



CNRA Connections

Center for Neurobehavioral Research on Addiction

Department of Psychiatry

The eyes have it: Eye-tracking technology is promising tool for relapse prevention

■ Nadeeka R. Dias, Graduate Student

High relapse rates remain a huge problem in addiction treatment efforts. Individuals with cocaine dependence relapse at rates greater than 50% over their lifetime. Those seeking treatment for this addiction, may enter programs that typically admit patients based on age and overall physical and mental health.

However, these factors do not predict relapse. A test that would provide more predictive information based on a patients' neural and cognitive function would be an advantage for treatment evaluation. Unfortunately, there are no methods of effectively predicting treatment outcomes or preventing relapse at this time.



As the participant views each image, saccade eye movements are measured through an infrared eye-tracker located below the monitor.

Led by Dr. Scott Lane, Professor in Psychiatry & Behavioral Sciences, and Graduate School for Biomedical Sciences (GSBS) graduate students Nadeeka Dias and Nuvan Rathnakaya, this team has recently developed methods in our laboratory aimed at finding

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Newsletter layout and design by Kathryn Tipton

CNRA launches new treatment approach for PTSD and cocaine dependence

■ Anka A. Vujanovic, Ph.D.

Post traumatic stress disorder (PTSD) is an anxiety disorder resulting from exposure to a traumatic event and marked by re-experiencing, avoidance/numbing, and hyper-arousal symptoms. PTSD is associated with significant functional impairment and deleterious health outcomes, including a substantially elevated risk for substance

use disorders (SUD). PTSD is estimated to co-occur at exceptionally high rates among SUD samples, with prevalence ranging from 20-60% among treatment-seeking SUD samples. Trauma exposure is reported by as many as 90-95% of individuals with SUD. PTSD also has been documented as a significant risk factor for poorer SUD treatment outcomes. PTSD

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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:

Joy Schmitz, Ph.D.

Scott Lane, Ph.D.

Charles Green, Ph.D.

Anka Vujanovic, Ph.D.

Jin Yoon, Ph.D.

Prashant Gajwani, M.D.

Interested in research?**Contact us!****(713) 486-2823**

Rolanda Johnson
CNRA Program Manager

Director's Message



Joy Schmitz, Ph.D.

I hope you enjoy the inaugural issue of our CNRA newsletter. This is an exciting, challenging, and invigorating time for CNRA. In 2010, we were proud to be officially recognized as a research center within the University of Texas Medical School at Houston. Along with this designation came the renewal of our National Institute of Drug Abuse (NIDA) Research Center of Excellence (P50) grant program, now in its 19th year of continuous funding.

Best of all, in 2010 our department moved to its new location in the Behavioral and Biomedical Sciences Building (BBSB) on the south campus of the Texas Medical Center. The first floor of the BBSB is occupied by the CNRA and features a specially constructed Treatment Research Clinic and the Neurobehavioral Research Laboratory. The move has been a huge success in terms of improving subject capacity and throughput. Since 2010, we have evaluated over 1,946 participants, of whom 594 have enrolled in a research study. As a result, our infrastructure now supports a broader range of funded research projects, collaborations, and training opportunities.

CNRA is perfectly positioned and strongly committed to generating new scientific data that will advance our understanding of how drugs of abuse change the brain and behavior – ultimately translating into improved treatment outcomes. The creation of this newsletter is just one sign of the exciting efforts underway to chart the next chapter in the Center's history!



CNRA's location on the first floor of the BBSB improves subject capacity and throughput.

Eye Tracking contd from page 1

improved markers of relapse risk. These methods are based on two features: 1) a cocaine user's reactivity to drug cues, and 2) the sensitivity of the visual system (eye-movements) to neural dysfunction (brain insult and injury).

When a cocaine user is shown an image of cocaine, he quickly focuses his attention towards the image---a phenomena known as attentional bias, recognized as a strong predictor of drug craving and relapse. Rapid eye movements, called saccades, serve as a precise physiological measure of attention. Saccades can be measured with an eye-tracker, an infrared device that tracks the movement of the pupil.

This team developed a novel attentional bias task that used eye-tracking to record eye movements while two groups, cocaine and healthy controls of similar age, gender, and education, looked at images related to cocaine or neutral objects.

The results indicated that when cocaine users are instructed to make voluntary eye movements *away* from

a cocaine image, they are unable to consistently do so and make significantly more errors than controls, in other words they fail to look away from the cocaine images.

