Genetic and Environmental Analysis of Behavioral Risk Factors for Adolescent Drug Use in a Community Twin Sample

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We investigated the etiology of six problem behaviors that might facilitate an understanding of behavioral pathways to substance use and abuse in adolescents. These behavioral measures, classified as Conduct Problems, Hyperactivity, School Problems, Low Self-esteem, Neuroticism, and Social Withdrawal were the result of a previously reported (Siewert et al., 2003) modification of the Drug Use Screening Inventory (DUSI; Tarter, 1990; Tarter & Hegedus, 1991). We developed these measures as interpretable components of risk for substance use and abuse in a community based sample of 633 twin pairs, who were under the legal drinking age of 21 (mean age = 15.0 years). Using multivariate analyses, model comparisons indicated that these six behavioral measures could be thought of as two heritable, and genetically distinct, dimensions of problem behavior. Two closely competing models resulted from our analyses. The best fitting model hypothesized a general genetic factor loading on all 6 behavioral measures with a second genetic factor loading on only the three internalizing behavioral measures with loadings of 0.25–0.59 and 0.26–0.44, respectively. A second model, which fit the data almost as well, hypothesized one genetic factor loading only on the externalizing behavioral measures, and a second genetic factor loading only on the internalizing behavioral measures, with a correlation between the two latent factors of 0.75. Because our analyses show that there are two genetically distinct factors influencing these six problem behaviors, we anticipate that there may be different patterns of relationship of these factors to risk for substance use, abuse, and dependence.

In a previous paper (Siewert et al., 2003) we reported on the psychometric and predictive properties of subscales derived from the Drug Use Screening Inventory (DUSI; Tarter, 1990; Tarter & Hegedus, 1991). We found that these subscales may contribute to a description of behavioral components of risk for substance use and abuse in nonclinical samples of adolescents, even though the DUSI was developed for use in clinical settings. Our goal in exploring the behaviors assessed by the DUSI was to understand the behavioral pathways to substance use and abuse in adolescence. By choosing to assess behaviors that show good discriminant validity between clinical and nonclinical samples (Kirisci et al., 1995), and which have been nominated by clinicians as of particular importance in describing the syndrome of behavioral problems often comorbid with substance use disorders, we hope to focus our study of adolescent problem behaviors on those that show an especially close relationship to the risk for substance use and abuse.

To develop behavioral measures that might be used as predictors of substance use and abuse within an adolescent community sample, we modified the Drug Use Screening Inventory resulting in six subscales that characterize the common behavioral problems of adolescence: Conduct Problems, Hyperactivity, Low Self-esteem, Neuroticism, Social Withdrawal, and School Problems (Siewert et al., 2003). Although these six subscales remain moderately inter-correlated, much of the explicit overlap in the assessment of behaviors using the four DUSI domains was eliminated. Thus, these resulting six subscales were more easily interpretable as separable behavioral risk factors, even though some or all of them may share a common underlying etiology.

Young et al. (2000) and Krueger et al. (2002) have reported that substance problems in adolescence are part of a general spectrum of behaviors that may be characterized as manifestations of behavioral disinhibition (Iacono et al., 1999) or a general externalizing factor. Young et al. (2000) examined the relationships between symptoms of conduct disorder, attention deficit hyperactivity disorder, breadth of substance experimentation, and the personality trait of novelty seeking in a sample of 336 pairs of twins aged 12–18 years. Multivariate genetic modeling resulted in the identification of a highly heritable (86%) general factor, labeled behavioral disinhibition, that linked these four phenotypes. Krueger et al. (2002) studied 626 pairs of 17-year-old twins and also found a highly heritable (81%) general factor labeled the "externalizing factor" linking measurements of adolescent antisocial behavior, conduct disorder, alcohol dependence, drug dependence, and a personality assessment of "lack of constraint." In either characterization, individual differences in the underlying factor were found in these twin studies to be familial, largely due to genetic rather than environmental reasons. The importance of this is that at least some aspects of behavioral problems in adolescence that predispose to substance use

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and abuse may reflect biological factors as well as, or perhaps instead of, social factors. To explore this possibility we wanted to determine the extent to which individual differences in our six behavioral problem subscales were influenced by genetic factors, as well as by shared environmental and non-shared environmental factors. Additionally, we wanted to determine the extent to which the different aspects of problem behavior chosen to be clinically predictive of substance use disorders, might reflect a common underlying factor and, if so, to what extent the etiology of individual differences in that factor were genetic.

