Examination of the Causes of Covariation Between Conduct Disorder Symptoms and Vulnerability to Drug Dependence

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Conduct disorder (CD) symptoms and substance dependence commonly co-occur. Both phenotypes are highly heritable and a common genetic influence on the covariation has been suggested. The aim of this study was to determine the extent to which genes and environment contribute to the covariance between CD and drug dependence using twins from the Colorado Longitudinal Twin Sample and the Colorado Twin Registry. A total of 880 twin pairs (237 monozygotic [MZ] female, 195 MZ male, 116 dizygotic [DZ] female, 118 DZ male and 214 DZ opposite-sex) aged 13 to 18 (mean = 15.65) were included in the analysis. CD was assessed by lifetime *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; DSM-IV; American Psychiatric Association, 1994) symptom count and a polysubstance dependence vulnerability index was developed from responses to the Composite International Diagnostic Interview — Substance Abuse Module. A bivariate Cholesky Decomposition model was used to partition the cause of variation and covariation of the two phenotypes. No sex-limitation was observed in our data, and male and female parameter estimates were constrained to be equal. Both CD symptoms and dependence vulnerability were significantly heritable, and genes, shared environment and nonshared environment all contributed to the covariation between them. Genes contributed 35% of the phenotypic covariance, shared environment contributed 46%, and nonshared environmental influences contributed the remaining 19% to the phenotypic covariance. Therefore, there appears to be pleiotropic genetic influence on CD symptoms and dependence vulnerability.

Conduct disorder (CD) commonly co-occurs with substance dependence disorders (SD; Arseneault et al., 2000; Bukstein et al., 1989; Disney et al., 1999; Neighbors et al., 1992). For instance, it has been shown using a clinical sample of inpatients that 52% of adolescents with CD also meet the criteria for substance use disorders (Reebye et al., 1995), a prevalence that is higher than those reported for samples without CD (Regier et al., 1990; Somers et al., 2004). This high comorbidity is also found in population-based samples (Boyle & Offord, 1991). The high rates of comorbidity, along with similar developmental trends for CD and SD (Rutter et al., 1998), indicate the possibility of a common etiology for the two disorders.

Both CD and SD display moderate heritability, although findings vary across populations. For CD, estimates of approximately .33 to .61 have been reported (Jacobson, Neale et al., 2000; Miles et al., 2002; Rhee & Waldman, 2002). The heritability of SD has usually been reported for specific substances. For instance, estimates of .08 to .60 (Kendler et al., 1992, 1994) for alcoholism, .40 to .70 (Sullivan & Kendler, 1999) for tobacco use, and .25 to .45 for illicit substance disorders (Grove et al., 1990; Miles et al., 2002; Tsuang et al., 1996) have been reported. However, there is also evidence of substantial genetic covariance across substances (Kendler et al., 2003; Tsuang et al., 1998) and evidence that a composite measure of vulnerability to develop substance specific dependence in adolescence, irrespective of the substance, is itself heritable (Corley et al., 2001).

Previous analyses of the causes of comorbidity have indicated a genetic contribution. Adoption studies have demonstrated that adopted-away offspring of biological fathers with alcohol problems frequently suffer from aggressive CD (Jary & Stewart, 1985), indicating either differential manifestation of a single underlying vulnerability or two disorders influenced by a similar underlying biological basis. Twin studies also support the hypothesis of a common genetic influence. For example, bivariate genetic analysis of CD and alcohol dependence implied that genes explain 75% of the phenotypic correlation

Received 22 July, 2005; accepted 5 October, 2005.

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between them (Slutske et al., 1998). Other twin studies have demonstrated a substantial genetic contribution to the covariance of CD with tobacco use (Silberg et al., 2003), marijuana use (Miles et al., 2002), and other illicit drug use (Grove et al., 1990). An underlying latent factor has also been proposed to explain the covariation between CD and substance use (Young et al., 2000) or dependence (Hicks et al., 2004; Krueger et al., 2002), as well as a number of other externalizing disorders. This factor has been called Behavioral Disinhibition, is substantially heritable, and contributes to the variance of both CD and substance use disorder.

