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Genetic and Environmental Influences on the Familial Transmission of Externalizing Disorders in Adoptive and Twin Offspring

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Abstract

Context—Twin-family studies have shown that parent-child resemblance on substance use disorders and antisocial behavior can be accounted for by the transmission of a general liability to a spectrum of externalizing disorders. Most studies, however, include only biological parents and offspring, which confound genetic and environmental transmission effects.

Objective—Examine the family transmission of externalizing disorders among both adoptive (who are genetically unrelated) and biological relatives to better distinguish genetic and environmental mechanisms of transmission.

Design—Family study design wherein each family included the mother, father, and two offspring, including monozygotic twin, dizygotic twin, non-twin biological and adoptive offspring. Structural equation modeling was used to estimate family transmission effects and their genetic and environmental influences.

Setting—Participants were recruited from the community and assessed at a university laboratory.

Participants—1590 families with biological offspring and 409 families with adoptive offspring. Offspring participants were young adults (mean age = 26.2 years).

Main outcome measures—Symptom counts of conduct disorder, adult antisocial behavior, and alcohol, nicotine, and drug dependence.

Results—There was a medium effect for the transmission of the general externalizing liability for biological parents ($r = 0.27$ - 0.30), but not for adoptive parents ($r = 0.03$ - 0.07). In contrast, adoptive siblings exhibited significant similarity on the general externalizing liability ($r = 0.21$). Biometric analyses revealed the general externalizing liability was highly heritable ($a^2 = 0.61$), but also exhibited significant shared environmental influences ($c^2 = 0.20$).

Conclusions—Parent-child resemblance for substance use disorders and antisocial behavior is primarily due to the genetic transmission of a general liability to a spectrum of externalizing disorders. Including adoptive siblings revealed a greater role of shared environmental influences on the general externalizing liability than previously detected in twin studies, and indicates sibling

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rather than parent-child similarity indexes important environmental risk factors for externalizing disorders.

Determining whether a disorder is transmitted within families—and if so, the genetic and environmental mechanisms of transmission—is fundamental to understanding its etiology, as a familial disorder suggests specific theoretical models by which to investigate risk mechanisms. Antisocial behavior and substance use disorders, collectively referred to as *externalizing* disorders, exhibit substantial familial transmission¹⁻³. Externalizing disorders not only run in families, but also tend to run together in the same individual; that is, they exhibit high levels of comorbidity or co-occurrence⁴. As such, one theory is that rather than risk for specific disorders, what is transmitted from parents to offspring is a broad liability that increases risk for a spectrum of externalizing disorders⁵.

Consistent with this model, we previously showed that the similarity between parents and their 17-year old twin offspring for child and adult antisocial behavior, alcohol dependence, and drug dependence could be accounted for by the transmission of a general externalizing factor ($r = 0.30$)⁵. There were, however, disorder specific effects across siblings, that is, effects that contributed to sibling similarity for a specific disorder over and above the general externalizing factor. Results from twin studies indicated that genetic influences accounted for most familial transmission, as the heritability of the externalizing factor in late adolescence was estimated at 0.80-0.85 with no shared environmental influences (environmental influences that contribute to similarity among relatives)⁵⁻⁸.

We extended this finding to childhood manifestations of the externalizing liability by examining the link between substance use disorders and antisocial behavior in parents and disruptive behavior disorders (attention deficit hyperactivity disorder, conduct disorder, oppositional defiant disorder) in their pre-adolescent offspring⁹. Again, we found that the transmission of a general externalizing factor could account for the similarity between adult externalizing disorders in parents and childhood disruptive behavior disorders in their 11-year old twin offspring ($r = 0.23$). Disorder specific effects were again detected for sibling—but not parent-child—similarity. The childhood externalizing factor was also highly familial, exhibiting strong genetic (0.65) and significant shared environmental influences (0.23).

