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Two-part random effects growth modeling to identify risks associated with alcohol and cannabis initiation, initial average use and changes in drug consumption in a sample of adult, male twins

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ABSTRACT

Aims: Our aim was to profile alcohol and cannabis initiation and to characterize the effects of developmental and environmental risk factors on changes in average drug use over time.
Design: We fitted a two-part random effects growth model to identify developmental and environmental risks associated with alcohol and cannabis initiation, initial average use and changes in average use.
Participants: 1796 males aged 24–63 from the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders.
Measurements: Data from three interview waves included self-report measures of average alcohol and cannabis use between ages 15 and 24, genetic risk of problem drug use, childhood environmental risks, personality, psychiatric symptoms, as well as personal, family and social risk factors.
Findings: Average alcohol and cannabis use were correlated at all ages. Genetic risk of drug use based on family history, higher sensation seeking, and peer group deviance predicted both alcohol and cannabis initiation. Higher drug availability predicted cannabis initiation while less parental monitoring and drug availability were the best predictors of how much cannabis individuals consumed over time.
Conclusion: The liability to initiate alcohol and cannabis, average drug use as well as changes in drug use during teenage years and young adulthood is associated with known risk factors.
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1. Introduction

Alcohol and cannabis use disorders are complex traits influenced by genetic and environmental risks. Attempts to prevent use, avoid health and psychiatric consequences and identify prophylaxes (Degenhardt and Hall, 2002; Leweke and Koethe, 2008; Nurnberger et al., 2004) require distinguishing between processes that increase liability to drug use versus processes influencing patterns of use following initiation. Although genetic risks impact drug use and drug use disorders (Goodwin et al., 1973; Heath et al., 1997, 1991; Hettema et al., 1999; Kaprio et al., 1991; Pickens et al., 1991; Prescott et al., 1994; Prescott and Kendler, 1999; Sigvardsson et al., 1996), liability to alcohol and cannabis use can be predicted by a variety of social–environmental factors in early to mid-childhood (Caspi et al., 1996; Casswell et al., 2002; Chassin et al., 2002; Colder et al., 2002; Dubow et al., 2008; Ellickson et al., 2004; Englund et al., 2008; Jackson and Sher, 2006; Li et al., 2001; Maggs et al., 2008; Manzardo et al., 2005; Oxford et al., 2003; Pitkanen et al., 2008; Wiesner et al., 2007; Windle et al., 2005; Windle and Wiesner, 2004), personality dimensions (McGue et al., 1999), and externalizing behaviors (Boyle et al., 1992; Fergusson and Lynskey, 1998; Helzer et al., 1992; Lynskey and Fergusson, 1995; Szobot and Bukstein, 2008; Young et al., 1995). In addition, alcohol and cannabis use can be predicted during adolescence and teenage years by exposure to environmental risks and protective factors, e.g., parental monitoring (Dishion and Loeber, 1985b), childhood sexual or physical abuse (Fergusson and Mullen, 1999; Kendler et al., 2000a), parental attitudes toward drug use (McDermott, 1984), household drug use (Gfroerer, 1987), deviant peer group affiliation (Kandel et al., 1978), drug availability (Freisthler et al., 2005), participation in pro-social activities (Kendler et al., 1997; Werner, 1982; Werner and Smith, 1989). Yet despite the number of significant associations, it is unclear exactly how these risk factors covary with (i) the liability to use

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alcohol and cannabis and (ii) patterns of consumption following initiation.

When combining risks factors into a predictive developmental model, the distribution of the data must be taken into account. Although alcohol and cannabis are initiated on average by age 18 (Gillespie et al., 2009b; Wagner and Anthony, 2002), the distribution of initiation and average drug use at any given point remains semi-continuous. Such distributions have a characteristic histogram with a substantive proportion of zero responses alongside a skewed response pattern for the remainder of the response range. For cannabis, zero responders are high with lifetime abstinence among males of 46% (Gillespie et al., 2009b). Although the number of males who do not consume at least one full alcoholic drink in their lives is lower (3%) the proportion of zero responders only declines after adolescence so that abstemious subgroups can be observed in epidemiological samples (Kendler et al., 2008).

Therefore, our exploratory approach to unravel the role of risk factors over time is to fit a two-part random-effects model (Olsen and Schafer, 2001) which was specifically designed to take into account semi-continuous distributions. Specifically, the model assumes two processes underlie observed semi continuous responses. The first process is binary which differentiates between users and non-users, i.e., whether a response is zero or not. The second process is continuous and reflects the degree of use among drug users only. Both processes are modeled over time. At each time point, a zero response results in a zero for the first process and missing for the second process. In other words, non-users are not considered for modeling the second process. For users (non-zero responders), a latent growth curve model is fitted to the continuous consumption measures. Importantly, both processes are evaluated at each time point, permitting subjects to switch between the two regimes over time, e.g., a subject may be a non-user at time one, user at time two, and a non-user again for the remaining periods. These two processes may be equivalent or qualitatively distinct, i.e., they covary with different genetic and environmental risk factors. Although this method cannot identify subtypes among drug users, it is computationally stable, appropriate for semi-continuous longitudinal data and allows comparisons between abstainers and drug users in terms of known risk factors over developmental time (Olsen and Schafer, 2001).

