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## Nicotine dependence predicts cannabis use disorder symptoms among adolescents and young adults



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#### ABSTRACT

Purpose: We evaluate if cigarette smoking and/or nicotine dependence predicts cannabis use disorder symptoms among adolescent and young adult cannabis users and whether the relationships differ based on frequency of

Methods: Data were drawn from seven annual surveys of the NSDUH to include adolescents and young adults (age 12-21) who reported using cannabis at least once in the past 30 days (n = 21,928). Cannabis use frequency trends in the association between cigarette smoking, nicotine dependence and cannabis use disorder symptoms were assessed using Varying Coefficient Models (VCM's).

Results: Over half of current cannabis users also smoked cigarettes in the past 30 days (54.7% SE 0.48). Cigarette smoking in the past 30 days was associated with earlier onset of cannabis use, more frequent cannabis use and a larger number of cannabis use disorder symptoms compared to those who did not smoke cigarettes. After statistical control for socio-demographic characteristics and other substance use behaviors, nicotine dependence but not cigarette smoking quantity or frequency was positively and significantly associated with each of the cannabis use disorder symptoms as well as the total number of cannabis symptoms endorsed. Higher nicotine dependence scores were consistently associated with the cannabis use disorder symptoms across all levels of cannabis use from 1 day used (past month) to daily cannabis use, though the relationship was strongest among infrequent cannabis users.

Conclusion: Prevention and treatment efforts should consider cigarette smoking comorbidity when addressing the increasing proportion of the US population that uses cannabis.

#### 1. Introduction

Cannabis is the most commonly used illicit substance in the U.S. and adolescence and young adulthood represents the period of greatest risk for the development of cannabis use and cannabis use disorder symptoms (Substance Abuse and Mental Health Services Administration, 2015). Early use has been found to be associated with poor academic performance, higher dropout rates, greater unemployment, lower life satisfaction (Stiby et al., 2015; Mokrysz et al., 2014; Georgiades and Boyle, 2007) and deficits in executive function (Gruber et al., 2012). The Monitoring the Future Study reports that 9.4% of 8th graders, 23.9% of 10th graders and 35.6% of 12th graders used cannabis in the past year (Johnston et al., 2016). Nearly 8% of 19- to 22-year-olds report using cannabis daily, double the rate of use among young adults in

1996 (Johnston et al., 2016). Though often viewed as less addictive than other licit and illicit substances (Nutt et al., 2007), cannabis dependence has been shown to develop in nearly one in ten (approximately 9%) individuals who have ever tried cannabis (Wagner and Anthony, 2002). Those initiating cannabis use during adolescence, compared to those who first use in young adulthood, have also been found to be at increased risk for experiencing cannabis use disorder symptoms soon after initiation and developing associated problems in adulthood (Degenhardt et al., 2001; Mewton et al., 2010). In a recent study examining adolescent cannabis users who initiated within the past two years, nearly one-third of those using cannabis no more than 5 days per month reported experiencing at least some cannabis use disorder symptoms (Dierker et al., 2017).

A strong association between tobacco cigarette smoking and

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cannabis use has been found in cross-sectional and longitudinal investigations in which both cigarette use and symptoms of nicotine dependence have been shown to be associated with cannabis use (Kapusta et al., 2007; Lai et al., 2000; Ramo et al., 2013a,b), cannabis dependence (Ream et al., 2008), a decreased likelihood of successful quitting of cannabis use (Haney et al., 2013) and increased risk of relapse to illicit substance use among those with remitted substance use disorders (Weinberger et al., 2017). In fact, the prevalence of cannabis use has been increasing over the past decade (Compton et al., 2016) with estimates of cigarette smoking among current cannabis users ranging from 41 to 94% (Peters et al., 2012). Although support for the order of onset has been mixed, with evidence for cigarette smoking being a risk factor for later cannabis use (Beenstock and Rahay, 2002; Bentler et al., 2002), and cannabis use a risk factor for tobacco initiation and the development of nicotine dependence symptoms (Badiani et al., 2015; D'Amico and McCarthy, 2006; Patton et al., 2005), their co-occurrence has been consistently established.

The mechanisms underlying this association remain somewhat less clear. The link between cigarette smoking and cannabis use has been discussed with regard to the role each behavior plays in increasing risk for exposure to the other substance, either through a "gateway effect" in which the use of one substance may increase susceptibility to the other, or through regular pairing and/or co-administration of each substance. For example, in one study among college students who reported smoking both tobacco and cannabis, 65% had smoked tobacco and cannabis in the same hour (Tullis et al., 2003). Additionally, in cases of simultaneous use, the repeated pairing of cannabis and tobacco (e.g., blunts) is believed to lead to each substance serving as a behavioral cue for the other (Amos et al., 2004; Highet, 2004). Alternative explanations for the observed associations include genetic and individual factors thought to increase the risk of use for multiple substances (Huizink et al., 2010). Given that substance use disorder symptoms are known to play a central role in sustaining regular and chronic use, their role in the link between cigarette smoking and cannabis use may shed light on these alternate mechanisms of association.