Adoption studies can also help to delineate the genetic and environmental influences on the family transmission of externalizing disorders. The strength of the adoption design is the power to detect shared environmental effects; that is, because family members are genetically unrelated, any similarity must be due to environmental influences. Adoption studies have made fundamental contributions to understanding genetic and environmental risk for externalizing disorders by showing that adoptees tend to more closely resemble their biological parents than their adoptive parents¹⁰⁻¹². However, few adoption studies have been large enough to provide sufficient statistical power to adequately parse general versus specific transmission effects. Also, adoption studies have often focused on parent-child similarity (vertical transmission), rather than similarity among siblings (horizontal transmission). The few that have, however, found moderate similarity among adoptive siblings ($r = 0.26$) for adolescent substance use¹³⁻¹⁵, suggesting that sibling rather than parent influences may be an important environmental risk factor for externalizing disorders.

We sought to further our understanding of the family transmission of externalizing disorders by combining the strengths of the twin (high power to detect genetic influences) and adoption (high power to detect shared environmental influences) family designs. We were particularly interested in the extent to which the inclusion of adoptive families affected findings for (1) general versus specific transmission of externalizing disorders, and (2) estimates of the genetic and environmental influences on general and specific transmission

effects. Based on previous findings¹⁰⁻¹⁴, we anticipated little similarity between adoptive parents and offspring, but small to medium effects for the similarity between adoptive siblings, indicating a greater role of shared environmental influences than previously found in twin studies^{5-7,16-19}. We also included nicotine dependence, a disorder that is part of the externalizing spectrum in late adolescence and young adulthood^{15,20,21}, but one for which we had not examined the general versus specific nature of familial transmission. Also, unlike our previous studies that examined family transmission when the offspring were children or adolescents^{5,9}, the offspring in this study were adults, being on average 26 years old. As such, the vast majority of offspring had reached or passed the period of greatest risk for antisocial behavior and substance use disorders²²⁻²⁴, allowing us to account for most of the lifetime risk and familial resemblance for externalizing disorders.

Method

Additional details of sample recruitment, demographic characteristics, and measures is provided in the online supplemental material (eMethod). All participants provided informed consent and all study protocols were reviewed by an institutional review board.

Sample

Participants were members of the longitudinal Minnesota Twin and Family Study (MTFS)²⁵ or Sibling Interaction and Behavior Study (SIBS)^{25,26}, both of which utilized a family design that included the mother, father, and two siblings. Offspring from the MTFS were either monozygotic (MZ) or dizygotic (DZ) twins, while the SIBS included non-twin biological or adoptive offspring. The mean age of placement for the adoptive offspring was 4.7 months (SD = 3.4). The total sample included 1999 families: 902 families with MZ twins, 480 families with DZ twins, 208 families with two non-twin biological offspring, 124 families with one biological and one adoptive offspring, and 285 families with two adoptive offspring. All twin pairs were same-sex; non-twin biological and adoptive siblings were a mix of same-sex (61%) and opposite-sex (39%). The mean age was 44.0 years (SD = 6.2) for mothers (n = 1993), 45.4 years (SD = 8.2) for fathers (n = 1790), and 26.2 years (SD = 3.8, range 16.2 to 32.4) for offspring (n = 3877; 53.3% female) at their most recent assessment. Over 90% of the combined MTFS-SIBS sample reported European American ancestry, though a large number of the adoptive offspring reported Korean ancestry (n = 433).

Assessment

Externalizing disorders were assessed via structured interviews administered by trained staff. DSM-III-R criteria were used in all analyses as it was assessed at intake and all follow-up assessments. Symptoms of alcohol, nicotine, and illicit drug abuse and dependence were assessed using the Substance Abuse Module of the World Health Organization's Composite International Diagnostic Interview²⁷. Conduct disorder and adult antisocial behavior (the adult criteria for antisocial personality disorder) were assessed using a structured interview comparable to the Structured Clinical Interview for DSM-III-R Axis II. Rates of lifetime diagnoses for the full sample were: 21.3% alcohol dependence and 11.6% drug dependence, 31.0% nicotine dependence, 10.8% conduct disorder, and 7.5% adult antisocial behavior. Externalizing disorders exhibit age and sex effects and even secular trends for drug use that might affect comparisons of familial similarity^{28,29}. Therefore, all symptom counts were regressed on age, age², sex, the interactions between the age and sex variables, and whether the participant was a member of the parent or offspring generation. The mean correlation among the symptom count variables was 0.42 (range 0.30 to 0.55).

