Childhood externalizing and internalizing psychopathology in the prediction of early substance use

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ABSTRACT

Aims To examine the prospective relationships between childhood externalizing and internalizing disorders and substance use in early adolescence.

Design Longitudinal, community-based study of twins (aged 11 at intake; aged 14 at follow-up).

Setting and participants The sample was composed of twins participating in the Minnesota Twin Family Study, an epidemiological sample of twins and their families representative of the state population of Minnesota. A total of 699 twin girls and 665 twin boys participated at both time-points.

Measurements Twins participated in in-person, life-time diagnostic assessments of the following childhood DSM III-R externalizing and internalizing disorders at age 11: conduct disorder, oppositional defiant disorder, attention deficit hyperactivity disorder, major depressive disorder and in addition, for girls only, overanxious disorder and separation anxiety disorder. At ages 11 and 14, substance use and abuse were assessed.

Findings Externalizing psychopathology predicted having tried alcohol, nicotine and cannabis by age 14 as well as regular and advanced experience with these substances. Internalizing disorders showed weak effects, with only major depression at age 11 showing a significant relationship with substance use at age 14.

Conclusion The results suggest that externalizing psychopathology is a robust prospective predictor of a variety of early onset substance use behaviors and is systematically related to degree of substance use involvement. The results also suggest that depression may predict initiation of licit substance use in early adolescence.

KEYWORDS Alcohol use, drug use, externalizing, internalizing, prospective study, smoking.

INTRODUCTION

Substantial evidence indicates that childhood psychopathology is associated with elevated rates of early substance use and a range of problem substance use behaviors (Wilens & Biederman 1993; Disney *et al.* 1999; Iacono *et al.* 1999; Marmorstein & Iacono 2001; McGue *et al.* 2001a), both prospectively and concurrently (Bardone *et al.* 1998; Chassin *et al.* 1999; McGue *et al.* 2001a). Child psychopathology researchers distinguish between 'externalizing', or disorders characterized by behavioral disinhibition (disruptive behavior disorders of childhood), and 'internalizing', or disorders characterized by negative mood states and inhibition (depression, anxiety). Prospective studies of substance use behaviors can help disentangle the effects of concurrent psychopathology

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and incipient factors exerting influence over development. Because the early initiation of substance use relates predictably to future substance problems and psychopathology (Boyle *et al.* 1992; Clapper *et al.* 1995; Grant & Dawson 1998; Dewit *et al.* 2000; Muthén & Muthén 2000), identifying the precursors to early substance use offers considerable potential for understanding the growth of problematic substance use behaviors.

Externalizing psychopathology and substance use problems

Recent findings highlight the importance of understanding sequencing of psychopathology and substance use behaviors over time. McGue *et al.* (2001b) demonstrated that childhood disorders characterized by behavioral disinhibition predated an early age at first drink. An early age at first drink was associated with alcohol, nicotine, illicit drug use disorders and a variety of childhood problem behaviors and psychophysiological risk factors (McGue *et al.* 2001b). There is evidence to suggest that the genetic risk for childhood externalizing psychopathology [conduct disorder (CD), oppositional defiant disorder (ODD) and attention-deficit/hyperactivity disorder (ADHD)] is causally related to the familial transmission of an early age at first drink (McGue *et al.* 2001a). Thus, early behavioral disinhibition may precede early substance use and these two sets of behaviors may share a common origin. In their study, McGue *et al.* (2001a) found that though the relationship between externalizing disorders and early alcohol use was not different for boys and girls, the environmental and genetic origins underlying the association did differ by gender. Less is known about whether the behavioral correlates of early drinking are related to using other substances and to engaging in problematic substance use behaviors.

Despite strong support for a connection between externalizing psychopathology and substance use and abuse, it is unclear to what extent externalizing confers risk for the early initiation of a broad array of substance use behaviors. Many studies focus on the early use of one substance (e.g. alcohol; Johnson *et al.* 1995; Grant & Dawson 1997). A 'substance-specific' approach to research may impede our understanding of the shared etiological contributions to various forms of substance use. Beyond having tried alcohol, an early pattern of repeated alcohol use has been related to future problems (Jackson *et al.* 2001). Prospective developmental studies investigating etiological influences can benefit greatly from adopting a research focus that includes variables that sample the natural progression of early substance use (Collins *et al.* 2000). Early substance use may progress through predictable transitions or 'stages'. Collins *et al.* (2000) tested a model in the following order of cumulative progression (adding to the previous stages): (a) ever tried alcohol or nicotine; (b) ever been drunk; (c) ever tried marijuana; and (d) use of another illicit substance. Despite our growing knowledge of this natural progression, few researchers have attempted to unite this approach with etiological models of substance use. In summary, it is important to determine if the risk factors associated with early initiation of alcohol use are similarly associated with more developmentally extreme substance use behaviors (e.g. heavy drinking, regular smoking).

Internalizing psychopathology and substance use problems

Although the link between childhood externalizing disorders and substance use has been the source of considerable attention, there is evidence that internalizing problems (depression and anxiety) are etiologically related to substance use, particularly in females (Chassin *et al.* 1999). Researchers have suggested that the two 'domains' of internalizing and externalizing psychopathology may carry different etiological importance in the development of substance use and problem use in girls and boys (Windle 1990; Chassin *et al.* 1999). Perhaps because later-developing substance use disorders are more prevalent in women, there have been relatively few studies investigating the precursors of early substance use in females. It is unclear whether gender differences in the relationship between psychopathology and substance use emerge earlier or later in development.

Investigators have suggested that internalizing psychopathology [major depressive disorder (MDD) and anxiety disorders] may influence substance use through the mechanisms of tension reduction and/or common genetic influence on the two phenotypes (Kendler *et al.* 1993; Greeley & Oei 1999). With cross-sectional evidence alone, it is difficult to determine whether internalizing is a cause or consequence (or both) of using substances. Some longitudinal studies have found that internalizing disorders have failed to predict the development of substance use disorders (Bardone *et al.* 1998; Rao, Daley & Hammen 2000), whereas others have found that internalizing problems are related to the development of substance use psychopathology (Pandina *et al.* 1992; Marmorstein & Iacono 2001). Because there is little agreement among studies in this area, the impact of internalizing psychopathology on risk for substance problems remains unclear.

Other community-based studies have examined psychopathology in the prediction of substance use involvement in adolescence. (Kendler *et al.* 1993) Later-onset forms of alcoholism are more strongly associated with anxiety, depression and negative emotionality, whereas

earlier onset alcoholism is more strongly related to general disinhibition and novelty seeking (Gomberg 1997). Wide variation has existed in definitions of childhood internalizing problems, ranging from established checklists covering a variety of internalizing behaviors, to inventories focusing only on depression or anxiety. Few studies of early substance use have employed comprehensive diagnostic assessments including more than one major childhood internalizing disorder. Including multiple childhood internalizing disorders can help reveal if specific childhood internalizing disorders predict substance use outcomes.