The outcomes show that the task is a sensitive measure of "inhibitory control" (self-control), which provides insight into neural deficits related to cocaine use. In addition, cocaine dependent subjects show greater attentional bias (a strong relapse predictor), which is shown by the high amount of errors and faster eye-movements in the presence of cocaine images compared to neutral images. Essentially, the presence of these cocaine images is related to differential attention and craving for the drug.

This new task will serve as a quick, non-invasive tool in assessing reactivity to drug cues and relapse risk. Currently, this team is integrating this task into clinical trials for the treatment of cocaine dependence, encouraged that it may aid in the improvement of treatment outcomes and prevention of relapse in cocaine addiction. ■

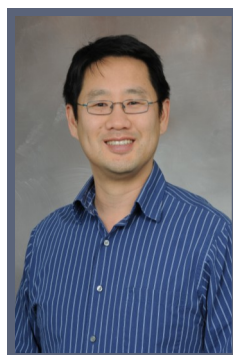
High Cost of Addiction

Considering their combined medical, economic, criminal, and social impact, drug abuse and addiction cost Americans nearly half a trillion dollars a year.

CNRA Welcomes New Faculty



Anka Vujanovic, Ph.D. an Assistant Professor and Director of Psychology Services at the UT-Harris County Psychiatric Center, joined the CNRA in June 2013. Anka received her doctoral degree in clinical psychology from the University of Vermont in 2009. Her research focuses on examining biopsychosocial mechanisms underlying the comorbidity between PTSD (and other trauma-related psychopathology) and substance use disorders in order to inform the development of novel treatments.



Jin Yoon, Ph.D. received his Ph.D. in the experimental analysis of behavior from the University of Florida in 2006. His research interest is in developing treatments and identifying mechanisms of drug addiction, with a focus on nicotine dependence. Additionally, he is interested in the use of novel technological innovations in addictions research.

Pharmacogenetics in cocaine treatment: One size may not fit all

■ Joy Schmitz, Ph.D.

Presently there are no proven medications to treat cocaine addiction. Much of the NIDA-supported research at the CNRA has focused on identification and testing new pharmacological interventions to treat cocaine addiction safely and effectively. Since 1998, we have tested over 20 different medications, reporting some positive and some negative findings.

Even when medications show efficacy, not all treated patients benefit, suggesting considerable individual variability in drug response. Understanding the source of individual variation in drug response to cocaine medications has proven difficult, but is receiving more attention now than ever before.

In a recent study CNRA investigated the role of *genetic factors* in modulating response to cocaine treatment. Seventy-one cocaine-dependent patients participated in a 12-week randomized double-blind placebo-controlled trial of levodopa with carbidopa (Sinemet®, 800/200 mg per day). Adult participants who were interested in quitting cocaine returned



for outpatient clinic visits three times a week (MWF) to provide a urine drug screen, participate in weekly individual drug counseling, receive medication, and complete measurements. Thirty-eight patients were randomly assigned to the levodopa medication group and 33 patients received placebo. Levodopa is a medicine that the brain converts to dopamine.

Pharmacologically, levodopa is thought to work by replenishing dopamine stores that are depleted as a result of chronic cocaine use. CNRA and others have reported on the efficacy of levodopa in reducing cocaine use, but with a wide range in treatment response rates.

In the present study we sought to better identify the subgroup of “responders” according to their dopaminergic genotype. Using DNA samples collected at the start of the study, participants were genotyped (retrospectively) according to their level of a dopamine metabolizing enzyme: dopamine β -

hydroxylase (D β H). D β H is the enzyme that converts dopamine to norepinephrine. Individuals with genetically low D β H activity (carriers of the CT/TT genotype) exhibit higher endogenous dopamine levels due to converting less dopamine to norepinephrine. In contrast, individuals with genetically higher (normal) D β H enzyme activity (carriers of the CC genotype) have been shown to have lower endogenous dopamine levels.

We speculate that the dopamine-increasing effects of levodopa work best in patients who already have higher endogenous levels of dopamine.

At the end of the study we tested whether treatment helped patients stop using cocaine and found an interesting interaction. Levodopa treatment was more effective than placebo, but only in the subgroup of patients having the low D β H genotype. The other subgroup of patients having “normal” D β H activity responded about the same whether they received treatment with levodopa or placebo.

Based on these findings we speculate that the dopamine-increasing effects of levodopa work best in patients who already have higher endogenous levels of dopamine. Perhaps in these patients the therapeutic goal of replacing or re-

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Pharmacogenetics contd

plenishing dopamine is more likely to be achieved than in patients with higher enzyme levels who promptly convert dopamine to norepinephrine.

