

University of Pennsylvania

Annual Progress Report: 2010 Nonformula Grant

Reporting Period

June 1, 2011 – June 30, 2011

Formula Grant Overview

The University of Pennsylvania received \$4,999,999 in nonformula funds for the grant award period June 1, 2011 through May 31, 2015. Accomplishments for the reporting period are described below.

Research Project: Project Title and Purpose

CURE Addiction Center of Excellence: Brain Mechanisms of Relapse and Recovery - The overall purpose of the proposed project, a “CURE Addiction Center of Excellence: Brain Mechanisms of Relapse and Recovery”, is to develop an understanding of the biological mechanisms of relapse that may be common across drugs of abuse – knowledge that is lacking, but critical for changing the harsh relapse statistics for addiction (up to 80% of treated individuals have relapsed by 6 months following treatment). The expected scientific yield is a brain-based understanding of relapse vulnerability that will enable targeted, novel (medication and behavioral) interventions to improve the health of addicted Pennsylvanians, save billions in addiction-related costs, and offer new hope for recovery to all those afflicted with these painful disorders.

Anticipated Duration of Project

6/1/2011 - 5/31/2015

Project Overview

The extraordinary cost of addiction – financially, medically and socially – is directly related to the stubborn clinical problem of relapse. The striking similarity of relapse rates across a wide range of addictive drugs, demographics, and treatments suggests shared biologic vulnerabilities that, if understood, could offer new treatment targets -- saving billions in addiction-related costs, and offering dramatically improved odds for recovery from addiction. This critical knowledge is lacking, but rapid advances in the clinical neuroscience of addiction have put it within our reach.

Understanding the biological mechanisms of relapse shared by drugs of abuse is thus the overarching goal of our CURE project. The expected scientific yield is a brain-based understanding of relapse vulnerability – generating treatments that will permanently alter the harsh relapse statistics for addiction.

The proposed CURE Addiction Center of Excellence will use functional magnetic resonance imaging (fMRI) and specific probes of reward and inhibition as biomarkers predicting drug use during (Aim 1) and after (Aim 2) treatment in 216 patients addicted to cocaine (Component 1), marijuana (Component 2), and prescription opioids (Component 3). Participants will be scanned before, during, and after a 12-week active treatment specific to each of these drugs of abuse. The brain fMRI measures will be correlated with the primary clinical outcome of drug use (by urine drug screen) during the treatment and follow-up phase. Exploratory Aim 3 will examine the impact of genetic (e.g., polymorphisms modulating reward and inhibition) and epigenetic factors (e.g., history of prior trauma/abuse) on the relapse-relevant brain measures. The Minority Training Aim 4 will offer mentored research internships within the CURE projects to selected Lincoln University undergraduates.

The proposal reflects an integrated collaborative effort between the University of Pennsylvania School of Medicine, Philadelphia Department of Veteran's Affairs Medical Center, Lincoln University, and two community addiction treatment organizations, with guidance from (internal and external) Scientific Advisors and from Community Advisors in organizations supporting the recovery of addicted individuals (The Philadelphia Alliance, PROACT, Re-Enter, Gaudenzia, and PeerStar).

Principal Investigator

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Other Participating Researchers

Charles P. O'Brien, MD, PhD, Teresa R. Franklin, PhD, Marina Goldman, MD, Daniel D. Langleben, MD, Kyle M. Kampman, MD, Ze Wang, PhD, Jeremy F. Magland, PhD, Wade H. Berrettini, MD, PhD, Kevin G. Lynch, PhD, David S. Metzger, PhD - employed by University of Pennsylvania
Ronald N. Ehrman, PhD, Anita V. Hole, PhD, Jesse J. Suh, PsyD, Regina P. Szucs-Reed, MD, PhD, Chris Tjoa, MD, James W. Cornish, MD, Sabrina A. Poole, MS – employed by Philadelphia VA Medical Center
Patricia Joseph, PhD – employed by Lincoln University

Expected Research Outcomes and Benefits

The field of human addiction neuroscience has advanced rapidly in the past decade, often using brain imaging to identify a number of ways in which the brains of addicted individuals differ - in function or even in structure - from the non-addicted. What has not been determined is which (or whether) these many "brain differences" may explain the most painful feature of addiction: relapse. *This knowledge is critical for changing the harsh statistics of relapse (nearly 80%*

relapse by 6 months after treatment), and for reducing the enormous health, social and economic toll of addiction.

The field has lagged in attempting to connect brain-imaging findings to clinical outcomes. There are a few hundred (by now) brain imaging studies in addiction, and also a few hundred clinical trials of various interventions (behavioral and pharmacologic), but the two efforts have not been joined on a scale that would offer stable, replicable results to guide new treatments. Unfortunately, this “separate but parallel” approach severely limits the scientific yield from both arenas: the clinical significance of the brain findings is indeterminate, and the clinical trials are uninformed by brain science that could provide new targets, or help match patients to existing treatments.

Our CURE project will provide the first large scale effort, in the nation, to link brain measures with drug use outcomes in a large cohort of underserved individuals receiving well-characterized treatments for addiction. *The expected scientific yield is a brain-based understanding of relapse vulnerability – an understanding that may provide a sea-change in addiction treatment, and permanently alter the dark relapse statistics for addiction.* These benefits would extend beyond our immediate community, to the Commonwealth, and to the nation.

Summary of Research Completed

The notice of grant award for this new CURE project arrived June 17, 2011; the funding itself is due to arrive within 45 days of the grant award notice.

This initial report thus covers only the two weeks following the award notice, and there are no research results yet to report.

We do have preliminary progress toward CURE preparations:

*We have completed preparation and submission of our master research protocol for the CURE project to the Penn IRB; it was recently reviewed and we are awaiting the outcome.

*We hired two CURE Minority Interns (Ms. Sabrina Smalls and Ms. Kori Devaughn) for summer 2011. They are enjoying their mentored research experience, and will present posters at our site on data concerning HIV risk behaviors in adolescents on August 4, 2011.

Though research activity with human subjects cannot begin until full board approval of our CURE protocol, we have begun preliminary hiring of research personnel involved in preparation of the research study protocols and research materials for the upcoming studies. This ongoing hiring includes research support for the PI (Childress), Co-PIs (O’Brien and Ehrman), several Co-Investigators (Drs. Magland, Franklin, Goldman, Langleben, Kampman, Suh and Szucs-Reed), the senior coordinator (Ms. Fornash) and the study clinicians (Dr. Hole and Ms. Marquez). Salary support is also now in place for the CURE Minority Training Directors at Penn (Cornish and Poole), and the subcontracts with Lincoln University and the VA Medical Center are in process. Enthusiasm for the CURE project is high, and we greatly look forward to initiating the research.