ORIGINAL ARTICLE

Intergenerational Transmission of Childhood Conduct Problems

A Children of Twins Study

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Context: The familial nature of childhood conduct problems has been well documented, but few genetically informed studies have explicitly explored the processes through which parental conduct problems influence an offspring's behavior problems.

Objective: To delineate the genetic and environmental processes underlying the intergenerational transmission of childhood conduct problems.

Design: We used hierarchical linear models to analyze data from a Children of Twins Study, a quasiexperimental design, to explore the extent to which genetic factors common to both generations, unmeasured environmental factors that are shared by twins, or measured characteristics of both parents confound the intergenerational association.

Setting: Participants were recruited from the community and completed a semistructured diagnostic telephone interview.

Participants: The research used a high-risk sample of twins, their spouses, and their young adult offspring (n=2554) from 889 twin families in the Australian Twin Registry, but the analyses used sample weights to produce parameter estimates for the community-based volunteer sample of twins.

Main Outcome Measure: Number of conduct disorder symptoms.

Results: The magnitude of the intergenerational transmission was significant for all offspring, though it was stronger for males (effect size [Cohen d]=0.21; 95% confidence interval, 0.15-0.17) than females (d=0.09; 95% confidence interval, 0.05-0.14). The use of the Children of Twins design and measured covariates indicated that the intergenerational transmission of conduct problems for male offspring was largely mediated by environmental variables specifically related to parental conduct disorder (d=0.13; 95% confidence interval, 0.02-0.23). In contrast, the intergenerational transmission of conduct problems was not because of environmentally mediated causal processes for female offspring (d=−0.09; 95% confidence interval, −0.20 to 0.03); a common genetic liability accounted for the intergenerational relations.

Conclusions: The mechanisms underlying the intergenerational transmission of conduct problems depend on the sex of the offspring. The results are consistent with an environmentally mediated causal role of parental conduct problems on behavior problems in males. Common genetic risk, however, confounds the entire intergenerational transmission in female offspring.

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THE FAMILIAL NATURE OF conduct problems has been well documented,[1] but the mechanisms through which parental and social factors cause conduct problems in offspring remain poorly understood.[1-3] Parental conduct problems may have a direct influence on an offspring's behavior problems through specific environmentally mediated processes, such as modeling, which has been the predominant historical view.[4] Parents with a history of conduct problems also put their offspring at greater risk of experiencing environmental risk factors, such as relationship violence[5] and childhood abuse,[6] which may mediate the intergenerational transmission.

The influence of parental conduct problems, however, could also be explained by confounds that account for psychopathology in both generations. Behavioral genetic studies have noted a prominent role of genetic factors in conduct problems[7,8] and broadly measured externalizing problems.[9] Therefore, genetic factors influencing parental conduct problems could be transmitted to their offspring and influence their behavior.[1,10] Environmental factors that affect both generations, such as socioeconomic status[11] and neighborhood characteristics,[12] could also con-

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found the association between parental and offspring conduct problems. Finally, the role of assortative mating, exposing offspring to 2 parents with greater externalizing problems, could further increase conduct problems in offspring.[13]

Etiological research needs to move beyond merely identifying risk factors for offspring conduct problems and test alternative hypotheses by using designs that can differentiate co-occurring genetic and environmental processes and account for unmeasured confounds.[1,14] Although studying genetic risk associated with parental conduct problems is difficult, especially with female offspring,[15] there are genetically informed approaches that can pull apart the underlying mechanisms,[14] particularly the Children of Twins (CoT) design.[16-19] The CoT design is an extension of the typical twin study that compares the offspring of dizygotic (DZ) and monozygotic (MZ) twins, an approach that may be particularly helpful in the study of conduct problems.[1] The design compares cousins who differ in their genetic and environmental risks, a model that can separate the intergenerational associations into 3 processes: environmental risk factors specific to the measured factor, genetic confounds, and environmental confounds that twins share.[16] The CoT design is best suited for studying intergenerational transmission of individual characteristics, rather than dyadic variables,[20] especially when both parents are included in the analyses.[21,22]

We used a high-risk sample of twins, their spouses, and their offspring drawn from a population-based registry in Australia.[8,23] The high-risk sample included a sufficient number of families with a history of conduct problems and related psychopathology, but sample weighting provided estimates of risk based on the entire Australian sample of twins. Previous analyses of the adult twin sample indicated no sex difference in the underlying biometric models for conduct disorder, a large genetic contribution, and a possible moderate role of shared environmental factors.[8] Using the CoT design with the sample therefore could account for genetic confounds and unmeasured environmental factors that make twins similar. Furthermore, statistically controlling for measured covariates of both parents, including conduct problems in the spouses of the twins, helped account for selection factors and assortative mating. Finally, the analyses explored sex differences in the offspring.[24,25] Thus, the analyses present a rigorous examination of the underlying etiological processes involved in the intergenerational transmission of conduct problems.