Using a community twin sample, we were able to differentiate between shared environmental influences and genetic influences that are largely confounded in non-twin sibling samples. Initially, univariate analyses were performed in order to assess the components of the variance within each behavioral measure. Following that, we conducted multivariate twin analyses to develop the best account of the relationships among the behaviors and to test the hypothesis that there would be an underlying genetically influenced trait common to some or all of the six assessed areas of behavioral problems.

Methods

Subjects

We obtained the data used in these analyses from adolescents who participated in the Colorado Adolescent Twin Study (1102 individuals who were at least 12 years of age) and the Colorado Adult Twin Study (164 individuals who were younger than the legal drinking age of 21 years). Informed consent was obtained from the individual twins or their parents (if twins were under age 18). Research protocols and consent forms were approved by the Human Research Committee at the University of Colorado at Boulder and the data are protected by a Confidentiality Certificate issued by the Department of Health and Human Services. These subjects all completed and returned a mailed questionnaire that was designed to assess behavioral patterns, health issues, personality characteristics, and alcohol and drug use in a community sample. The questionnaire was mailed to 4232 individual twins that had been previously identified by searching multiple birth records through the Colorado Department of Health and Colorado school records.

Of the 2053 surveys returned (48.5 % response rate) there were 868 complete twin pairs (1736 individuals), of which 633 pairs (1266 individuals) were between the ages of 12 and 20 with a mean of 15.0 years (*SD* = 2.36). The mean number of years of school completed was 8.7 (*SD* = 2.22) with a minimum of 4 years completed and a maximum of 16 years (bachelor's degree) completed. There were 119 MZ male, 208 MZ female, 76 DZ male, 100 DZ female, and 130 DZ opposite sex pairs.

Zygosity Determination

Zygosity for same-sex twin pairs was determined in the following manner. As part of the registration for the twin study, the twins and a rater (usually a parent) were asked if they were identical or fraternal and how frequently they were mistaken for each other. Additionally, in some cases, two testers rated the similarity of the twins based on a10-item assessment comparable to the form developed by Nichols and Bilbro (1966). Using this information, the twins were classified as MZ or DZ. Subsequently, the zygosity assignment was confirmed for 253 out of 259 twin pairs (97.7%) by genotyping the twins' DNA using 9 highly polymorphic Short Tandem Repeat markers.

Measures

Part of the Colorado Adolescent (and Adult) Twin Study questionnaire that was mailed to the participants consisted of 75 yes/no type questions from the Drug Use Screening Inventory (Tarter & Hegedus, 1991). Items from Domain II (Behavior Patterns), Domain IV (Psychiatric Disorder), Domain V (Social Competency), and Domain VII (School Performance/Adjustment) were incorporated in order to assess behavioral patterns of the participant. Because our questionnaire was a self-report assessment, we avoided using the DUSI domain headings, and simply titled the four sections Behavior Patterns I, Behavior Patterns II, Social Behavior, and School Behavior. A principal components analysis was performed on all the items across the four sections which resulted in six scales: Conduct Problems (CP), Hyperactivity (Hyp), School Problems (Sch), Low Self-esteem (LSE), Neuroticism (Neu), and Social Withdrawal (SW) (Siewert et al., 2003). The items for each scale were then summed. Additionally, the sums were transformed so that the data were more nearly normally distributed resulting in a measure of behavior for each of the six scales centered on 0 with a variance of 1. The measures were regressed onto age, age squared, sex, sex × age, and sex × age squared, and all further analyses were performed on the residuals. The correlations of the original scales with the transformed data ranged from 0.93–0.99.

The six measures were evaluated for differences among the means and variances among the five zygosity groups. A standard one-way ANOVA was used to test the equality of the means, and Levene's Improved test was used to test the equality of the variances. The correlations between Twin 1 and Twin 2 for each behavioral measure were also calculated for each of the five zygosity groups.

