthCNRA!](http://www.facebook.com/UTHealthCNRA)



## Upcoming Events

### UTHealth Stomp Out Stroke Festival

Saturday April 30<sup>th</sup> 2016

Water-Works Buffalo Bayou Park

- Free, open to the public, family-friendly event
- Stroke and brain health education
- Free health screenings
- Entertainment, performances, & music

**Visit the CNRA at the Brain on Drugs booth in the Kid's Zone.**



*Register at [www.strokefestival.org](http://www.strokefestival.org)*

## Role of the Orexin Receptor, continued from page 1

strategy for substance use disorders.

### **Drug Cues**

Reactivity to drug cues is a robust predictor of relapse. This relationship has been established for a variety of abused drugs, including cocaine. Craving and biased attention toward drug-related stimuli (i.e., settings, drug paraphernalia) are two of the best-documented indices of reactivity to drug cues, and have been identified as factors in nearly every major drug of abuse.

These factors are predictive of relapse following treatment, and are now considered hallmark char-



acteristics of addiction. Importantly, both craving and biased attention toward drug cues bias can be reduced through medications.

### **Novelty and promise of the orexin system**

The orexins are a class of recently discovered peptides that are widely distributed throughout the brain. The orexin system is neuromodulatory, meaning that it activates a number of brain circuits through the regulation of two major neurotransmitters: glutamate and GABA. The primary role of the orexin system appears to be in balancing the brain's energy needs (e.g., arousal and awareness). Accordingly, blocking the action of the orexin system (a process called *antagonism*) promotes sleep.

Importantly, research suggests that orexin antagonists modify three key cocaine-related variables described above: stress/anxiety, sleep, and drug-cue reactivity. Suvorexant is currently the only FDA approved compound that acts on the orexin receptor system. It is indicated for treatment of insomnia.

In the present study, funded by an award from the Peter McManus Charitable Trust to **Dr. Scott Lane**, CNRA researchers will in-

vestigate the effect of suvorexant to regulate the interactions among drug-cue reactivity, anxiety/stress, and sleep in individuals with cocaine abuse – hypothesizing that suvorexant may be an effective medication for the prevention of relapse in cocaine abuse.

The CNRA research team will use laboratory measures of risk for relapse, including measurement of eye-movements in the presence of drug-related cues, developed by Dr. Lane (described in CNRA Newsletter, January 2014). Additionally, **Dr. Jin Yoon** will coordinate state of the art wearable activity/sleep monitors and text-messaging services to be utilized in data collection and adherence to taking the medication daily over several weeks.

This study will represent the first examination of the orexin system in humans struggling with substance abuse. CNRA researchers hope to show medications that modulate the orexin system may be effective in the quest to treat those with substance use disorders, especially in the prevention of relapse.

**The CNRA will begin to recruit research volunteers with cocaine dependence in the Spring of 2016.**

*Stress is one of the most powerful triggers of relapse, even after prolonged periods of abstinence from drug abuse.*

National Institute on Drug Abuse

# Ensuring Best Practices in Scientific Research



## Joy Schmitz, Ph.D.

It starts with the right ingredients – an intriguing scientific premise, a compelling research question, a testable hypothesis, pilot funds, and enthusiastic researchers. Two years and thirty enrolled participants later, the results are organized and critically assessed with the possible outcomes. Positive findings → race to present, publish, and apply for more funding. Negative findings → identify study limitations, file under “failed studies,” and move on with a stiff upper lip.



Increasingly in recent years, this “recipe” for scientific discovery has come under close scrutiny and calls for reformulation. “Enhancing reproducibility

through rigor and transparency” is the new buzz-phrase at the National Institutes of Health (NIH). It is time to improve the recipe by adding a generous dose of checks and balances to ensure best practices in scientific research.

