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Research paper

Probability and predictors of the cannabis gateway effect: A national study

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ABSTRACT

Background: While several studies have shown a high association between cannabis use and use of other illicit drugs, the predictors of progression from cannabis to other illicit drugs remain largely unknown. This study aims to estimate the cumulative probability of progression to illicit drug use among individuals with lifetime history of cannabis use, and to identify predictors of progression from cannabis use to other illicit drugs use.

Methods: Analyses were conducted on the sub-sample of participants in Wave 1of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC) who started cannabis use before using any other drug ($n = 6624$). Estimated projections of the cumulative probability of progression from cannabis use to use of any other illegal drug use in the general population were obtained by the standard actuarial method. Univariate and multivariable survival analyses with time-varying covariates were implemented to identify predictors of progression to any drug use.

Results: Lifetime cumulative probability estimates indicated that 44.7% of individuals with lifetime cannabis use progressed to other illicit drug use at some time in their lives. Several sociodemographic characteristics, internalizing and externalizing psychiatric disorders and indicators of substance use severity predicted progression from cannabis use to other illicit drugs use.

Conclusion: A large proportion of individuals who use cannabis go on to use other illegal drugs. The increased risk of progression from cannabis use to other illicit drugs use among individuals with mental disorders underscores the importance of considering the benefits and adverse effects of changes in cannabis regulations and of developing prevention and treatment strategies directed at curtailing cannabis use in these populations.

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Introduction

The gateway hypothesis holds that substance use progresses in sequential stages beginning with alcohol and tobacco use, followed by cannabis use and, later, the use of other illicit drugs (Kandel, 1975, 2003; Kandel, Yamaguchi, & Chen, 1992; Kandel, Yamaguchi, & Klein, 2006). According to the gateway hypothesis, individuals rarely use certain substances, such as heroin or cocaine, without having first used "gateway" substances, such as legal drugs or cannabis. The validity of the gateway hypothesis has been the topic of intense debate since the early 1970s. Although some studies have found that use of legal drugs or cannabis are not a requirement for the progression to other illicit drugs (Golub & Johnson, 1994; Mackesy-Amiti, Fendrich, & Goldstein, 1997; Malone, Lamis, Masyn, & Northrup, 2010; Morral, McCaffrey, & Paddock, 2002; Tarter et al., 2012; Tarter, Vanyukov, Kirisci, Reynolds, & Clark, 2006), most studies have supported the "gateway sequence" (Degenhardt et al., 2009; Fergusson, Boden, & Horwood, 2006; Fergusson & Horwood, 2000; Grau et al., 2007; Makanjuola, Oladeji, & Gureje, 2010; Mayet, Legleye, Falissard, & Chau, 2012; Rebellon & Van Gundy, 2006; Van Ours, 2003; Yamaguchi & Kandel, 1984).

In recent years there has been a growing interest in the effects of cannabis on mental health and psychosocial functioning (Blanco et al., 2014; Copeland, Rooke, & Swift, 2013; Moore et al., 2007; van Gastel et al., 2013; Van Ours & Williams, 2012), including the extent to which cannabis acts as a 'gateway drug' (Fergusson et al.,

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2006; Vanyukov et al., 2012). Cannabis would meet the conditions for gateway drug if (a) its use was initiated prior to the onset of other illicit drug use; and, (b) cannabis use increased the likelihood of using other illicit drugs (Fergusson et al., 2006).

While most of the studies have shown a high degree of association between cannabis use and use of other illicit drugs (Agrawal, Neale, Prescott, & Kendler, 2004; Fergusson & Horwood, 2000; Khan et al., 2013; Lynskey et al., 2003; O'Donnell & Clayton, 1982; Van Ours, 2003), the predictors of progression from cannabis to other illicit drugs remain largely unknown (Kandel et al., 2006; Van Gundy & Rebellon, 2010). Identification of those predictors is a crucial step in understanding the etiology of substance use disorders that could help in the development of more effective treatment and preventive interventions.

Prior research has indicated that genetic predisposition (Agrawal et al., 2004), higher frequency of cannabis use (Fergusson & Horwood, 2000; Mayet et al., 2012) and early onset of cannabis use (Fergusson et al., 2006; Van Gundy & Rebellon, 2010) are associated with increased risk of progression to other illicit drug use. Presence of depressive symptoms (Yamaguchi & Kandel, 1984), stress and unemployment (Van Gundy & Rebellon, 2010), peer influence (Wagner & Anthony, 2002) or drug availability (Degenhardt et al., 2010) have also been linked to increased risk of progression to other illicit drug use. Despite this body of knowledge, important questions remain regarding predictors of progression from cannabis use to use of other drugs (Kandel et al., 2006). For example, several sociodemographic, psychopathologic and substance use related predictors previously reported for other types of drug use transitions (Florez-Salamanca et al., 2013; Lopez-Quintero, Perez de los Cobos, et al., 2011; Ridenour, Maldonado-Molina, Compton, Spitznagel, & Cottler, 2005) have not been examined. With the exception of one study that examined depression, no published study has investigated the effect of psychiatric comorbidity (i.e., anxiety, conduct or personality disorders) on progression from cannabis use to use of other drugs.

