CRAN

COLLABORATIVE RESEARCH ON ADDICTION AT THE NATIONAL INSTITUTES OF HEALTH

STRATEGIC PLAN 2016-2021

NIH Collaborative Research on Addiction at NIH

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CONTENTS

** Note that each of the participating CRAN Institutes have their own comprehensive and detailed Strategic Plans that can be found on their respective websites: **www.niaaa.nih.gov**, **www.drugabuse.gov**, **www.nci.nih.gov**. Additionally, the National Institutes of Health Office of AIDS Research has developed a strategic plan for HIV research that can be found at **http://www.oar.nih.gov/strategicplan**.*

The CRAN Strategic Plan is intended to inform the research and other communities about opportunities for common areas of research for the three Institutes. They include those emerging from recent scientific advances and policy changes, as well as the original areas identified by the Scientific Management Review Board in 2010.

MISSION

The mission of the National Institutes of Health (NIH) partnership, Collaborative Research on Addiction at NIH (CRAN), is to provide a strong collaborative framework to enable the National Institute on Alcohol Abuse and Alcoholism (NIAAA), the National Institute on Drug Abuse (NIDA), and the National Cancer Institute (NCI) to leverage resources and expertise that will advance substance use, abuse, and addiction research to improve public health outcomes.

The CRAN framework was created to foster synergies in addiction science, provide new research opportunities, and meet public health needs by broadening the research focus of participating Institutes to better address poly- or multiple substance use, abuse, and addiction. Its main priorities are to elucidate the common, specific, and interacting causes and consequences of substance exposure, and to develop effective prevention and treatment interventions. By recognizing that there are some common connections among substances of abuse, approaches taken to understand risk factors, mechanisms of action, prevention, treatment, consequences, and service delivery can be improved. To this end, CRAN seeks to fill gaps in research through implementing the following:

1) Expansion of research training to increase scientific expertise in multi-substance research;
2) Creation of core technical facilities and common databases for such research; and
3) Facilitation of a paradigm shift in addiction research culture both within NIH and across the research community.

In this way, research related to one drug will be better leveraged to inform research on others, and help achieve the common goal of reducing the enormous toll of all substance use on patients, families, and society.

BACKGROUND AND OVERVIEW

Epidemiological and clinical research studies indicate that both single substance abuse (e.g., alcohol) as well as poly-substance abuse are common, and the cause of significant morbidity and mortality in the United States and around the world. Basic research studies on behavioral and neural mechanisms involved in alcohol, drug, and tobacco use reveal both unique as well as common substrates and consequences of exposure. The NIH research structure contains three separate Institutes (i.e., NIAAA, NIDA, and NCI—focusing on alcohol, drugs, and tobacco, respectively) that contribute important knowledge about individual substances. At the same time, resulting in part from prioritization of particular substances by each Institute and their discrete resource streams, there have been missed scientific opportunities to capitalize on shared approaches. Certain areas (e.g., epidemiology, prevention, and health services) have been relatively successful in realizing an integrated scientific approach to poly-substance research. However, in other research domains, a comprehensive, well-integrated understanding of multiple substances of abuse remains to be fully addressed.

While differences exist among alcohol, licit and illicit drugs, and tobacco, there are also important commonalities. Addiction to any substance is a disorder, the pathophysiology of which is influenced by multiple risk and protective factors (e.g., genetics, epigenetics, development, temperament, other mental illnesses, social/cultural milieu, economic status, stress level, etc.). Addiction is a chronic relapsing disorder characterized by a compulsion to seek and take a substance, loss of control over intake, and emergence of a negative emotional state (dysphoria, anxiety, irritability) when access to the substance is prevented.

Addiction involves dramatic changes in the function of the brain reward, stress, executive control, learning, and mood systems that can manifest to a greater or lesser extent (depending on the substance) as a relapsing three-stage cycle—binge/intoxication, withdrawal/negative affect, and preoccupation/anticipation. The conceptual framework of the three cycles derives from common elements, such as impulsivity, compulsivity, positive reinforcement, and negative reinforcement, which are associated with addiction for all substances, despite significant differences in overt symptoms. For example, the binge/intoxication stage forms a minor component of tobacco use disorder, in which the pattern involves the highly titrated intake of the drug that does not interrupt daily activities and that is maintained throughout the day, only to be interrupted during periods of sleep.

CRAN will capitalize on opportunities to integrate research where there is overlap in vulnerability, use, mechanisms, prevention, and treatment of tobacco, alcohol, marijuana, and other drugs of abuse. The functional integration of research that will be supported through CRAN allows for an evolution in science to not only respond to new discoveries, but also to lead ongoing efforts to advance understanding of the fundamental bases of one of this nation's most pressing public health problems. The mission of CRAN is to capitalize on evolving synergies between and among programs to create research opportunities focused on multiple substances and address the broad public health needs in the addiction field.

GOALS AND OBJECTIVES

CRAN builds upon the existing research of the participating Institutes focused on genetic, epigenetic, molecular, neurobiological, behavioral, and environmental factors that underlie substance use, abuse, and addiction. The ultimate goal is for CRAN to investigate and differentiate the common and distinctive features of the different manifestations of addiction along the disease continuum. In conjunction with results from other research conducted by NIDA, NIAAA, and NCI, this knowledge will identify means of preventing initiation/escalation of substance use, and provide effective means of helping affected individuals and populations quit and remain abstinent.