### ✓ Check 1: Is there a strong scientific premise for the research?

Even the newest avant-garde entrees from high-end restaurants are based on previous successes and failures. Likewise, all research builds upon prior research: The

stronger the base, the sturdier the foundation or premise for new research. Sometimes the enthusiastic researcher, armed with positive findings from a pilot study, forges ahead with the next study without carefully addressing the strengths and weaknesses of existing data. The discouraged researcher may shove negative findings into the proverbial file drawer, out of side and out of mind, without considering that research done properly will produce negative results – as much as half of the time! Reporting negative results, especially when they point out scientific flaws in previously published work, is an important step toward enhancing reproducibility. Bottom line: A good scientist must evaluate the premise for their research by identifying strengths and weaknesses of prior work in order to propose ways to improve going forward.

### ✓ Check 2: Is the research consistent with rigorous experimental design?

A good recipe carefully describes the ingredients and techniques required to make a dish. In science, this means including critical methodological details and procedures – step-by-step – so that even a novice can follow the well-written recipe to obtain the same results. The message here is to document and report every aspect

of your work. Start with participants. What eligibility criteria were used for selection? How were participants assigned to experimental conditions? How was the size of the study sample determined? How many participants completed the study? How many dropped out and why? End with results. What statistical analyses were undertaken? How precise (or uncertain) are the estimated effect sizes of the intervention? Do any study results generalize to other individuals with different characteristics in regard to age, sex, gender? Full transparency in reporting study details will allow other researchers to reproduce and extend the findings.

### ✓ Check 3: Is the trial registered?

Think of national registries such as ClinicalTrials.gov as the public “menu” for researchers. Enter your protocol (recipe) with standard reporting elements

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(ingredients), and then submit timely updates and summary results. Everyone benefits. Patients and clinicians can search for a new treatment study for a specific disease. Journal editors and granting agencies can find detailed information about the trial design, procedures, and results. The general public can learn how research results contribute to medical knowledge.

## Check out the CNRA trials posted on ClinicalTrials.gov!

NCT00439049 Substance Abuse Pre-Treatment Screening Study

NCT01535573 Citalopram for Cocaine Dependence

NCT01393457 Cognitive Remediation for Cocaine Dependence

NCT02461732 Trial of a Novel Cognitive-Behavioral Treatment for Posttraumatic Stress and Substance Dependence



## New Faces at the CNRA

**Jafar Bakhshaie, M.D.** is a practicum student, currently working on the *Trial of Novel Treatment of Posttraumatic Stress and Substance Dependence* study. He is a third-year doctoral student in the clinical psychology program at the University of Houston. Dr. Bakhshaie's research focuses on exploring emotional regulatory mechanisms and cognitive processes underlying substance use disorders and panic/PTSD comorbidities. His research interests include emotional regulatory and reactivity processes as underlying processes of substance use-anxiety/stress comorbidity with important clinical implications.

**Melissa Fasteau, M.A.**, is a pre-doctoral intern from Yeshiva University/Ferkauf Graduate School of Psychology. She has trained in a variety of clinical settings, including college counseling centers, outpatient community and hospital clinics, and an inpatient psychiatric hospital. Her training focuses on evidenced-based interventions, including CBT for anxiety, depression, and addictions, Motivational Interviewing, and Exposure and Ritual Prevention. She is completing a 6 month rotation at the CNRA. Her dissertation research focuses on the intersection of low-income adolescents' perceptions of political fairness, dispositional optimism, and goal-setting behavior.

**Ilana Haliwa, B.A.**, is a Research Assistant working with Dr. Jin Yoon on the *Assessment of Cigarette Smoking among Candidates for Cardiovascular Sur-*

*gery and Perioperative Outcome* study, the *Nicotine and Tobacco Use in Cardiac Patients* study, as well as the *Abuse Liability of E-cigarettes following Administration of Alcohol and Exposure to Alcohol Cues among College Students* study. She earned her B.A. in Psychology from the University of North Carolina at Chapel Hill and is currently in the process of completing her Master's in Public Health through Nova Southeastern University.

