

Advance-CTR Pilot Project Application

Mechanisms responsible for substance use are diverse, and potentially specific to each individual. Etiological heterogeneity impacts the potential precision of interventions, and hence is an obstacle in developing more efficacious treatments¹⁻⁴. This application seeks to build upon an NIH funded study (NIAAA K08 AA024794) that aims to “unpack” distinct dysregulatory phenotypes of drug use. The primary study is not powered to test the cross-cultural validity of the proposed framework. Being awarded the Advanced-CTR Pilot Project (Category 1) award would augment the aims of the PI’s K08 to support the infrastructure needed to competitively apply for a Research Project Grant (R01) application that seeks to test contemporaneous, “cutting edge” etiological models of drug use across Latino and non-Latino White youth. Validating etiological models in minority populations is an important step to reduce disparities in the development of drug use.

Decades worth of scientific data have shown that environmental adversity impacts health outcomes; and several emerging theories have begun to postulate cognitive and motivational dysregulation as a potential link between adversity and health outcomes⁵⁻⁸. In other words, environmental adversity is thought to become “embedded” within the individual, and this acquired phenotype is thought to bias health related decision-making. **This application aims to: 1) Test the validity of a novel framework to “unpack” dysregulatory phenotypes of substance use across ethnicity; and 2) Test if ethnic differences in exposure to “environmental dosages” can explain the emergence of distinct phenotypes of drug use.**

This proposal seeks to quantify etiological heterogeneity by drawing from the literatures on dual-process models of drug use. Dual-process models explain etiological heterogeneity of drug use by postulating individual differences in motivation and cognitive control as underlying mechanisms driving drug use. This is analogous to proposing that risk for drug involvement depends on the relative balance of a “brake” (*executive functioning*) and an “accelerator” (*motivational processes*). People can be at risk because of faulty brakes, faulty accelerators, or both. Different dual-process models have emerged, and although they generally conceptualize the executive system similarly, there are radical differences in the conceptualization of motivational mechanisms. Models diverge in their conceptualization of motivational impulses as generated by: 1) **reinforcement sensitivity** (sensitivity to reward and punishment)⁹⁻¹¹; or 2) **associative memory** (drug specific memory associations)¹²⁻¹⁴. There is support for both views, though the assessment tools and empirical evidence has been developed in predominantly non-minority populations.

This proposal seeks to add 50 Latino participants to a project that is scheduled to recruit 150 predominantly non-Latino White youth between the ages of 18-20. The proposal will utilize structural equation modeling to test the measurement invariance of instruments that have been previously validated in predominantly non-Latino White populations to assess: executive functioning, reinforcement sensitivity, and associative memory. Participants will be brought to my laboratory at Brown University, and will be administered a battery of performance-based tasks and questionnaire measures (see *Figure 1* for conceptual model).

In sum, developing a more homogenous way to classify drug involvement can lead to increased precision in how we intervene. Hence, clinical implications involve the potential to inform personalized medicine approaches to the treatment of drug use. For example, users whose phenotype involves hypersensitivity to reward may react better to contingency management approaches as such individuals may be more reactive to reinforcement¹⁵, and/or may be particularly responsive to intervention efforts that incorporate non-drug use sources of reinforcement¹⁶. Users whose phenotype involves memory associations between drugs and positive outcomes may be more responsive to cognitive restructuring techniques that build memory structures that are antagonistic to drug use¹⁷. The PI is currently on track to test the conceptual framework in predominantly non-minority populations. This framework was deemed highly innovative by the NIH, as indicated by an impact score of 20 on the first submission of the K08. Being awarded this Advance-CTR pilot grant would allow me to build upon my federally funded work in order to launch a new, parallel, and culturally sensitive branch to my program of research.

