Early Onset Problem Behavior, Young Adult Psychopathology, and Contextual Risk

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A prospective study of 692 male twins was undertaken to investigate the relationships among early adolescent problem behavior, contextual risk, and disinhibitory psychopathology. Early adolescent problem behavior was assessed by the number of the following behaviors engaged in by the time of the age-14 assessment: (1) tobacco use, (2) alcohol use, (3) marijuana use, (4) other illicit drug use, (5) sexual intercourse, and (6) police contact. Contextual risk was assessed as a composite of measures of peer models, parent-offspring conflict, and academic engagement from the age-14 assessment. Disinhibitory psychopathology was assessed by symptoms of nicotine dependence, alcohol dependence, drug dependence, and adult antisocial behavior at the age-18 assessment. Early adolescent problem behavior and contextual risk were strongly correlated (r = .53) and both were strongly and independently associated with symptoms of disinhibitory psychopathology (r from .35 to .60). The association of early adolescent problem behavior with both contextual risk and disinhibitory psychopathology was mediated entirely by genetic factors while the association between contextual risk and disinhibitory psychopathology was mediated by both genetic and nonshared environmental factors. The results are discussed in the context of emerging research on the prognostic significance of early adolescent problem behavior for risk of adult psychopathology.

One of the most influential observations to emerge from the substance abuse field over the past 10 years has been the finding that adolescents who experiment with alcohol early in life are at a substantially elevated risk of developing alcoholism in early adulthood relative to those who delay drinking onset. Using data from a large epidemiological survey of US adults, Grant and Dawson (1997) found that individuals who reported first trying alcohol prior to age 15 were four times more likely to be diagnosed with alcoholism as adults than individuals who first tried alcohol after the age of 20. Since this initial study, several research groups have replicated this essential finding: individuals who first try alcohol early in adolescence are much more likely to become alcoholic than individuals who postpone drinking initiation into early adulthood (Dewit et al., 2000; McGue et al., 2001a; Prescott & Kendler, 1999). The finding that early alcohol use is a potent risk factor of alcoholism underscores the importance of efforts to prevent and delay the onset of adolescent drinking (Stewart et al., 2005). Nonetheless, the implications of the finding of a correlation between early drinking and alcoholism depend necessarily on the mechanisms underlying the association.

Two alternative hypotheses have been advanced to account for the association of early onset adolescent drinking with alcoholism risk. First, early drinking may exert a causal influence on alcoholism risk by affecting the course of adolescent development (Dewit et al., 2000). In particular, early use of alcohol may increase the likelihood that adolescents associate with deviant peers, decrease the likelihood that they have a close relationship with their parents, and diminish their commitment to and interest in academic pursuits. In this scenario, early drinking influences alcoholism risk by both increasing the likelihood adolescents affiliate with individuals who model and encourage deviance and decreasing the likelihood of their attachment to individuals and institutions that encourage sobriety. Early drinking may also disrupt adolescent development through biological mechanisms. Rodent studies have revealed that the adolescent brain is especially sensitive to alcohol's cognitive impairing effects but relatively insensitive to its sedating effects (Spear, 2002; White & Swartzwelder, 2004). Findings with human adolescents provide additional support for the hypothesis that drinking in adolescence may result in biological changes that promote subsequent drinking. Specifically, heavy alcohol exposure in adolescence has been associated with neurocognitive changes that may make it more likely that an adolescent continues to abuse alcohol (Brown & Tapert, 2004). Thus, early onset of drinking may initiate a series of social and biological changes that promote a pattern of chronic

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abusive drinking by altering the typical course of adolescent development.

Prescott and Kendler (1999) have proposed an alternative, noncausal, explanation for the association of early drinking with alcoholism risk. Specifically, they hypothesize that both early drinking and alcoholism are manifestations of a common inherited liability. Consistent with this hypothesis, they report findings from a large sample of adult twins that show that the association between age at drinking onset and alcoholism is mediated predominantly by common genetic effects. In a series of research publications, we have provided additional support for this common-liability model. First, we have found that the association of early drinking and alcoholism risk is nonspecific. That is, early drinking is associated not only with an increased risk of alcoholism but also with an increased risk for a wide range of disorders of disinhibition, including drug abuse, nicotine dependence, and antisocial behavior, as well as with personality and psychophysiological markers of disinhibition (McGue et al., 2001a, 2001b). Conversely, rate of alcoholism is elevated not only among individuals who drank early in adolescence but also among individuals who smoked, used illicit drugs, had sexual intercourse, or had police contact early in adolescence (McGue & Iacono, 2005). This research thus implicates the existence of a spectrum of early adolescent problem behavior (Jessor & Jessor, 1977) that is associated with a spectrum of disinhibitory behaviors and psychopathology in adulthood (Krueger et al., 2002; Young et al., 2000). Moreover, consistent with what Prescott and Kendler (1999) found for alcohol, we have found that the association of early adolescent problem behavior with general adult disinhibitory psychopathology is mediated predominantly by common genetic factors (McGue et al., 2006).