**Nausheen Noor, M.A., M.Ed.**, is a doctoral student in Counseling Psychology at University of Houston. Her research focuses on cultural factors that influence the adjustment of immigrants in the U.S. She has worked with trauma and substance use disorders in various settings. She is doing her doctoral practicum at the CNRA as a therapist working on the *Trial of Novel Treatment of Posttraumatic Stress and Substance Dependence* study and *Clinical Trial of Citalopram in Cocaine Dependence* studies.

**Jonika Tannous** is a first year neuroscience PhD student at GSBS. She has a background in cognitive science, psychology, and neuroimaging. She intends to investigate Diffusion-Weighted Tensor Imaging (DTI) as a diagnostic tool in psychiatry throughout her graduate career. She is currently rotating in Dr. Scott Lane's lab and is studying white matter abnormalities in patients with cocaine and alcohol disorders.

# Research Update

## 2016 Selected Faculty Publications

- Alcorn III JL, **Green CE**, **Schmitz JL**, **Lane SD**: Effects of oxytocin on aggressive responding in healthy adult males. *Behavioural Pharmacology* (special issue on behavioral pharmacology of social behavior), 26: 798-804, 2015.
- Alcorn III, JL, Rathnayaka N, Swann AC, Moeller FG, **Lane SD**: Effects of intranasal oxytocin on aggressive responding in Antisocial Personality Disorder. *The Psychological Record*, in press.
- Asby AT, **Heads AM**, Dickson JW: Living with maternal HIV: Spirituality, Depression, and Family Functioning. *American Journal of Health Sciences*, in press.
- Bershada AK, Weafer JJ, Kirkpatrick MG, **Wardle MC**, Miller MA, de Wit H: Oxytocin receptor gene variation predicts subjective responses to MDMA. *Social Neuroscience*, in press.
- Brown ES, Peterson JT, Hu LT, **Schmitz JM**, Carmody TJ, Nakamura A, Sunderajan P, Rush AJ, Adinoff B: A randomized double-blind placebo-controlled trial of citicoline for cocaine dependence in bipolar I disorder. *Am J Psychiatry*, 172: 1014-1-21, 2015.
- Dias NR, **Schmitz JM**, Rathnayaka N, Red SD, Sereno AB, Moeller FG, **Lane SD**: Anti-saccade error rates as a measure of attentional bias in cocaine dependent subjects. *Behavioural Brain Research*, 292, 493-499, 2015.
- Hamilton JE, **Heads AM**, Cho RY, **Lane SD**, Soares JC: Racial disparities during admission to an academic psychiatric hospital in a large urban area. *Comprehensive Psychiatry* 63:113-22, 2015.
- Lijffijt M, Maili L, **Lane SD**, Moeller FG, Steinberg JL, Swann AC: Impulsivity and risk seeking relate differentially to intensity-sensitivity of N1 and P2 auditory evoked potentials. *Journal of Neuropsychiatry and Clinical Neurosciences*, in press.
- Steingroever H, Fridberg DJ, Horstmann A, Kjome KL, Kumari V, **Lane SD**, Maia TV, McClelland JL, Pachur T, Premkumar P, Stout J, Wetzels R, Wood S, Worthy DA, Wagenmakers EJ: Data from 617 Healthy Participants Performing the Iowa Gambling Task: A “Many Labs” Collaboration. *Journal of Open Psychology Data*, in press. DOI: <http://dx.doi.org/10.5334/jopd.ak>.
- **Vujanovic AA**, Rathnayaka N, Amador C, **Schmitz JM**: Distress tolerance: Associations with posttraumatic stress disorder symptoms among trauma-exposed, cocaine dependent adults. *Behavior Modification*, 40, 120-143. DOI: 10.1177/0145445515621490
- **Vujanovic AA**, **Wardle MC**, Liu S, Dias NR, & **Lane SD**: Attentional bias in adults with cannabis use disorders. *Journal of Addictive Diseases*, in press. doi: 10.1080/10550887.2015.1116354.
- **Wardle MC**, Bershada AK, & de Wit H: Naltrexone alters the processing of social and emotional stimuli in healthy adults. *Social Neuroscience*, in press.
- **Weaver MF**, Carlat D: Understanding the dangers of designer and club drugs. *The Carlat Addiction Treatment Report*, 3(7): 1-8, 2015.
- **Weaver MF**: “Alcohol Use Disorder and Chronic Pain,” Presentation at PAINWeek 2015 National Conference, Las Vegas, NV, September 2015.
- **Weaver MF**: “Medication-Assisted Treatment,” Panelist at Spectrum 2015 conference, Texas Association of Addiction Professionals, Houston, TX, October 2015.
- **Yoon JH**, **Lane SD**, **Weaver MF**: Opioid analgesics and nicotine: More than blowing smoke. *Journal of Pain & Palliative Care Pharmacotherapy*, 29(3):281-289, 2015.