METHODS

PARTICIPANTS

Twins were drawn from the Australian Twin Registry (ATR), a volunteer registry. Three major health and behavioral surveys have been conducted on the twins in the ATR cohort. The assessment of the twins included a mailed survey during 1980-1982 (8183 individual twins; 69% response rate),[26] a second mailed questionnaire during 1988-1990 (6327 individual twins; 83% response rate),[27] and a telephone interview in 1992 (5889 individual twins; 86% response rate).[23] Relatives of the twins (n=14 421), including 3318 spouses, were assessed with a questionnaire in 1988,[28] and the spouses (n=3844) were reassessed with a telephone interview in 1994. The demographics of the sample are broadly consistent with the population, and tests for self-selection biases in the longitudinal sample have found few detectable differences in risk for abnormal behavior.[8,23]

Data were collected from the offspring of the adult twins (CoT Study) in 3 high-risk subgroups and a control group. The targeted subgroups included offspring of twins with (1) a history of alcohol dependence and/or conduct disorder, (2) a history of major depressive disorder, and (3) a history of divorce. If either twin met criteria for any of the high-risk subgroups, offspring from both twins were included in the study. The adults were contacted to give consent to contact their children. If consent was given, the staff contacted the offspring to complete a telephone interview and mailed survey. Of the twins selected to be in the high-risk and control groups, 85% consented and 82% (2554) of their possible offspring completed the telephone interview. The offspring were drawn from 1286 nuclear families nested under 889 twin families. The age of the offspring ranged from 14 to 39 years (mean, 25.1 years); 51% were female. At the time of the assessment, 28% were married, 4% were divorced or separated, and 68% had never been married. A subsample of the offspring (n=176) completed the interview a second time (mean of 1.1 years later) to establish the reliability of the instrument. The study was approved by the ethics or institutional review boards at the authors' institutions. Extensive details about the sample, including the proportions of twins and their offspring in the high-risk groups, can be found elsewhere.[22]

ASSESSMENT

Adult Twin and Spouse Characteristics

We assessed the adult twins and their spouses by using the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA).[29] The SSAGA is based on previously validated research interviews and demonstrates moderate to high interrater reliability,[29] particularly with conduct disorder.[8] The SSAGA was originally developed for studies in the United States, but it has been adapted for use in Australia.[30] Assessment of childhood conduct problems was based on the *DSM-III-R* diagnosis for conduct disorder. Report of the number of conduct problem symptoms before the age of 18 years was used so that the analyses could also explore subthreshold conduct problems.

A number of characteristics of the adult twins and their spouses were included in the analyses to determine whether the measured covariates confound the intergenerational transmission of childhood conduct problems. Lifetime symptoms for alcohol abuse and major depressive disorder were included. The current analyses also included lifetime measures of cigarette use and any illegal substance use. The twins' and spouses' history of suicidality was calculated based on a 5-point Likert scale.[31] Parents' age at the birth of their first child, their highest level of education (7-point Likert scale), and lifetime history of divorce/marital separation (separation of a relationship that had lasted >6 months) were also assessed.[22] Less than 1% of the twin values and less than 20% of the spouse values for each covariate were missing.

Spousal correlations (polychoric) for conduct problems were significant for female (r=0.13; SE=0.04; n=2417) and male (r=0.17; SE=0.03) twins, based on 5 multiply imputed data sets[32] that included variables reflecting the individual's sex, psychiatric history, and measured covariates. The magnitude of all of the spouse-spouse correlations (the association between the twins' spouses), calculated on the multiply imputed data sets

for the same-sex twins, were small and did not differ by genetic relatedness: MZ female (r=0.10; SE=0.06), MZ male (r=0.11; SE=0.09), DZ female (r=0.10; SE=0.06), and DZ male (r=0.10; SE=0.11) pairs. Thus, the results suggest minimal spousal similarity for childhood conduct problems, and the similarity is not due to genetic assortative mating.

Offspring Characteristics

The offspring were also assessed using the SSAGA, which included items related to conduct disorder as defined by the *DSM-III-R* and *DSM-IV*. The analyses presented in this article are based on the *DSM-III-R* criteria, but the same pattern of results was found when the *DSM-IV* criteria and *DSM-III-R* symptoms occurring before the age of 15 years were analyzed. Test-retest reliability after 1 year for the *DSM-III-R* symptom count for conduct disorder (r=0.80) in the offspring was high. The amount of contact among twin families, the sum of 4 items assessing the closeness of the offspring to their aunt or uncle's family, was calculated at the 3 levels of the CoT Study model: offspring, nuclear family (twin, his or her spouse, and their offspring), and twin family (both twins, their respective spouses, and all of their offspring).[22]

