Psychological Medicine, 2004, **34**, 1113–1127. © 2004 Cambridge University Press
DOI: 10.1017/S0033291703001788 Printed in the United Kingdom

Specificity in the familial aggregation of overt and covert conduct disorder symptoms in a referred attention-deficit hyperactivity disorder sample

M. C. MONUTEAUX*, G. FITZMAURICE, D. BLACKER, S. L. BUKA AND J. BIEDERMAN

Pediatric Psychopharmacology Unit, Psychiatry Department, Massachusetts General Hospital, Boston, MA, USA

ABSTRACT

Background. To examine the familial associations of overt and covert antisocial behavior within the diagnosis of conduct disorder (CD) in families ascertained by referred children with attention-deficit hyperactivity disorder (ADHD), and to test if these familial associations differed between male and female probands.

Method. Subjects were clinically-referred male and female ADHD children ($n=273$) and their first-degree biological relatives ($n=807$). Scores for overt and covert conduct problems were calculated by summing the DSM-III-R conduct disorder symptoms, as derived from structured diagnostic interviews. Familial aggregation analyses were conducted with multivariate regression modeling methodology.

Results. Proband overt scores significantly predicted the overt scores of their relatives, and proband covert scores significantly predicted the covert scores of their relatives. There was no evidence of covert symptom scores predicting overt scores or vice versa. There was some evidence that the aggregation of covert symptoms was stronger in the families of female probands.

Conclusions. These results provide preliminary evidence that overt and covert conduct disorder symptoms are independently transmitted through families and may represent distinct familial syndromes.

INTRODUCTION

Conduct disorder (CD) is a DSM-IV Axis I childhood onset mental disorder. It is characterized by a chronic pattern of behavior that violates the fundamental well-being of other people and is in conflict with accepted social standards of conduct (APA, 1994). The pervasive public health burden of CD and its associated antisocial behaviors has been repeatedly recognized (Institute of Medicine, 1989; Beitchman *et al.* 1992; APA, 1994; Moore *et al.* 1994; Offord & Bennett, 1994).

* Address for correspondence: Dr M. C. Monuteaux, Massachusetts General Hospital, Warren 705, 55 Fruit Street, Boston, MA 02114, USA.
(Email: mmonuteaux@partners.org)

Because CD, like other psychiatric disorders, is likely to be highly heterogeneous, several approaches have been made to help identify more homogeneous subtypes. One such approach is to subtype CD youth based on the nature of the CD symptoms into overt or covert CD (Loeber & Schmaling, 1985). Covert CD symptoms refer to clandestine or stealthy behaviors, such as burglary, theft and lying. In contrast, overt CD symptoms are confrontational and apparent, such as starting fights, robbery and violence.

There is empirical evidence supporting the notion that CD symptoms tend to cluster into these covert and overt domains. For example, in a meta-analytic review, Frick *et al.* (1993) examined 60 factor analyses of youth behavior problems from 44 published studies. Using

multi-dimensional scaling techniques, their results suggest that antisocial behaviors in children could be plotted along two dimensions, a destructive/non-destructive pole and an overt/covert pole. Two of the quadrants created by the intersection of these axes were labeled covert property violations and overt aggression. Also, Fergusson *et al.* (1994) performed a confirmatory factor analysis on reports of behavior problems in a sample of 739 New Zealand youth and found evidence that CD symptoms could be parceled into an overt domain and a covert domain. Achenbach *et al.* (1991), in a large study of parent-reported problems in a national sample of 2600 clinically referred 4- to 16-year-olds and 2600 demographically matched non-referred children, presented evidence supporting a distinction between overt CD and covert CD symptoms.

In one of the earliest works empirically demonstrating the heuristic value of dividing CD symptoms into overt and covert subtypes, Loeber & Schmaling (1985) suggested that these two sets of symptoms may represent different clinical disorders. However, because these sets of aberrant symptoms tend to co-occur, uncertainties remain as to whether overt and covert CD symptoms are separate but co-occurring, or diverse manifestations of the same disorder. However, it has been argued that observing high rates of co-occurring disorders in the study of child psychopathology does not preclude the consideration that each condition may represent a separate entity, in terms of developmental course and causation (Loeber & Stouthamer-Loeber, 1998). Based on this argument, it is reasonable to hypothesize that overt and covert CD symptoms may represent distinct, yet correlated, disorders. If overt and covert CD symptoms do in fact represent separate disorders, there may be different associations between risk factors for CD and each of its symptomatic subtypes. For example, there is some evidence that maladaptive parenting practices and measures of cortisol activity may have such discordant associations (Loeber & Stouthamer-Loeber, 1998).