Recognizing the value of the systems approach, CRAN encourages funding to target emerging and/or under-recognized opportunities addressing multiple substance use and comorbidity across the lifespan, involving different levels of analysis, from the cellular/molecular to health services and policy research.

STRATEGIES AND ACTIONS

A first step toward eliminating any disease is understanding its nature, incidence, prevalence, and etiology. CRAN will support research to understand better the factors that predispose a person to initiate use of substances of abuse and engage in behaviors ranging from experimentation to harmful use. These factors need to be taken into account to prevent addiction and other associated negative consequences. CRAN will support research to develop successful treatments for multi-substance addiction and improve treatment accessibility and implementation. Additionally, CRAN will leverage data systems and share resources among the CRAN Institutes and others, as appropriate. Examples of research efforts include, but are not limited to the following:

Advancing Basic Science:

- Develop animal models of multiple or poly-substance use.
- Identify new targets (e.g., genes, epigenetic marks, biochemical pathways, neural circuits) to serve as biomarkers or leads for medications development to treat multiple addictions.

Promoting Clinical Research:

- Determine the efficacy/utility of coordinated efforts to screen for multiple substances.
- Implement multi-armed clinical trials to assess outcomes for various substances alone and in combination to maximize resources and speed medications and other treatment development.
- Develop innovative and integrative approaches for treating multi-substance addictions and other comorbid conditions (e.g., mental illness, chronic pain, HIV).

Improving Public Health and Reducing Health Disparities:

- Focus on poly-substance use in vulnerable populations (e.g., pregnant women, the elderly; people with medical comorbidities, such as HIV or HCV).
- Identify and test strategies to overcome barriers and disincentives to adoption of research-based treatments for multiple addictions in the community, criminal justice system, and healthcare systems.
- Conduct implementation research to improve treatment accessibility in various populations, leveraging provisions in the Affordable Care Act that increase access to care.
- Promote research on the adverse health consequences of poly-substance use.
- Support research to develop more effective program, policy, and communication interventions targeting substance use and substance use disorders, and to disseminate and implement existing evidence-based interventions more effectively.

Additionally, CRAN's efforts to change the culture of addiction research within NIH and across the research community will include the following:

- Coordination of communication strategies across the ICs to provide timely information to the public.
- Development of Funding Opportunity Announcements in areas of shared interest.
- Coordination of substance use and addiction training programs across ICs.
- Encouragement of CRAN-related presentations/workshops at key scientific conferences.

HIGHLIGHTS

The Adolescent Brain Cognitive Development Study

One of the landmark initiatives that CRAN has spearheaded is the Adolescent Brain Cognitive Development (ABCD) Study, a national longitudinal study that will use advanced brain imaging as well as psychological and behavioral research tools to observe brain growth and maturation with unprecedented precision. The project, now supported by multiple NIH Institutes, Centers, and Offices (e.g., National Institute of Child Health and Human Development, National Institute of Mental Health, National Institute on Minority Health and Health Disparities, National Institute of Neurological Disorders and Stroke, Office of Behavioral and Social Sciences Research) in addition to CRAN, will recruit 10,000 youths beginning at ages 9 to 10 and follow them over 10 years into early adulthood.

The ABCD project is expected to:

- Identify individual developmental trajectories (e.g., brain, cognitive, emotional, academic), and the factors that can affect them.
- Develop national standards of normal brain development in youth.
- Understand the role of genetic versus environmental factors on development, enriched by comparisons of twin participants.
- Examine the effects of physical activity, sleep, as well as sports injuries and other injuries on brain development and other outcomes.
- Study the onset and progression of mental disorders, factors that influence their course or severity, and the relationship between mental disorders and substance use.
- Determine how exposure to different substances such as alcohol, marijuana, tobacco, caffeine, and others, individually or in combination, affect various developmental outcomes and vice versa.

Findings from the ABCD study will greatly increase our understanding of the environmental and genetic factors relevant to brain and cognitive development, in order to inform a number of public health strategies.

Using Social Media to Understand and Address Substance Use and Addiction

Interactive platforms such as Facebook and Twitter have become important sources of public information, and are powerful tools to help scientists identify prevailing attitudes and myths, and convey accurate information to the public about alcohol, tobacco, and other addictive substances. An emerging approach is for researchers to analyze social media interactions to gain insights into patterns of use, risk factors, and behaviors associated with substance use. In addition, by providing a platform for communicating science-based, health-related messages, social media may also enhance screening, prevention, and treatment of substance use and addiction.

CRAN issued two funding opportunities in early 2014 to (1) support research that leverages social media platforms to advance the scientific understanding of substance use; and (2) use social media to improve the treatment and prevention of behaviors related to substance use. Eleven awards were made in September 2014 and more projects have been funded, as investigators who were not awarded under the original RFA resubmitted proposals based on their original idea. Research on social media generated by these awards will begin to fill important gaps in current paradigms for alcohol, tobacco, and other drugs prevention and treatment.

CONCLUSION

ABCD and the Social Media projects illustrate the potential that CRAN efforts can synergize—reaching beyond the three participating Institutes and the mission of CRAN. CRAN provides a forum and resources for broad-based research agenda, whose benefits and outcomes are dependent on the collaborative efforts of the research community, NIH, and other stakeholders. When considering research priorities, we encourage the research community to leverage the opportunities provided by CRAN in order to develop a better understanding of the influence of multiple substances on brain development, drug use patterns and trajectories, health and public health consequences, treatment, prevention, and implementation science.

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