The current study

The present study offers a number of advantages over previous work. First, few community-based studies employ comprehensive diagnostic assessments of more than one major internalizing and externalizing disorder, while combining parent and child reports of psychopathology to arrive at diagnoses. Using multiple informants reduces the problems associated with child self-reports and the advantages of multi-informant clinical assessment procedures are well documented (see Achenbach 1995). In the current investigation, we used multi-informant diagnostic information to determine if major depression and externalizing disorders at age 11 predicted prospectively the early use (by age 14) of three common substances (alcohol, nicotine and cannabis) in a community-based sample of girls and boys. In addition, we were able to take advantage of childhood anxiety disorder assessments in our female sample to determine how these disorders related to subsequent substance involvement in girls. Another advantage of our study was the ability to examine the first reports of experimentation, prior to engaging in prolonged use of a substance. Examining multiple substances in a parallel framework allowed us to determine the degree to which externalizing psychopathology predicted different forms of substance use and different degrees of involvement. Informed by the literature on the natural progression of substance use involvement, we examined whether these two forms of psychopathology relate more strongly to substance use behaviors falling on the more extreme end of a developmental sequence. In summary, our study sought to address three complementary sets of questions:

1 Is the presence of an externalizing disorder (ADHD, ODD, or CD) by age 11 related to an increased risk for the early initiation, regular use, and advanced use of alcohol, nicotine, and cannabis by age 14? What is the increase in the odds of the substance use outcomes given the presence of a specific externalizing disorder?
2 Is the presence of an internalizing disorder [i.e. MDD, separation anxiety disorder (SAD), or overanxious disorder (OAD)] by age 11 related to increased risk for a range of substance use behaviors by age 14? What is the increase in the odds of the substance use outcomes given the presence of each internalizing disorder?
3 Are the relationships different for boys and girls? For example, are externalizing disorders, which are less prevalent in girls, likely to lead to similar substance involvement in both genders?

METHOD

Sample description

The sample comprised 708 twin girls and 694 twin boys ranging in age from 10 to 12 years (average age 11 years), participating in the Minnesota Twin Family Study (MTFS). Twin pairs were excluded from participation if either twin had a physical or cognitive handicap that would interfere with participation in our full day assessment, or if a family lived more than a day's drive from our laboratory. The MTFS is a longitudinal investigation of the development of substance use disorders and related psychopathology. Data collection lasted 3–4 years for intake (1990–94 for males; 1993–96 for females) and follow-up assessments (1993–97 for males; 1996–99 for females). The mean age of the twins at follow-up assessment was 14.8 years (SD = 0.5 years). The sample for this study was ascertained through public birth records in the State of Minnesota (for a complete description of the MTFS sampling method, see Iacono *et al.* 1999).

Measures

Childhood internalizing and externalizing disorders

Semi-structured clinical interviews of DSM III-R disorders were used to obtain diagnostic information. Child symptomatology was assessed via independent child and mother interviews conducted by trained interviewers who had a minimum of a BA in psychology. Using a modified version of the Diagnostic Interview for Children and Adolescents—Revised (DICA-R; Reich & Welner 1988) and the parent version of this interview, children and mothers were asked to report on the child's life-time symptoms of externalizing (ADHD, CD, ODD) and major depressive disorder (MDD) at age 11. Boys were not assessed for anxiety disorders, but at the time the assessment of girls was initiated in 1993, mother and daughter DICA-R coverage of separation anxiety disorder (SAD) and overanxious disorder (OAD) was included in the battery.

For all internalizing and externalizing disorders, mother and child interviews were reviewed blindly and independently by two or more advanced clinical

psychology graduate students and symptoms were then assigned based on consensus. Parent and child reports of symptomatology were then combined by computer following DSM III-R guidelines to produce a best estimate of child symptoms. Data from both informants were entered into the computer and computer algorithms were used to combine parent and child diagnoses. To yield diagnoses that made the best use of all clinical information, data from both sources were combined using the provisional rules on combining data from mother and child interviews outlined by Reich & Earls (1987). This approach placed more weight on evidence that a symptom is present than absent, particularly when there is substantial evidence that the symptom carries impairment or there is convergence from multiple sources. A more complete description of the clinical assessment protocol can be found in Iacono *et al.* (1999). Contrary to DSM III-R guidelines, which preclude a diagnosis of ODD in a child with CD, we allowed these two disorders to be diagnosed in the same person. Kappa reliability estimates for externalizing and internalizing disorders were acceptable (0.74 for ADHD, 0.76 for ODD, 0.83 for CD, 0.87 for MDD, 0.72, for SAD and 0.60 for OAD). In this report, children meeting full criteria or falling one symptom short were assigned a diagnosis. This decision was made based on four considerations. First, because we use life-time diagnoses in a community sample, our approach accommodates imperfect memory of symptoms, a procedure that has been followed in studies of life-time psychopathology (Spitzer *et al.* 1978). Secondly, our 11-year-olds are still passing through the age of risk for many of these disorders. Our approach allowed for the likelihood that those falling one symptom short of a diagnosis represent a group of children well on their way to developing a disorder. Thirdly, there is evidence to suggest that childhood internalizing and externalizing disorders are expressed to varying degrees along a continuum and those individuals who do not meet the DSM criteria for definite diagnoses nevertheless have significant problems (Achenbach 1995; Levy *et al.* 1997; Slutske *et al.* 1997; Pickles *et al.* 2001; Kessler *et al.* 2003). Finally, this approach is consistent with other community-based studies of childhood internalizing and externalizing psychopathology (Merikangas *et al.* 1998). The two categorical variables of externalizing (EXT; examined in boys and girls) and internalizing (INT; examined only in girls) were defined by the presence of at least one relevant disorder by age 11.

Substance use by age 14

For intake assessment, boys and girls completed a substance use assessment administered in person. However, some children could not return for in-person assessments at age 14, and these individuals were interviewed by telephone. Of those with complete data at both time-points, only a small percentage (8.4%) completed a telephone interview for their follow-up assessment. χ^2 significance tests indicated no significant differences in rates of substance use outcomes based on method of interview (telephone versus in person). To encourage accurate and honest reporting over the telephone, interviewers requested that the adolescent find a private place in the home prior to starting any interview. If it became apparent that privacy could be compromised during the interview (e.g. someone entered the room), the interview was stopped and re-scheduled.