Sample Weights

The adult twin families in the CoT Study were selected from the ATR. Based on a standard procedure for weighting twin samples,[33] we used multiple logistic regression to identify predictors of whether a twin pair (ie, at least 1 co-twin) from the ATR participated in the CoT Study. Psychiatric and demographic characteristics of the ATR, assessed in the SSAGA study in 1992, were used as predictors.[34] **Table 1** includes the variables used to predict participation in the CoT sample, the frequency of the sociodemographic and psychiatric characteristics in the original ATR, the frequency in the unweighted CoT subsample, and the frequency in the weighted CoT subsample. Sample weights were calculated using the predicted probability of the pair participating in the CoT Study for both discordant and concordant pairs. The regression results indicated that birth cohort, male-male pairs, family alcohol use, family depression history, and self-reported psychiatric problems predicted participation in the high-risk CoT Study, findings that are consistent with the sampling strategy of the CoT Study. The comparison of the unweighted and weighted frequencies in the CoT subsample revealed that weighting the sample either removed or greatly reduced the bias of using the high-risk CoT sample.[35] Sensitivity analyses revealed that the residual differences in the frequency of psychiatric disorders were partially due to the differences in the birth cohort.[34] Given that the weighting of the sample reflected the original distribution in the ATR and the sampling was based on the twin-pair level,[36] the analyses in our article used the sample weights for each twin family.[33]

DATA ANALYSIS

MEAN COMPARISONS OF OFFSPRING OF ADULT TWINS

Exploring the mean number of conduct problems for offspring of twins discordant for conduct problems can provide an initial perspective on the underlying processes responsible for the intergenerational transmission.[16,17] The mean number of offspring symptoms for conduct disorder was calculated separately for adult twins who had no childhood conduct problems and adults who had any childhood conduct problems. For descriptive purposes, the level of adult conduct problems was based on 1 or more symptoms of conduct disorder. To establish the intergenerational relation, offspring in the entire sample were initially used, which compared unrelated offspring. The offspring of all discordant twins, regardless of zygosity, were subsequently compared, an approach that contrasts cousins differentially exposed to parents with a history of conduct problems. If the intergenerational relation was causal, the effects would be evident at all levels of analysis, particularly within twin families.[37] Conduct problems in offspring of discordant DZ twins were then explored. The comparison of the cousins in discordant DZ twin families controls for possible unmeasured confounds and other characteristics specific to twins.[22] The comparison of offspring of MZ twins discordant for conduct problems is the most rigorous test of causality in the CoT design, because it accounts for unmeasured environmental and genetic factors from the twin parents that may confound intergenerational associations.[16,17] The mean number of offspring conduct problems was calculated as the least squares mean in a hierarchical linear model (HLM) to control for the influence of the offspring's age and age squared and to incorporate the sample weights.

HIERARCHICAL LINEAR MODELING

Hierarchical linear models were used to explore the processes underlying the intergenerational transmission of conduct problems using continuous measures in both generations. The advantages of using HLMs for analyzing data from CoT studies and the algebraic representations of the models are presented elsewhere.[22] Briefly, HLMs allow for regression-based analyses that can measure the magnitude of the intergenerational relations using nested data (ie, the SEs and significance testing are appropriate for the nonindependent observations). Unstandardized regression weights were used to compare effect sizes within and between models.[38] Parental and offspring conduct problems were independently normalized using a Blom transformation, an approach that has been shown to help analyze counts of psychiatric symptoms.[39] The scores were also standardized so that the effect sizes were on an understandable scale (the Cohen d scale). Because there were missing values for some parental characteristics, the HLMs were completed on 5 multiply imputed data sets.[32] The imputed parental data sets were based on the psychiatric history, demographic characteristics, and sex of both parents, in addition to the mean number of symptoms for psychiatric problems assessed by the SSAGA for all offspring in the family.

The first HLM estimated the phenotypic relation between parental and offspring conduct problems. The model included conduct problems in the adult twin and his or her spouse, controlling for the age and age squared of the offspring. The second HLM used effect codes to estimate an approximation of the between–twin family effect, which is the comparison of unrelated offspring, based on the mean number of conduct problems in the twin pair.[40] The model also estimated the within–twin family effect. The parameter (the difference between each

Table 1. Comparison of Sociodemographic and Psychiatric Characteristics of the ATR[a] and CoT Subsample[b] Before and After Data Weighting[c]