Statistical Analysis

Structural equation modeling was used to estimate the general and specific transmission effects for externalizing disorders. The general liability to externalizing disorders was operationalized as a latent externalizing factor, defined by the covariance among symptoms of conduct disorder, adult antisocial behavior, and alcohol, nicotine, and drug dependence. General transmission effects were operationalized as the correlations among the latent externalizing phenotypes between parents and offspring (vertical transmission) and between siblings (horizontal transmission). We estimated disorder specific transmission effects by allowing the residual variance of the parent symptom counts (i.e., the variance of each disorder that was unrelated to the general externalizing liability) to covary with the residual variance of the corresponding offspring symptom counts (e.g., residual variance of mother alcohol dependence was allowed to correlate with the residual variance of offspring alcohol dependence). The same procedure was used to estimate specific transmission effects between siblings.

Models of family transmission were fit using Mplus 5.0. We used the MLR estimator that adjusts for the non-independence of the family-level data and the non-normal symptom count variables, and accommodates missing data. Model fit was evaluated using the mean-adjusted χ^2 ,³⁰ the Bayesian information criterion (BIC; $\chi^2 - df[\ln N]$)³¹ and the root mean-square error of approximation (RMSEA)³². The mean adjusted χ^2 provides an estimate of overall fit for non-normal data. The BIC balances overall fit with parsimony such that model fit is penalized for the inclusion of unnecessary parameters. Negative BIC values indicate a good fit with lower (more negative) values indicative of better fit. The RMSEA provides an estimate of discrepancy in model fit per degree of freedom; values less than 0.080 and 0.050 indicate an adequate fit and very good fit, respectively. Nested models can be compared by conducting a likelihood ratio test calculated as the difference in the χ^2 values and degrees of freedom between the two models. Such tests, however, are overpowered for large samples, especially with non-normal data. Therefore, we used differences in BIC values to compare the relative goodness of fit of competing models given its greater weight to model parsimony. A difference in BIC of 0-2 is considered weak evidence of support for the model with the lower BIC value, a difference of 2-6 is considered positive evidence, a difference of 6-10 is considered strong evidence, and a difference greater than 10 is considered very strong evidence³¹.

We also fit biometric models to obtain estimates of the genetic and environmental influences on the general and specific transmission effects using the offspring data. These models conceptualize the variance of phenotypes as attributable to additive genetic (A), shared environmental (C), and nonshared environmental (E) influences. Additive genetic influences refer to the cumulative effects of genes summed across loci, and are inferred if the correlation between MZ twins is greater than the correlation between DZ twin and non-twin biological siblings, which in turn should be greater than the correlation between adoptive siblings. Shared environmental influences refer to environmental influences that contribute to similarity among relatives. As adoptive siblings have no genes in common, the correlation between adoptive siblings provides a direct estimate of shared environmental influences. Shared environmental influences are also inferred if the correlation between DZ twins and non-twin biological siblings is greater than one-half the correlation between MZ twins. Nonshared environmental influences refer to environmental influences that contribute to differences among relatives, including measurement error. MZ twin correlations less than 1.0 are evidence of nonshared environmental influences. Biometric models were fit using the computer program Mx³³ with a full information maximum likelihood estimator that accommodates missing data. Symptom counts were $\log(x+1)$ transformed to reduce skew and kurtosis.

Results

General and Specific Transmission of Externalizing Disorders

First, a general transmission only model was fit to the five family types. To simplify the model, the general transmission effects across siblings were constrained to be the same for the families with (1) DZ twins and non-twin biological offspring, and (2) families with two adoptive children and families with both an adoptive and biological child. This general transmission model provided a good fit to the data, with values for the fit indices listed in Table 1. This model served as the baseline model for all subsequent models that incorporated disorder specific transmission effects.

