Alcohol and Substance Abuse Disorders Research Program

Program History

The problem of alcohol and substance abuse is a growing concern among the general public, as well as military personnel and Veterans alike. In 2013 the Institute of Medicine (IOM) report, Substance Use Disorders in the U.S. Armed Forces, characterized the overall prevalence of heavy drinking at 20% and the overall prevalence of illicit drug use at 12%. Rates of acute and chronic incident alcohol diagnoses increased from 2001 through 2010, especially for the active duty component. The results indicate the increasing medical burden imposed on the Military Health System by excessive alcohol use. Substance abuse was involved in 30% of the Army's suicide deaths from 2005-2009 (National Institute of Drug Abuse 2011). Furthermore Alcohol and Substance Use Disorders (ASUD) significantly worsen the hyper-arousal effects of PTSD, a disorder that affects 14% of all previously deployed U.S. military personnel (RAND 2012). Veterans have their PTSD complicated by chronic TBI-effects, which are worsened by ASUD. The 2013 IOM report recommended that the Department of Defense assume leadership to ensure the consistency and quality of treatment services available to those with ASUDs given the burden of ASUD in the military. The Alcohol and Substance Abuse Disorders Research Program (ASADRP) was established in FY10 with a congressional appropriation of $6.375M. Since then, the program has established a network of multidisciplinary, translational research teams with the explicit goal of accelerating the delivery of new or improved treatments for ASUDs, and federal funding for its research has led to a total appropriation of $32.075M to the ASADRP. The goal of the program is to identify and develop new medications to improve treatment outcomes for SUDs, especially related to TBI and PTSD. The program's approach is to organize multidisciplinary, team-based translational research efforts to identify promising compounds, conduct proof-of-principle basic research to determine which compounds are most appropriate for human research trials, and conduct human proof-of-principle trials with promising compounds. If successful, this approach could result in translation of contemporary basic science knowledge into enhanced clinical pharmacological treatment protocols for ASUDs.

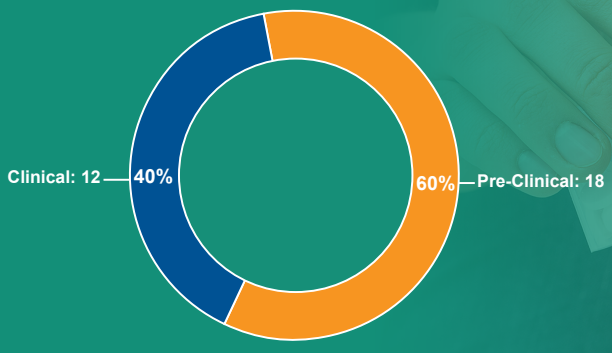
Vision

Decrease the clinical impact of alcohol and substance abuse

Mission

Explore new opportunities to address alcohol and substance abuse disorders, especially related to TBI and PTSD, through multidisciplinary, team-based research efforts that translate basic knowledge into enhanced clinical protocols

FY10–FY14 Portfolio by Research Area



Total number of awarded projects: 30
Total number of active projects: 18

Glial Regulators for Treating Comorbid Posttraumatic Stress Disorder and Substance Use Disorders

Sudie E. Back, Ph.D., Medical University of South Carolina

Data from the Proof-of-Principle study among 35 Veterans with PTSD and SUDs (primarily alcohol use disorder) showed that NAC treatment was associated with an 81% reduction in craving, which was significantly greater than the placebo group (32%). Scores on the Clinician Administered PTSD Scale (CAPS) and the Beck Depression Inventory (BDI) were also significantly reduced in the NAC but not the placebo group. These robust results led to a recently initiated full scale, 8-week, randomized controlled trial of NAC (2400 mg) vs. placebo among Veterans (N=90) with PTSD and alcohol use disorder. In addition, the new study is utilizing functional magnetic resonance imaging (fMRI) and proton magnetic resonance spectroscopy (1H-MRS) before and after treatment.

Epigenetic Modulation of Interactions between Fear and Substance Abuse

Kennon M. Lattal, Ph.D., Oregon Health & Science University

SUDs and PTSD are highly comorbid, with PTSD symptoms causing relapse in drug seeking, even after successful treatment and long periods of abstinence. This project aims to develop a novel rodent model for the comorbidity between SUDs and PTSD, and use this model to test a novel pharmacological intervention that, when paired with behavioral interventions, reverses drug-seeking and anxiety induced by specific memories. The investigators have successfully established a novel procedure for studying the interactions between fear conditioning and drug-seeking and have established HDAC3 inhibitors as a potential therapeutic for promoting extinction of fear and drug-seeking behaviors. Importantly, they have demonstrated that the fear conditioning procedure that they previously found to have lasting effects on methamphetamine seeking also has an effect on alcohol-seeking behavior and may provide data relevant to multiple types of drug abuse.

Development of an Animal Model and Novel Treatments for Comorbid PTSD and Cocaine Addiction

Lori A. Knackstedt, Ph.D., University of Florida

The objective of this project is to develop a novel animal model of comorbid PTSD and cocaine use disorder and examine medications that target the glutamate and endocannabinoid systems for their ability to reduce both PTSD symptoms and cocaine-seeking. The investigators have successfully shown that stress-susceptible (PTSD-like) rats displayed enhanced cocaine-seeking compared to resilient and unstressed control rats. The antibiotic ceftriaxone effectively prevented cocaine-seeking only in the resilient and unstressed control rats, indicating that medications that treat cocaine addiction in non-PTSD individuals may be unable to do so in PTSD patients. However, the combination of ceftriaxone with CDPPB, which also targets the glutamate neurotransmitter system, completely prevented cocaine-seeking in PTSD rats. Future studies will examine additional experimental compounds in an effort to guide successful treatment of comorbid PTSD and cocaine use in those suffering from these disorders.

The Pharmacotherapies for Alcohol and Substance Abuse (PASA) Consortium

Rick Williams, Ph.D., Research Triangle Institute International (RTI)

The PASA is a multicenter collaboration led by Dr Rick Williams of RTI and its partners Baylor College of Medicine and the Uniformed Services University of Health Sciences. PASA uses a translational approach (from animal models to humans) to understand the complex interaction of substance abuse with the now-common military stress comorbidity of associated PTSD and TBI. New pharmacotherapies for treatment of ASUD and combined disorders are needed to improve health outcomes and adherence to treatment, as well as reduce costs to the military. PASA has recently funded 4 studies, (2 pre-clinical and 2 clinical):

- **Assessing pharmacotherapies in animal models of post-traumatic stress disorder and alcohol use disorder (AUD),**
- **Preclinical Analysis of Combined Carisbamate and Doxazosin Treatments in Stress-Alcohol Drinking Models,**
- **Carisbamate as a New Treatment for PTSD & Co-Occurring AUD,**
- **Efficacy and Safety Study of ORG 34517 in Veterans with Co-morbid PTSD/AUD**