Twin Pair Characteristic[d]	ATR Sample[a]	CoT Subsample[b]	Weighted CoT Subsample[b]
Sociodemographics			
Sex/cohort[e]			
Female/< 35 y	18.47	5.96[f]	16.93
Female/35-45 y	22.47	32.13[f]	23.05[f]
Female/> 45 y	26.80	30.11[f]	22.07[f]
Male/< 35 y	11.75	1.46[f]	18.04
Male/35-45 y	10.96	16.97[f]	11.43[f]
Male/> 45 y	9.55	13.37[f]	8.59
Age, mean, y[e]	44.09	45.14[f]	42.39
Sex of pair[e]			
Male-male	19.50	24.38[f]	20.00
Female-male	24.81	21.46[f]	28.82
Female-female	55.69	54.16	51.18
Discordant Pairs			
History of family alcohol use			
Twin[e]	11.44	12.47	14.37[f]
Father	10.83	11.57	12.05[f]
Mother	2.93	2.81	2.20
Spouse	13.40	17.53[f]	14.55[f]
History of family depression			
Twin[e]	29.81	37.42[f]	31.06[f]
Father	18.07	20.11	18.22
Mother	23.68	24.94	27.21[f]
Spouse[e]	22.80	30.67[f]	23.55[f]
Agoraphobia[e]	5.58	6.52	5.61
Panic[e]	5.55	2.41[f]	5.07
Social phobia	3.63	5.06[f]	3.65
Other phobias	3.05	4.27[f]	3.17
Abstain from alcohol	3.36	3.26	3.13
High-frequency drinking	28.41	31.80[f]	30.58
High-density drinking	19.84	20.67	20.32
High maximum No. of drinks[e]	19.84	18.99	20.37
Suicidal ideation	4.46	6.63[f]	6.29[f]
Major depression[e]	33.69	41.69[f]	35.92[f]
Alcohol dependence[e]	15.38	21.91[f]	17.44[f]
Conduct disorder[e]	9.70	13.60[f]	11.02[f]
Concordant Pairs			
History of family alcohol use			
Twin	1.53	2.92[f]	4.03[f]
Father[e]	9.92	15.06[f]	12.38[f]
Mother	1.65	2.81[f]	1.95
Spouse	1.01	1.57[f]	0.80
History of family depression			
Twin	8.06	13.15[f]	8.47[f]
Father	6.19	8.54[f]	6.54
Mother[e]	10.68	17.08[f]	9.96
Spouse	2.38	4.49[f]	2.28
Agoraphobia[e]	0.55	1.57[f]	0.66[f]
Panic	0.40	0.56	0.24
Social phobia	0.15	0.34	0.14
Other phobias	0.12	0.22	0.11
Abstain from alcohol	0.82	1.01	0.76
High-frequency drinking	11.26	13.60[f]	14.21[f]
High-density drinking	4.00	4.94	7.03[f]
High maximum No. of drinks	4.21	3.82	6.74[f]
Suicidal ideation	0.31	0.21[f]	0.34
Major depression[e]	9.80	16.97[f]	12.51[f]
Alcohol dependence[e]	3.45	5.51[f]	4.44[f]
Conduct disorder[e]	1.86	3.26[f]	2.37[f]

Abbreviations: ATR, Australian Twin Registry; CoT, Children of Twins.
[a] Unselected twin sample.
[b] High-risk subsample.
[c] All values are percentages, unless otherwise indicated.
[d] Characteristics were measured by the Semi-Structured Assessment for the Genetics of Alcoholism, a psychiatric interview.
[e] Variable that predicted inclusion in CoT subsample from a logistic regression analyses.
[f] Univariate comparisons with nonselected participants from the ATR are significant ($P < .05$).

Table 2. Offspring Conduct Problems by Twin History of Conduct Problems, Offspring Sex, and Family Type[a]

	Female		Male	
Twin Parent Conduct Problems[b]	No. of Conduct Problems, Mean (SE)	No. of Offspring	No. of Conduct Problems, Mean (SE)	No. of Offspring
Entire sample				
None	0.86 (0.05)	794	1.74 (0.07)	799
Some	1.12 (0.07)	499	2.57 (0.10)	462
All discordant twins				
None	0.95 (0.10)	213	1.72 (0.15)	199
Some	0.85 (0.10)	209	2.63 (0.16)	179
Discordant dizygotic twins				
None	0.89 (0.17)	123	1.87 (0.21)	106
Some	0.98 (0.18)	126	2.94 (0.21)	105
Discordant monozygotic twins				
None	1.05 (0.15)	90	1.55 (0.22)	93
Some	0.69 (0.16)	83	2.14 (0.25)	73

[a] The influence of the offspring's age and age squared was partialled from the mean conduct disorder scores. High conduct problems in the twins were based on 1 or more conduct disorder symptoms.