Substance use was assessed at three 'levels' (first-time, regular and advanced use), each reflecting more serious involvement with the substance and greater substance use deviancy. At intake and follow-up, boys and girls were asked if they had used tobacco, alcohol without parental permission and cannabis. Only individuals with substance use assessments at both time-points were used in the analyses. At age 11, a small percentage of boys and girls with available data at both time-points had used alcohol without parental permission (2.3%, $n = 32$), nicotine (7.3%, $n = 101$) and cannabis (0.2%, $n = 3$).

At follow-up assessment, we gathered reports of frequency of use via an in-person computerized substance use assessment. Using data on frequency of use, we operationalized 'regular' alcohol, cigarette (the only form of nicotine included) and cannabis use as reporting using one or more times per month during the past 12 months. Fourteen-year-olds reporting using at least once or more a month were considered regular users, and in all analyses were compared to those who used substances less frequently or not at all.

Two questions from the DICA-R child report served as indicators of advanced drinking experience: (a) 'Have you ever been drunk?' and (b) 'What's the most you have ever drank at one time?' All individuals who had drunk the equivalent of a six-pack of beer, a bottle of wine or four to five drinks of hard liquor at one time were considered heavy drinkers. An item gathered from the DICA-R was used as an indicator of advanced smoking experience: 'Have you ever smoked (used tobacco) regularly every day or just about every day?' Individuals responding yes to this question were grouped in the advanced smoking category. Finally, we defined advanced cannabis use experience as the presence of any DSM III-R cannabis abuse or dependence symptom reported by the child (gathered from the DICA-R).

Statistical analyses

To account statistically for the correlated observations of individuals due to the clustering of twins within pairs

(and families), we used generalized estimating equations (GEEs) in PROC GENMOD, a procedure in the Statistical Analysis Software (SAS) computing package (see Diggle, Liang & Zeger 1994 for a description). Each generalized estimating equation treated individual twins as clustered within pairs. We computed prevalence rates and odds ratios (ORs; males to females) for EXT, each externalizing disorder individually and MDD. Prevalence rates of girls with INT and each anxiety disorder were computed separately. Where parallel assessments were available for boys and girls, we computed a χ^2 statistic to determine if rates of disorders differed significantly by gender. Using the entire eligible sample, we utilized log-linear analyses (for dichotomous independent and dependent variables) to test a model including the effects of sex, EXT and the sex–EXT interaction on rates of substance use, regular substance use and extensive substance use. For all analyses, where we found a non-significant interaction term we dropped the interaction and reported the results of a model including EXT and sex only. ORs and 95% confidence intervals (CIs) were obtained as a measure of the strength of association. Taking advantage of our anxiety disorders assessment, the INT effect was tested in girls only. We then conducted the same statistical procedures with all individual psychiatric disorders and when we found a non-significant sex–disorder interaction term, it was dropped from the analysis.

RESULTS

Life-time diagnoses by age 11 and substance use rates by age 14

The life-time prevalence and frequency of age 11 DSM III-R internalizing disorders (SAD and OAD in the girls and MDD for both genders) and externalizing disorders (CD, ODD and ADHD for both genders) are presented in Table 1, along with substance use rates by age 14. Boy-to-girl odds ratios were computed and χ^2 analyses were used to test differences for each diagnostic category or

Table 1 Prevalence of age 11 life-time DSM III-R externalizing and internalizing disorders and age 14 substance use outcomes by gender.

	Boys (%)[a] *n = 665*	*Girls (%)*[a] *n = 699*	*Odds ratio (M : F)*	*95% CI*
Age 11 diagnoses				
Externalizing disorders				
Conduct	19.7	4.8	5.08****	(1.16, 2.09)
Oppositional defiant	15.3	10.0	1.64**	(1.12, 2.42)
Attention-deficit/hyperactivity	9.1	4.5	2.13**	(1.29, 3.51)
Any externalizing disorder	27.9	14.1	2.49****	(1.81, 3.44)
Internalizing disorders				
Major depressive	3.6	2.9	1.24	(0.66, 2.32)
Separation anxiety	–	19.3	–	–
Overanxious	–	6.1	–	–
Any internalizing disorder	–	23.7	–	–
Both internalizing and externalizing	–	5.4	–	–
Age 14 substance use outcomes				
Ever used				
Alcohol	31.1	29.0	1.11	(0.84, 1.47)
Nicotine	35.6	28.5	1.41*	(1.06, 1.88)
Cannabis	12.0	8.8	1.39	(0.91, 2.13)
Regular use				
Alcohol	12.4	9.6	1.33	(0.87, 2.03)
Cigarettes	16.1	13.7	1.20	(0.82, 1.76)
Cannabis	6.6	4.8	1.39	(0.78, 2.50)
Advanced substance use experience				
Alcohol (ever drunk)	13.3	10.7	1.25	(0.83, 1.88)
Alcohol (heavy drinking)	11.2	8.8	1.26	(0.83, 1.93)
Nicotine (used every day)	11.1	8.7	1.31	(0.84, 2.03)
Cannabis (any symptom)	4.5	2.4	1.90	(0.95, 3.79)

Dashes indicate not applicable, as girls had a supplemental assessment covering anxiety disorders. CI = confidence interval. [a]We report the number of boys and girls available for the 'ever used' alcohol analyses. The total number of boys and girls available (with relevant data at both time-points) varied slightly for alcohol, nicotine, and cannabis. *$P < 0.05$, **$P \leq 0.01$, ****$P \leq 0.0001$.

group. Pre-adolescent boys did not have significantly higher odds of a MDD diagnosis than girls, but they did have elevated rates of externalizing disorder (OR = 2.49, $P \leq 0.0001$). Males had a significantly greater odds of having tried nicotine (OR = 1.41, $P < 0.05$). Although substance use prevalence rates were uniformly higher in boys, there were no significant gender differences in the rates of any other substance use outcome (see Table 1). Only a small percentage of children who tried marijuana by age 14 had not also tried alcohol (1.3%) or nicotine (0.6%), indicating that use of these more socially acceptable substances almost always preceded use of marijuana.

Externalizing in the prospective prediction of substance use

We examined the effects of EXT, sex and their interaction across all measures of first-time substance use and advanced substance use. For the analyses of first-time substance use at age 14, we eliminated those who had already used the substance by age 11. This gave us the opportunity to determine how the presence of the disorder at age 11 predicted first-time use at age 14. For the analyses of regular and advanced use, we did not eliminate those who had used the substance at age 11. This allowed us to estimate how the presence of disorder affected the odds of a higher level of use at age 14, regardless of use at age 11. The results of these analyses are presented in Table 2. Not reported in Table 2 are results for the higher levels of use variables after eliminating those who used the substance for the first time at age 11. However, we also carried out these analyses, and they differed little from those we report in Table 2. Controlling for the effects of sex, EXT at age 11 was significantly associated with increased odds of substance use involvement across all substance outcomes. Only one sex–EXT interaction was found. This interaction indicated that EXT significantly elevated the odds of heavy drinking in males, but not females ($Z = -2.28$, $P < 0.05$).