There is evidence that comorbid CD negatively impacts the outcome of treatment for substance abuse (Fiscenscher & Novins, 2003; Rowe et al., 2004). Understanding the causes of this comorbidity may aid development of effective techniques for each disorder, occurring alone or jointly. Knowledge of the cause of comorbidity will also aid the search for genetic or environmental risk factors specific to each as well as those that potentially influence both. This will lead to a better understanding and diagnosis of these clinical disorders.

The aim of the current study was to determine the extent to which genes and environment contribute to the covariance between CD and drug dependence, using a large, population-based twin study. We hypothesize that both genes and environmental factors contribute to the covariance of the two phenotypes.

Materials and Methods

Participants

Twins were recruited from the Colorado Longitudinal Twin Sample (LTS; Emde & Hewitt, 2001) and the Colorado Twin Registry (CTR; Young et al., 2000). The LTS twins were recruited through the Colorado Department of Health's Division of Vital Statistics and were included in the Center for the Genetics of Antisocial Drug Dependence (CADD) sample as they reached their 12th birthday. The CTR were recruited through the Department of Health and 170 of the 176 school districts in Colorado. Written informed consent or assent (from minor participants) was obtained and assessments were administered by trained interviewers. Twins used in this analysis were aged 13 to 18 (mean = 15.65, *SD* = 1.65). Of the 881 twin pairs aged 13 to 18 years, one twin pair was eliminated due to uncertain zygosity, resulting in a total of 880 twin pairs (1760 individuals: 432 monozygotic [MZ] pairs — 237 female, 195 male; 448 dizygotic [DZ] pairs — 116 female, 118 male, 214 opposite-sex).

Zygosity

Zygosity was determined using a 9-item assessment questionnaire (Nichols & Bilbro, 1966) and by genotyping for a minimum of 11 informative short tandem repeat polymorphisms (STRPs) using DNA from cheek swabs. Zygosity was assigned as MZ if at least nine STRPs were identical in both twins.

Psychiatric Assessment

CD symptoms were measured by administration of the Diagnostic Interview Schedule for Children — IV (DISC-IV; Shaffer et al., 1997), a structured interview which assesses DSM-IV symptoms. A score of one was given for each CD symptom presented by the subject throughout his or her lifetime, and a lifetime symptom count for CD was calculated by adding up each of these endorsed behaviors.

Drug dependence was assessed using the Composite International Diagnostic Interview — Substance Abuse Module (CIDI-SAM; Cottler et al., 1989), a structured diagnostic interview which assesses the frequency of consumption of tobacco, alcohol, marijuana, cocaine, amphetamines, sedatives, inhalants, hallucinogens, opiates and phencyclidine (PCP). We follow Stallings et al. (2003) in focusing on nonspecific substance dependence. This focus reflects the observation that, especially in adolescence, use of multiple substances, rather than specializing in any single substance, is typical, especially among those with substance dependence (Glantz & Leshner, 2000; Johnston et al., 2001; Young et al., 2002). Moreover, there is increasing empirical evidence that, perhaps especially in adolescence, genetic influences are responsible for the comorbidity across substances and even across substance use and other externalizing problems (Kendler et al., 2003; Krueger et al., 2002; Slutske et al., 1998; Stallings et al., 2003, 2005; Young et al., 2000). Stallings et al. (2003) considered 10 alternative phenotypes that might quantify an adolescent's vulnerability to develop nonspecific substance dependence. Of these 10 alternatives, dependence vulnerability (DV) as defined here best met their criteria for a phenotype that would be clinically valid, familial, and heritable. Therefore, a polysubstance dependence vulnerability index was produced by taking a total count of dependence criteria endorsed across all classes of substances, ascertained from lifetime symptom counts of the individual substances, and dividing it by the number of substances used (use defined as using almost daily for at least 30 days for tobacco, having six or more drinks during one's lifetime for alcohol, and using more than five times during one's lifetime for illegal drugs; Corley et al., 2001; Stallings et al., 2003); those who had never used any substance more than five times were assigned a DV score of zero. These scores were age and sex corrected using standard regression procedures (i.e., residual scores were obtained).