[b] Five offspring were from twin families in which the twin's or co-twin's measure of conduct problems was missing and thus could not be identified as coming from discordant or concordant twin pairs.

co-twin's conduct problems and the mean conduct problems in the twin pair) estimated whether an offspring with a twin parent with more conduct problems had more conduct problems than their cousins, whose adult twin parent had fewer conduct problems. The third HLM separated the within–twin family effect by the zygosity type of the adult twins by including the interaction between a zygosity variable (coded as MZ = 0 and DZ = 1) and the within–twin family measure of conduct problems. The model therefore estimated the within–twin family estimate for MZ families—the most stringent test of a causal connection in the design—and the difference between the 2 estimates (difference between within DZ twin family and within MZ twin family). If the within–twin family effect is larger in DZ than in MZ families, genetic factors would be implicated, because offspring of MZ twins share the same genetic risk associated with the twins' conduct problems, whereas offspring of DZ twins do not.[16,17] The fourth model controlled for measured covariates of both parents, including demographic characteristics, measures of lifetime psychopathology, and the level of contact in the twin families. Models (not shown) that included the interaction of the parents' conduct problems and testing the difference between maternal and paternal conduct problems indicated that the effects of parental conduct problems were independent of each other and not based on the sex of the parent.

RESULTS

MEAN COMPARISONS OF OFFSPRING OF ADULT TWINS

The mean number of conduct disorder symptoms in offspring based on the parental level of conduct problems is presented in **Table 2** for the entire sample and by twin pair history of conduct problems. In the entire sample, the mean number of symptoms in female offspring was lower if their parents reported no conduct problems (no symptoms mean, 0.86 symptoms; conduct problems mean, 1.12 symptoms). Female cousins differentially exposed to twin parents with a history of conduct problems, however, did not differ (no symptoms mean, 0.95 symptoms; conduct problems mean, 0.85 symptoms). For females, the comparison of offspring from discordant DZ families (no symptoms mean, 0.89 symptoms; conduct problems mean, 0.98 symptoms) was somewhat similar to the comparison in unrelated offspring, but the difference between female offspring of discordant MZ twins (no symptoms mean, 1.05 symptoms; conduct problems mean, 0.69 symptoms) was in the reverse direction. The pattern of results suggests that the intergenerational transmission of conduct problems was because of genetic factors for female offspring.

Conduct problems among male offspring were associated with parental conduct problems in the entire sample (no symptoms mean, 1.74 symptoms; conduct problems mean, 2.57 symptoms). Male cousins from discordant twin families also differed greatly (no symptoms mean, 1.72 symptoms; conduct problems mean, 2.63 symptoms). In contrast to the results in female offspring, the comparison of male offspring of discordant DZ twins (no symptoms mean, 1.87 symptoms; conduct problems mean, 2.94 symptoms) and discordant MZ twins (no symptoms mean, 1.55 symptoms; conduct problems mean, 2.14 symptoms) was significant. Thus, the mean comparisons imply that environmental factors specific to parental conduct problems mediate the intergenerational relationship for male offspring.

HIERARCHICAL LINEAR MODELS

Intergenerational Transmission to Female Offspring

The HLMs were run separately for female and male offspring, because the mean analysis suggested sex differences in the underlying processes. The HLM results for

Table 3. Parameter Estimates of Hierarchical Linear Models Predicting Conduct Disorder Symptoms in Females[a]

	Model 1		Model 2		Model 3		Model 4	
Parameter	b	SE	b	SE	b	SE	b	SE
Twin conduct disorder								
Phenotypic	0.09[b]	0.02	...	...	...	...	...	...
Between twin family	...	...	0.13[b]	0.03	0.13[b]	0.03	0.07[b]	0.03
Within twin family	...	...	0.01	0.04	...	...	...	...
Within MZ twins	...	...	...	...	− 0.09	0.07	− 0.08	0.06
Difference between within-DZ and within-MZ estimates	...	...	...	...	0.19[b]	0.09	0.13	0.08
Spouse conduct disorder	0.07[b]	0.03	0.07[b]	0.03	0.07[b]	0.03	− 0.01	0.03
Offspring age	0.08[b]	0.03	0.08[b]	0.03	0.08[b]	0.03	0.08[b]	0.03
Offspring age squared	− 0.001[b]	< 0.0001	− 0.001[b]	< 0.0001	− 0.001[b]	<0.0001	− 0.001	< 0.0001
Parental divorce	...	...	...	...	...	...	0.12[b]	0.06
Twin covariate								
Education	...	...	...	...	...	...	0.00	0.02
Age at first child's birth	...	...	...	...	...	...	− 0.01	0.01
Cigarette use	...	...	...	...	...	...	0.08	0.05
Alcohol abuse	...	...	...	...	...	...	0.03	0.04
Depression	...	...	...	...	...	...	0.01	0.01
Illicit drug use	...	...	...	...	...	...	0.08	0.07
Suicidality	...	...	...	...	...	...	0.02	0.02
Spouse covariate								
Education	...	...	...	...	...	...	0.03	0.02
Age at first child's birth	...	...	...	...	...	...	0.00	.01
Cigarette use	...	...	...	...	...	...	0.01	0.08
Alcohol abuse	...	...	...	...	...	...	0.08[b]	0.03
Depression	...	...	...	...	...	...	0.01	0.01
Illicit drug use	...	...	...	...	...	...	0.01	0.08
Suicidality	...	...	...	...	...	...	0.01	0.03