2. Methods

2.1. Sample and assessment procedures

As part of an ongoing study of adult male twins from the Virginia Adult Twin Study of Psychiatric and Substance Use Disorders (VATSPSUD) this report is based on data collected from three waves of interviews (1994–2004; Kendler and Prescott, 2006). Briefly, twins were eligible for participation if one or both were successfully matched to birth records, were a member of a multiple birth with at least one male, were Caucasian, and were born between 1940 and 1974. Of the 9417 eligible individuals for Wave 1 (1993–1996), 6814 (72.4%) completed the interview. This included 5074 males (the figure excludes third-born member of triplets) from 1499 complete and 2076 incomplete twin pairs (or singletons). Subjects who completed the Wave 1 interview were contacted approximately 1 yr later to schedule a second interview (1994–1998). Wave 2 was completed by 4203 (83%) males from 1189 complete twin pairs and 1825 singletons. A third interview targeting the complete male twin pairs who participated in Wave 2 was launched (2000–2004) to study the nature and pattern of risk and protective factors for psychoactive substance use (PSU) and psychoactive substance use disorders (PSUD) across adolescence and young adulthood. Wave 3 was completed by 1778 males (75%), aged 24–62 yrs (μ = 40.3, SD = 9.0) from 745 complete twin pairs and 288 singletons.

At each wave the Committee for the Conduct of Human Research at Virginia Commonwealth University approved protocols given subjects along with a full explanation. Signed informed consents were obtained before all face-to-face interviews. Verbal assent was obtained before all telephone interviews. Most subjects were telephone interviewed. However, a small number were interviewed in person because of subject preference, residence in an institutional setting, or not having telephone service.

Interviewers possessed a master's degree in social work, psychology, another mental health related field, or a bachelor's degree in one of these areas plus a minimum of 2 yrs relevant clinical experience. They received 40 h of training plus regular individual and group review sessions. Two senior staff members reviewed interviews for completeness and consistency. Each member of a twin pair was interviewed by different interviewers blind to clinical information about the co-twin.

Table 1
Summary of risk factors measured at the first(1993–1993), second (1994–1998) and third (2000–2004) interviews. The third interview included retrospective assessments spanning five development periods (8–11 yrs, 12–14 yrs, 15–17 yrs, 18–21 yrs, and 22–25 yrs).

Risk factors	Scales	Wave
Genetic risk		
Alcohol|illicit drug problem	DSM-IV (115)	2
Externalizing disorder	DSM-IV (115), FH-RDC (71)	1,2
Childhood environmental risks		
Church attendance at 8–17 yrs[FS]	Monitoring the Future (80, 81)	3
Household drug use[a,FS]		3
Parental attitudes toward drugs[a,FS]	Monitoring the Future (80, 81)	3
Physical or sexual abuse		1
Temperamental and symptom		
Disruptive behavior at 15–17 yrs[b,FS]	DSM-IV (115)	3
Neuroticism[FS]	EPQ-R (116)	1
Sensation seeking[FS]	Sensation Seeking Scale (117)	3
Early onset anxiety disorder	DSM-IV (115)	2
Personal, family and social risks		
Conduct disorder at 15–17 yrs[FS]	DSM-IV (115), DBD Scale (75)	3
Parental monitoring[a,FS]	Stattin (76), Kerr (78)	3
Peer group deviance at 15–17 yrs[FS]	Tarter (79), Johnston (80)	3
Alcohol/cannabis availability 8–25 yrs[FS]	Monitoring the Future (80, 81)	3

Note: FH-RDC = Family History – Research Diagnostic Criteria, EPQ-R = Eysenck Personality Questionnaire – Revised, DBD = Disruptive Behavior Disorders. [FS]Individual Marginal Maximum Likelihood factor score calculated based on a single principle component.

[a] Retrospective assessment period of "growing up" defined as ages 8–17 yrs or until left home.

[b] Based on attention deficit, hyperactivity disorder and oppositional defiance disorder psychiatric criterion.

2.2. Model variables

After a systematic review of the literature, the 15 risk factors in Table 1 were selected because of previous significant associations with drug use and drug use disorders. Risks are divided into four developmental tiers reflecting: (i) genetic risks and year of birth; (ii) aspects of the childhood environment; (iii) critical temperamental and symptom variables; and (iv) key personal, social and environmental risk factors in late adolescence. The third interview included a number of retrospective assessments spanning five development periods (8–11 yrs, 12–14 yrs, 15–17 yrs, 18–21 yrs, and 22–25 yrs) to coincide with the timing of major developmental milestones, i.e., leaving the parental home, finishing school, college entry and completion. Also included in the third interview were items assessing the period of "growing up" we defined as between the ages of 8 and 18 yrs.

2.3. Quality control and reliability

Because a number of the childhood environmental risks, temperamental and symptom variables, as well as personal, family and social risk factors measured at the Wave 3 interview are retrospective, these data are potentially contaminated by recall bias and telescoping effects our study used a Life History Calendar format developed by Thornton (Freedman et al., 1988) to improve the quality of the data. Empirically, this method has been shown to improve the accuracy of retrospective reporting by providing multiple cues to increase the chances of accurate recall (Belli, 1998). The method makes the task more akin to the accurate and well-retained process of recognition than to the less reliable task of free recall.

2.4. Genetic risks

Given significant heritability for alcohol and cannabis use (Heath et al., 1997; Kendler et al., 2000b; Kendler and Prescott, 1998; Lynskey et al., 2002; McGue et al., 2000; Miles et al., 2001; Pickens et al., 1991; Prescott et al., 1999; Prescott and Kendler, 1999; Rhee et al., 2003; van den Bree et al., 1998) we included estimates of individual genetic risk for problematic alcohol and cannabis use. These were based on Wave 2 interview self-reports asking twins to report on their paternal, maternal and cotwin's drug use. Specifically, the response distributions to three questions: (i) "*Did your father ever have a problem with [drinking/cannabis] that lasted at least a month?*"; (ii) "*Did your mother ever have a problem with [drinking/cannabis] that lasted at least a month?*"; and (iii) "*Has your twin ever had a problem with [drinking/cannabis] that lasted at least a month?*"