Continuity or Discontinuity between Substance Experimentation, Regular Use, and Dependence Symptoms in Adolescence: Twin and Adoption Results

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Abstract

Heath and colleagues (A.C. Heath, J. Meyer, L. J. Eaves, and N.G. Martin, 1991, ***Journal of Studies on Alcohol***, **52**: 345-352) have suggested that abstinence from consumption is qualitatively distinct from quantity and frequency dimensions of alcohol use in adults. In adolescent substance use, it is harder to distinguish between abstinence and still-pending initiation because assessments are made during the transitional age of risk. This may result in substantial overlap between liability dimensions for experimentation, regular use, and dependence. Data on adolescent substance use has been collected from a Colorado twin sample and participants in the Colorado Adoption Project using interview and questionnaire instruments. For a measure of substance dependence that includes alcohol, tobacco, marijuana, and other drugs, adjusted for the number of substances tried, and corrected for age within gender, the correlation for 297 MZ twin pairs was 0.64, for 268 DZ twin pairs was 0.39, for 140 non-adopted sibling pairs was 0.35, and for 131 adopted sibling pairs was 0.21. We used the multiple threshold approach for ordinal data implemented in Mx to examine whether the dependence dimension could be distinguished from dimensions of use and experimentation.

Introduction

The Colorado Center on Antisocial Drug Dependence is a collaboration between researchers at the University of Colorado at Boulder, and the University of Colorado's Health Science Center in Denver. Clinical probands at residential treatment facilities and outpatient clinics present with high levels of substance dependence across multiple substances and high levels of conduct disorder. Familial resemblance between probands and their family members for substance dependence and antisocial personality/conduct disorder suggests the possibility of an underlying genetic vulnerability. A primary goal of the collaborative Center is to use data from genetically-informative unselected community samples to guide selection of phenotypes prior to genetic analyses using a selected sample.

Crowley et al. (2001) have demonstrated that a multiple substance dependence measure strongly discriminates adolescent patients from community controls. We have explored age and gender effects, and familial resemblance among siblings for alternate formulations of this Dependence Vulnerability measure in a combined, unselected sample of adolescents and young adults (Corley et al., 2001). The phenotype chosen for future genetic analysis represents a sum of dependence symptoms across ten substance classes (including alcohol and tobacco), adjusted for number of substances tried to criterion, and further adjusted for age at assessment and gender of subject. In this adolescent sample, subjects not yet experimenting are assigned a raw score of zero.

Heath and colleagues (Heath et al., 1991) have suggested that abstinence from consumption is qualitatively distinct from quantity and frequency dimensions of alcohol use in adults. Retrospective data from adult twins (e.g., Heath et al., 1999; Stallings et al., 1999) suggest that different aspects of smoking and drinking behaviors may be at least partially distinct etiologically, with shared environmental effects more important in initial use. Epidemiological studies of adolescent substance use trajectories (e.g., Chassin et al., 2000) have demonstrated that early sampling during adolescence may miss a substantial portion of subjects whose substance use begins later, but approaches the levels of use of early-onset subjects in adulthood.

This study reports developmental trends for initial substance use, regular use, and number of dependence symptoms during adolescence, and reports familial estimates for siblings for each multiple substance composite. In addition, we begin to explore how differences in timing of initial use may potentially confound different dimensions of use in this largely cross-sectional study.

Methods

Participants

Between January, 1993 and March 15, 2001, we have conducted 3676 diagnostic interviews with community-based samples of twins, full siblings, and adoptive siblings recruited without regard to substance use or conduct disorder symptoms. Of these interviews, 1692 (46%) have been with female subjects. The subjects ranged in age from 11 through 25 years. The first sample consisted of 2026 twins and a near-in-age sibling if available. The second sample consisted of 720 participants in the Colorado Adoption Project (CAP; DeFries, Plomin, & Fulker, 1994), of whom 295 have been interviewed twice, once as adolescents, and once as young adults. The third sample consisted of adolescents and their siblings matched to adolescent probands in the treatment and outpatient facilities on the basis of ethnicity, gender, and age.

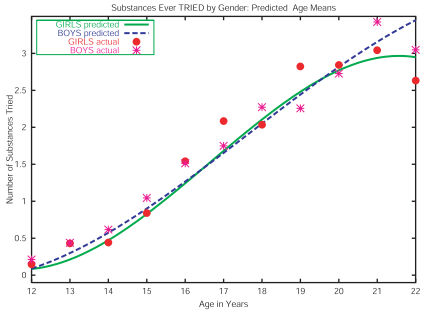
Measures

The Composite International Diagnostic Interview-Substance Abuse Module (CIDI-SAM) questions on tobacco, alcohol, and illicit substances were administered by a trained lay interviewer. Scoring algorithms based on whole life substance use were used to derive the number of Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV) dependence symptoms for each of ten drug classes: tobacco, alcohol, cannabis, stimulants, sedatives, cocaine, opioids, phencyclidine (PCP), hallucinogens, and inhalants. **Dependence Vulnerability** is defined as the average number of symptoms for each substance tried to criterion (nearly daily use for tobacco, six times or more for alcohol, five times or more for others).

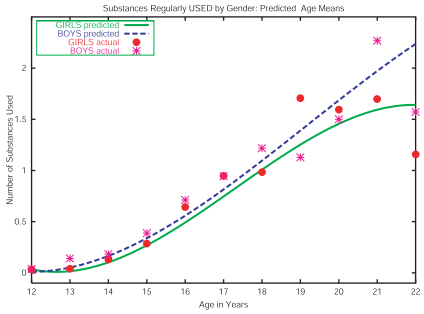
Questions from the Monitoring the Future instrument were asked via questionnaire for lifetime, last year, and last month use of each of 13 substance classes. Sedative, hallucinogen, and narcotic subclass questions were combined to yield categories comparable to the interview (with the exception of PCP, blended into the hallucinogen category). Initial use was defined as any use for illicit substances, and more than 2 uses for tobacco and alcohol. Regular use was defined as more than 40 lifetime, or more than 10 last year, or as more than 3 last month occurrences of use.

