

## **1. Characterizing Cannabis Use in Veterans with Posttraumatic Stress Disorder**

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Description: Rates of cannabis use, misuse and cannabis use disorders (CUD) are high among individuals with posttraumatic stress disorder (PTSD). Over twenty states have legalized cannabis for medicinal use, including nine states that list PTSD as an approved condition. Four states have legalized the sale of cannabis for recreational use. Thus, cannabis misuse may become even more prevalent within this vulnerable population as access increases and legal consequences are removed. Empirical studies have contributed to our early understanding of the cross-sectional relations between PTSD symptom severity and cannabis use, however, this work has lacked the methodological rigor required to draw meaningful conclusions regarding the potential bi-directional relations between PTSD, cannabis use, and related variables (e.g., motives to use, craving). Developing a greater understanding of how, what, and why individuals with PTSD choose to use cannabis and how this use interacts with PTSD symptoms will be essential to the development of appropriate services for individuals with PTSD who use cannabis.

The objective of this study is to build our understanding of cannabis use in individuals with PTSD by: 1) characterizing cannabis use patterns and motives in individuals with PTSD symptoms, 2) conducting the first prospective examination of the day-to-day relations between PTSD and cannabis use, and 3) conducting the first effort to qualitatively describe the perspective of patients with PTSD who use cannabis. To achieve this objective the research group will utilize a mixed methods approach incorporating an online survey (n = 200), daily symptom and use monitoring (i.e., interactive voice response; n = 48), and in-depth qualitative interviews (n = 30) with Veterans enrolled in PTSD treatment who report at least weekly cannabis use. These data will provide an essential foundation on which to build a range of future research efforts along with educational, assessment, and intervention resources.

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## **2. Steps Toward a Nation-wide Examination of the Effect of Marijuana-related Legislation on Adolescent Substance Use and Related Risk Factors**

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Description: A wave of changes in marijuana laws has swept across U.S. states in recent years. Almost half of states now allow for medical marijuana, and four states (Washington, Colorado, Oregon, and Alaska), as well as the District of Columbia, have also legalized recreational marijuana. The shifting legal climate with respect to marijuana could potentially lead to increased availability of marijuana for adolescents, as well as more favorable community and parent attitudes towards marijuana use. This could, in turn, result in increased use of marijuana and other drugs among adolescents, which would have important public health consequences. Understanding the effects of law changes is imperative for guiding public policy and crafting and implementing laws that minimize the harms of adolescent marijuana use.

The proposed study builds on and extends to new territories the current NIDA-funded R21 project that evaluates cannabis-related policies in five states. The proposed study will gather and harmonize data on marijuana and other substance use and marijuana-related risk factors from an additional 18 states that have medical or recreational legislations and develop detailed state-specific marijuana policy timelines for these states. This work will be the foundation for further extramural funding and a nationwide examination of the impact of state-level marijuana legislation – including Washington State’s I-502 – on marijuana-related risk factors and substance use outcomes among youth.

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### **3. Marijuana Use and Disorders from Adolescence into Young Adulthood: Examining Descriptive Epidemiology and Mental Health Risk Factors in a Community-based Prospective Cohort**

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Description: For this study, we will conduct secondary data analyses (SDA) on eight waves of longitudinal data from the Developmental Pathways Project (DPP). The first study aim is to document the descriptive epidemiology and developmental trajectories of marijuana use and disorders over the developmental period from early adolescence through young adulthood. The second aim is to use marginal structural modeling to elucidate the role of depression and conduct problems in the etiology of marijuana use and disorders.

With ADAI small grant funding we will prepare longitudinal data, conduct analyses, and write up results to invest as preliminary studies in an R-01 to be submitted to NIDA in June 2016. The aims of the R-01 SDA proposal will be to address pressing questions about the phenomenology, etiology, and consequences of marijuana use and disorders across the developmental period from early adolescence to young adulthood, to understand differences and similarities in developmental patterns of marijuana and alcohol use and disorders, and to evaluate the effects of marijuana policy changes on young adult marijuana use, perceived norms and harms, and motives.

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### **4. Development of a Novel and Translational Model of Binge Ethanol and Tetrahydrocannabinol Intake in Adolescent Rats**

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Description: Alcohol and marijuana are the most commonly used drugs among adolescents and are often used in combination. Initial experimentation with alcohol and marijuana typically occurs early in life and age of first use is predictive of abuse or dependence of one or both of these substances later in life. Drug exposure during adolescence is thought to alter normal brain development producing long-term neurobiological and behavioral changes that may underlie increased risk for chronic alcohol abuse problems in adulthood, but less is known about the long-term consequences of combined alcohol and marijuana use. Adolescents frequently consume alcohol in a highly dangerous pattern of intake known as heavy episodic or binge drinking that produces substantial behavioral intoxication and pharmacologically relevant blood alcohol levels in a short period of time.

A recurring issue in preclinical research is the availability of rodent models of oral drug self-administration that produce significant levels of intake and effectively model the human condition. Particularly, this absence of relevant models has proven to be a hindrance in the neurobiological examination of alcohol dependence after adolescent binge drinking and in the development of effective preventative and treatment strategies. Further, animal models of polydrug self-administration (e.g., alcohol and marijuana) are missing. For these reasons, the development of a rodent model of binge alcohol intake and concurrent marijuana use that closely models the human condition is crucial for advancing our understanding of the role of early-life drug use in the pathology of alcohol use disorders.

The proposed work seeks to establish and validate a translational model of adolescent binge ethanol intake, and to develop a novel model of polydrug self-administration, with the long-term goal of expanding our current understanding of the neurobiological and behavioral consequences of this harmful pattern of intake on learning and decisionmaking systems as a potential basis for addiction.