## Clinical Corner:

# Innovations

# Combining Therapy with Medications to Treat Addiction

CNRA is pleased to announce that the **INNOVATIONS Clinic** is offering behavioral therapy services to compliment the Medication-Assisted Treatment (MAT) program for substance use disorders. **Dr. Angela Heads**, a licensed psychologist, is accepting new patients who are interested in receiving individual therapy to help in their recovery from drug addiction, including tobacco, alcohol, prescription medications, and other illegal substances.

“Working with **Dr. Weaver** (MAT director), I believe the combination of medication with behavioral therapy is the right formula for success. I’m proud to be part of a program that adheres to current best practice guidelines as defined by national and international health organizations, such as the American Society of Addiction Medicine (ASAM), the Substance Abuse and Mental Health Services Administration (SAMHSA) and the World Health Organization.”

Dr. Heads has over 15 years of experience as a psychotherapist. She is also a clinician-scientist with research publications and presentations on topics related to health disparities, gender, trauma, and addiction. Her goal as a therapist is to assist each individual in setting value-based goals and taking actions toward changing how they

think and behave.

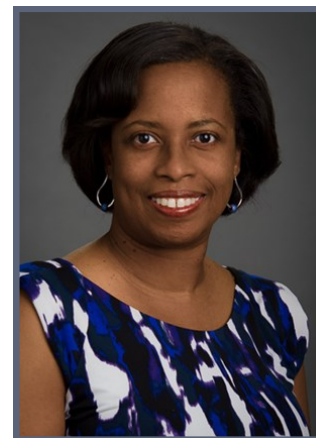
**Drs. Weaver and Heads** work as a team in evaluating and developing a personalized and comprehensive treatment plan that involves medication management and ongoing psychotherapy.

“Psychotherapy is sometimes referred to as ‘talk therapy,’” Heads explains. “Research has shown that psychotherapy is an essential part of substance use treatment for many people. Specifically, the use of interventions such as cognitive behavioral therapies, motivational interviewing and mindfulness-based interventions have been shown to be effective in helping people to recover from addiction.”

For individuals who achieve abstinence, psychotherapy has been shown to reduce the risk of relapse by providing strategies for managing stress, dealing with cravings, and developing healthy coping strategies. Psychotherapy can also help people stay in treatment longer, thereby allowing them to experience the full effectiveness of their medications.

Psychiatric comorbidity (the occurrence of a mental health condition) is known to complicate treatment for individuals with substance use disorders. Research has shown a tendency for poorer outcomes including higher relapse

rates among substance users who also have a comorbid psychiatric condition such as depression or posttraumatic stress disorder. The first-line treatment approach for all comorbid disorders is **integrated** psychotherapy that targets comorbid conditions concurrently. The most promising integrated treatments for patients with comorbid conditions are offered at the **INNOVATIONS clinic**.



**Dr. Angela Heads**

The **INNOVATIONS Clinic** participates with multiple health insurance plans, including Medicare and Medicaid. Appointments are currently available with minimal wait time. The **INNOVATIONS Clinic** is located on the campus of the Texas Medical Center close to the CNRA, with ample surface parking nearby. For additional information, to refer a patient, or to schedule an appointment, please call the UT Psychiatry Clinic.