Analyses and Results

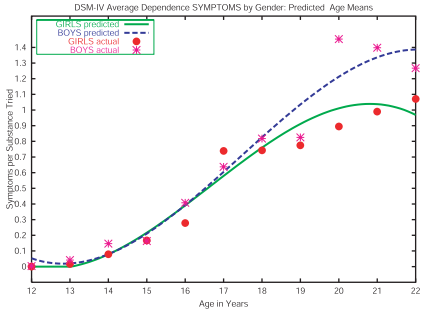
The combined samples yield at least 100 subjects for each age category between 12 and 22. Nine subjects younger than 11.5 and 42 subjects between 22.5 and 26 have been folded into the age 12 and age 22 age categories, respectively. Proportions of males and females are approximately equal across the age range. Figure 1 shows the predicted age effects for boys and girls on the number of substances ever **tried** as a function of age, along with the mean number of substances tried by age category. The regression predictions for girls and boys overlap substantially, and range from a little more than 0 substances at age 12 to approximately 3 substances by age 22.



The second figure shows the predicted age effects for boys and girls on the number of substances regularly used as a function of age, along with the mean number of substances **used** by age category. The regression predictions for girls and boys again overlap substantially, and range from essentially 0 substances at age 12 to approximately 2 substances by age 22.



The third figure shows the corresponding data for the **Dependence Vulnerability** measure, the average dependence **symptoms** across ten substance classes (including tobacco & alcohol). Just as the number of substances ever tried increased over this age range, the number of dependence symptoms adjusted for the number of substances tried increases, from a low of 0 at age 12 to approximately 1 by age 22. Even in these samples unselected for substance dependence, subjects show some dependence symptoms by early adulthood for the substances they have tried to criterion.



Individual scores for the three measures of TRIED, REGULAR USE, and SYMPTOMS were corrected within sex for liinear, quadratic, and cubic age effects, and then standardized. We used Mx to estimate the familial resemblance for MZ twin pairs, DZ twin pairs, full siblings from the sample matched to treatment probands, and full and adoptive (biologically-unrelated) siblings from the Colorado Adoption Project, using a multiple threshold approach. A univariate ACE model was also fit for each measure. The results are shown in Table 1, below.

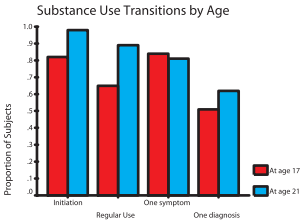
Table 1: How familial are the three multiple substance phenotypes (using gender- and age-adjusted scores) estimated using a multiple-threshold Mx model?

Multiple Substance Phenotypes	MZ Twin Pairs (361)	DZ Twin Pairs (351)	Cntrl. Biol. Sibs (475)	CAP Biol. Sibs (162)	CAP Adop. Sibs (143)	*Est. for h^2*	*Est. for c^2*
Number of substances ever **tried**	0.85	0.64	0.36	0.36	0.25	*0.36*	*0.20*
Number of substances regularly **used**	0.87	0.54	0.42	0.26	0.18	*0.56*	*0.10*
Number of average **symptoms**	0.80	0.74	0.19	0.27	0.20	*0.11*	*0.16*
Average age difference in years	*0.00*	*0.00*	*3.62*	*3.18*	*3.84*		
Average age at testing difference in years	*0.00*	*0.01*	*3.65*	*1.25*	*1.77*		

Analyses and Results, continued

Longitudinal Results:

Of the 295 CAP subjects interviewed once in late adolescence and once in early adulthood, 281 (95%) had completed both the interview and the questionnaire at both time points. The average age at first interview was 17.5 years, and at second interview was 21.3 years. We used this longitudinal data to compare four transition probabilities at each age: the probability of trying at least one substance, the probability of moving to regular use of at least one substance having initiated, the probability of developing at least one symptom having begun regular use, and the probability of manifesting three or more dependence symptoms (the clinical threshold for a diagnosis of dependence) having manifested at least one dependence symptom. Figure 4 shows these transition probabilities separately for the first and second interviews. Clearly, there is still an increase in initial use between adolescence and adulthood, and an increased probability of moving on to regular use by the later interview age



Discussion

We are using data from unselected community samples of twins and siblings to inform our choice of a phenotype for genetic analysis in a selected sample of adolescent probands undergoing treatment for antisocial substance dependence and their siblings. We have focused on multiple substance composites in the interests of compatibility across samples, because the selected sample probands show high levels of dependence across several substances. Although we believe such composites are justifiable on the basis of at least partially overlapping etiological factors, it is the case that they are vulnerable to variation in the time course of the development of and transitions between initiation, use, and dependence for different substances.

In the community samples, composite measures of initiation, use, and symptoms show strong, nearly linear increases through adolescence to early adulthood. When combining data from siblings tested at different ages, some sort of correction or control for age effects is a prerequisite. But this type of adjustment can not control for variations in latencies to transitions for subjects with comparable underlying vulnerabilities, as suggested by the longitudinal data.

The low estimate of the genetic contribution to the dependence **symptoms** composite in Table 1 may partially be attributable to this type of transition latency variability. Analyses based on either simple age-corrected data, or on rank-normalized data, but limited to pairs in the adolescent age range (through age 18) yield substantially higher heritability estimates. We intend to further explore the role of variations in latency through both simulation and more detailed analysis of data collected prospectively in CAP during adolescence.

Acknowledgements

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