Topic DAT18-05: Gene-Environment Interplay in Substance Use Disorders **(R01, R21)**

Purpose

To encourage the submission of research project applications studying the interplay of genetic and environmental factors in the onset, developmental trajectories, comorbidity, and outcomes of substance use disorders (SUDs), elucidating phenotypes and development of methodologic approaches, to enhance opportunities for translation to treatment, prevention, gene-finding and molecular studies.

Background

Research applying genetic epidemiologic and molecular genetic approaches has contributed increasingly significant advances to understanding the causes of use, misuse, and use disorders of addictive substances, including alcohol, illicit drugs, nicotine, and prescription medications [Substance Use Disorders (SUDs)]. These studies have established that SUDs are complex developmental disorders, with high heritability, and strong shared environmental effects particularly early in adolescence and at drug use initiation. Genetic epidemiologic approaches have highlighted the roles of gene-environment interactions and correlations in understanding SUD risk and trajectories and to apply methodologies to explicate etiological mechanisms, often in combination with molecular approaches. New studies continue to be needed to elucidate the complex interplay of genetic and environmental (GxE) factors in developmental trajectories of SUDs and comorbid conditions, deepen and refine phenotypic definitions of SUDs, and meet methodologic challenges.

Research Objectives

NIDA welcomes applications studying the interplay of genetic and environmental factors to elucidate risk trajectories and underlying mechanisms of risk and progression of substance use disorders. Applicants are strongly encouraged to explain how their work can enhance opportunities for translation to treatment, prevention, gene-finding and molecular studies.

Examples of approaches that are encouraged include, but are not limited to:

- Studies of GxE interplay to explicate the contributions of both genetic and environmental risk factors to risk for initiation, progression, comorbidity, adverse outcomes, and cessation of SUDs and underlying mechanisms
- Studies using genetically informed methods to refine phenotyping, including alternative phenotypes such as affective or inhibited subtypes
- Use of animal models to better control for genetic, environmental, and/or developmental factors in the study of GxE interactions and of potential trans-generational implications of GxE interactions
- Use of post-mortem brain tissue to study the intersections of genomic and epigenomic factors with specific drug exposures
- Impact of HIV on GxE interactions
- Studies of GxE interplay in outcomes for offspring exposed in utero to substances including marijuana, prescription opioids, alcohol or nicotine
- Studies of the impact of genetic factors on response to preventive or treatment interventions

Cost effective approaches that take advantage of existing data or research infrastructure are also encouraged, including:

- Secondary data analyses: single databases or harmonizing data among multiple studies
- Adding environmental, genetic, or diagnostic measures to ongoing studies with sufficient power to address GxE
- Developing or testing methodologic approaches to improve yield from existing data, to address challenges in data reduction, harmonization and analysis of large, heterogeneous datasets,
- Using existing data to replicate prior findings
- Existing datasets include but are not limited to the following sources:
    - The database of Genotypes and Phenotypes (dbGaP)
    - Collaborative Studies on Genetics of Alcoholism (COGA) Study
    - NIDA Center for Genetics Studies (NGC)
    - Adolescent Brain Cognitive Development (ABCD) Study
    - Population Assessment of Tobacco and Health (PATH) Study

Relevant Funding Opportunities

Funding opportunities that can be used to pursue these and other research activities include, but are not limited to:

R01 NIH Research Project Grant (Parent R01 Clinical Trial Not Allowed) PA-18-484
R01 NIH Research Project Grant (Parent R01 Clinical Trial Required) PA-18-345
R21 NIH Exploratory/Developmental Research Grant Program (Parent R21 Clinical Trial Not Allowed) PA-18-489
R21 NIH Exploratory/Developmental Research Grant Program (Parent R21 Clinical Trial Required) PA-18-344
Administrative Supplements to Existing NIH Grants and Cooperative Agreements (Parent Admin Supp Clinical Trial Optional) PA-18-591

Scientific/Research (Program) Contacts

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AREAS OF EXPERTISE
- Gene-environment interplay in SUD risk trajectories
- Comorbid developmental psychiatric conditions
- Twin, adoption, and other population-based designs

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AREAS OF EXPERTISE
- Genetics and epigenetics
- Human genetics
- Data integration