Univariate Models

For each of the six behavioral measures, a univariate twin model was fit to the 2 × 2 (Twin 1 by Twin 2) variance-covariance matrices for the five zygosity groups using the Mx software. (Neale, 1999). The most saturated model allowed the phenotypic variances for each of the behavioral measures to be explained by additive genetic, shared environmental, and non-shared environmental influences (ACE model). The magnitudes of these genetic and environmental influences were permitted to differ between males and females. A series of alternative models was tested with each model incorporating additional constraints by restricting either the genetic and/or shared environmental influences to be 0, or by restricting the magnitude of the influences for both sexes to be equal to or a scalar multiple of one another. Two additional models were tested by allowing the genetic correlation and the shared environmental correlation for the opposite sex twins to depart from 0.5 and 1.0, respectively (Neale & Cardon, 1992).

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In the same way, models were also fit allowing for non-additive (dominance) genetic influences (ADE model) as an alternative to the ACE model. The best model was selected using the Akaike Information Criterion (AIC), a fit index which takes into account the parsimony, as well as the fit, of the model to the observed data (Akaike, 1987).

Multivariate Models

In addition to univariate analyses, multivariate twin models were used to decompose the covariation among the behavioral measures into genetic and environmental sources. A 12 × 12 variance-covariance matrix (i.e., six measures for Twin 1 and six measures for Twin 2) was calculated for each of the five zygosity groups. Initially, a Cholesky decomposition (Neale & Cardon, 1992) was used to partition the variance/covariance matrix into three latent sources of variation: additive genetic, shared environmental, and non-shared environmental factors. Reduced Cholesky factorization models were also examined, by constraining the male and female factor loadings to be equal, and/or by dropping the shared environmental latent factors. Again, the Akaike Information Criterion was used to select the best fitting model.

We then explored the factor structure by hypothesizing two latent additive genetic factors to explain the covariation among the 6 behavioral measures. Additionally, genetic factors specific to each measure were included in the models. Non-shared environmental influences were left as a fully parameterized Cholesky factorization, while shared environmental influences (which had been found to be non-significant) were dropped from the models. Several alternative forms of the two-factor genetic models were considered. Figure 1 shows a path diagrammatic representation of these models for the additive genetic factors. For clarity, only one twin is represented, and the non-shared environmental loadings are not shown. These alternative models included two orthogonal factors (paths a_{11}, a_{21}, a_{31}, a_{42}, a_{52}, a_{62}) or two correlated factors (paths a_{11}, a_{21}, a_{31}, a_{42}, a_{52}, a_{62}, r_g) corresponding to hypothesized externalizing and internalizing dimensions, or one general factor together with an additional factor specific to either the internalizing cluster (paths a_{11}, a_{21}, a_{31}, a_{41}, a_{51}, a_{61}, a_{42}, a_{52}, a_{62}) or the externalizing cluster (paths a_{11}, a_{21}, a_{31}, a_{12}, a_{22}, a_{32}, a_{42}, a_{52}, a_{62}) of behaviors.

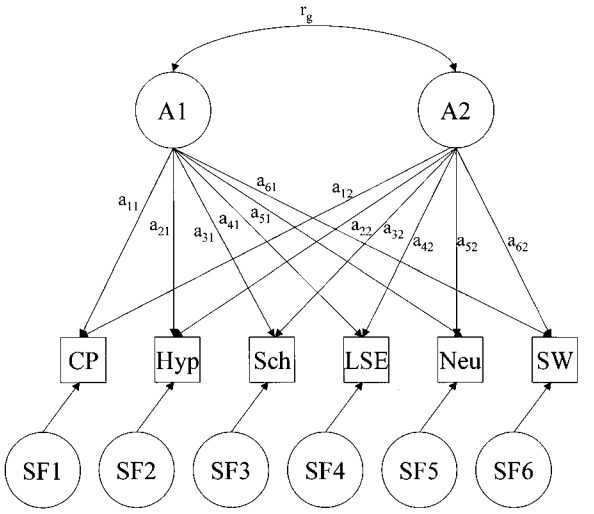

Figure 1

Bivariate Cholesky model for 2 general (A) and 6 specific (SF) additive genetic factors.