One important risk factor in CD is genetics (Simonoff, 2001). Genetic risk factors have been associated with antisocial behavior (Raine, 1993) and CD (Wamboldt & Wamboldt, 2000). It has also been suggested that genetic risk factors may have a differential influence on covert and overt CD symptoms (Edelbrock *et al.* 1995; Simonoff *et al.* 1998). Although there are no criteria with which to define overt and covert CD 'cases', several studies have empirically examined the genetic influence on these symptomatic subtypes using forensic categories or dimensional measures. A pair of large adoption studies evaluating criminal behavior found that criminal convictions in biological parents were significantly associated with property crime in their adopted-away offspring, but not with violent crimes (Bohman *et al.* 1982; Mednick *et al.* 1984). In contrast to these findings, a family study found that parents of early-onset, aggressive CD children had more antisocial behaviors than the parents of late-onset, less aggressive CD children (Lahey *et al.* 1998). In an adoption study of 197 males and females (Cadoret *et al.* 1995), antisocial personality disorder in the biological parents was significantly associated with dimensional measures of aggression and DSM-III conduct disorder symptoms in the adopted-away offspring. Likewise, in a study of 181 twin pairs aged 7–15, Edelbrock *et al.* (1995) found significant genetic effects on a dimensional measure of aggressive behavior, but not for a measure of non-violent delinquent behavior. This putative genetic effect on aggressive behavior is consistent with a prior report, which studied younger (aged 4–7 years) children (Ghodsian-Carpey & Baker, 1987).

A recent molecular genetic study found an association between the tryptophan hydroxylase gene, which codes for an enzyme involved in serotonin biosynthesis, and measures of aggression and anger (Manuck *et al.* 1999). Another study has found an association between the gene for monoamine oxidase-A (MAO-A) and aggression (Manuck *et al.* 2000). However, a twin study of a community sample of 434 male twin pairs aged 8–16 years found a genetic liability for both property violations (covert) and aggression (overt) (Simonoff *et al.* 1998). In summary, while studies that examined overt CD symptoms are consistent in regards to finding genetic effects (Cadoret *et al.* 1995; Manuck *et al.* 1999, 2000), studies that examined both constructs are inconsistent, with some reporting effects for covert CD symptoms only (Bohman *et al.* 1982; Mednick *et al.* 1984), and others for overt only (Ghodsian-Carpey & Baker,

1987; Edelbrock *et al*. 1995) and others for both (Simonoff *et al*. 1998). Questions of statistical power notwithstanding, it is not clear from these findings how genetic risk operates in the pathogenesis of CD symptoms.

A major drawback to these studies and a challenge to research efforts investigating the differential correlates of overt and covert CD symptoms is that there are other sources of heterogeneity in CD beyond the overt-covert symptomatic dichotomy. For example, there have been suggestions of defining subtypes of CD by co-morbidity with attention-deficit hyperactivity disorder (ADHD; Loeber *et al*. 2000). The high degree of co-morbidity between ADHD and CD has been extensively documented in several studies, as well as the poor long-term prognosis for children with both disorders (Moffitt, 1990; Hinshaw *et al*. 1993; Mannuzza *et al*. 1993; Loeber *et al*. 2000). While methodological flaws and nosological shortcomings could explain high rates of co-morbidity (Caron & Rutter, 1991), the ICD-10 endorsed the conclusion that this overlap represents a separate condition labeled hyperkinetic conduct disorder (WHO, 1986). This view is supported by work showing ADHD and CD to be a distinct familial subtype (Faraone *et al*. 1997, 2000; Smalley *et al*. 2000). Furthermore, a large twin study by Silberg *et al*. (1996) found that the covariation between hyperactivity and conduct/oppositional problems is attributable to genetic factors, suggesting that the co-morbid condition is a distinct subtype that is genetically mediated.

Also, several studies have found that males are three to four times more likely to manifest CD than females (Earls, 1994; Biederman *et al*. 2002). In a review of studies examining gender effects in overt behavior, Loeber & Hay (1997) concluded that gender differences in aggression and violence emerge in the preschool years and persist throughout the lifespan, with boys being more likely to engage in these behaviors and also to perpetrate serious violent acts. In contrast, antisocial behavior in females tends to onset in adolescence, and tends to be more covert than overt (Loeber & Stouthamer-Loeber, 1998). In a longitudinal cohort study of children in New Zealand, the prevalence rates of CD in males and females at age 15 years were very similar (7·2% for males; 7·4% for females). However, rates of aggressive CD (3·1% for males; 0% for females) and non-aggressive CD (4·1% for males; 7·4% for females) revealed stark gender differences (McGee *et al*. 1990). Furthermore, a large adoption study found the biological parents of female property criminals to have a higher proportion of property offenders compared to the biological parents of male property criminals. This finding suggests that genetic effects for criminal behavior differ by gender, being stronger in females than in males (Sigvardsson *et al*. 1982; Brennan *et al*. 1991). Another interpretation compatible with these data predicts weaker environmental factors operating on females relative to males. Contrary to this finding, a recent review of twin studies of CD did not find evidence of gender differences in genetic liability (Simonoff, 2001). Considering these conflicting results, research attempting to clarify the genetic risk for overt and covert subtypes of CD should attend to both the co-morbidity with ADHD and gender effects.