Abbreviations: DZ, dizygotic; MZ, monozygotic; ellipses, parameter was not included in model.
[a]The analyses were weighted to estimate population-based parameters. Differences in contact between MZ and DZ twin families did not alter the findings.
[b]$P < .05$.

females are presented in **Table 3**. For females, model 1 indicated that for every 1 SD increase in the parents' number of childhood conduct problems, conduct problems increased significantly in female offspring (adult twin, b=0.09; 95% confidence interval [CI], 0.05-0.13; spouse of the twin, b=0.07; 95% CI, 0.01-0.13). Model 2 indicated that the intergenerational association was only found at the between–twin families level (b=0.13; 95% CI, 0.07-0.19) and not at the within–twin family level (b=0.01; 95% CI, −0.07 to 0.09). The results imply that the relationship between parental and offspring conduct problems for female offspring is not causal, but the results do not indicate whether the confounds are genetic or environmental. Model 3 indicated that there was no association with the adult twin's conduct problems in MZ families (b=−0.09; 95% CI, −0.23 to 0.05), but at the within–DZ twin family level, effect was larger than the within–MZ twin family estimates (b=0.19; 95% CI, 0.01-0.37). The results for model 4 show the same pattern of findings. Parental conduct problems were only associated at the between–twin family level (b=0.07; 95% CI, 0.01-0.13). There was no intergenerational relationship within MZ twins who differed in their level of conduct problems (b=−0.08; 95% CI, −0.20 to 0.04), and the difference in the within–twin family effect between DZ and MZ twin pairs was large (b=0.13; 95% CI, −0.03 to 0.29). The pattern suggests that shared genetic liability accounts for the intergenerational transmission of conduct problems in females, because the confound was related to genetic risk associated with parental conduct problems. It is difficult to interpret the parameters for the parental characteristics, because the parameters represent unique contributions to offspring conduct problems controlling for all of the variables in the model, though parental divorce was still independently associated with female conduct problems.

Intergenerational Transmission to Male Offspring

The results for males are presented in **Table 4**. Model 1 indicated a phenotypic relationship between parental and offspring conduct problems (adult twin, b=0.21; 95% CI, 0.15-0.27; spouse of the twin, b=0.15; 95% CI, 0.07-0.23). Model 2 revealed that the intergenerational association was large at both levels of analysis (between twin families, b=0.21; 95% CI, 0.13-0.29; within twin families, b=0.21; 95% CI, 0.11-0.31). The results from model 3 show that the relationship was still great for offspring of MZ twins who differed in their conduct problems (b=0.16; 95% CI, 0.02-0.30), which is consistent with an environmentally mediated process specifically related to parental conduct problems. The difference between the within–MZ twin family and within–DZ twin family effects (b=0.08; 95% CI, −0.14 to 0.30) suggests the possibility of a small genetic confound, but the pa-

Table 4. Parameter Estimates of Hierarchical Linear Models Predicting Conduct Disorder Symptoms in Males[a]

	Model 1		Model 2		Model 3		Model 4	
Parameter	b	SE	b	SE	b	SE	b	SE
Twin conduct disorder								
Phenotypic	0.21[b]	0.03	...	...	...	...	...	...
Between twin family	...	...	0.21[b]	0.04	0.21[b]	0.04	0.17[b]	0.04
Within twin family	...	...	0.21[b]	0.05	...	...	...	...
Within MZ twins	...	...	...	...	0.16[b]	0.07	0.13	0.08
Difference between within-DZ and within-MZ estimates	...	...	...	...	0.08	0.11	−0.01	0.11
Spouse conduct disorder	0.15[b]	0.04	0.15[b]	0.04	0.15[b]	0.04	0.13[b]	0.04
Offspring age	0.10[b]	0.04	0.10[b]	0.04	0.10[b]	0.04	0.10[b]	0.04
Offspring age squared	−0.002[b]	< 0.0001	−0.002[b]	< 0.0001	−0.002[b]	< 0.0001	−0.002[b]	< 0.0001
Parental divorce	...	...	...	...	...	...	0.14[b]	0.07
Twin covariate								
Education	...	...	...	...	...	...	0.01	0.02
Age at first child's birth	...	...	...	...	...	...	0.00	0.01
Cigarette use	...	...	...	...	...	...	0.07	0.06
Alcohol abuse	...	...	...	...	...	...	0.06	0.05
Depression	...	...	...	...	...	...	0.00	0.01
Illicit drug use	...	...	...	...	...	...	−0.01	0.10
Suicidality	...	...	...	...	...	...	0.04	0.03
Spouse covariate								
Education	...	...	...	...	...	...	0.00	0.02
Age first child's birth	...	...	...	...	...	...	0.01	0.01
Cigarette use	...	...	...	...	...	...	0.02	0.10
Alcohol abuse	...	...	...	...	...	...	0.01	0.04
Depression	...	...	...	...	...	...	0.00	0.01
Illicit drug use	...	...	...	...	...	...	0.07	0.10
Suicidality	...	...	...	...	...	...	−0.04	0.03