Table 2 Prevalence of age 14 substance use as a function of gender and age 11 externalizing disorders.

	Prevalence (%, n)		*Odds ratio (95% CI)*		
Levels of use	*No Ext*	*Ext*	*Boys*	*Girls*	*Common*
First time use after age 11					
Alcohol	26.9 (291)	41.9 (119)	2.02****	1.38	1.72****
(*n* = 1364)			(1.41, 2.90)	(0.87, 2.17)	(1.30, 2.28)
Nicotine	28.2 (290)	47.1 (120)	1.94***	1.63*	1.79****
(*n* = 1288)			(1.32, 2.87)	(1.03, 2.59)	(1.39, 2.50)
Cannabis	6.9 (75)	23.1 (69)	3.71****	2.14*	2.96****
(*n* = 1388)			(2.30, 6.00)	(1.13, 4.07)	(2.04, 4.28)
Regular substance use[a]					
Alcohol	9.2 (90)	17.1 (48)	1.82*	2.21***	1.95***
(*n* = 1256)			(1.08, 3.07)	(1.27, 3.87)	(1.31, 2.90)
Cigarettes	11.7 (114)	26.1 (73)	2.37****	2.48**	2.38****
(*n* = 1256)			(1.54, 3.66)	(1.43, 4.30)	(1.69, 3.35)
Cannabis	3.6 (35)	12.9 36)	3.62***	1.69	2.68***
(*n* = 1255)			(1.75, 7.52)	(0.69, 4.14)	(1.59, 4.52)
Advanced drinking experience					
Ever drunk	9.2 (100)	21.8 (66)	2.43***	1.33	1.89***
(*n* = 1389)			(1.50, 3.91)	(0.80, 2.24)	(1.30, 2.64)
Heavy drinking	7.9 (86)	18.3 (55)	2.65****	1.11	†
(*n* = 1388)			(1.63, 4.32)	(0.61, 2.02)	
Advanced nicotine use experience					
Used every day	7.4 (81)	19.2 (58)	2.13**	2.76***	2.38****
(*n* = 1395)			(1.28, 3.55)	(1.57, 4.85)	(1.62, 3.51)
Advanced cannabis use experience					
Any symptom	1.6 (18)	9.9(30)	3.63***	5.38****	4.74****
(*n* = 1399)			(1.64, 8.02)	(1.99, 14.50)	(2.56, 8.76)

CI = confidence interval; Ext = externalizing disorder. The number of participants included for regular use measures was smaller because not all participants received the in-person, computerized assessment. †The common OR is not reported for this analysis because we found a significant interaction term. The sex-specific OR estimates are reported in the two columns to the left. [a]Regular substance use was defined as use once or more a month in the past 12 months. *$P < 0.05$, **$P \leq 0.01$, ***$P \leq 0.001$, ****$P \leq 0.0001$, two-tailed.

Individual externalizing diagnoses in the prospective prediction of substance use

To test the effect of individual externalizing diagnoses on substance use at age 14, we computed ORs for each age 11 externalizing diagnosis following the same procedure outlined in the preceding section. Results are presented in Table 3. We re-analyzed the data, replacing all binary diagnostic variables with symptom counts (EXT, CD, ODD and ADHD). Results indicated that all effects remained intact. However, excluding those who had used a substance at age 11 and recalculating effects for regular and advanced use caused three of the 24 significant ORs to become non-significant. These ORs are reported in the footnotes to Table 3. After testing the interaction term for all analyses, only one significant sex–disorder interaction was found (ADHD × sex effect in predicting heavy drinking, $Z = -2.03$, $P < 0.05$). The interaction indicated that ADHD was somewhat more predictive of heavy drinking in men than women; however, the main effect of ADHD was not significant (see note to Table 3). Therefore, we fitted a model including the sex and diagnosis main effects and reported common ORs using the entire eligible sample (sex-specific ORs for the ADHD–sex interaction are reported in a footnote to Table 3). Overall, 24 of the 30 ORs showed the diagnoses to be significantly associated with substance use. Of the three externalizing disorders, ADHD demonstrated the weakest prospective relationships with substance use (four of the 10 ORs were significant). ADHD did not significantly predict an alcohol use outcome. Of the three substances, individual EXT disorders showed the weakest prospective relationships with having tried alcohol. Across substances, CD and ODD tended to predict the greatest increase in the odds of

Table 3 Prevalence of age 14 substance use as a function of age 11 individual externalizing disorders.

	Prevalence (%, n)								
	Boys			*Girls*			*Common odds ratio (95% CI)*		
Levels of use	*CD*	*ODD*	*ADHD*	*CD*	*ODD*	*ADHD*	*CD*	*ODD*	*ADHD*
First time use after age 11									
Alcohol (*n* = 1364)	44.6 (54)	43.5 (40)	50.8 (31)	29.0 (9)	44.1 (30)	33.3 (10)	1.50* (1.07, 2.10)	1.73** (1.23, 2.43)	1.53 (0.97, 2.42)
Nicotine (*n* = 1288)	50.5 (53)	52.9 (45)	60.4 (29)	35.5 (11)	42.6 (26)	40.0 (10)	1.54* (1.07, 2.22)	1.78** (1.25, 2.54)	1.87* (1.12, 3.10)
Cannabis (*n* = 1388)	30.5 (40)	19.8 (20)	27.9 (17)	18.2 (6)	20.3 (14)	19.4 (6)	2.60**** (1.62, 4.16)	1.75** (1.14, 2.70)	2.90**** (1.72, 4.89)
Regular use									
Alcohol (*n* = 1256)	20.5 25)	15.8 (15)	16.1 (9)	21.9 (7)	18.8 (13)	13.3 (4)	2.18*** (1.38, 3.43)	1.95** (1.29, 2.95)	1.34 (0.67, 2.69)
Cigarettes (*n* = 1256)	30.3 37)	26.3 (25)	30.4 (17)	28.1 (9)	24.6 (17)	20.0 (6)	1.88** (1.22, 2.92)	2.13*** (1.42, 3.18)	2.28**[a] (1.30, 4.00)
Cannabis (*n* = 1255)	18.9 (23)	12.6 (12)	8.9 (5)	12.5 (4)	11.6 (8)	6.7 (2)	2.88*** (1.50, 5.52)	2.01* (1.11, 3.65)	1.29 (0.52, 3.18)
Advanced drinking experience									
Ever drunk (*n* = 1389)	29.9 4)	22.9 (24)	23.0 (14)	18.8 (6)	19.1 (13)	9.7 (3)	1.83** (1.13, 2.97)	1.76** (1.14, 2.70)	1.36 (0.72, 2.56)
Heavy drinking (*n* = 1388)	25.0 (34)	21.0 (22)	21.3 (13)	12.5 (4)	14.7 (10)	3.2 (1)	1.85* (1.10, 3.12)	1.95** (1.27, 3.00)	†
Advanced nicotine use experience									
Used every day (*n* = 1395)	20.6 (28)	20.9 (22)	21.3 (13)	18.2 (6)	18.6 (13)	19.4 (4)	1.66*[b] (0.98, 2.82)	2.45**** (1.61, 3.73)	2.38**[c] (1.22, 4.67)
Advanced cannabis use experience									
Any symptom (*n* = 1399)	12.4 (17)	10.5 (11)	6.3 (4)	9.1 (3)	8.7 (6)	3.2 (1)	3.45*** (1.70, 7.06)	3.22**** (1.76, 5.89)	1.35 (0.43, 4.22)