Next, we tested for any disorder specific transmission effects by allowing the residual variance of each parental symptom count to covary with residual variances of the corresponding offspring symptom count variable. Parent-child transmission effects were allowed to vary for biological and adoptive parent-child relationships. To maximize power to detect effects, we tested for one disorder at a time (2 *df* test). None of the father-child disorder specific effects resulted in a lower BIC value, the criterion by which we used to judge a significant improvement in model fit. For mother-child disorder specific effects, only the effect for nicotine dependence resulted in a lower BIC value. The effect was small, but statistically significant for biological mothers ($r = 0.11$, 95% Confidence Interval [CI] = 0.06-0.17), but not adoptive mothers ($r = 0.03$, 95% CI = -0.06-0.13).

We also tested for disorder specific transmission effects across siblings, allowing these effects to vary for MZ twins, DZ twins and non-twin biological siblings, and adoptive siblings. Including specific transmission effects across siblings resulted in a lower BIC value for each disorder. The specific effect for adult antisocial behavior, however, was no longer significant when the other disorder specific effects were included in the model; therefore, this effect was dropped. Specific transmission effects for siblings were medium to large for MZ twins (0.32 to 0.58), small to medium for DZ twins and non-twin biological siblings (0.08 to 0.36), and mostly non-significant for adoptive siblings (-0.05 to 0.13). The final best fitting model is depicted in Figure 1.

The correlation between the mother and father latent externalizing factor was medium to large ($r = 0.45$, 95% CI = 0.35-0.55), indicative of assortative mating. For the general transmission effects, the parent-child correlations for the latent externalizing factors were medium for biological mothers ($r = 0.27$, 95% CI = 0.20-0.34) and fathers ($r = 0.30$, 95% CI = 0.23-0.38), but were not significantly different from zero for adoptive mothers ($r = 0.07$, 95% CI = -0.01-0.15) and fathers ($r = 0.03$, 95% CI = -0.07-0.12). Families that included both a biological and adoptive offspring provided a particularly elegant demonstration of this pattern of family transmission. The general transmission effects were significant for biological children (mother $r = 0.26$, 95% CI = 0.14-0.37; father $r = 0.35$, 95% CI = 0.25-0.46), but not for adoptive children (mother $r = 0.06$, 95% CI = -0.02-0.14; father $r = 0.02$, 95% CI = -0.07-0.11). These findings suggest that parent-child resemblance on externalizing disorders is almost entirely attributable to genetic transmission. We also tested whether the general transmission effects differed by mother and father. Equating the mother and father general transmission effects did not result in a higher BIC value (see Table 1) indicating the correlations were not significantly different from each other.

The correlation between the two siblings on the latent externalizing factor was large for MZ twins ($r = 0.79$, 95% CI = 0.73-0.84), while the correlation was medium to large for DZ twins and non-twin biological siblings ($r = 0.45$, 95% CI = 0.36-0.55), and smaller but statistically significant for adoptive siblings ($r = 0.21$, 95% CI = 0.09-0.33). The adoptive

sibling correlation is a direct estimate of shared environmental influences, indicating that sibling similarity was due to a combination of genetic and shared environmental influences.

Genetic and Environmental Influences on the General Externalizing Liability and Disorder Specific Liabilities

Next, we fit standard biometric models to derive more precise estimates of the genetic and environmental influences on each externalizing disorder and the general externalizing liability. Table 2 provides the sibling correlations and univariate ACE parameter estimates for each externalizing disorder. Each externalizing disorder exhibited moderate heritability (0.35 to 0.49) and nonshared environmental influences (0.38 to 0.48). Each disorder except alcohol dependence also exhibited significant shared environmental influences (0.09 to 0.26).

Next, we fit a biometric factor model to estimate the genetic and environmental influences on the general externalizing liability, as well as disorder specific genetic and environmental liabilities (Figure 2). The general externalizing factor was highly heritable ($a^2 = 0.61$, 95% CI = 0.50-0.71), but also exhibited significant shared environmental influences ($c^2 = 0.20$, 95% CI = 0.10-0.29), with the remaining variance attributable to non-shared environmental influences ($e^2 = 0.19$, 95% CI = 0.16-0.23).