Although the common-inherited liability model has received considerable support in the behavioral genetic literature, it is important to recognize that the two alternative explanations for the association of early drinking with alcoholism risk are not necessarily mutually exclusive. That is, early drinking in adolescence may both be a manifestation of a highly heritable disposition that can manifest in adulthood as alcoholism and also cause an alteration of the course of adolescent development that increases the likelihood of chronic abusive drinking. The present study aims to further explore this joint model using a prospective study of a cohort of male twins. Specifically, we sought to first replicate using our prospective design the frequently replicated observation from retrospective studies that an early onset of adolescent problem behavior is associated with risk of disinhibitory psychopathology. Second, we sought to determine the extent to which early problem behavior was associated with contextual markers of risk including peer group exposure, parent-offspring conflict, and academic motivation. Finally, we used multivariate biometric methods to investigate genetic and environmental contributions to the association of disinhibitory psychopathology in early adulthood with both early adolescent problem behavior and contextual risk.

Method

Overview of the Minnesota Twin Family Study

The Minnesota Twin Family Study (MTFS) is an ongoing, population-based, longitudinal study of approximately 1400 like-sex adolescent twins, ascertained from Minnesota state birth records between 1971 and 1985, and their parents. Families were eligible to participate if they lived within a day's drive of the University of Minnesota and if the twins had no physical (e.g., blindness) or psychological (e.g., mental retardation) disability that would interfere with their completing an assessment. Using birth certificates, death records, phone books, driver's license records, reverse directories and Internet telephone directories, we located addresses for over 90% of those twins still alive. Of these, approximately 17% refused to participate. A brief assessment was conducted by phone or mail with over 80% of nonparticipating families. A comparison of participating and nonparticipating parents showed no significant difference in self-reported mental health although participating parents were slightly but significantly better educated (by less than 0.3 years of education). Approximately 90% of participating families were Caucasian, which is generally representative of the population of Minnesota in the years in which these twins were born.

The MTFS intake sample includes an 11-year-old and a 17-year-old cohort. Intake and follow-up assessments are scheduled to coincide with major transitions in the lives of these adolescents and young adults. The younger cohort was initially assessed when the twins reached 6th grade, typically prior to substance use initiation. They were followed-up for the first time at age 14 to 15 years, when early substance use initiation could be assessed, and a second time at age 17 to 18 years in their senior year of high school. The older cohort was initially assessed their senior year of high school and followed up initially at age 20 to 21 years, a time in when substance use and abuse tend to peak. They were subsequently followed up at age 24 to 25 years, when many had begun to moderate their substance use.

Both biological parents plus any step parents of the twins were invited to participate in the intake assessment for both cohorts and at the age 17 to 18 assessment of the younger cohort; only the primary caretaker participated at the age 14 to 15 assessment. An intake assessment was completed by 99% of the biological mothers, 91% of living biological fathers, and over 85% of stepparents, providing us with comprehensive information on the biological and rearing backgrounds of the participating twins. Analysis of participation at both follow-ups reveals high rates of

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participation and minimal diagnostic differences between participants and nonparticipants.

Intake and follow-up day-long assessments are conducted in person at the University of Minnesota and include a clinical diagnostic interview and psychophysiological assessment. In addition, twins and their parents complete a variety of self-reports designed to measure individual and environmental risk and protective factors, including personality, parent-offspring relationships and family context, peer group characteristics, and academic interests and achievements. Parents and teachers supply diagnostic and social adjustment data to supplement the information obtained during interviews with the twins.

Participants

So that we could investigate associations using a prospective design, only male twins from the 11-year-old cohort are included in this study.[1] These twins participated in three waves of assessment scheduled to coincide with key transitions in the lives of adolescents.The intake sample included 252 monozygotic (MZ) and 122 dizygotic (DZ) twin pairs whose average age was 11.2 years (*SD* = .39).

Ninety-two per cent (*N* = 692) of the sample returned to participate in the first follow-up at a mean age of 14.8 years (*SD* = .49), and 85% (*N* = 645) participated in a second follow-up at mean age 18.0 years (*SD* = .66). The current study primarily makes use of data from the first (which for ease of presentation we will designate the age-14 assessment) and second (age-18 assessment) follow-up assessments.

Assessments

Six indicators of early adolescent problem behavior were obtained through self-reports at the age-11 and age-14 assessments. These were (1) tobacco use, (2) alcohol use (without parent permission), (3) marijuana use, (4) other illicit substance use, (5) police contact (not including traffic violations), and (6) sexual intercourse. Each behavior was coded as positive if the respondent indicated he had engaged in that behavior at least one time by the time of their age-14 assessment. To obtain an overall measure of early involvement in problem behavior, we computed an Early Problem Behavior index by summing the six individual problem behaviors (α = .75). Prior to statistical and biometric analyses, the Early Problem Behavior index was log-transformed to reduce skew.