Results

Comparison of the Means, Variances, and Correlations

There were no significant differences among the means of the five zygosity groups for each of the six behavioral measures. Also, with the exception of Neuroticism, there were no significant differences among the variances of the five zygosity groups for each of the six behavioral measures. The twin variances for Neuroticism were significantly larger in the females than in the males ($p < .0001$).

The correlations between Twin 1 and Twin 2 for each of the six behavioral measures for the five zygosity groups are presented in Table 1. An examination of the correlations reveals that, in general, the MZ correlations are approximately twice the value of the DZ correlations for all 6 behavioral measures for females. This pattern of correlations suggest that additive genetic influences contribute substantially to the individual variability seen in these six behavioral measures. For males, MZ correlations also generally exceed DZ correlations (the one exception is for Low Self-esteem). However, DZ correlations for conduct problems (CP), hyperactivity (HYP), and neuroticism (NEU) are less than half the MZ correlations, suggesting the presence of nonadditive (dominance) influences.

Univariate Models

Each behavioral measure was initially analyzed using a univariate twin model. For each behavioral measure, the 2 × 2 covariance matrix (Twin 1 by Twin 2) was fitted to the full ACE model and to 14 other reduced models. Additionally, the full ADE model and 10 alternative models were also tested. Table 2 presents the best fitting model based on the lowest Akaike statistic. All of the best fitting models fit the data extremely well. The *p*-values range from 0.398–0.961. Notice that all of the best fitting models are some form of an AE model, generally confirming the indications of the correlation data. Although the male twin correlations suggested the presence of nonadditive genetic influences for some measures, there was insufficient power to detect these effects with the current sample sizes.

Heritability estimates range from 35% for Social Withdrawal to as much as 61% for Hyperactivity in males. In females, heritability appears to be about 40–60% for all 6 behavioral measures. The lowest genetic influence in females is for the Low Self-esteem behavioral measure which is estimated to be 35% and the highest genetic influence in females is for the School Problems behavioral measure which is estimated to be 58%. In general, the heritabilities appear to be higher for Conduct Problems, Hyperactivity, and School Problems, than for Low Self-esteem, Neuroticism, and Social Withdrawal.

Multivariate Models

Table 3 presents the results of the Cholesky decomposition models. Model 1 is the full Cholesky decomposition, with

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Table 1

Correlations of Behavioral Measures Between Twin 1 and Twin 2 by Zygosity

	Male		Female		M/F
	MZ (n = 116)	DZ (n = 72)	MZ (n = 201)	DZ (n = 97)	DZ (n = 127)
CP	0.642	0.226	0.494	0.226	0.285
Hyp	0.659	0.187	0.501	0.237	0.183
Sch	0.619	0.300	0.563	0.301	0.287
LSE	0.183	0.303	0.430	0.214	0.165
Neu	0.424	0.023	0.434	0.206	0.220
SW	0.318	0.264	0.559	0.244	0.206

Table 2

Best Fitting Univariate Models Based on Akaike Statistic

Behavior Measure		Model	Parameter Estimates[1]				Fit Statistics			
			a^2	c^2	e^2	Scalar	χ^2	df	p-value	AIC
CP	AE (m = f)[2]	Male	0.5311	—	0.4689	—	13.657	13	0.398	–12.343
		Female	0.5311	—	0.4689	—				
Hyp	AE[3]	Male	0.6137	—	0.3863	—	7.782	11	0.733	–14.218
		Female	0.4851	—	0.5149	—				
Sch	AE (m = f)[2]	Male	0.5830	—	0.4170	—	5.554	13	0.961	–20.446
		Female	0.5830	—	0.4170	—				
LSE	AE (m = f)[2]	Male	0.3516	—	0.6484	—	11.880	13	0.537	–14.120
		Female	0.3516	—	0.6484	—				
Neu	Scalar AE[4]	Male	0.4119	—	0.5881	—	5.378	12	0.944	18.622
		Female	0.4119	—	0.5881	1.1668				
SW	AE[3]	Male	0.3462	—	0.6538	—	4.368	11	0.958	–17.632
		Female	0.5449	—	0.4551	—				