Analyses

Basic analyses (means, standard deviations, Mann–Whitney *U* test, and correlations) were conducted using SPSS (SPSS Inc., 2004). Structural equation modeling was performed using the Mx program (Neale, 1997). A bivariate Cholesky Decomposition model was fit to covariance matrices using the maximum likelihood function in Mx (Neale, 1997). This model was used to estimate the magnitude

https://doi.org/10.1375/twin.9.1.38 Published online by Cambridge University Press

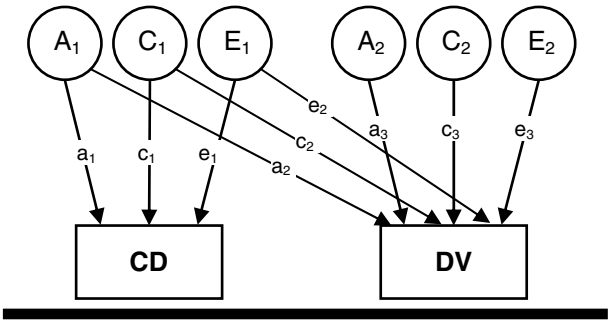

Figure 1

A Bivariate Cholesky Decomposition model decomposing the relative contribution of genetic, shared environmental and nonshared environmental influences on the variances and covariance of conduct disorder symptoms (CD) and dependence vulnerability (DV).

Variance components: A_1, genetic effects common to both disorders; A_2, genetic effects specific to DV. C_1, shared environmental effects common to both disorders; C_2, shared environmental effects specific to DV; E_2, nonshared environmental effects specific to DV. Path coefficients: a_1 = effect of A_1 on CD; a_2 = effect of A_1 on DV; a_3 = effect of A_2 on DV; c_1 = effect of C_1 on CD; c_2 = effect of C_1 on DV; c_3 = effect of C_2 on DV; e_1 = effect of E_1 on CD; e_2 = effect of E_1 on DV; e_3 = effect of E_2 on DV.

of effect of genetic, shared environmental and nonshared environmental influences on the phenotypic variance of both symptoms of CD and symptoms of DV. Furthermore, the Cholesky model enables us to decompose the genetic, shared environmental and nonshared environmental influences on DV (Neale & Cardon, 1992) into those in common with CD, as well as those specific to DV. Therefore, the full model tests the influence of nine pathways; a genetic influence on CD that also influences DV and a genetic contribution to DV that is not shared with CD, and similarly for shared and nonshared environmental influences. This model is represented in Figure 1. From this model it is possible to estimate the genetic correlation, shared environment correlation and nonshared environment correlation between CD and DV symptomatology.

The fit of all models was tested using both the χ^2 fit function, and Akaike's Information Criterion (AIC), calculated as χ^2 minus twice the degrees of freedom, to provide an index of both parsimony and goodness-of-fit (Akaike, 1987). A smaller, nonsignificant, χ^2, and a corresponding low (negative) AIC, indicates a good fitting model. To test the significance of each pathway, models in which each pathway in turn was constrained to zero were tested and a χ^2 difference test was applied.

Results

Table 1 shows the means and standard deviations for CD symptoms and DV split by age and sex. A Mann–Whitney *U* test on the total sample confirmed that males scored significantly higher than females for both CD symptoms ($z = -18.225$; $p < .001$) and DV ($z = -12.083$; $p < .001$). Both scores also correlated significantly with age (CD: $r = .085$, $p < .001$; male $r = .076$, $p < .001$; female $r = .109$, $p < .001$; DV: $r = .193$, $p < .001$; male $r = .175$, $p < .001$; female $r = .228$, $p < .001$). Both CD symptoms and DV scores were first regressed on age and age^2 separately within sex and the residual deviance scores were standardized. As the scores were skewed they were then log-transformed to approximate a normal distribution using the equation $(x) = \ln(2 + x)$, where x is the original raw score, (x) is the transformed score, and a constant of 2 is added to each score as some scores were negative.