Four indicators of contextual risk were also collected at the age-14 assessment. These included self-report measures of conflict with parents (12-item scale; e.g., 'My parent often criticizes me'; α = .88), academic engagement (6-item scale; e.g., 'Have a good attitude about school'; α = .84), and affiliation with both positive peers (8-item scale; e.g., 'Liked by teachers', 'Get good grades'; α = .78) and deviant peers (9-item scale; e.g., 'Break the rules', 'Get into trouble with police'; α = .85). We created a Contextual Risk index by summing the standardized scores (the positive peer measure was reflected before summing) on these four measures (α = .67).

All diagnostic data were obtained from structured clinical interviews conducted at the age-18 assessment using the expanded substance abuse module, developed by Robins et al. (1987) as a supplement to the World Health Organization's Composite International Diagnostic Interview for substance use disorders; and the Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; DSM-IV; American Psychiatric Association, 1994) personality disorders antisocial personality disorder section (Spitzer et al., 1987). Diagnoses were considered to be positive if either all (definite) or all but one (probable) of the DSM-IV criteria were met. Probable diagnoses were included in an effort to minimize false negatives in a sample of young people who had not passed through the full period of risk for these diagnoses.

Four diagnostic outcomes indicative of disinhibitory psychopathology were included from the age-18 assessment: nicotine dependence, alcohol dependence, drug dependence, and adult antisocial behavior (i.e., symptoms of antisocial behavior manifest after age 15). Kappa reliability coefficients for these diagnoses are .90 or more (Iacono et al., 1999). In addition to individual diagnoses, symptom counts were created for each diagnosis, and an overall Disinhibitory Psychopathology symptom scale was created by summing the symptoms for each of the four diagnoses (α = .83). Prior to statistical and biometric analyses, symptom scales were log-transformed to reduce skew.

Zygosity

Zygosity was based on agreement among three separate indices: (1) parent's report of physical similarity, (2) ponderal and cephalic indices and fingerprint ridge count, and (3) the judgment of two senior staff members. If these three estimates did not agree, serological analysis was performed. We have shown previously that this method of zygosity determination is highly valid (Iacono et al., 1999).

Statistical Analysis

The prospective relationship of early adolescent problem behavior and young adult disinhibitory psychopathology was assessed for each of the six problem indicators with each of the diagnostic outcomes using logistic regression. Hierarchical linear methods represented by the Statistical Analysis System (SAS) PROC GENMOD (Liang & Zeger, 1986) were employed to account for the correlated nature of the twin data. In addition, we examined the effect of early problem behavior in the aggregate by estimating the likelihood of meeting criteria for any disinhibitory psychopathology by age 18 as a function of the Early Problem Behavior index. We also assessed the relationship between the symptom outcome scales and the Early Problem Behavior and Contextual Risk indexes using standard correlational methods.

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Twin correlations for the Early Problem Behavior index, the Contextual Risk index, and the Disinhibitory Psychopathology symptom scale were estimated, and biometric models were subsequently fit to the twin data using the Mx software program (Neale et al., 1999). The aim of the model-fitting analyses was to partition the variance in and covariance among the three variables into their additive genetic, shared environmental, and nonshared environmental components using standard biometrical approaches (Neale & Cardon, 1992). Model-fitting analyses were performed using Mx full-information maximum-likelihood raw data techniques to correct for cases missing at follow-up. Model fitting began by fitting a general three-variable Cholesky model, after which a series of submodels were fit to identify a 'best fitting' model that both fit the data well and was parsimonious (i.e., had a low number of parameters). Model fit was evaluated using both the goodness-of-fit χ^2 test statistic and the Akaike Information Criteria (AIC = $\chi^2 - 2df$). The minimized value of –2ln(likelihood) from the full Cholesky model was used as the base for the computation of the model fit statistics.

Results

Analysis of Attrition and Descriptive Statistics

A total of 692 twins returned for the age-14 assessment, and 645 twins completed an age-18 assessment. Early Problem Behavior and Contextual Risk were assessed at the age-14 assessment, while the disinhibitory outcomes were assessed at age 18. We assessed the impact of attrition by comparing the Early Problem Behavior index and Contextual Risk scores of participants and nonparticipants at age 18. Nonparticipants had Early Problem Behavior scores that were borderline significantly greater than those of participants (standardized mean difference of .28, t (690 df) = 1.94, p = .052), but Contextual Risk scores did not vary significantly as a function of participation status (standardized mean difference of .18, t (557 df) = 1.08, p = .28). There is thus some evidence that participants at follow-up were at slightly lower risk than nonparticipants. Nonetheless, it seems likely that these differences did not markedly affect the results presented here because the differences are small, the participation rate is high, and full-information maximum-likelihood methods were used to minimize any biasing effects of sample attrition.

Rates at which each adolescent problem behavior was endorsed by the time of the age-14 assessment are reported in Table 1. As expected, early use of alcohol and tobacco are the most common behavior problems by age 14, with about 30 to 40% reporting each; police contact and marijuana use occurred at an intermediate rate, with about 10 to 15% of the sample endorsing each; and sexual intercourse and other illicit drug use were the least common, with endorsement rates of about 3% to 4%. On average, participants reported one problem behavior at the time of the age-14 assessment, although there was marked variability as the full range of scores on the Early Problem Behavior index (i.e., 0 to 6) was observed in our sample.