The discipline of pharmacogenetics has been practiced for decades. In the field of oncology, for example, genetic testing has revolutionized the approach to cancer treatment. In the field of drug addiction, genetic factors may unlock

Genetic factors may unlock the key to predicting the type of pharmacological treatment that will be most effective for the individual patient.

the key to predicting not only the risk of developing a substance use disorder, but also the type of phar-

macological treatment that will be most effective for the individual patient.

Unfortunately, there is no “one size fits all” approach for treating a complex disorder like cocaine dependence. Recognizing individual differences and how these differences are expressed in genetic information may help overcome current limitations in the treatment of drug addiction. ■

PTSD contd from page 1

is predictive of stronger drug cravings, greater tendency to use substances to alleviate negative mood states, less improvement during SUD treatment, and faster time to relapse post-treatment.

According to the self-medication hypothesis, trauma-exposed individuals with subclinical or clinical PTSD use substances to escape/avoid aversive PTSD symptoms. Given the transactional associations between PTSD and SUD and the high rates of treatment failure documented among individuals with PTSD-SUD comorbidities, integrated treatments that address both aspects of this highly prevalent and difficult-to-treat comorbidity are imperative for improving treatment outcomes and thus alleviating the related public health burden.

Yet, the literature for integrated PTSD-SUD treatment is strikingly limited. The most well-studied integrative treatment for PTSD-SUD to date- the *Seeking*

Safety program, a manualized, group-based treatment program focused on cognitive-behavioral skills relevant to PTSD and SUD - has yielded only equivocal results. An examination of the literature indicates a significant paucity of research in the area of integrative treatments, both cognitive-behavioral and pharmacological. Thus, it is imperative for future research to address this clinically significant gap in order to improve outcomes for this common though difficult-to-treat population.

A newly funded study at CNRA (KL2TR000370-07; PI: Vujanovic) aims to develop an integrative cognitive-behavioral treatment for PTSD-cocaine dependence. The treatment will integrate evidence-based cognitive-behavioral principles for the treatment of PTSD and SUD into one 12-session individualized treatment. In the context of a randomized-controlled trial, CNRA will compare the efficacy of the integrative treatment with a standard cognitive-behavioral

treatment for SUD in terms of both PTSD- and SUD-related outcomes.

We will compare the efficacy of the integrative treatment with a standard cognitive-behavioral treatment for SUD in terms of both PTSD- and SUD-related outcomes.

In the context of the trial, CNRA also will experimentally examine mechanisms of change, including drug- and trauma-cue reactivity and distress tolerance, with the goal of utilizing the information gleaned to further refine the next iteration of the treatment. CNRA will recruit adults with PTSD and cocaine dependence to participate in the study beginning in early 2014. ■

Recent Awards & Honors

Research Update

Scott Lane

R21 DA034825

Bupirone, Stress, and Attentional Bias to Marijuana Cues

Anka Vujanovic

KL2TR000370-07

Randomized Controlled Trial of a Novel Cognitive-Behavioral Treatment for PTSD and Cocaine Dependence

Joy Schmitz

P50 DA009262 Supplement

PPAR γ Agonist as a Treatment for Cocaine Dependence**Jin Yoon**

P30 CA125123-06S3

Perceptions of E-Cigarettes and Effects on Craving, Withdrawal and Smoking Severity After Exposure to Virtual Reality Cues

Angela Heads

SAMHSA

The Knowledge Awareness and Prevention on Wheels (KAPOW!) Project

Nilesh Tannu & Samet Kose

Travel Award

American Association of Addiction Psychiatry (AAAP)