MZ and DZ correlations both prior to and after splitting by sex are presented in Table 2. As the MZ correlations are higher than the DZ for both CD symptoms and DV they suggest a genetic influence on each.

The phenotypic correlation between CD symptoms and DV is .489. The cross-twin cross-trait correlations were higher for MZ twins than for DZ twins, indicating the importance of genetic influences on the association between the two.

The results of model fitting are presented in two ways. First, the models were fit to the full set of five separate zygosity and sex groups, and the results of this series of models are presented in Table 3. All the models in this series fit the data poorly. The source of the poor overall fit was that the variance of DV for opposite-sex DZ twins was significantly lower in both male and females. We explored a number of post hoc models, including sex-limited sibling interaction models, but could not provide an adequate rationale for this observation. Our current interpretation is that the result reflects sampling variation leading to an attenuated range of dependence symptoms in this group. Despite the poor overall fit, hierarchical nested χ^2 tests indicate that parameters of our models can be constrained to be equal across sex, but otherwise, only the shared environment specific to DV could be dropped. Because of the poor overall fit of the first series of models, together with the indication of homogeneity across sexes, we refit the series of models to data collapsed over sex groups, and results of this series of models are presented in Table 4. In this case the models provided a good fit to the data, $\chi^2_{(df)} = 8.804_{(11)}$; $p = .640$, as well as resulting in

Table 1

The Means and Standard Deviations for Conduct Disorder Symptoms and Dependence Vulnerability Split by Age and Sex

	Conduct Disorder symptoms		Dependence Vulnerability	
Age	Male	Female	Male	Female
13	1.14 (2.04)	0.47 (1.16)	0.25 (0.70)	0.09 (0.36)
14	1.77 (2.59)	0.72 (1.52)	0.55 (1.23)	0.27 (0.78)
15	2.76 (2.90)	0.98 (1.56)	1.09 (1.42)	0.45 (0.91)
16	2.76 (2.88)	1.06 (1.45)	1.14 (1.41)	0.61 (1.04)
17	2.39 (2.44)	1.01 (1.23)	1.15 (1.36)	0.70 (1.06)
18+	2.04 (2.23)	1.00 (1.13)	1.08 (1.24)	0.79 (1.09)

https://doi.org/10.1375/twin.9.1.38 Published online by Cambridge University Press

Table 2

Cross-Twin and Cross-Twin Cross-Trait Correlations for Conduct Disorder Symptoms and Dependence Vulnerability Split First by Zygosity and Then by Zygosity and Sex

	CD	DV	CD1–DV2
MZ	.562	.610	.392
DZ	.400	.387	.293
MZ male	.585	.576	.357
DZ male	.453	.423	.350
MZ female	.540	.640	.426
DZ female	.512	.359	.393
DZ opposite-sex	.291	.396	.329 (male CD, female DV)
			.129 (female CD, male DV)

almost identical parameter estimates for the best fitting model as the first series.

In both series, with the exception noted above, it was not possible to drop any of the genetic or environmental influences on either phenotype without significantly reducing the fit of the model. This indicates a significant influence of all parameters. The best fitting model was one which did not drop any of the correlation pathways. However, as noted, it was possible to drop the shared environment specific to DV, thereby constraining the shared environment correlation to 1, $\Delta\chi^2_{(df)} = 0.000_{(1)}$; $p = 1.000$, indicating that all the shared environmental influences are common to both phenotypes.

The genetic correlation was estimated to be .50, explaining approximately 39% of the phenotypic covariance between the two. Shared environment influences had a correlation of 1.0 and contributed the greatest proportion (43%) to the phenotypic covariance. Nonshared environmental influences correlated .22 and contributed 18% to the phenotypic covariance.

Discussion

A number of studies have identified a significant correlation between the occurrence of conduct and substance use disorders, as well as identifying the possibility of common etiology for the two. The current study examined the etiology of the comorbidity between symptom counts for CD and the vulnerability to develop dependence on drugs of abuse, including alcohol and tobacco, in a large population-based twin study.

