

OVPR Revise and Resubmit Seed Grant Program

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Project Title: Astrocyte iNOS regulates cocaine-induced vasoconstriction in cocaine addiction

Project Summary

Cocaine use can lead to stroke and cerebral ischemia. Previous research effort was focused on cocaine's effects on neurons, and the role of astrocytes in addiction and cocaine-induced brain pathology was under investigated. The goal of this study is to investigate the role astrocyte iNOS plays in chronic cocaine-induced vasoconstriction and addiction. We hypothesize that 1) through an iNOS-mediated pathway, chronic cocaine use can cause astrocyte activation and loss, which will lead to vasoconstriction and cerebral blood flow reduction, causing downstream ischemic responses; and 2) inhibiting astrocyte iNOS upregulation may be an effective approach to prevent cocaine-induced vasoconstriction and addiction. There are two specific aims. Aim 1 is to investigate effects of chronic cocaine exposure on astrocytes and neurovascular pathophysiology in the prefrontal cortex, and characterize iNOS' participation. In Aim 2, iNOS inhibitors will be used to inhibit astrocyte iNOS expression in a cocaine self-administration animal model, to inhibit the over production of nitric oxide, and downstream vasoconstriction responses. Results obtained from this novel study will significantly improve our current understanding of cocaine-induced hypofunction in prefrontal cortex with addiction, and help with the identification of new drug target that can treat (or prevent) brain tissue damage in cocaine addiction.