

Topic DAT18-01: Neuroimmune Signaling and Function in Substance Use Disorders (R01, R21)

Purpose

To encourage research project submissions examining the molecular, cellular, circuit, and behavioral responses to neuroimmune signaling in the CNS in relation to: the trajectory (i.e. initiation, escalation, and maintenance) of drug misuse; consequences of chronic exposure to misused drugs; abstinence and withdrawal from prolonged use; and relapse or reinstatement of drug taking.

Background

Repeated exposure to drugs of abuse can cause changes in neuronal structure and function that contribute to and sustain drug use. Research has largely focused on the interactions of drugs with specific neuronal targets, and on the consequences of drug exposure on neuronal function, excitability, neuroplasticity, and neurochemistry. However, emerging evidence shows that glia activation and the release of neuroimmune factors can promote neuron-glia interactions that modulate neuronal structure and function. Yet the role of glia and neuroimmune signaling in the modulation of neuronal function and expression of substance use behaviors is poorly understood. Research has shown that drugs of abuse, including methamphetamine, morphine, cocaine and nicotine, can elicit neuroinflammatory responses from glia. Stress, an important contributor to relapse, can also elicit neuroimmune responses. Consequently, it is probable that neuroimmune signaling from glial cells contributes to drug misuse, addiction, and other consequences of repeated drug use. Further, because the molecular targets and receptors for abused substances differ, the complement of neuroimmune factors released in response to exposure to a particular drug may differ. Research to identify the linkages between specific drugs of abuse, the neuroimmune factors released by drug use, and the neuroanatomical location of the responses is needed. It is expected that the contributing actions of neuroimmune signaling to addictive behaviors are most likely due not to obvious brain damage and overt pathology, but to the consequences of such signaling in altering specific molecular and cellular processes within glia, neurons, and neural circuits.

Research Objectives

NIDA seeks to stimulate research on the identification and characterization of neuroimmune factors expressed by glial cells and the mechanism(s) by which these factors may mediate substance use, misuse, and addictive behaviors. NIDA is particularly interested in the identity, diversity, chronicity, and functional consequences of the neuroimmune factors released from microglia and astrocytes in response to intermittent or chronic drug exposure or withdrawal, their effects on neuron-glia signaling, and how these factors may facilitate or protect against developing substance use disorders. Applications may focus on all areas of research relevant to understanding neuroimmune signaling in substance misuse, such as genetic and epigenetic components; molecular, cellular, and physiological responses; neural circuitry; and behavior. Applications may propose to study lifespan and vulnerable periods, comorbidity, and sex differences. Applications that incorporate clear behavioral measures are especially encouraged.

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](#)

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AREAS OF EXPERTISE

- Neuronal structure and function
- Glial neurobiology
- Neural circuits