Note: [1] Standardized parameter estimates for heritability (a^2) and shared (c^2) and non-shared (e^2) environmentalbility
[2] AE model, Sexes constrained to be equal
[3] AE model, Sex differences allowed
[4] AE model, Sexes constrained to differ by a scalar

genetic, and environmental effects allowed to have different influences on males and females. Model 2 constrains the genetic and environmental effects to have equal influences on both males and females. Model 3 further constrains the shared environmental effects to be zero. Model 4 constrains the shared environmental effects to be zero, while allowing different genetic and non-shared environmental loadings for each sex. Results confirm the univariate results that the most parsimonious, best fitting model based on the Akaike statistic is the AE model with equal loadings for both sexes (χ^2 = 329.237, df = 348, p = 0.751, AIC = –366.237).

An analysis of the factor loadings from the Cholesky decomposition models indicated that a model with 2 latent and 6 specific genetic factors loading on the behavioral measures would be appropriate (see Figure 1). The non-shared environmental factors were modeled as a Cholesky decomposition and the effects of the latent factors were constrained to load equally on both sexes. Based on the results of both the univariate and the Cholesky decomposition analyses, the shared environmental factors were not included in this model. Table 4 lists the series of nested models tested within this model. The first sub model, Model 2, allows for only 1 latent additive genetic factor loading on all six behavioral measures. The goodness of fit for this model, in comparison to the full model was poor ($\Delta\chi^2$ = 26.827, df = 5, p = 0.0001).

The successive alternative models investigated the pattern of loadings of the two latent additive genetic factors on the 6 behavioral measures. Initially, we hypothesized two orthogonal factors. Model 3 represents an externalizing latent factor (as measured by Conduct Problems, Hyperactivity, and School Problems), and an internalizing latent factor (as measured by Low Self-esteem, Neuroticism, and Social Withdrawal). This orthogonal model was not supported by the data, however ($\Delta\chi^2$ = 94.352, df = 5, p < .0001).

Subsequently, we investigated various overlapping patterns of loadings of the 2 latent additive genetic factors on

Table 3

Comparison of Cholesky Decomposition Models

Cholesky Models	χ^2	df	p-value	AIC
1 Chol ACE m~ = f	269.928	264	0.388	–258.072
2 Chol ACE m = f	324.119	327	0.535	–329.881
3 Chol AE m = f	329.237	348	0.751	–366.237
4 Chol AE m~ = f	284.750	306	0.803	–327.250

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Table 4

Comparison of Alternative Nested Models to Full Model of Two Latent Genetic Factors Loading on all Six Behavioral Measures

Nested Models	χ^2	*df*	*p*-value	AIC	Compare	$\Delta\chi^2$	Δdf	*p*-value
1 Full Model-2 Latent A loading on all 6 measures	337.123	352	0.707	–366.877				
2 1 Latent A loading on all 6 measures	363.950	357	0.388	–350.050	vs. 1	26.827	5	0.0001
3 2 Latent A loading orthogonally (CP, Hyp, Sch) & (LSE, Neu, SW)	431.475	357	0.004	–282.525	vs. 1	94.352	5	<0.0001
4 2 Latent A loading 6 & 3 (LSE, Neu, SW)	337.640	354	0.726	–370.360	vs. 1	0.517	2	0.7722
5 2 Latent A loading 3 (CP, Hyp, Sch) & 6	344.951	354	0.625	–363.049	vs. 1	7.828	2	0.0200
6 2 Latent A loading 6 & 2 (Neu, SW)	362.988	355	0.374	–347.012	vs. 1	25.865	3	<0.0001
7 2 Latent A loading 6 & 2 (LSE, SW)	353.395	355	0.514	–356.605	vs. 1	16.272	3	0.0010
8 2 Latent A loading 6 & 2 (LSE, Neu)	363.592	355	0.365	–346.408	vs. 1	26.469	3	<0.0001

the 6 behavioral measures. Models 4–5 hypothesize a general genetic factor loading on all 6 behavioral measures and a second factor loading on particularly the internalizing (Model 4) or externalizing (Model 5) behavioral measures. While Model 4 fit the data very well ($\Delta\chi^2$ = 0.517, *df* = 2, *p* = .7722), Model 5 did not ($\Delta\chi^2$ = 7.828, *df* = 2, *p* = .0200).