2013 Selected Faculty Publications

- Liu S, **Lane SD**, **Schmitz JM**, Cunningham KA, John VP, Moeller FG: Effects of escitalopram on attentional bias to cocaine-related stimuli and inhibitory control in cocaine-dependent subjects. *Journal of Psychopharmacology*, 27, 801-807, 2013.
- **Schmitz JM**, Rathnayaka N, **Green CE**, Moeller FM, Dougherty AE, Grabowski J.: Combination of modafinil and d-amphetamine for the treatment of cocaine dependence: A preliminary investigation. *Front. Psychiatry*, 3, 77, 2012.
- Bough KJ, Amur S, Lao G, Hemby SE, Tannu NS, Kampman KM, **Schmitz JM**, Martinez D, Merchant KM, **Green CE**, Sharma J, Dougherty AH, Moeller FG: Biomarkers for the development of new medications for cocaine dependence. *Neuropsychopharmacology*, 139, 202-19, 2014.
- Lindsay JA, Minard C, Hudson S, **Green CE**, **Schmitz JM**: Using prize-based incentives to enhance daily interactive voice response (IVR) compliance: A feasibility study. *Journal of Substance Abuse Treatment*, 46, 74-77, 2014.
- **Alcorn JL**, **Gowin JL**, **Green CE**, Swann AC, Moeller FG, **Lane SC**: Aggression, impulsivity, and psychopathic traits in combined antisocial personality disorder and substance use disorder. *J Neuropsychiatry Clin Neurosci*, 25, 229-32, 2013.
- Kollins SH, English JS, Roley ME, O'Brien B, Blair J, **Lane SD**, McClernon FJ: Effects of smoking abstinence on smoking-reinforced responding, withdrawal, and cognition in adults with and without attention deficit hyperactivity disorder. *Psychopharmacology*, 227, 19-30, 2013.
- **Vujanovic AA**, Farris SG, Harte CB, Smits JAJ, Zvolensky MJ: Smoking status and exercise in relation to PTSD symptoms: A test among trauma-exposed adults. *Mental Health and Physical Activity*, 6, 132-138, 2013.
- **Vujanovic AA**, Hart AS, Potter CM, Berenz EC, Niles BL, Bernstein A: Main and interactive effects of distress tolerance and negative affect intensity in relation to PTSD symptoms among trauma-exposed adults. *Journal of Psychopathology and Behavioral Assessment*, 35, 235-243, 2013.
- Boden MT, Babson KA, **Vujanovic AA**, Short NA, Bonn-Miller MO: Post-traumatic stress disorder and cannabis use characteristics among military veterans with cannabis dependence. *The American Journal on Addictions*, 22, 277-284, 2013.
- Garcia-Rodriguez O, Weidberg S, **Yoon JH**, Garcia-Fernandez G, Secades-Villa R: Assessment of impulsivity using a delay discounting task in cocaine addicts. *Revista Iberoamericana da Psicologia y Salud*, 4, 23-35, 2013.
- Bordnick PS, **Yoon JH**, Kaganoff E, Carter B: Virtual-reality cue reactivity assessment: A comparison of treatment- vs. non-treatment seeking smokers. *Research on Social Work Practice*, 23, 407-418, 2013.
- Ross EL, **Yoon JH**, Mahoney III JJ, Omar Y, Newton TF, De La Garza II R: The impact of self-reported life stress on current impulsivity in cocaine dependent adults. *Progress in Neuro-Psychopharmacology & Biological Psychiatry*, 113-119, 2013.
- Garcia-Rodriguez O, Secades-Villa R, Weidberg S, **Yoon JH**: A systematic assessment of delay discounting in relation to cocaine and nicotine dependence. *Behavioral Processes*, 99, 100-105, 2013.

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: UHealth—CNRA, P.O. Box 301413, Dallas, TX 75303 or by calling

(713) 500-5217

Training Leads to Success

The CNRA is committed to the training and career development of the next generation of addiction scientists, educators, and clinicians. This year we broadened our training program by successfully recruiting positions at the graduate school, residency, and fellowship level. Meet our new cohort of six trainees!

Angela M. Heads, Ph.D. is currently a postdoctoral research fellow in the Department of Psychiatry and Behavioral Sciences at UT Medical School at Houston. She obtained her Ph.D. in Counseling Psychology at Texas A&M University. She is a fully licensed psychologist whose research interests include stress and coping, psychocultural variables related to health and mental health and gender and race/ethnicity related health and mental health disparities.

Rob Suchting, Ph.D. is a first year postdoctoral research fellow at UT Houston. He received a Ph.D. in social psychology at the University of Houston with a minor in quantitative methods. His research interests include substance dependence, motivation, and the relationship between frequentist and Bayesian statistics.

Samet Kose, MD, PhD, is a third year research track resident in the general psychology program at UT Houston. Dr. Kose earned his medical degree at Hacettepe Uni-

versity School of Medicine in Ankara, Turkey. He completed his residency in psychiatry at Dokuz Eylul University School of Medicine, Department of Psychiatry in Izmir, Turkey. Dr. Kose completed his Psychiatric Neuroimaging Fellowship at the Center for Advanced Imaging Research, Medical University of South Carolina in Charleston. Dr. Kose's current research at the University of Texas focuses on cerebral blood volume mapping in patients with unipolar and bipolar depression and brain stimulation using TMS for treatment of cocaine dependence.