CI = confidence interval; CD = conduct disorder; ODD = oppositional defiant disorder; ADHD = attention deficit hyperactivity disorder. Common odds ratios were calculated using the entire available sample. The *ns* for regular substance use are relatively smaller than other measures because there were fewer individuals who received the in-person assessment. The odds ratio is a measure of the increase in odds of a substance outcome, given the presence of a diagnosis. †In this analysis we found a significant interaction term, so the common OR is not reported. The sex-specific OR estimates were 1.95 (CI = 0.91, 4.19) for males, P = NS and 0.22 (CI = 0.02, 1.66) for females, P = NS. After controlling controlling for age 11 tobacco initiation, some effects changed ([a]OR = 1.82 CI = 0.92, 3.53, P = NS; [b]OR = 1.38, CI = 0.72, 2.64, P = NS; [c]OR = 1.50, CI = 0.64, 3.44, P = NS). *$P < 0.05$, **$P \leq 0.01$, ***$P \leq 0.001$, ****$P \leq 0.0001$, two-tailed.

substance use, particularly for regular and advanced use. Finally, a diagnosis of CD was associated with notably high ORs across multiple levels of cannabis use (ORs ranged from 2.60 to 3.45).

Internalizing in the prospective prediction of substance use

Using GEE-based χ^2 analyses to test group differences and estimate odds ratios to measure strength of association, we examined whether having an internalizing disorder by age 11 (INT) was associated with elevated rates of involvement with alcohol, nicotine and cannabis by age 14 in the girls only (see Table 4). INT did not predict significantly greater odds of any substance use outcome. We re-analyzed the data using symptom counts in place of all binary diagnostic independent variables (INT, SAD, MDD and ODD) and all effects remained intact.

Individual internalizing diagnoses in the prospective prediction of substance use

Next, we tested the effect of individual internalizing disorders on substance use (see Table 4). ORs for SAD and OAD were calculated for girls only. MDD was examined for the combined sample of boys and girls because no significant sex–MDD interactions were found. Of the 40 ORs computed for internalizing disorders only three, all involving MDD, reached statistical significance. Because of the comorbidity between MDD and EXT, we recalculated the effects for MDD statistically adjusting for the effects of EXT and sex. After this adjustment, all the MDD effects met criteria for statistical significance (first-time use of alcohol = 1.95, 95% CI = 1.14, 3.39, $P < 0.05$; first-time use of nicotine = 1.98, 95% CI = 1.15, 3.41 $P < 0.05$; regular alcohol use = 2.24, 95% CI = 1.09, 4.58, $P < 0.05$).

Table 4 Prevalence of age 14 substance use as a function of age 11 internalizing disorders.

	Prevalence (%, n)									
	Boys			*Girls*				Odds ratio (95% CI)		
	MDD	*No INT*	*INT*	*MDD*	*SAD*	*OAD*	*INT*[a]	*MDD*[b]	*SAD*[a]	*OAD*[a]
First time use after age 11										
Alcohol	37.5	26.9	35.5	55.0	35.6	30.2	1.32	2.16**	1.38	0.82
	(9)	(144)	(59)	(11)	(48)	(13)	(0.92, 1.90)	(1.27, 3.68)	(0.92, 2.07)	(0.45, 1.49)
Nicotine	45.0	27.0	33.8	55.6	30.9	35.9	0.99	2.13**	0.84	1.09
	(9)	(142)	(52)	(10)	(38)	(14)	(0.68, 1.45)	(1.22, 3.71)	(0.56, 1.25)	(0.55, 2.16)
Cannabis	17.4	8.5	9.5	15.0	8.8	9.3	1.31	2.04	1.21	1.02
	(4)	(46)	(16)	(3)	(12)	(4)	(0.72, 2.38)	(0.97, 4.31)	(0.63, 2.31)	(0.34, 3.05)
Regular use										
Alcohol	17.4	8.0	14.5	25.0	12.9	11.1	1.62	2.55**	1.32	0.81
	(4)	(40)	(22)	(5)	(16)	(4)	(0.88, 2.97)	(1.26, 5.18)	(0.71, 2.47)	(0.81, 3.60)
Cigarettes	21.7	21.7	20.0	20.0	16.9	11.1	1.11	1.94	1.18	0.76
	(5)	(5)	(4)	(4)	(21)	(4)	(0.68, 1.82)	(0.95, 3.96)	(0.68, 2.04)	(0.25, 2.34)
Cannabis	8.7	8.7	0.0	0.0	5.6	5.6	1.98	1.11	1.89	0.85
	(2)	(2)	(0)	(0)	(7)	(2)	(0.99, 3.96)	(0.33, 3.82)	(0.89, 4.04)	(0.12, 5.95)
Advanced drinking experience										
Ever drunk	17.4	9.7	13.7	5.3	13.9	9.3	1.50	1.14	1.57	0.99
	(4)	(52)	(23)	(1)	(19)	(4)	(0.98, 2.30)	(0.55, 2.36)	(0.96, 2.58)	(0.64, 1.54)
Heavy drinking	13.0	8.8	10.1	0.0	10.9	9.3	1.18	0.94	1.36	1.00
	(3)	(47)	(17)	(0)	(15)	(4)	(0.68, 2.04)	(0.46, 1.87)	(0.72, 2.57)	(0.42, 2.41)
Advanced nicotine use experience										
Used every day	4.4	8.9	8.3	10.0	8.7	10.0	1.08	0.83	1.25	1.21
	(1)	(48)	(14)	(2)	(12)	(2)	(0.57, 2.05)	(0.23, 2.93)	(0.66, 2.38)	(0.39, 3.77)
Advanced cannabis use experience										
Any symptom	4.2	2.4	2.4	0.0	2.2	2.3	1.16	0.77	0.99	0.97
	(1)	(13)	(4)	(0)	(3)	(1)	(0.41, 3.29)	(0.11, 5.15)	(0.32, 3.06)	(0.11, 8.95)