Models 6–8 test whether any of the three internalizing behavioral measures can be dropped from the path of Model 4. All three of these models show a significant $\Delta\chi^2$ result. Thus the most parsimonious model that best fits the data is Model 4. This model allows the first latent factor to load on all six behavioral measures and the second latent factor to load on the three internalizing behavioral measures of Low Self-esteem, Neuroticism, and Social Withdrawal.

We further investigated the orthogonal factor model (Model 3). This model is especially appealing as it theorizes two latent factors, one of which influences externalizing behavior, and the second one influences internalizing behavior. We wanted to see whether allowing the two latent factors to correlate would improve this model. The resulting correlation between the two latent factors in this model was 0.75. By allowing this correlation between the internalizing and externalizing latent factors of Model 3, we obtain a much better fit than the orthogonal latent factor model (χ^2 = 347.093, *df* = 356, *p* = .622, AIC = –364.907). However, this model, although theoretically appealing, did not provide as good a fit as Model 4 which hypothesized a general latent factor with a specific internalizing latent factor.

Figure 2 represents the best fitting model. Model 4 is shown with the estimated loadings from the latent genetic factors. Although one general latent genetic factor can adequately explain the externalizing behavioral measures, the genetic influence on the internalizing behavioral measures is more complex. Table 5 partitions the components of the variances observed for the 6 behavioral measures. The general latent factor accounts for approximately 33% of the variance observed in the externalizing behavioral measures. The remaining variance is accounted for by specific additive genetic factors (~21%), and non-shared environmental factors (~46%). The variance components for the internalizing behavioral measures has a more complex structure. While Low Self-esteem appears to be affected mostly by the Internalizing Genetic Factor, Neuroticism appears to be affected mostly by the General Factor and Social Withdrawal appears to be affected by both the General and the Internalizing Factors. The largest influence on these

Table 5

Variance Components for Six Behavioral Measures

	Genetic Factors			Environmental Factors
Measure	General Factor	Internalizing Factor	Specific Factor	Non-shared
CP	0.318	0.000	0.199	0.483
Hyp	0.333	0.000	0.178	0.489
Sch	0.348	0.000	0.233	0.419
LSE	0.060	0.159	0.128	0.652
Neu	0.190	0.070	0.134	0.606
SW	0.146	0.196	0.120	0.538

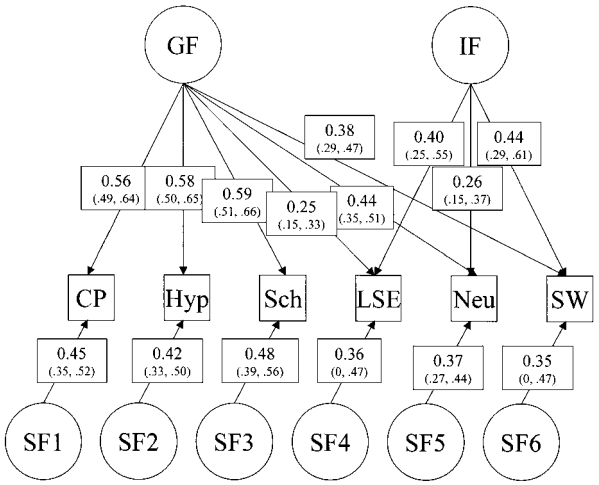

Figure 2

Estimated loadings (95% CI) of latent genetic factors in best fitting multivariate model. General factor (GF), Internalizing factor (IF), Specific factor (SF).

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three internalizing behavioral measures, however, are nonshared environmental factors.