In terms of disorder specific liabilities, each disorder exhibited specific genetic effects (drug dependence $a^2 = 0.27$, 95% CI = 0.17-0.32; conduct disorder $a^2 = 0.24$, 95% CI = 0.15-0.33; nicotine dependence $a^2 = 0.21$, 95% CI = 0.13-0.28; alcohol dependence $a^2 = 0.16$, 95% CI = 0.09-0.20), though the effect for adult antisocial behavior was only marginally significant ($a^2 = 0.07$, 95% CI = 0.003-0.14). Only conduct disorder exhibited a specific shared environmental effect ($c^2 = 0.19$, 95% CI = 0.11-0.26). Each disorder also exhibited specific nonshared environmental influences: adult antisocial behavior $e^2 = 0.30$, 95% CI = 0.27-0.34; conduct disorder $e^2 = 0.39$, 95% CI = 0.35-0.43; alcohol dependence $e^2 = 0.38$, 95% CI = 0.35-0.42; drug dependence $e^2 = 0.40$, 95% CI = 0.36-0.44; nicotine dependence $e^2 = 0.32$, 95% CI = 0.29-0.36).

Comment

Previously, we showed that most parent-child similarity on substance use disorders and antisocial behavior can be attributed to the transmission of a general liability to a spectrum of externalizing disorders^{5,9}. Here, we extended this finding by leveraging the strengths of the twin and adoptive family designs in a single analysis, showing a medium effect for this general transmission among biological parents and offspring, but a near zero effect for adoptive parents and offspring. Especially persuasive was that this pattern was found in families that included both biological and adoptive offspring. That is, even among children who shared the same rearing environment, biological offspring exhibited greater similarity than adoptive offspring to the same rearing parents. This indicates that—for the most part—the mechanism of parent to child transmission is not only general, but also genetic in nature. That is, rather than disorder-specific risk, what parents pass on to their (biological) offspring is a non-specific, genetic liability to multiple externalizing disorders.

In contrast to adoptive parents and offspring, we detected significant similarity between adoptive siblings on the general externalizing liability, which was solely attributable to environmental influences. This was reflected in the results of the biometric factor model, as we detected significant shared environmental influences on the general externalizing factor, more so than in previous twin studies^{6,7}. Previous MTFs studies also identified shared environmental influences on a general externalizing factor in childhood⁹ and middle adolescence²⁰, but this is the first to do so in adulthood. Though the mechanism of these

shared environmental effects is not yet known, it seems sibling rather than parent-child similarity indexes shared environmental risk for multiple externalizing disorders.

We did detect a specific transmission effect for maternal nicotine dependence. The effect was small, however, and may be a false positive. The slightly stronger effect for biological mothers relative to adoptive mothers suggests either a specific genetic effect or a maternal smoking effect on fetal development. Regarding the former, a strong association was detected between the nicotinic receptor gene *CHRNA3* and cigarettes smoked per day in a large genome wide association study, but only among current smokers³⁴. This suggests the *CHRNA3* gene confers a specific genetic risk for nicotine addiction that is likely unrelated to externalizing, which might be evident in the specific effect we detected.

Disorder-specific transmission effects appear to be robust for sibling-to-sibling transmission. To some extent, this could be attributable to differences in assessment, that is, siblings are more similar in age, are assessed on multiple occasions, and are more actively engaging in externalizing behaviors relative to parents who were assessed for lifetime symptoms on a single occasion in middle adulthood. Conduct disorder was the most distinctive of the externalizing phenotypes exhibiting specific genetic and shared environmental influences. This distinctiveness is likely due to being a childhood disorder with multiple contributing etiological factors. That is, conduct disorder is a risk factor for almost all forms of adult psychopathology³⁵, suggesting that only a portion of conduct disorder cases are attributable to the general externalizing liability. The disorder specific effects for the substance use disorders were primarily attributable to genetic factors, suggesting genes that confer increased risk for addiction to specific substances. Very little of the variance in adult antisocial behavior was attributable to specific genetic or shared environmental effects, indicating it is the disorder most strongly determined by the general externalizing liability.