While it is true that exposure to cannabis is a necessary requirement for developing cannabis use disorder symptoms, recent evidence suggests that frequency of cannabis use is a markedly imperfect index for determining an individual's probability of developing DSM-5 cannabis use disorder symptoms among recent onset cannabis users drawn from the National Survey on Drug Use and Health (NSDUH; Dierker et al., 2017). Further, previous research has shown alcohol use disorders (Dierker et al., 2011, 2016) to be a risk factor for DSM-IV nicotine dependence and DSM-IV nicotine dependence symptoms even when smoking cigarettes infrequently and/or at low levels of use. Moreover, cross-over between alcohol use disorder symptoms and nicotine dependence symptoms may promote chronic smoking independent of one's level of smoking or drinking. For example, an investigation of young adult smokers from the National Epidemiologic Study of Alcohol and Related Conditions (NESARC) demonstrated that daily smokers with DSM-IV alcohol dependence were at increased risk for DSM-IV nicotine dependence regardless of how much they smoked (Dierker and Donny, 2008). Similarly, based on a 4-year longitudinal follow-up of adolescents at risk for chronic smoking behavior, we have previously demonstrated that, among novice smokers at entry into the study, the association between alcohol-related problems at baseline and smoking frequency at the 4 year follow-up could be largely explained by experiences of nicotine dependence symptoms measured by the Nicotine Dependence Symptom Scale, rather than directly through measures of smoking or drinking behavior (Dierker et al., 2016).

This evidence independently linking alcohol use disorder symptoms to nicotine dependence rather than smoking or drinking per se provides evidence for a developmental mechanism that recognizes symptoms associated with one type of substance use disorder as a sign or signal for symptoms of another substance use disorder regardless of levels of exposure to either substance. If nicotine dependence is independently

linked to cannabis use disorder symptoms over and above level of exposure to either substance, this would provide evidence that nicotine dependence may indicate sensitivity to cannabis use disorder symptoms across a potentially wide range of cannabis use behaviors. To our knowledge, there has been little research evaluating the link between nicotine dependence and cannabis use disorders symptoms controlling for level of exposure to both substances. Given this gap in the literature, the present study aims to (1) determine the prevalence of cannabis use disorder symptoms among adolescents and young adults who do or do not smoke cigarettes within a nationally representative sample of current cannabis users; (2) evaluate whether cigarette smoking or nicotine dependence better predicts cannabis use disorder symptoms among adolescents and young adults using both substances: (3) determine the strength of the association between nicotine dependence and cannabis use disorders symptoms according to the frequency with which cannabis is used and (4) investigate differences in these relationships across socio-demographic subgroups. Specifically, we were interested in whether the relationships between cigarette and cannabis use and their association with nicotine dependence and cannabis use disorder symptoms are consistent across gender, age (adolescents vs. young adults), and race/ethnicity subgroups.

We hypothesize that, while frequency of cannabis use will be a significant predictor of cannabis use disorders symptoms, nicotine dependence will also be independently associated with individual cannabis use disorder symptoms and with the total number of cannabis use disorder symptoms reported. With respect to the strength of the association between nicotine dependence scores and cannabis use disorder symptoms across the continuum of cannabis use frequency from 1 day per month to daily use, we hypothesize that nicotine dependence scores will be significantly associated with cannabis use disorder symptoms even among those reporting infrequent use, given the evidence that the development of cannabis use disorder symptoms in the context of nicotine dependence need not be driven by heavy use.

#### 2. Methods

#### 2.1. Participants

The sample was drawn from seven annual NSDUH surveys (2009–2015), consisting of n=21,928 individuals age 12–21 who reported cannabis use at least once in the past 30 days. The 2009 survey was chosen as the earliest cohort due to changes to the mental health module between 2008 and 2009. The NSDUH utilized multistage area probability methods to select a representative sample of the non-institutionalized U.S. civilian population aged 12 or older. Persons living in households, military personnel living off bases, and residents of non-institutional group quarters including college dormitories, group homes, civilian dwellings on military installations, as well as persons with no permanent residence are included. More than half of the sample was male (58.8% SE 0.44) and the mean age was 18.3 years (SE = 0.02). Racial/ethnic representation was 60.0% Non-Hispanic White, 14.9% non-Hispanic Black, 18.3% Hispanic, and 6.8% Other.

All procedures performed in this study involved human participants and were in accordance with the ethical standards of the Wesleyan Institutional Review Board and with the 1964 Helsinki declaration and its later amendments. Informed consent was obtained from all individual participants included in the study.

#### 2.2. Measures

#### 2.2.1. Cannabis use frequency

Cannabis use frequency was measured by asking participants: "During the past 30 days, on how many days did you use marijuana or hashish?"

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