Bivariate model fitting provided parameter estimates for the univariate components of CD symptoms and DV, both of which were found to be moderately heritable, with heritability estimates of .35 (95% confidence intervals [CI]: 0.18–0.51) and 0.40 (95% CI: 0.24–0.55) respectively. Furthermore, our study also demonstrated a significant influence of the shared environment contributing towards the between twin pair covariances for both disorders (.22; 95% CI: 0.08–0.36) for CD symptoms and .19 (95% CI: 0.06–0.33) for DV. Nonshared environmental influences including error were found to account for 43% (95% CI: 0.37–0.49) of the variance of CD and 41% (95% CI: 0.36–0.47) of the variance of dependence vulnerability. These findings are consistent with other studies of similar phenotypes (Jacobson, Prescott et al., 2000; Tsuang et al., 1996).

There was a substantial and significant phenotypic correlation of approximately .49. Results of bivariate analysis showed that the two traits shared approximately half their genetic influence in common (rG = .50), as well as all their shared environmental influences (rC = 1.00) and a small but significant proportion of their nonshared environment influences (rE = .22). The contribution of genes, shared environment and nonshared environment to the phenotypic covariance were 39%, 43% and 18% respectively. Consequently, it appears that CD symptoms and DV share substantial genetic influences, and thus genes and shared environment contribute to the co-occurrence of the two traits, whereas disorder-specific genes and also nonshared environment influences account for the etiological differences and thus the development of two distinct disorders. Again, these findings are generally consistent with those from adult studies (Miles et al., 2002).

Age trends and sex differences for CD symptoms and DV in this sample have previously been noted (Young et al., 2002). These mean effects were regressed out of the data prior to analysis and age effects on genetic and environmental parameters were not tested for here. We tested for sex differences in etiology using this sample but found that genetic and environmental parameters could be constrained to be the same for males and females for both the individual disorders and for the covariation between the two disorders. Consequently, we conclude that the relative influences of genetic and environmental risk factors on CD symptoms, DV and their covariation are the same in male and female adolescents despite different degrees of manifestation in the observed variables. This is in contrast to the conclusions drawn from retrospective studies (Slutske et al., 1998).

There are a number of limitations of this study. The overall fit of models to the five zygosity and sex groups was poor. This occurred because the variance in the opposite-sex twin pairs for DV was significantly lower than those for the same-sex groups. A number of post hoc tests were conducted to explain this observation, such as fitting a sex-limited sibling imitation model. However, these did not improve the fit of the model. Despite this, nested models in which male and female parameter estimates were equated did not result in a worsening of the fit. Consequently, we conducted a second series of analyses in which matrices were collapsed across sex. This resulted in good fitting models and resulted in the same parameter estimates. Our conclusion is that the opposite-sex DZ twins have been subject to some unusual sampling variance for DV, resulting in an attenuated range of scores.

https://doi.org/10.1375/twin.9.1.38 Published online by Cambridge University Press

https://doi.org/10.1375/twin.9.1.38 Published online by Cambridge University Press