Table 1

Rates of Adolescent Problem Behavior at the Age-14 Assessment

	Problem behavior	*N*	Rate or mean (*SD*)
Tobacco use	%	692	40.6
Alcohol use	%	692	32.8
Marijuana use	%	692	12.3
Other substance use	%	691	3.8
Police contact	%	687	16.3
Sexual intercourse	%	684	3.2
Early Problem Behavior Index	Mean (*SD*)	692	1.1 (1.4)

Note: Sample sizes vary somewhat because of nonresponse on some of the problem behavior items. Early Problem Behavior Index was coded as missing if an individual had more than two missing responses.

Rates of age-18 DSM-IV diagnoses at the definite plus probable level of certainty for each of the four disinhibitory disorders are given in Table 2.[2] Also given is the mean number of symptoms for each of the diagnoses. Nearly 40% of the sample had at least one of the disinhibitory diagnoses and on average participants reported 3.2 symptoms of disinhibitory psychopathology (*SD* = 5.08) at the age-18 assessment. There clearly is marked variation in outcome by age 18 in this community ascertained sample of twins.

Table 2

DSM-IV Diagnostic Outcomes at Age-18 Assessment[3]

DSM diagnosis	*N*	% with diagnosis[1]	Mean (*SD*) symptom count
Nicotine dependence	645	28.7	1.00 (1.59)
Alcohol dependence	645	13.5	0.52 (1.13)
Drug dependence	644	14.1	0.72 (2.10)
Adult antisocial behavior	612	24.4	0.97 (1.44)
Any disinhibitory diagnosis[2]	645	39.7	3.20 (5.08)

Note: Sample sizes vary somewhat because of nonresponse.

[1]Diagnoses were made at the definite (all criteria met) and probable (one symptom short of definite) levels of certainty.

[2]Rate of Any Disinhibitory Diagnosis is the percentage with at least one of the four listed diagnoses; symptom count for this category is the sum of the symptom counts for the four diagnoses.

[3]Disorders were present between the age-14 and age-18 assessment. For over 90% of participants diagnosed with a nicotine, alcohol, or drug disorder, evidence of the disorder (i.e., tobacco use, intoxication, or illegal drug use, respectively) was present in the year prior to their age-18 assessment.

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Table 3

Relationship Between Early Problem Behaviors and Age-18 DSM-IV Diagnoses

	Odds ratio (95% confidence interval)				
Early problem behavior	Nicotine dependence	Alcohol dependence	Drug dependence	Adult antisocial	Any disinhibitory
Tobacco	7.4 (5.0, 11.0)	4.9 (3.0, 8.2)	5.8 (3.5, 9.7)	5.9 (3.9, 8.9)	8.1 (5.6, 11.7)
Alcohol	4.9 (3.4, 7.1)	5.0 (3.1, 8.2)	5.3 (3.3, 8.5)	7.2 (4.8, 10.8)	5.3 (3.7, 7.6)
Marijuana	7.5 (4.4, 12.9)	6.0 (3.5, 10.3)	12.1 (7.0, 21.0)	8.7 (5.1, 14.9)	12.3 (6.2, 24.5)
Other substance	15.2 (4.4, 52.6)	7.2 (2.9, 17.8)	15.3 (5.6, 41.4)	13.4 (4.4, 40.9)	NC
Police contact	4.5 (2.8, 7.0)	4.4 (2.6, 7.4)	4.3 (2.6, 7.2)	5.9 (3.6, 9.4)	5.1 (3.2, 8.3)
Sexual intercourse	17.1 (3.8, 76.6)	6.1 (2.1, 17.2)	16.8 (5.2, 55.0)	46.4 (6.1, 356.3)	22.1 (2.9, 169.0)

Note: Diagnoses are at the definite plus probable level.

NC — Odds ratio could not be computed because one of the cells in the 2×2 table had a zero count.

The Association of Early Problem Behavior and Contextual Risk with Age-18 Disinhibitory Psychopathology

The odds ratios (ORs), and associated 95% confidence intervals, relating each of the adolescent problem behaviors with each of the outcome diagnoses, are given in Table 3. Every early problem behavior was significantly associated with each of the four disinihibitory diagnoses as well as with any disinhibitory diagnosis. Indeed, the smallest OR reported in the table is 4.3, and the majority of the ORs exceed 5.0, indicating a very strong and general relationship between early problem behavior and age-18 disinhibitory psychopathology. The Early Problem Behavior score is meant to provide a general measure of early adolescent problem behavior. The correlations between the log-transformed Early Problem Behavior score and each of the log-transformed symptom outcome scales are reported in Table 4. These correlations are all significant and large (from .41 to .60). Also reported in Table 4 are the correlations between the Contextual Risk score and the log-transformed symptom scales. These correlations are also all statistically significant and generally large (.35 to .51), although in every case the correlation for the Contextual Risk composite is slightly lower than the corresponding correlation for the Early Problem index.