We sought to build on prior work by drawing on data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), a large nationally representative study of the United States (US) adult population (Grant & Kaplan, 2005). The main goals of this study were to: (1) estimate the cumulative probability of progression to illicit drug use among individuals with lifetime history of cannabis use; and, (2) assess the association between several sociodemographic characteristics, psychiatric comorbidity and substance use-related variables and the risk of progression from cannabis use to other illicit drugs use.

Methods

Sample

The NESARC target population at Wave 1 (2001–2002) was the civilian non-institutionalized population 18 years and older residing in households and group quarters. The final sample included 43,093 respondents. Blacks, Hispanics, and adults 18–24 were oversampled, with data adjusted for oversampling, household- and person-level non-response. The overall survey response rate was 81%. Data were adjusted using the 2000 Decennial Census, to be representative of the US civilian population for a variety of sociodemographic variables. Interviews were conducted by experienced lay interviewers with extensive training and supervision (Grant et al., 2009; Grant, Hasin, et al., 2004). All procedures, including informed consent, received full human subjects review and approval from the US Census Bureau and US Office of Management and Budget. This study examined data of the sub-sample of individuals who started cannabis use at Wave 1 before using any other drug ($n = 6624$). Those who used other illicit drug before cannabis ($n = 484$) and those who only used other illicit drug ($n = 964$) were not included in the current analyses.

Data were collected using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV (AUDADIS-IV) (Grant et al., 2003). The AUDADIS-IV is a structured diagnostic interview, developed to advance measurement of substance use and mental disorders in large-scale surveys (Grant, Stinson, et al., 2004). Computer algorithms produced DSM-IV diagnoses based on AUDADIS-IV data.

Measures

Sociodemographic variables

Sociodemographic factors included gender, self-reported age, race/ethnicity (Whites, Blacks, Hispanics, Asians and Native Americans), urbanicity (urban vs. rural), nativity (U.S.-born vs. foreign-born), educational attainment, marital status and employment status. Family history of substance use disorders (SUD) was defined as any alcohol or drug use disorder among first degree relatives (Heiman, Ogburn, Gorroochurn, Keyes, & Hasin, 2008).

Substance use, abuse and dependence

Extensive AUDADIS-IV questions covered DSM-IV criteria for nicotine, alcohol and cannabis use disorders. For nicotine and alcohol dependence, 3 or more of 7 criteria within a 12-month period are required. The diagnosis of cannabis dependence required that at least 3 criteria from a list of six during a 12-month period be met. Because DSM-IV does not describe a withdrawal syndrome for cannabis, the AUDADIS-IV withdrawal criterion was not included in the diagnosis of cannabis dependence. For alcohol and cannabis abuse, participants had to meet 1 or more of 4 criteria within a 12-month period and not meet the criteria for dependence (American Psychiatric Association, 1994). Age of substance use onset was determined by asking respondents about the age at which they first used: cannabis, sedatives, tranquilizers, analgesics, stimulants, cocaine or crack, hallucinogens, inhalants/solvents, heroin, and other. Consistent with prior reports (Blanco et al., 2007, 2013; Martins et al., 2012) non-medical use of a prescription drug was defined to respondents as using a prescription drug (sedatives, tranquilizers, analgesics, and stimulants) "without a prescription, in greater amounts, more often, or longer than prescribed, or for a reason other than a doctor said you should use them". After the initial probe item, the respondent was given an extensive list of examples of prescription drugs and asked if s/he used any of the prescription drugs on the list or similar drugs 'nonmedically'. The good to excellent test–retest reliability and validity of AUDADIS-IV SUD diagnoses is well documented in clinical and general population samples (Grant et al., 2003; Ruan et al., 2008).

Psychiatric disorders

Mood disorders included DSM-IV primary major depressive disorder, dysthymia, and bipolar I and II disorders. Anxiety disorders included DSM-IV panic disorder, social anxiety disorder, specific phobia and generalized anxiety disorder. AUDADIS-IV methods to diagnose these disorders are described in detail elsewhere (Grant, Hasin, et al., 2004; Grant et al., 2005; Hasin, Goodwin, Stinson, & Grant, 2005; Stinson et al., 2007). Avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic and antisocial personality disorders were assessed on a lifetime basis at Wave 1 and described in detail elsewhere (Grant, Hasin, et al., 2004).

Test–retest reliabilities for AUDADIS-IV mood, anxiety and personality disorders diagnoses in the general population and clinical settings were fair to good ($\kappa = 0.40$–0.77) (Canino et al., 1999; Grant et al., 2003; Ruan et al., 2008). Convergent validity was good to excellent for all affective, anxiety, and personality disorders

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