CI = confidence interval; Int = internalizing disorder; MDD = major depressive disorder; SAD = separation anxiety disorder; OAD = overanxious disorder. [a]Estimates were computed using girls only because girls received the supplemental assessment covering anxiety disorders. [b]The odds ratio and 95% CI computed represents a common estimate (boys and girls). **$P \leq 0.01$, two-tailed.

DISCUSSION

The results of our study indicate that externalizing psychopathology substantially elevates the risk for early initiation of alcohol, nicotine and cannabis use, as well as regular and advanced forms of use by age 14. The pattern of findings generally support the idea that externalizing psychopathology tends to be a more potent predictor of higher level substance use (e.g. the strongest associations were observed between externalizing disorders and advanced cannabis use) falling on a progression of behaviors similar to those outlined by Collins *et al.* (2000). These findings are consistent with the literature documenting an association between the childhood externalizing disorders and the emergence and persistence of a constellation of deviant problem behaviors (Elkins *et al.* 1997; Iacono *et al.* 1999).

Our findings support the idea that externalizing psychopathology is a relatively stronger predictor of marijuana use than for the other two substances (see Table 2). One explanation for the relatively stronger effects of externalizing psychopathology on cannabis use is that children who have 'progressed' to cannabis have probably tried the other two substances (i.e. 'the gateway phenomenon'; we found over 98% of our marijuana users to have used cigarettes and alcohol) and may be particularly behaviorally deviant by age 11. Indeed, our findings are commensurate with a recent study of later adolescence conducted on another sample of adolescent twins (average age 17 years) in which illicit drug disorders were associated with particularly high levels of behavioral disinhibition compared to alcohol disorders (Elkins *et al.* 2004).

The stronger effects found for marijuana use (an illicit substance) are also consistent with findings from a recent longitudinal, community-based study which demonstrated that conduct disorder was associated with relatively greater effects for cannabis and hard drug use compared to alcohol or nicotine (Boyle *et al.* 1992). While Boyle *et al.* did not find a significant association between CD and future nicotine and alcohol use, important distinctions between their study and ours should be considered. Boyle *et al.* (1992) examined substance use in late adolescence, whereas the current investigation only covers early adolescence and spans a period of about 3 years. One possible reason for the discrepancy may be that during the period of later adolescence, alcohol and nicotine use may be more the norm than the exception. Also, substance use in later adolescence may follow a relatively different progression compared to earlier onset substance use. Between the ages of 11 and 14, having used these substances is probably more developmentally deviant than use at other ages, possibly explaining why early use of all three substances was related to CD. The current investigation makes use of structured diagnostic interviews to collect diagnostic information, whereas Boyle *et al.* (1992) used items selected from an established behavior checklist (i.e. Child Behavior Checklist) to determine diagnostic status. Despite differences in methodology and age groups, it is striking that both studies found relatively stronger effects of an externalizing disorder (conceptualized in two different ways) on cannabis use relative to alcohol or nicotine.

We examined the degree to which individual externalizing disorders elevated the risk for different degrees of substance use involvement. CD tended to yield the strongest individual effects of substance use across levels of use (ORs ranged from 1.50 for having tried alcohol to 3.45 for advanced cannabis use). ODD demonstrated the same general pattern as CD. Among externalizing disorders, ADHD tended to be the weakest prospective predictor of substance use. Interestingly, ADHD predicted only nicotine and cannabis use. Perhaps ADHD has its strongest effects on nicotine use because of the stimulant properties of the drug. Consistent with this hypothesis, a recent cross-sectional study found that ADHD was related to nicotine dependence in 17-year-old girls (Disney *et al.* 1999). Our pattern of results suggests that the degree to which a diagnosis predicts that substance use involvement may be associated with its degree of antisocial content. Specifically, CD and ODD contrast to ADHD in the manifestation of antisociality, with CD and ODD reflecting severe to milder antisociality (i.e. stealing, harming others; arguing with adults) and ADHD reflecting behavioral hyperactivity and attentional difficulties.

Our study indicates that boys and girls appear to be at relatively similar risk for substance use involvement during early adolescence. Other studies of early adolescence have reported comparable rates in both genders for having tried alcohol and using substances regularly (Boyle *et al.* 1992; Rose *et al.* 2001). Additionally, the degree to which externalizing predicts future substance involvement is relatively similar for both genders. One exception was the effect of externalizing on heavy drinking (conceptualized as having had a six-pack or more) being relatively stronger for boys than girls. Although this finding is intriguing, given the lack of sex–externalizing interactions found for all other measures, it seems deserving of replication before we speculate regarding its causes.

When we examined whether internalizing psychopathology predicted early initiation of use in girls, a consistent pattern of results emerged. Effects associated with internalizing disorders were weak, and internalizing was not associated with significantly elevated odds of any substance use outcome. In line with our results, other studies have found that an internalizing pathway for substance problems may not be operating until late adolescence (Zucker 1994; Chassin *et al.* 1999). Although we did not

find strong evidence for internalizing in the prediction of substance use, it should be noted that this may be attributable to lowered power to detect effects because anxiety disorders were assessed in girls only.

Although less robust than effects found for externalizing, we found that MDD at least doubled the odds of first-time use of nicotine and alcohol and regular use of alcohol by age 14. After controlling for the effects of externalizing psychopathology, MDD was still predictive of the three substance use outcomes. Perhaps the effects of MDD are relatively weaker than externalizing because the etiological relevance of MDD to substance use emerges later in development (Zucker 1994). Although these MDD effects warrant replication, they may indicate that MDD places children on a pathway to early substance use initiation that does not lead to more deviant use by age 14. Children with MDD may experiment with substances in order to try to self-medicate to reduce their depressed mood. Also, because a diagnosis of MDD represents a general tendency to experience low mood, it may increase children's vulnerability to deviant peer influences. Due to low mood and self-esteem, children with depression may be influenced more easily to try substances in an effort to gain or maintain acceptance in peer networks. However, high levels of behavioral inhibition may preclude them from further experimentation and progression to higher-level use, an illegal set of behaviors with a high probability of serious consequences. Given the data available these notions are necessarily speculative, but can be more fully evaluated by following our sample into adolescence and young adulthood.