In interpreting the associations of Early Problem Behavior and Contextual Risk with symptom outcomes it is important to recognize that Early Problem Behavior and Contextual Risk are themselves strongly related. The overall correlation between the Early Problem Behavior index and Contextual Risk is .53, and Figure 1 gives the mean Contextual Risk score as a function of number of early problem behaviors. Because Contextual Risk is scaled on a *T*-score metric (overall mean of 50 and standard deviation of 10), the figure shows that adolescents who have engaged in five to six early problem behaviors score more than two standard deviations higher than adolescents with no early problem behaviors. The two dimensions of risk are clearly highly interrelated. Nonetheless, both contribute independently to the prediction of each of the symptom outcome scales. This can be seen from the multiple correlations, where both dimensions of risk contribute uniquely to the prediction of the symptom outcome scales (see Table 4). Each of the multiple correlations is significantly greater than both of the corresponding zero-order correlations, indicating that both dimensions of risk contribute independently to the prediction of disinihibitory psychopathology.

Biometrical Analysis of the Twin Data

Biometric analyses focused on the Early Problem Behavior index, the Contextual Risk composite, and the Disinhibitory Psychopathology symptom scale. Twin correlations for these three variables are given in Table 5. In every case the MZ twin correlation exceeds the corresponding DZ twin correlation, implicating the existence of genetic influences. Additionally, the DZ correlations are consistently greater than half the corresponding MZ correlations, implicating the existence of shared environmental influences. We sought to formalize these observations by fitting a series of biometric models to the twin data. Specifically, we first fit a general 3-factor Cholesky model and then a series of submodels. Because our interest was in accounting for variation in the age-18 outcome as a function of the two dimensions of risk assessed at the age-14 assessment, the submodels we fit to the data focused on testing the significance of parameters relating age-14 effects to age-18 outcomes.

Table 4

Correlation of Age-18 Symptom Outcome Scales With Early Problem Behavior Index and Contextual Risk Composite Assessed at Age 14

Symptom scale	Early problem behavior	Contextual risk	Multiple correlation
Nicotine dependence	.47	.41	.51
Alcohol dependence	.42	.35	.45
Drug dependence	.41	.38	.46
Adult antisocial	.54	.48	.59
Disinhibition composite	.60	.51	.65

Note: All zero-order and multiple correlations significant at $p < .01$. In every case, the multiple correlation is significantly greater than both of the zero-order correlations.

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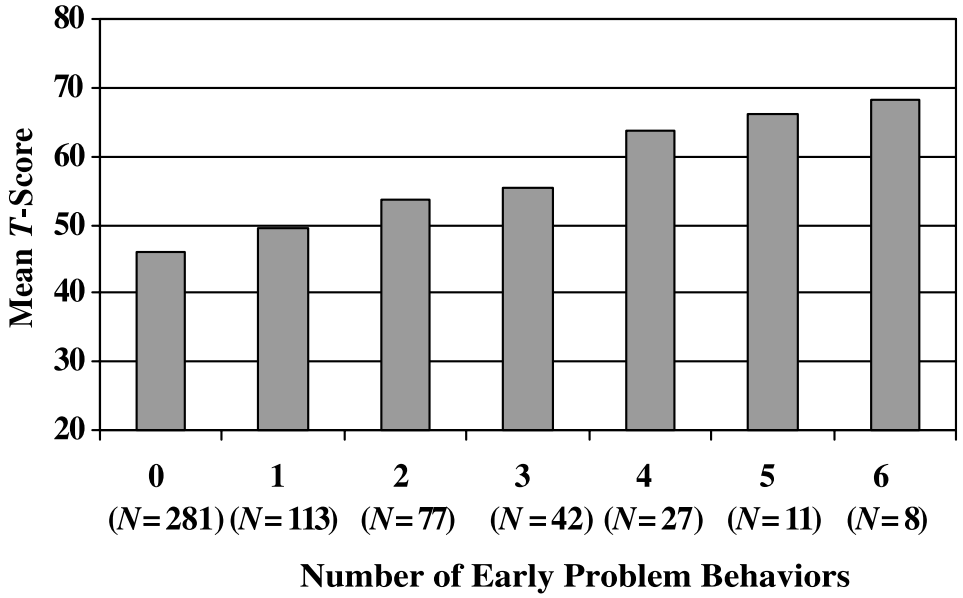

Figure 1

Mean Contextual Risk composite as a function of the number of early adolescent problem behaviors. In the full sample the composite score is scaled to a *T*-score metric (mean of 50 and standard deviation of 10). The correlation between the composite and the log-transformed number of early problem behaviors is .53 ($p < .001$).

Model fit indexes for the submodels relative to the general Cholesky model are given in Table 6.