Abbreviations: DZ, dizygotic; MZ, monozygotic; ellipses, parameteer was not included in model.
[a]The analyses were weighted to estimate population-based parameters. Differences in contact between MZ and DZ twin families did not alter the findings.
[b]$P < .05$.

rameter could not be precisely estimated. Model 4 included the measured covariates of both parents. The within–MZ twin family effect was great (b=0.13; 95% CI, −0.03 to 0.29), though the SEs around the estimate were sizeable, and the difference between the within–twin family effects was small (b=−0.01; 95% CI, −0.22 to 0.22). Excluding the interaction between zygosity and the within-family effect from model 4 resulted in a large and statistically significant effect of the twin parent's conduct problems (b=0.13; SE=0.05; 95% CI, 0.03-0.22).

To further test whether the sex differences in underlying processes were statistically significant, a full model was fit in the entire data set that tested the interaction between each twin conduct problems variables and offspring sex. The 3-way interaction (offspring sex × within–twin family effect × twin zygosity) was statistically significant (b=0.27; SE=0.12; 95% CI, 0.03-0.51), signifying that the difference between the within–MZ twin family and within–DZ twin family effects was statistically greater in females. Additional analyses without the sample weights (results not shown) and controlling for levels of contact among the twin families found the same pattern of results.

COMMENT

The results suggest that shared genetic liability accounts for the intergenerational transmission of conduct problems for female offspring because (1) the comparison of cousins raised by parents with different levels of childhood conduct problems revealed no relationship between parental and offspring conduct problems, a crucial test of causality,[37] and (2) the confound varied according to genetic risk associated with parental conduct problems. In contrast, the results for male offspring indicate that the intergenerational transmission of childhood conduct problems was largely mediated by environmental risk factors specifically related to parental conduct problems. We conclude that most of the underlying causal risk mechanisms are environmental, in as much as the intergenerational transmission cannot be accounted for by shared genetic liability between the twin parent and the offspring, unmeasured environmental factors that make adult twins similar, assortative mating in the parent generation for conduct problems, demographic characteristics, measures of lifetime psychopathology in both parents, or greater levels of contact in MZ than DZ twin families. The analyses also suggest some role of selection factors in males, which may be genetic in origin.

Our results emphasize the importance of environmental risk factors that are specifically associated with intergenerational transmission of male conduct problems. Environmental influences, such as parental divorce[22,41,42] and harsh or abusive parenting,[43] have also been associated with offspring externalizing problems independent of parental externalizing and shared ge-

netic liability. It is important to note, however, that the current findings do not conflict with the behavioral genetic literature that highlights the importance of genetic factors for male conduct problems.[1,7] The current analyses, similar to previous CoT studies using the sample,[22,34,35,41,43,44] focused on explaining the association or covariation between parental and offspring characteristics, not accounting for all of the variance in the offspring phenotype. The current HLMs for male conduct problems also suggest genetic factors may partially confound the intergenerational association. Furthermore, genetic factors unrelated to the parental conduct problems that occurred a generation earlier could influence externalizing problems in parents' offspring. The current results, therefore, do not negate the overall importance of genetic factors for male conduct problems.

The current results reinforce the necessity of using quantitative genetic designs to distinguish between correlated genetic and environmental risk processes.[14,45] The analyses represent one of the most stringent tests of the underlying causal mechanisms responsible for the intergenerational transmission of childhood conduct problems. The CoT design can separate genetic and environmental processes and includes different, if not fewer, assumptions than other behavioral genetic designs that explore intergenerational associations.[14,16] In particular, the design does not require the assumption that conduct problems in both generations have equivalent etiologies.[17] The study used a high-risk sample that contained a sufficient number of families containing parents with conduct problems to test for small environmental effects (as evidenced by statistically significant estimates of small effect sizes). The sample was also drawn from a large twin study; this enabled the use of sample weighting to produce estimates based on the entire ATR. Finally, we used measures of conduct problems, demographic characteristics, and lifetime psychopathology in both parents to account for assortative mating and other confounding variables.