Some limitations should be noted. First, the sample had limited racial and ethnic diversity, which constrains generalizability to other populations. A second limitation regards restriction of range among adoptive families. Specifically, relative to biological families, mean-levels of externalizing symptoms were lower among the adoptive parents, but not among the adoptive offspring²⁶. However, a thorough analysis of restriction of range in the SIBS sample²⁶ showed that such effects were relatively small and would have little impact on our results. Third, our measure of drug dependence assessed illicit drug problems in general, when there are likely different genetic influences for different drug classes. Fourth, there was a notable age range among the offspring participants, leaving open the possibility that the results could differ slightly for different ages. Additionally, because data collection of the longitudinal data spanned two decades, there may be small cohort effects within the offspring sample. Finally, we used standard biometric models rather than more complex extended twin-family models³⁶ (though they are unlikely to yield substantively different results) or models that incorporate the presence of gene x environment interactions that seem to be present for externalizing disorders³⁷.

To conclude, we again demonstrated the primacy of general rather than disorder-specific transmission from parents to offspring for externalizing disorders, and leveraged the adoption data to strengthen the case for genetic transmission. We also detected a greater role for shared environmental influences on the general externalizing liability in adulthood than previous twin studies, and were able to link these environmental influences to sibling rather than parent similarity. An important future direction will be to identify more specific mechanisms of these shared environmental and their interplay with genetic risk in the development of externalizing disorders.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1.

EXT = Externalizing factor; AAB = adult antisocial behavior; CD = conduct disorder; ALD = alcohol dependence; NCD = nicotine dependence; DRG = drug dependence. The three numbers listed above the paths linking the specific disorders across sibling 1 and 2 refer to the effects for MZ twins, DZ twins and biological siblings, and adoptive siblings, respectively. All path coefficients are standardized and the weighted mean across the family types. All paths greater than 0.10 are significant at $p < 0.01$. The latent externalizing variables represent the general liability factors that contribute to each disorder. The smaller circular variables associated with each disorder are the residual variances, and represent all liability factors that are specific to each disorder and unrelated to the general externalizing liability. The double-headed arrows linking the mother and father externalizing factors to the offspring (sibling) externalizing factors represent the general transmission effects. The double-headed arrows linking the sibling 1 and sibling 2 externalizing factors indexes sibling similarity for the general externalizing liability, and was allowed to vary across MZ twins, DZ twins and non-twin biological siblings, and adoptive siblings. The double-headed arrows linking the residual variances for conduct disorder and alcohol, nicotine, and drug dependence across siblings represent disorder specific liability factors that increase sibling similarity, but that are independent of the general externalizing factor. Correlations among the residual variances are from left to right for MZ twins, DZ twins and non-twin biological siblings, and adoptive siblings. To reduce the figure's complexity, we did not depict a small but statistically significant specific effect for maternal nicotine dependence (biological mothers $r = 0.11$, 95% CI = 0.06-0.17; adoptive mothers $r = 0.03$). If included, this would be

a double-headed arrow linking the residual variance of maternal nicotine dependence to residual variance of sibling 1 and sibling 2 nicotine dependence.

Figure 2.

All path coefficients are standardized and 95% confidence intervals are shown in parentheses beneath each coefficient. All coefficients that do not include zero are significant. The percentage of variance accounted for by a given variable in another variable can be determined by squaring the path coefficient on the path connecting the first variable to the second variable. The sum of the squared loadings (effects from the general externalizing factor as well as the specific ACE loadings) equals 1.0. The total effect for A, C, and E can be calculated by summing the general effect (squared loading for a given disorder multiplied by the squared A, C, and E loadings on the externalizing factor) and the specific effect (squared A, C, or E specific effect on a given disorder). Using conduct disorder as an example, $a^2 = \text{general} (0.61^2 \times 0.50^2) + \text{specific} (0.49^2) = 0.33$; $c^2 = \text{general} (0.45^2 \times 0.50^2) + \text{specific} (0.43^2) = 0.24$; $e^2 = \text{general} (0.44^2 \times 0.50^2) + \text{specific} (0.62^2) = 0.43$. A = additive genetic; C = shared environment; E = nonshared environment; EXT = Externalizing factor; AAB = adult antisocial behavior; CD = conduct disorder; ALD = alcohol dependence; NCD = nicotine dependence; DRG = drug dependence.