Deleting either the genetic, χ^2 (2 *df*) = 18.7, $p < .001$, or nonshared environmental, χ^2 (2 *df*) = 24.9, $p < .001$, correlations between the age-14 dimensions of risk and the age-18 outcome resulted in a significant decrease in model fit. Deleting the shared environmental correlations between risk and outcome did not, however, result in a significant decrement in model fit, χ^2 (2 *df*) = 3.5, $p = .17$. The residual genetic effect on the outcome measure was not statistically significant, χ^2 (1 *df*) = 0.0, $p = .99$, and a single genetic factor could account entirely for the genetic effects on the three observed phenotypes, χ^2 (3 *df*) = 6.3, $p = .10$. A model that eliminated shared environmental correlations between age-14 risk and age-18 outcome, and constrained genetic factors to a single factor fit the data well, χ^2 (6 *df*) = 11.4, $p = .08$, and this model could be further reduced by eliminating the nonshared environmental correlations between the Early Problem Behavior index and both Contextual Risk and Disinhibitory Symptoms, χ^2 (8 *df*) = 13.8, $p = .09$. Standardized parameter estimates for the latter, best fitting, model are reported in Figure 2.

Table 5

MZ and DZ Twin Correlations for Risk Factors and Symptom Outcomes

	Twin correlations	
Variable	MZ	DZ
Age 14 risk factors		
Early problem behavior	.75 (*N* = 232)	.54 (*N* = 109)
Contextual risk	.66 (*N* = 178)	.49 (*N* = 78)
Age 18 outcome		
Disinhibitory psychopathology	.78 (*N* = 198)	.43 (*N* = 94)

Note: Early Problem Index and disinhibition symptom outcome scale were log-transformed prior to estimation of correlations.

Table 6

Indexes of Model Fit

Model	χ^2	*df*	*p*	AIC
Genetic factors not correlated between risk dimensions and disinhibition outcome	18.7	2	<.001	14.7
Shared environmental factors not correlated between risk dimensions and disinhibition outcome	3.5	2	.17	–0.5
Nonshared environmental factors not correlated between risk dimensions and disinhibition outcome	24.9	2	<.001	20.9
No residual genetic effect on disinhibition outcome	0.0	1	.99	–2.00
Same genetic effect on risk dimensions and outcome	6.3	3	.10	0.30
Best fitting model (single genetic factor, uncorrelated shared environmental factors, and correlated nonshared environmental factors between only contextual risk and outcome	13.8	8	.09	–2.20

Note: The general 3-variable Cholesky model was used as the base model against which all other models were compared. Parameter estimates for 'best fitting' model are reported in Figure 2.

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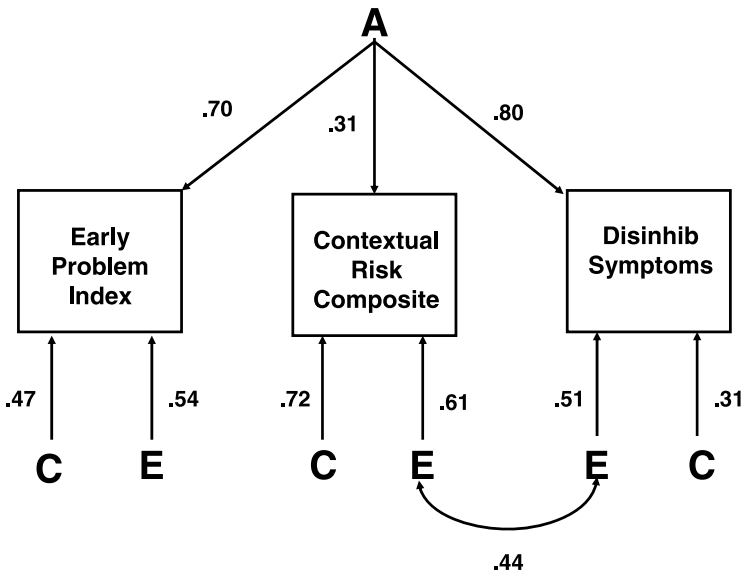

Figure 2

'Best fitting' biometric model relating Early Problem Behavior, Contextual Risk, both assessed at the age-14 assessment, and Disinhibitory Psychopathology symptoms, assessed at the age-18 assessment. A = additive genetic factors, C = shared environmental factors, and E = nonshared environmental factors.

Genetic factors were estimated to account for 49% of the variance in the Early Problem Behavior index, 10% of the variance in the Contextual Risk variable, and 64% of the variance in the composite measure of Disinhibitory Psychopathology symptoms. The corresponding estimates of shared environmental effects were, respectively, 22%, 52%, and 10%; while nonshared environmental factors were estimated to account, respectively, for 29%, 37%, and 26% of the observed variance. The association of Early Problem Behavior with the other two phenotypes was mediated entirely by common genetic effects, while the association between Contextual Risk and Disinhibitory Psychopathology was mediated by both common genetic and common nonshared environmental effects.

Discussion

A sample of 692 14-year-old male twins was followed through age 18 to investigate the association of early adolescent problem behavior and contextual risk with symptoms of disinhibitory psychopathology. Our analyses revealed: (1) early adolescent problem behavior is prospectively associated with risk of disinhibitory psychopathology, (2) early adolescent problem behavior is associated with increased exposure to contextual markers of risk, and (3) early problem behavior and contextual risk are significantly associated with disinhibitory psychopathology, although the genetic and environmental contributions to these associations appear to differ. We discuss each of these findings in turn.