**713-486-2525**

## Recent Awards, Recognition, Honors

- ◇ **Dr. Scott Lane** was awarded the Peter F. McManus Charitable Trust Foundation Grant for his study entitled, “Role of the orexin receptor system at the nexus of stress, sleep and drug abuse.”
- ◇ **Dr. Anka Vujanovic** was invited to present “PTSD and Substance Use Disorders: A Clinical Overview” at the Seventh Annual UTHealth Psychiatry Update in Houston, Texas, February 2016.
- ◇ **Dr. Angela Heads** joined the CNRA faculty as Lead Therapist of the behavioral treatment program at INNOVATIONS Clinic.
- ◇ **Dr. Michael Weaver** was invited to present “Alcohol Use Disorder and Chronic Pain,” at the PAINWeek 2015 National Conference, Las Vegas, NV, September 2015.
- ◇ **Dr. Michael Weaver** was invited as a Panelist to present “Medication-Assisted Treatment” at the Texas Association of Addiction Professionals, Houston TX, October 2015.
- ◇ **Jocelyn Abrams**, a visiting research assistant at the CNRA and pre-doctoral counseling trainee at the University of Houston was accepted into Yale School of Medicine Clinical Psychology Internship program.
- ◇ **Dr. Vujanovic**, in collaboration with Drs. Bonn-Miller and Petry, was invited to serve as Guest Editor of a special section on co-occurring posttraumatic stress and substance use disorders for an upcoming issue of Psychology of Addictive Behaviors.
- ◇ **Dr. Schmitz**, in collaboration with Drs. Copeland and Cropsey, was invited to serve as Guest Editor of a special issue on special populations and comorbidity issues in nicotine dependence for the Journal of Addiction.

## Your Support Is Needed

Contributions to CNRA help advance important research to develop science-based treatments for those who suffer from substance use disorders.

Donations can be made to:

Office of Development

Attn: B. Henry/CNRA

P.O. Box 1321 Houston, TX 77251-1321

Funds provided by the Faillace Endowed Professorship, established in 2011 by **Cynthia and Ray Wright** in honor of **Louis A. Faillace, M.D.**, supports excellence in psychiatric research and patient care, and envelops the mission of the CRNA – to develop evidence-based addiction treatment.



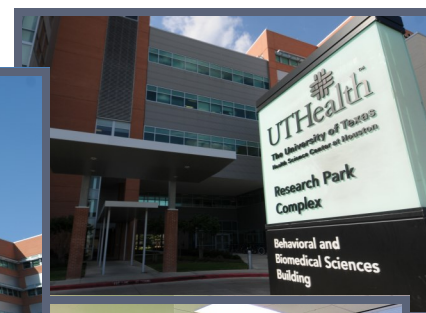
# Inside the CNRA

The CNRA currently has three ongoing studies of treatment for substance use disorders.

- ◆ Clinical Trial of Citalopram in Cocaine Dependence
- ◆ Cognitive-enhancing Dopamine Medications for Cocaine Dependence
- ◆ Treatment of Integrated Posttraumatic Stress and Substance Use

## CNRA Program Features:

- ◆ No Cost Treatment
- ◆ 100% confidential
- ◆ Medical & Behavioral Treatments
- ◆ Experienced and Professional Staff
- ◆ A Safe and Clean Atmosphere
- ◆ Free Parking and Metro Tickets
- ◆ Financial Compensation for Research Participation
- ◆ Funded by the National Institute on Drug Abuse (NIDA)



**Appointments:**  
**713-500-DRUG (3784)**

**Clinic Hours:**  
**Monday – Friday 7:30-4:00**

**Behavioral and Biomedical Sciences Building**  
**1941 East Road**  
**Houston Texas 77054**

<https://med.uth.edu/psychiatry/research/addiction/>