TABLE 1
Indexes of Fit for Alternative Models for Family Transmission of Externalizing Disorders

Model	χ^2	df	RMSEA	BIC	χ^2	df
General transmission only	2295.86	974	.058	-5106.93	--	--
Specific transmission effects						
Father						
Conduct disorder	2294.32	972	.058	-5093.27	1.54	2
Adult antisocial behavior	2288.44	972	.058	-5099.15	7.42	2
Alcohol dependence	2289.14	972	.058	-5098.45	6.72	2
Nicotine dependence	2281.19	972	.058	-5106.40	14.67*	2
Drug dependence	2280.98	972	.058	-5106.61	14.88*	2
Mother						
Conduct disorder	2288.96	972	.058	-5098.63	6.90	2
Adult antisocial behavior	2293.29	972	.058	-5094.30	2.57	2
Alcohol dependence	2293.08	972	.058	-5094.51	2.78	2
Nicotine dependence	2275.15	972	.058	-5112.44	20.71*	2
Drug dependence	2284.34	972	.058	-5103.25	11.52	2
Sibling						
Conduct disorder	1976.77	971	.051	-5403.22	319.09*	3
Adult antisocial behavior	2249.86	971	.057	-5130.13	46.00*	3
Alcohol dependence	2231.38	971	.057	-5148.62	64.48*	3
Nicotine dependence	2122.25	971	.054	-5257.74	173.61*	3
Drug dependence	2221.41	971	.057	-5158.58	74.45*	3
Best fitting model						
General transmission from parent to offspring, general transmission across siblings, specific effect for maternal nicotine dependence, cross-sibling specific effects for conduct disorder and alcohol, nicotine, and drug dependence	1648.22	960	.042	-5648.16	647.64*	14
Equate maternal and paternal general transmission	1662.45	962	.043	-5649.14	633.41*	12

Note. df = degrees of freedom; BIC = Bayesian information criterion; RMSEA = Root mean square error of approximation. Lower values for fit indices are indicative of better fit. Lower (more negative) BIC values were used to select the best fitting model.

* 2 significant at $p < 0.001$.

TABLE 2

Sibling Correlations and Univariate Parameter Estimates for Additive Genetic (A), Shared Environmental (C), and Nonshared Environmental (E) Influences (95% Confidence Interval) on Externalizing Disorders.

Variable	MZ Twin Pairs (n = 902)	DZ Twin Pairs (n = 480)	Non-twin Bio Sib Pairs (n = 208)	Adoptive Sib Pairs (n = 409)	A	C	E
Adult antisocial behavior	.58 (.54, .62)	.36 (.28, .44)	.46 (.33, .57)	.22 (.12, .32)	.44 (.35, .52)	.19 (.11, .25)	.38 (.34, .42)
Conduct disorder	.62 (.57, .65)	.49 (.41, .55)	.32 (.18, .44)	.25 (.16, .35)	.35 (.26, .44)	.26 (.19, .34)	.39 (.35, .43)
Alcohol dependence	.51 (.45, .55)	.28 (.20, .36)	.29 (.15, .41)	.06 (-.04, .17)	.47 (.37, .56)	.05 (.00, .13)	.48 (.44, .53)
Drug dependence	.55 (.50, .59)	.32 (.24, .40)	.37 (.24, .48)	.12 (.02, .22)	.49 (.40, .58)	.09 (.02, .16)	.41 (.37, .46)
Nicotine dependence	.61 (.57, .65)	.35 (.27, .43)	.33 (.20, .45)	.07 (-.03, .17)	.49 (.38, .59)	.10 (.00, .19)	.42 (.38, .46)