An association between early alcohol use and risk of alcoholism has been consistently observed by several different investigators, including ourselves (Dewit et al., 2000; Grant & Dawson, 1997; McGue et al., 2001a; Prescott & Kendler, 1999). Despite the consistency of these observations, research in this area is characterized by a common limitation: the retrospective assessment of early alcohol use. There are several mechanisms that could produce artifactual associations in retrospective designs, including faulty recall and telescoping (Groves, 1989). Consequently, it is essential that the association is also confirmed using a prospective design. Using a prospective design, we found that use of alcohol by the age-14 assessment was associated with a five-fold increase in the odds of alcohol dependence by age 18. As in our previous, retrospective research, however, early use of alcohol was not specifically associated with risk of alcohol dependence but rather was associated also with an increased risk of nicotine dependence (OR = 4.9), drug dependence (OR = 5.3), and adult antisocial behavior (OR = 7.2). Moreover, other problem behaviors when expressed early in adolescence were strongly and generally associated with increased risk of all forms of disinhibitory psychopathology by age 18. We have thus confirmed prospectively the observation we first made using retrospective data: early adolescent problem behavior is a generalized risk factor for adult disinhibitory psychopathology (McGue & Iacono, 2005). While the present prospective design has clear advantages relative to earlier retrospective research, it also has one important limitation. The associations we observe may reflect in part an increased opportunity

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to progress from the initial stages of substance use to substance dependence. For example, someone who has begun to drink at age 13 will have had a greater opportunity to progress to dependence by age 18 than someone who first tried alcohol at age 17. Nonetheless, the generality of the associations we observe argue against this limitation being a major explanation for our results (e.g., the association between early sexual intercourse and drug dependence, or between early marijuana use and nicotine dependence).

Consistent with the altered-course-of-development explanation for the association of early alcohol use with alcoholism risk, we found the individuals who engaged in problem behavior early in adolescence were more likely to affiliate with peers that modeled deviant behavior, were more likely to have a relationship with their parents that was marked by conflict, were less likely to affiliate with peers that modeled positive behavior, and were less likely to be engaged in academic pursuits. Moreover, we found that both early problem behavior and contextual risk were strongly and independently associated with age-18 disinhibitory psychopathology. While the causal basis of the association between early problem behavior and contextual risk cannot be unambiguously resolved in the present design, it is clear that individuals who engage in multiple problem behaviors early in adolescence are much more likely to be exposed to a high-risk environment than adolescents who have not engaged in problem behavior.

Joint biometric analysis of early adolescent problem behavior, contextual risk, and disinhibitory psychopathology revealed a significant genetic influence on all three phenotypes. Importantly, genetic influences on the three phenotypes could be accounted for by a single common genetic factor. Consistent with earlier research (Krueger et al., 2002; Young et al., 2000), we found a strong genetic influence for disinhibitory psychopathology (heritability, a^2 = 64%). Our estimate of the strength of genetic influence on early problem behavior (a^2 = .49), however, is larger than that which we recently reported in a retrospective twin study (a^2 = .23; McGue et al., 2006).

The small heritability estimate for the Contextual Risk index (10%) is consistent with our characterization of it as a marker of environmental risk. Nonetheless, we found that the association between Contextual Risk and Early Problem Behavior was mediated entirely by genetic factors. Although we cannot necessarily establish the causal basis for this association, these findings are consistent with a gene-environment correlation model in which heritable influences on early adolescent problem behavior result in the increased likelihood of exposure to environments that increase the risk of disinhibitory psychopathology. It is of interest in this regard that, while Disinhibitory Psychopathology's association with Early Problem Behavior was mediated entirely by genetic factors, its association with Contextual Risk was mediated by both genetic and (nonshared) environmental factors. The latter may account for our finding that, at the phenotypic level, Contextual Risk contributes independently of Early Problem Behavior to the prediction of Disinhibitory Psychopathology.

In summary, a prospective analysis of adolescent problem behavior in a sample of 692 male twins revealed that problem behavior when expressed early in adolescence is associated with a general and substantially increased risk of disinhibitory psychopathology by early adulthood and with increased exposure to risky environments. Biometric analysis of the twin data indicated that the association between problem behavior and disinhibitory psychopathology and between problem behavior and contextual risk is due to common genetic effects. These findings are consistent with a model that hypothesizes that early adolescent problem behavior is associated with disinhibitory psychopathology both because it is a marker of genetic liability and because it is associated with environmental risk by genotype-environment correlational processes.

Endnotes

1 Although the MTFS also includes a cohort of 11-year-old female twins followed longitudinally, assessment of the female twins lags that of the male twins. At the time of this report, data from the second follow-up of the 11-year-old female cohort was not fully available, so that the present report is focused exclusively on the male cohort, which has completed the second follow-up.