Table 3

Results of Fitting a Sex-Limitation Model

		Conduct Disorder symptoms			Dependence Vulnerability			Correlation			Fit					
		A	C	E	A	C	E	A	C	E	$\chi^2_{(df)}$	*p*	AIC	RMSEA	$\Delta\chi^2_{(df)}$	*p*
1.1	M	.27	.30	.43	.27	.29	.44	.18	1.00	.36						
		(.02–.49)	(.11–.51)	(.35–.53)	(.06–.57)	(.02–.48)	(.37–.53)	(.00–.76)	(.69–1.00)	(.25–.47)	$63.390_{(32)}$	.001	–.610	.072	—	—
	F	.46	.12	.42	.42	.20	.38	.64	1.00	.09						
		(.04–.61)	(.01–.51)	(.35–.50)	(.24–.58)	(.06–.35)	(.32–.46)	(.44–.82)	(.72–1.00)	(.00–.20)						
1.2#		.35	.22	.43	.39	.20	.41	.50	1.00	.22						
		(.18–.51)	(.08–.36)	(.38–.49)	(.23–.55)	(.06–.34)	(.36–.47)	(.25–.73)	(.67–1.00)	(.14–.30)	$78.308_{(41)}$	.001	–3.692	.070	$14.918_{(9)}$	.093
1.3*		.18	.35	.47	.22	.34	.44	[0]	1.00	.30						
		(.05–.29)	(.26–.45)	(.41–.53)	(.10–.32)	(.25–.44)	(.39–.50)		(.90–1.00)	(.23–.36)	$87.723_{(42)}$	< .001	3.723	.074	$9.415_{(1)}$	.002
1.4*		.53	.05	.42	.58	.02	.40	.73	[0]	.18						
		(.35–.63)	(.00–.12)	(.37–.49)	(.41–.65)	(.00–.16)	(.35–.46)	(.61–.93)		(.10–.27)	$90.084_{(42)}$	< .001	6.084	.082	$11.776_{(1)}$	< .001
1.5*		.39	.19	.42	.44	.16	.40	.81	.73	[0]						
		(.22–.57)	(.03–.33)	(.37–.48)	(.26–.61)	(.01–.32)	(.35–.46)	(.61–1.00)	(.10–1.00)		$103.223_{(42)}$	< .001	19.223	.084	$24.915_{(1)}$	< .001
1.6*		.17	.35	.48	.38	.21	.41	[1]	.59	.17						
		(.00–.45)	(.13–.50)	(.40–.55)	(.11–.58)	(.03–.42)	(.36–.49)		(.12–1.00)	(.08–.29)	$90.191_{(42)}$	.001	6.191	.079	$11.884_{(1)}$	.001
1.7*		**.35**	**.22**	**.43**	**.39**	**.20**	**.41**	**.50**	**[1]**	**.22**						
		(.18–.54)	**(.08–.36)**	**(.38–.49)**	**(.23–.55)**	**(.06–.34)**	**(.36–.47)**	**(.25–.67)**		**(.14–.30)**	**$78.307_{(42)}$**	**.001**	**–5.693**	**.068**	**$0.000_{(1)}$**	**1.000**

Note: 1.1: Full model with sex limitation; 1.2: full model with parameter estimates equated across sex; 1.3: sex-equated parameters testing the significance of the genetic correlation; 1.4: sex-equated parameters testing the significance of the shared environment correlation; 1.5: sex-equated parameters testing the significance of the nonshared environment correlation; 1.6: sex-equated parameters testing the significance of the dependence vulnerability (DV) specific genetic effects; 1.7: sex-equated parameters testing the significance of the DV specific shared environment effects; A: genetic contribution to the (co)variance; C: shared environment contribution to the (co)variance; E: nonshared environment contribution to the (co)variance; $\chi^2_{(df)}$ = chi-square; *df* = degrees of freedom; *p* = probability; AIC = Akaike's Information Criterion; RMSEA = Root Mean Square Error of Approximation; $\Delta\chi^2$ = chi-square difference between full and nested models.

#Fit compared to model 1.1; *fit compared to model 1.2; best fitting model is in bold; 95% confidence intervals in parentheses.