These results are generally consistent with other studies. Analysis of a large community sample similarly revealed no difference in the transmission of externalizing problems based on the sex of the parent.[9] The current study also replicates the findings of a previous adoption study that found that males may be more susceptible to environmental risk factors for conduct problems, while genetic factors account for the intergenerational transmission in females.[46] The overall magnitude of the intergenerational transmission is also consistent with research from the National Comorbidity Study.[6] The study found that the association between parental and offspring externalizing problems was robust for boys when child abuse was included in the model, but it was not for girls; this highlights sex-specific mechanisms underlying the intergenerational transmission of conduct problems.[6] Furthermore, the spousal correlations for childhood conduct disorder are significant in our study but not as large as spousal correlations for adult antisocial behavior.[13] The lower spousal correlations for childhood conduct problems (vs adult antisocial behaviors) are similar to a recent population-based study,[47] and the magnitude of the correlation is similar to findings for other externalizing problems, such as alcohol abuse or dependence.[48] Previous research has also reported that the spouse-spouse correlation of MZ twins was no more similar than the spouse-spouse correlation of same-sex DZ twins[49]; a finding that is consistent with our results. We must note, however, that the results are in contrast to research that suggests the correlates of conduct problems are generally the same for males and females on similar trajectories.[24]

Despite the strengths of the current research, there are also a number of limitations. First, as previously reported, the ATR is a community sample that may not include individuals with extreme scores for conduct disorder or antisocial personality disorder.[8,23] Twin parents, their spouses, or their offspring with high levels of antisocial traits may not have participated in the longitudinal assessments in the ATR or the high-risk CoT Study. If genetic risk for conduct problems is related to nonparticipation, the results of our study may not completely generalize to those at greatest genetic risk for externalizing problems. Our study was conducted on a high-risk sample and was weighted to produce estimates based on a volunteer sample of twins that is generally consistent with the population of Australia. The analyses used techniques to handle missing data to address this concern. Nevertheless, the study suffers from the limitations inherent in population-based research. The sample weighting also may not have entirely accounted for the selection of twins into the high-risk CoT Study. Second, the results rely on retrospective self-report of conduct problems. The analyses are also limited to *DSM*-based criteria for conduct disorder and do not reflect parental antisocial behavior as adults. The results also do not address the importance of relational aggression.[25] Third, large sample sizes are needed to separate genetic from environmental confounds in the CoT design,[18] limiting our ability to determine whether genetic or environmental factors partially mediate the intergenerational transmission in male offspring. Fourth, the CoT design does not account for genetic risk associated with conduct problems from the spouse of the twins.[20] The analyses controlled for measured covariates of the spouses, but it is impossible to determine whether every salient variable was measured accurately and was included in the models. For example, the study did not include the effects of maternal smoking during pregnancy.

Fifth, our study did not include an exploration of gene-environment interaction. To gather a more precise understanding of the causal mechanisms related to conduct disorder, both gene-environment interaction and gene-environment correlation will need to be explored.[10,50] The current results, however, have implications for studies exploring gene-environment interaction, using measured genotypes and environments. The current analyses strongly suggest that sex moderates an individual's response to environmental risk factors. Furthermore, characteristics frequently considered to be environmental risk factors may actually be epiphenomena that mark shared genetic risk rather than a causal agent (at least in females).[51]

Sixth, the analyses did not explore heterogeneity in parental and offspring conduct problems. The etiological processes in earlier-onset conduct problems, often

characterized by neurodevelopmental problems, have been found to differ from the risks associated with later-onset delinquent behavior.[52] Recent studies have also illustrated that comorbid maternal depression and antisocial history particularly puts offspring at risk for conduct problems.[53] Genetic risk transmitted from parents to their offspring that is associated with conduct problems may also extend to other externalizing problems, such as substance abuse.[9]

Thus, the findings of our study would be further strengthened by replication in nationally representative samples in other countries using different measures of conduct problems and exploring moderating variables. Additional studies will need to explore whether the heterogeneity in conduct problems reflects different underlying environmental and genetic processes.[52] Research must also consider whether sex differences in thresholds for conduct problems could account for the current findings.[54] These substantive issues are critical for truly understanding the causes of conduct problems.[24]

CONCLUSIONS

The results of the current investigation suggest that interventions in boys should focus on the role of parenting, delinquent peers, and other well-known environmental risk factors.[55] The role of genetic processes accounting for the intergenerational transmission of conduct problems in girls does not preclude effective environmental interventions, nor does it suggest that environmental factors are not important in the etiology of conduct problems. The magnitude of the intergenerational transmission was small, and changes in the environment can alter the role of genetic influences on conduct problems.[2] Nevertheless, a history of childhood conduct problems in parents suggests that their female offspring in particular are at greater genetic risk for behavior problems. Additional research is required to further specify the environmental and genetic processes responsible for the intergenerational transmission of conduct problems.

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