Our study improves and extends the literature in this area, although several limitations should be considered. First, due to the nature of our protocol, we could take advantage of anxiety disorder (OAD and SAD) assessments for girls only. Therefore, we could not examine thoroughly the role of internalizing disorders in predicting substance use in boys and girls. Also, later-onset anxiety disorders such as panic disorder were not assessed in the present study, although these disorders may emerge as relevant to the development of substance use behaviors later in development (Merikangas *et al.* 1998). Second, it is important to note that our findings do not necessarily generalize to the initiation of substance use during a later stage of development. Third, this study did not deal specifically with the continuity or progression of substance use over time and across substances. Consequently, future studies should seek to track the trajectories of children who develop regular patterns of use, compared to those who are 'one-time' (or infrequent) as well as polysubstance users. Fourth, our sample involved twins who may differ in some way from non-twin adolescents. However, despite speculations that twins may have unique psychological experiences, current evidence suggests that twins are psychologically similar to singletons on personality and psychopathology (Rutter & Redshaw 1991; Kendler *et al.* 1995; Johnson *et al.* 2002). Fifth, we did not control specifically for other potentially confounding factors that may be associated with adolescent substance use (i.e. socio-economic status, family environment and family history of substance use). Finally, although this study had the advantage of comprehensive assessments of childhood psychopathology prior to the first sip of alcohol, first cigarette or joint, we did not address the etiological origins of these relationships. Also, our definition of having tried alcohol excluded parent-sanctioned use which, by its nature, may be less deviant.

Our findings have implications for models of the etiology and prevention of early substance use. First, our results suggest that externalizing psychopathology relates broadly to early initial use of different substances to indicators of use that vary in degree of severity. Secondly, they predict substance use similarly in boys and girls, indicating that early prevention efforts should target both genders and that both share a common risk factor for early substance use: externalizing psychopathology. Our results revealed that externalizing demonstrates relatively stronger associations with more advanced, age-inappropriate substance use behaviors (i.e. tried marijuana, ever having been drunk). Overall, the more deviant the measure of use, the stronger the effect of externalizing psychopathology, suggesting that these disorders are associated with a developmental trajectory characterized by rapid progression through a sequence of substance use involvement. Given our results, it may be beneficial to consider externalizing psychopathology in evaluating the effectiveness of promising prevention programs aimed at delaying the onset of a natural progression of substance use (Spoth *et al.* 1999). Specifically, it may be advantageous to determine if prevention programs may be maximally effective by treating externalizing psychopathology itself.

Our findings indicated that externalizing psychopathology is prospectively predictive of deviant substance use by age 14, offering support for the idea that childhood externalizing disorders relate predictably to a natural progression of substance use onset. MDD was modestly related to early initiation of two 'entry' substances and regular alcohol use, but otherwise was not associated with substance use. An advantage of the present study was the systematic evaluation of multiple levels of substance use in a single prospective, mixed-gender, community-based study. This study also extended and elaborated on the findings of McGue *et al.* (2001b), which found that externalizing psychopathology predicted an early age at first drink. Our results indicate that externalizing psychopathology predicts the

early use of three different substances and may be systematically related to a pattern of early regularity of use and more advanced use behaviors.

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References

Achenbach, T. M. (1995) Empirically based assessment and taxonomy: applications to clinical research. *Psychological Assessment*, **7**, 261–274.

Bardone, M. S., Moffitt, T. E., Caspi, A., Dickson, N., Stanton, W. R. & Silva, P. A. (1998) Adult physical health outcomes of adolescent girls with conduct disorder, depression, and anxiety. *Journal of the American Academy of Child and Adolescent Psychiatry*, **37**, 594–601.

Boyle, M. H., Offord, D. R., Racine, Y. A., Szatmari, P., Fleming, J. E. & Links, P. S. (1992) Predicting substance use in late adolescence: results from the Ontario Child Health Study follow-up. *American Journal of Psychiatry*, **149**, 761–767.

Chassin, L., Pitts, S. C., DeLucia, C. & Todd, M. (1999) A longitudinal study of children of alcoholics: predicting young adult substance use disorders, anxiety and depression. *Journal of Abnormal Psychology*, **108**, 106–119.

Clapper, R. L., Buka, S. L., Goldfield, E. C., Lipsitt, L. P. & Tsaung, M. T. (1995) Adolescent problem behaviors as predictors of adult alcohol diagnoses. *International Journal of the Addictions*, **30**, 507–523.

Collins, L. M., Hyatt, S. L. & Graham, J. W. (2000) Latent transition analysis as a way of testing models of stage–sequential change in longitudinal data. In: Little, T. D., Schnabel, K. U. & Baumert, J., eds. *Modeling Longitudinal and Multilevel Data*, pp. 147–161. Mahwah, NJ: Lawrence Earlbaum.

Dewit, D. J., Adlaf, E. M., Offord, D. R. & Ogborne, A. C. (2000) Age at first alcohol use: a risk factor for the development of alcohol disorders. *American Journal of Psychiatry*, **157**, 745–750.

Diggle, P. L., Liang, K. & Zeger, S. L. (1994) *Analysis of Longitudinal Data*. New York: Oxford Science Publications.

Disney, E. R., Elkins, I. J., McGue, M. & Iacono, W. G. (1999) Effects of ADHD, conduct disorder, and gender on substance use and abuse in adolescence. *American Journal of Psychiatry*, **156**, 1515–1521.

Elkins, I. J., Iacono, W. G., Doyle, A. E. & McGue, M. (1997) Characteristics associated with the persistence of antisocial behavior: results from recent longitudinal research. *Aggression and Violent Behavior*, **2**, 101–124.

Elkins, I. J., Malone, S. M., McGue, M. & Iacono, W. G. (2004) Relationships of parental alcohol or drug diagnosis and offspring personality to substance disorders in late adolescence. *American Journal of Psychiatry*, **761**, 670–676.

Gomberg, E. S. L. (1997) Alcohol abuse: age and gender differences. In: Wilsnack, R. W. & Wilsnack, S. C., eds. *Gender and Alcohol: Individual Social Perspectives*, pp. 225–244. New Brunswick, NJ: Rutgers Center of Alcohol Studies.

Grant, B. F. & Dawson, D. A. (1998) Age of onset of drug use and its association with DSM-IV drug abuse and dependence: results from the National Longitudinal Alcohol Epidemiologic Survey. *Journal of Substance Abuse*, **9**, 103–110.