Marsal Sanches, MD, Ph.D. is currently a fourth-year research track psychiatry resident at UT Medical School at Houston. He obtained his medical degree from Santa Casa de Sao Paulo School of Medicine, in Brazil and underwent residency training at the Federal University of Sao Paulo. He also completed a PhD. in behavioral sciences and a postdoctoral research fellowship in mood disorders and neuroimaging at the Uni-

versity of Texas Health Science Center at San Antonio. His research interests include mood disorders, impulsivity, and personality disorders.

Nilesh Tannu, MD is a third year research track resident in the general psychiatry residency program at UT Houston. After completing medical school in India, he did a Masters in a Biomedical Engineering at UT Memphis followed by Clinical Neuroscience work at Wake Forest University. His interests include understanding the neuropathology of cocaine dependence by proteomics methodology, and pharmacotherapeutic interventions for cocaine dependence using neuroprotective mechanisms.

Billie Myers is a pre-doctoral clinical psychology intern from Fielding Graduate University. Her research interests are social anxiety, PTSD, anxiety disorders with co-occurring substance dependence, and relationship dynamics.

The Brain on Drugs

Brain imaging studies from drug-addicted individuals show physical changes in areas of the brain that are critical to judgment, decision-making, learning and memory, and behavior control.

Clinical Corner

CNRA Treatment Graduate Shares Inspiring Experience

Lauren Kitchens, LPC, interviewed a recent graduate of one of CNRA's clinical trials to get his perspective on his experience as a participant.

“So many people want to help, just take it.”

How did you find out about us?

My fiancé and my daughter sent me a picture text of [CNRA's] ad in the Greensheet. I don't think either one knew that they were both sending it to me at the same time. I waited a month and then finally called.

Why did you wait a month?

I wanted to stop, but I just couldn't. I started researching medications for addiction and then just finally made the call. I think I was scared to get clean.

What were your initial impressions?

This program changed my definition of treatment. Treatment before was like a job where you just showed up and didn't want to. Now it means something that helps you get right, get better.

How is CNRA different?

Previous programs were always telling me what I did wrong. “You've got to change. We don't trust you.” That doesn't work for people on cocaine. I can't be forced. [Cocaine users] are rebellious. I don't know if it's the drug or what, but we want to do stuff on our own.

...You didn't force anything on me and [no one looked] down on me. I looked down on myself, but you didn't do that. You are angels.

...This program helped me learn how to *live* my life. Before this I was just trying to quit getting high. Now I am clean and *living* a life.



What are your thoughts about the medication and research?

Maybe it was the medication that helped me get to a place of opening up in treatment. I don't know if I got [the medication] or not but I felt I could open up and talk. I knew what I was getting into [with research]. This was my last resort. I never tried medication and I never tried doing everything that treatment involves.

Any concerns or fears you had about research?

I had no fear, only hope. I was living the worst life possible and I

thought how could it get any worse?

What would you tell people about this program?

It worked for me. I was at the bottom. You are my angels. If you're on drugs, you know your life isn't right. People always say, “I can stop. My life is good.” If it's true then why aren't you stopping? Why isn't your life good? Why don't you do it if it's that easy? Just ask for help and give up the fight. I took advantage of this program and [others] can too.

What advice would you give others wanting to make a change?

Take all the help you can get. *All the help*. And do it to the best of your ability. So many people want to help, just take it. Give up, surrender. I was fighting cocaine all my life. One that could eventually lead to my death. I finally gave up the fight with it and walked away. Now here I am today graduating this program, working the steps in 12 step, and taking my recovery day by day. ■

To participate in one of our ongoing clinical trials for treatment of cocaine dependence, call **713-500-DRUG (3784)**.

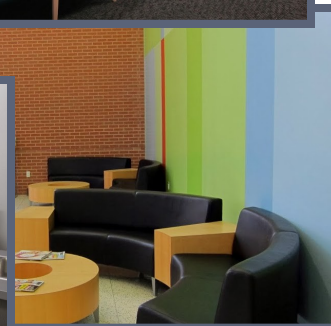
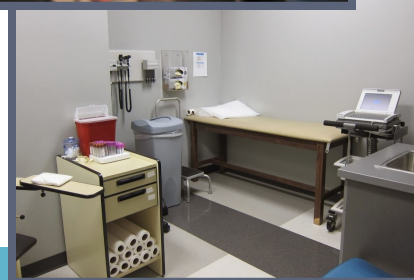
Inside the CNRA

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

- ◆ Clinical Trial of Citalopram in Cocaine Dependence
- ◆ Cognitive-enhancing Dopamine Medications for Cocaine Dependence
- ◆ PPAR Gamma Agonist Treatment for Cocaine Dependence

CNRA Program Features:

- ◆ No Cost Treatment for Cocaine Dependence
- ◆ 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