2 Diagnostic rates for alcohol and drug dependence can be compared to those reported by Kessler et al. (2005) in their report of DSM-IV diagnostic rates in the National Comorbidity Survey Replication. Alcohol and drug dependence rates reported in our current paper are necessarily high because we used a lower diagnostic threshold (definite and probable) to minimize false negatives in this sample of young men who had not yet passed through the full period of risk for these disorders. In our sample of 18-year-old males, diagnostic rates computed at the definite level only are 7% and 10%, for alcohol dependence and drug dependence, respectively. Comparable lifetime prevalence rates reported by Kessler et al. for 18- to 29-year-old men and women are 6% and 4%, for alcohol dependence and drug dependence, respectively. As expected, our rates are somewhat higher than those reported by Kessler et al., reflecting the all-male composition of the sample used in this article. Similarly, Grant et al. (2004) reported the lifetime prevalence of antisocial personality disorder from the National Epidemiologic Survey on Alcohol and Related Conditions. The reported prevalence of DSM-IV antisocial personality disorder in 18- to 29-year-old men and women is 6%. In this article, we reported the rate of adult antisocial behavior (i.e., symptoms of antisocial behavior evidenced after age 15) at the definite and probable level. If we restrict the diagnosis to

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those exhibiting adult antisocial behavior at the definite level with evidence of conduct disorder prior to age 15, the diagnostic rate in our sample is 8%, the slightly higher rate reflecting the all-male composition of our sample.

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References

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4th ed.). Washington, DC: Author.

Brown, S. A., & Tapert, S. F. (2004). Adolescence and the trajectory of alcohol use: Basic to clinical studies. *Annals of New York Academy of Sciences, 1021*, 234–244.

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.

Grant, B. F., Hasin, D. S., Stinson, F. S., Dawson, D. A., Chou, S. P., Ruan, W. J., & Pickering, R. P. (2004). Prevalence, correlates, and disability of personality disorders in the United States: Results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Journal of Clinical Psychiatry, 65*, 948–958.

Grant, B. F., & Dawson, D. A. (1997). Age at onset of alcohol use and its association with DSM-IV alcohol abuse and dependence: Results from the National Longitudinal Alcohol Epidemiologic Survey. *Journal of Substance Abuse, 9*, 103–110.

Groves, R. M. (1989). *Survey errors and survey costs*. New York: John Wiley and Sons.

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.

Jessor, R., & Jessor, S. L. (1977). *Problem behavior and psychosocial development: A longitudinal study of youth*. New York: Academic Press.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R., & Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry, 62*, 593–602.

Krueger, R. F., Hicks, B. M., Patrick, C. J., Carlson, S. R., Iacono, W. G., & McGue, M. (2002). Etiologic connections among substance dependence, antisocial behavior, and personality: Modeling the externalizing spectrum. *Journal of Abnormal Psychology, 111*, 411–424.

Liang, K. Y., & Zeger, S. L. (1986). Longitudinal data analysis using generalized linear models. *Biometrika, 73*, 13–22.

McGue, M., & Iacono, W. G. (2005). The association of early adolescent problem behavior with adult psychopathology. *American Journal of Psychiatry, 162*, 1118–1124.

McGue, M., Iacono, W. G., & Krueger, R. (2006). The association of early adolescent problem behavior and adult psychopathology: A multivariate behavioral genetic perspective. *Behavior Genetics, 36*, 594–602.

McGue, M., Iacono, W. G., Legrand, L. N., & Elkins, I. (2001a). The origins and consequences af 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.

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

Neale, M. C., Boker, S. M., Xie, G., & Maes, H. H. (1999). *Mx: Statistical modeling* (5th ed.). Box 126 MCV, Richmond VA 23298: Department of Psychiatry.

Neale, M. C., & Cardon, L. R. (1992). *Methodology for genetic studies of twins and families*. Dordrecht, the Netherlands: Kluwer.

Prescott, C. A., & Kendler, K. S. (1999). Age at first drink and risk for alcoholism: A noncausal association. *Alcoholism: Clinical and Experimental Research, 23*, 101–107.

Robins, L. M., Baber, T., & Cottler, L. B. (1987). *Composite International Diagnostic Interview: Expanded Substance Abuse Module*. St. Louis: Authors.

Spear, L. P. (2002). The adolescent brain and the college drinker: Biological basis of propensity to use and misuse alcohol. *Journal of Studies on Alcohol Supplement, 14*, 71–81.

Spitzer, R. L., Williams, J. B. W., & Gibbon, M. (1987). *Structured Clinical Interview for DSM-III-R*. New York: Biometrics Research Department, New York State Psychiatric Institute.

Stewart, S. H., Conrod, P. J., Marlatt, G. A., Comeau, M. N., Thush, C., & Krank, M. (2005). New developments in prevention and early intervention for alcohol abuse in youths. *Alcoholism: Clinical and Experimental Research, 29*, 278–286.

White, A. M., & Swartzwelder, H. S. (2004). Hippocampal function during adolescence: A unique target of ethanol effects. *Annals of New York Academy of Sciences, 1021*, 206–220.

Young, S. E., Stallings, M. C., Corley, R. P., Krauter, K. S., & Hewitt, J. K. (2000). Genetic and environmental influences on behavioral disinhibition. *American Journal of Medical Genetics (Neuropsychiatric Genetics), 96*, 684–695.