Table 4
Results of Fitting Models Constrained Across Sex

	Conduct Disorder symptoms			Dependence Vulnerability			Correlation			Fit				
	A	C	E	A	C	E	A	C	E	$\chi^2_{(df)}$	*p*	AIC	RMSEA	$\Delta\chi^2_{(df)}$	*p*
2.1	.35 (.18–.51)	.22 (.08–.36)	.43 (.37–.49)	.40 (.24–.55)	.19 (.06–.33)	.41 (.36–.47)	.50 (.26–.70)	1.00 (.71–1.00)	.22 (.13–.30)	$8.804_{(11)}$	.640	–13.196	.000	—	—
2.2*	.18 (.05–.29)	.36 (.27–.46)	.47 (.41–.53)	.23 (.11–.33)	.33 (.24–.43)	.44 (.39–.50)	[0]	1.00 (.91–1.00)	.29 (.22–.36)	$18.467_{(12)}$	.102	–5.533	.034	$9.663_{(1)}$	.002
2.3*	.53 (.36–.63)	.04 (.00–.18)	.42 (.36–.48)	.60 (.43–.65)	.00 (.00–.14)	.40 (.35–.46)	.71 (.61–.89)	[0]	.18 (.10–.27)	$20.605_{(12)}$	.056	–3.395	.031	$11.801_{(1)}$	< .001
2.4*	.40 (.22–.57)	.18 (.03–.33)	.42 (.37–.48)	.46 (.28–.61)	.14 (.01–.30)	.40 (.35–.45)	.76 (.60–1.00)	.82 (.18–1.00)	[0]	$33.167_{(12)}$	.001	9.167	.045	$24.363_{(1)}$	< .001
2.5*	.12 (.00–.41)	.39 (.16–.51)	.49 (.41–.56)	.42 (.15–.59)	.17 (.02–.39)	.41 (.35–.48)	[1]	.70 (.22–1.00)	.17 (.08–.31)	$21.912_{(12)}$	.039	–2.088	.043	$12.108_{(1)}$	< .001
2.6*	**.35 (.18–.51)**	**.22 (.08–.36)**	**.43 (.37–.49)**	**.40 (.24–.55)**	**.19 (.06–.33)**	**.41 (.36–.47)**	**.50 (.26–.67)**	**[1]**	**.22 (.13–.30)**	$\mathbf{8.804_{(12)}}$	**.720**	**–15.196**	**.000**	$\mathbf{0.000_{(1)}}$	**1.000**

Note: 2.1: Full model; 2.2: testing the significance of the genetic correlation; 2.3: testing the significance of the shared environment correlation; 2.4: testing the significance of the nonshared environment correlation; 2.5: testing the significance of the DV specific genetic effects; 2.6: testing the significance of the dependence vulnerability (DV) specific shared environment effects; A: genetic contribution to the (co)variance; C: shared environment contribution to the (co)variance; E: nonshared environment contribution to the (co)variance; $\chi^2_{(df)}$ = chi-square; *df* = degrees of freedom; *p* = probability; AIC = Akaike's Information Criterion; RMSEA = Root Mean Square Error of Approximation; $\Delta\chi^2$ = chi-square difference between full and nested models.
*Fit compared to model 2.1; best fitting model is in bold; 95% confidence intervals in parentheses.

Another possible limitation of this study is that it was conducted using a population-based sample, and thus the findings may not be applicable to those from clinical samples who will likely display greater prevalence of both disorders, and may be subject to unusual combinations of genetic and environmental risks. However, it has also been suggested that the use of population-based samples may be advantageous in the determination of causes of comorbidity (Caron & Rutter, 1991). Moreover, Stallings et al. (2005) report evidence for pleiotropic genetic influences on CD symptoms and DV in clinical probands and their siblings, indicating the possibility of a specific antisocial drug dependence phenotype.

Despite these limitations our study finds evidence in favor of a substantial genetic influence on the comorbidity of CD and DV symptomatology in adolescents. Another conclusion from this study is that 43% of the phenotypic covariance is attributable to common environment effects. This indicates that some of the shared environmental risk factors that have previously been associated with conduct problems in adolescents may also contribute to the development of DV and, consequently, account for the co-occurrence of the two disorders. This conclusion reflects previous literature, which has identified similar putative environmental risk factors for the development of both disorders (Guo et al., 2002; Hawkins et al., 1992; Rutter et al., 1998).

In summary, this study provides further evidence that both CD and dependence vulnerability in adolescence are heritable and that the comorbidity between these traits in adolescence is due, in part, to shared genetic influences, and shared environment and nonshared environment influences also contribute. Furthermore, the etiology of this comorbidity is similar in males and females.

Acknowledgments

This work was supported by National Institute on Drug Abuse grants DA-011015 and DA-012845, National Institute of Mental Health grant MH-43899, and National Institute of Child Health and Human Development grant HD-010333.

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