Greeley, J. & Oei, T. (1999) Alcohol and tension reduction. In: Leonard, K. E. & Blane, H. T., eds. *Psychological Theories of Drinking and Alcoholism*, pp. 14–53. New York: Guilford Press.

Iacono, W. G., Carlson, S. R., Taylor, J., Elkins, I. J. & McGue, M. (1999) Behavioral disinhibition and the development of substance use disorders: findings from the Minnesota Twin Family Study. *Development and Psychopathology*, **11**, 869–900.

Jackson, K. M., Sher, K. J., Gotham, H. J. & Wood, P. K. (2001) Transitioning into and out of large-effect drinking in young adulthood. *Journal of Abnormal Psychology*, **110**, 378–391.

Johnson, E. O., Arria, A. M., Borges, G., Ialongo, N. & Anthony, J. C. (1995) The growth of conduct problem behaviors from middle childhood to early adolescence: sex differences and the suspected influence of early alcohol use. *Journal of Studies on Alcohol*, **56**, 661–671.

Johnson, W., Krueger, R. F., Bouchard, T. J. & McGue, M. (2002) The personalities of twins: just ordinary folks. *Twin Research*, **5**, 125–131.

Kendler, K. S., Heath, A. C., Neale, M. C., Kessler, R. C. & Eaves, L. J. (1993) Alcoholism and major depression in women: a twin study of the causes of comorbidity. *Archives of General Psychiatry*, **50**, 690–698.

Kendler, K. S., Martin, N. G., Heath, A. C. & Eaves, L. J. (1995) Self-report psychiatric symptoms in twins and their non-twin relatives: are twins different? *American Journal of Medical Genetics*, **60**, 588–591.

Kessler, R., Merikangas, K., Berglund, P., Eaton, W. W., Koretz, D. S. & Walters, E. E. (2003) Mild disorders should not be eliminated from the DSM-IV. *Archives of General Psychiatry*, **60**, 1117–1122.

Levy, F., Hay, D. A., McStephen, M., Wood, C. & Waldman, I. (1997) Attention deficit hyperactivity disorder: a category or a continuum? Genetic analysis of a large-scale twin study. *Journal of the American Academy of Child and Adolescent Psychiatry*, **36**, 737–744.

Marmorstein, N. & Iacono, W. G. (2001) An investigation of female adolescents with both major depression and conduct disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, **40**, 299–306.

McGue, M., Iacono, W. G., Legrand, L. N. & Elkins, I. (2001a) Origins and consequences of age at first drink. II. Familial risk and heritability. *Alcoholism: Clinical and Experimental Research*, **25**, 1166–1173.

McGue, M., Iacono, W. G., Legrand, L., Malone, S. & Elkins, I. (2001b) The origins of age at first drink. I. Associations with substance-use disorders, disinhibitory behavior and psychopathology, and P3 amplitude. *Alcoholism: Clinical and Experimental Research*, **25**, 1156–1165.

Merikangas, K. R., Dierker, L. C. & Szatmari, P. (1998) Psychopathology among offspring of parents with substance abuse and/or anxiety disorders: a high-risk study. *Journal of Child Psychology and Psychiatry*, **39**, 711–720.

Muthen, B. O. & Muthen, L. K. (2000) The development of heavy drinking and alcohol-related problems from ages 18–37 in a US national sample. *Journal of Studies on Alcohol*, **61**, 290–300.

Pandina, R. J., Johnson, V. & Labouvie, E. W. (1992) Affectivity: a central mechanism in the development of drug dependence.

In: Glantz, M. & Pickens, R., eds. *Vulnerability to Drug Abuse*, pp. 179–210. Washington, DC: American Psychological Association.

Pickles, A., Rowe, R., Simonoff, E., Foley, D., Rutter, M. & Silberg, J. (2001) Child psychiatric symptoms and psychosocial impairment: relationship and prognostic significance. *British Journal of Psychiatry*, **179**, 230–235.

Rao, U., Daley, S. E. & Hammen, C. (2000) Relationship between depression and substance use disorders in adolescent women during the transition to adulthood. *Journal of the American Academy of Child and Adolescent Psychiatry*, **39**, 215–222.

Reich, W. & Earls, F. (1987) Rules for making psychiatric diagnoses in children on the basis of multiple sources of information: preliminary strategy. *Journal of Abnormal Child Psychology*, **15**, 601–616.

Reich, W. & Welner, Z. (1988) *Diagnostic Interview for Children and Adolescents—Revised: DSM III-R Version (DICA-R)*. St Louis: Washington University.

Rose, R. J., Dick, D. M., Viken, R. J., Pulkkinen, L. & Kaprio, J. (2001) Drinking or abstaining at age 14? A genetic epidemiological study. *Alcoholism: Clinical and Experimental Research*, **25**, 1594–1604.

Rutter, M. & Redshaw, J. (1991) Growing up as a twin: twin–singleton differences in psychological development. *Journal of Child Psychology and Psychiatry*, **32**, 885–895.

Slutske, W. S., Heath, A. C., Dinwiddie, S. H., Madden, P. A. F., Bucholz, K., Dunne, M. P., Statham, D. J. & Martin, N. G. (1997) Modeling genetic and environmental influences in the etiology of conduct disorder: a study of 2,682 adult twin pairs. *Journal of Abnormal Psychology*, **106**, 266–279.

Spitzer, R. L., Endicott, J. & Robins, E. (1978) Research diagnostic criteria: rationale and reliability. *Archives of General Psychiatry*, **35**, 772–782.

Spoth, R., Reyes, M. L., Redmond, C. & Shin, C. (1999) Assessing a public health approach to delay onset and progression of adolescent substance use: latent transition analysis and log-linear analyses of longitudinal family preventive intervention outcomes. *Journal of Consulting and Clinical Psychology*, **67**, 619–630.

Wilens, T. E. & Biederman, J. (1993) Psychopathology in pre-adolescent children at high risk for substance abuse: a review of the literature. *Harvard Review of Psychiatry*, **1**, 207–218.

Windle, M. (1990) A longitudinal study of antisocial behaviors in early adolescence as predictors of late adolescent substance use: gender and ethnic group differences. *Journal of Abnormal Psychology*, **99**, 86–91.

Zucker, R. A. (1994) Pathways to alcohol problems and alcoholism: a developmental account of the evidence for multiple alcoholisms and for contextual contributions to risk. In: Zucker, R., Boyd, G. & Howard, J., eds. *The Development of Alcohol Problems: Exploring the Biopsychosocial Matrix of Risk*, pp. 255–290. Rockville, MD: National Institute on Alcohol and Alcoholism.