Discussion

Consistent with several recent behavioral genetic studies of antisocial behavior, this investigation found evidence of moderate to substantial heritability for individual differences in externalizing behavioral problems (Eaves et al., 1997; Hudziak et al., 2000; Simonoff et al., 1995; Young et al., 2000). However, shared environmental influences were not significant for any of the six problem behavioral trait scores, a result consistent with some studies (e.g., Eaves et al., 2000), but inconsistent with others (e.g., Lyons et al., 1995). Some earlier studies of antisocial conduct, delinquency, and criminality suggested that genetic influences were likely to be greater for adult behavior than for juveniles (Cloninger & Gottesman, 1987). This pattern appeared to be confirmed in the report by Lyons et al. (1995), based on a large study of male twin pairs participating in the Vietnam Era Twin Registry. They reported that shared environmental influences explained about six times more variance in juvenile antisocial traits than in adult traits. However, Lyons et al.'s report was based on data collected by a telephone interview that required the subject with an average age of 45 years to recall behaviors engaged in 30 or more years earlier (i.e., prior to the age of 15). Thus, the increased shared environmental influences on the juvenile antisocial traits could be confounded with shared environmental influences on memory. In addition to the method of data collection, the rates of the phenotypic (and possibly genetic) variance of reported juvenile antisocial conduct were likely further reduced by inclusion in the data set of only those twin pairs where both adults independently participated (symptom counts were significantly higher for individuals whose co-twin did not participate) and by ineligibility for military service of individuals with serious criminal records as juveniles or young adults. Even given these limitations, significant genetic influences were reported for five antisocial behaviors: often truanting, initiating fights, using weapons, being cruel to animals, and often lying. Thus it would appear that the influence of genetic factors on adolescent externalizing behavioral problems or more extreme antisocial behavior is fairly robust, but that the role of shared family environments, not significant in our data, may vary with the behavior, the assessment instrument, or the sampling method.

Our heritability estimates for internalizing behavioral problems are somewhat lower and, in general, familial aggregation is somewhat less. Again, there was no evidence of a significant influence of shared family environment. These results are largely consistent with the behavioral and psychiatric genetic literature in both adults and adolescents (Eaves et al., 1997; Eaves et al., 1998; Hettema et al., 2001; Topolski et al., 1997).

Our multivariate analyses confirmed that the behavioral problems assessed by the items from the DUSI, that we used to assess problem behavior in a nonclinical adolescent sample, fall, to a good approximation, into the broadband groupings of externalizing and internalizing behavioral problems that have been found repeatedly in assessments of children, whether based on self-reports or when assessed by other observers such as parents (Hewitt et al., 1997). These two clusters cannot, however, be thought of as independent latent factors (see Table 4, Model 3). On the other hand, even though there were significant positive correlations between the externalizing and internalizing problems, as seen in either the General/Internalizing factor model or the correlated Internalizing/Externalizing factor model, it was not possible to treat the measures as indices of a single dimension of problem behavior (see Table 4, Model 2).

In this study, the externalizing traits of Conduct Problems, Hyperactivity, and School Problems, loaded on a general factor somewhat more unambiguously than the internalizing cluster of Low Self-esteem, Neuroticism, and Social Withdrawal. Although the general factor was required to load on all 6 behavioral measures, a comparison of Model 4 with Model 5 shows that the internalizing behavior cluster, rather than the externalizing behavior cluster requires an additional separate factor to obtain a good fit to the data.

Taken together, the results presented in this paper suggest that there are two heritable, and genetically distinct, dimensions of problem behavior that are being assessed by the six trait scales we have adapted from the DUSI for use in community studies of vulnerability to substance use, abuse, and dependence. Because they are heritable, and especially so in the case of the externalizing problems, we must consider individual differences in these problem behaviors as a biologically, as well as a socially determined, characteristic of the adolescent. Because the two clusters are, to some extent, genetically distinct, we should consider different patterns of relationship between the different kinds of adolescent psychopathology, such as vulnerability to substance abuse and dependence. For example, Cloninger (1987) distinguishes between Type 1 alcoholism, characterized by late onset and comorbid internalizing psychopathology, and Type 2 alcoholism, characterized by onset before age 25 and comorbid with antisocial behavior. Our findings further contribute to an accumulating literature suggesting that a substantial portion of the comorbidity among various problem behaviors in adolescence can be explained by common genetic factors, possibly reflecting two broad syndromes of externalizing and internalizing psychopathology. In a subsequent paper we will investigate the relationship between these two clusters of behavior and vulnerability to drug use and abuse in adolescence.

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