The purpose of this study was to examine the familial risk for overt and covert CD subtypes in a sample of families ascertained through an ADHD proband with and without co-morbid CD, attending to gender. First, we hypothesized that overt and covert CD symptoms represent distinct familial disorders. This hypothesis predicts that both symptomatic subtypes will aggregate in families, and these symptom subtypes will not coaggregate, meaning they will be independently transmitted. Secondly, based on the literature (Sigvardsson *et al*. 1982; Brennan *et al*. 1991; Simonoff *et al*. 1998), we hypothesized that familial effects for CD symptoms differ by gender, being stronger in females. This hypothesis predicts a significant proband gender-by-symptom interaction, in that the familial risk will be greater in the families of female probands compared to male probands.

METHOD

Subjects

Data from two identically designed case-control family studies of ADHD in male and female probands were combined. Both studies ascertained families on the basis of a case (ADHD) or control (non-ADHD) child aged 6–17 years at time of ascertainment. The study of boys (Biederman *et al*. 1992) with ADHD was

https://doi.org/10.1017/S0033291703001788 Published online by Cambridge University Press

composed of 140 ADHD probands (with 174 siblings and 280 parents) and 120 non-ADHD control probands. The study of girls (Biederman *et al*. 1999) ascertained families on the basis of a female case or control proband child also aged 6–17 years at time of ascertainment. In this study of girls with ADHD, there were 140 ADHD probands (with 143 siblings and 274 parents) and 120 non-ADHD control probands. Since control probands and families were not used in this study, they will not be described further. Potential probands were excluded if they had been adopted, or if their nuclear family was not available for study. We excluded subjects if they had major sensorimotor handicaps (paralysis, deaf-ness, blindness), psychosis, autism, inadequate command of the English language, or a Full Scale IQ estimate (Wechsler, 1974) less than 80. We also excluded ADHD probands if they did not have complete CD symptom data ($n=7$). Thus, the final sample used in this analysis included 273 ADHD probands (138 boys and 135 girls) and their 807 first-degree relatives (171 siblings and 252 parents of male probands and 134 siblings and 250 parents of female probands).

All of the ADHD subjects met full DSM-III-R diagnostic criteria for ADHD according to clinical assessment at the time of the clinical referral; at the time of recruitment for this study they all had active symptoms of the disorder. Parents provided written informed consent for their children. In addition, children and adolescents provided written assent to participate.

Two independent sources provided the index children. We selected psychiatrically referred ADHD probands from consecutive referrals to a pediatric psychopharmacology clinic at the Massachusetts General Hospital. Pediatrically referred ADHD subjects consisted of pediatric patients from a Health Maintenance Organization. A three-stage ascertainment procedure was used to select the subjects. The first stage was the ascertainment of patients referred to a psychiatric or pediatric clinic. The second stage confirmed the diagnosis of ADHD by screening all children using a telephone questionnaire administered to the mother. The questionnaire asked about the 14 DSM-III-R symptoms of ADHD and questions regarding study exclusion criteria. The third stage further confirmed the diagnosis made via the telephone questionnaire with face-to-face structured interviews with the mother. Only patients who received a positive diagnosis at all three stages were included in the final analysis.

Assessments

Psychiatric assessments of probands and their siblings were made with the Schedule for Affective Disorders and Schizophrenia for School-age Children: Epidemiologic Version (K-SADS-E; Orvaschel & Puig-Antich, 1987). Data were based on independent interviews with the mothers and the children. For children 12 years of age and older, interviews were combined by considering a diagnostic criterion positive if it was endorsed in either interview. Children younger than 12 years of age (51% of all offspring) were not interviewed directly, so diagnoses in these children were based solely on the maternal report. Diagnostic assessments of parents and siblings over age 18 were based on direct interviews with each parent using the Structured Clinical Interview for DSM-III-R (SCID; Spitzer *et al*. 1990). To assess childhood diagnoses in the parents, we administered modules from the K-SADS-E covering childhood diagnoses. Raters were blind to the child's diagnosis (ADHD or non-ADHD control) and ascertainment site. Socio-economic status (SES) was assessed with the Hollingshead four-factor scale (Hollingshead, 1975). The scale measures SES on a 5-point ordinal scale, with 1 corresponding to the highest level of SES and 5 corresponding to the lowest level of SES.

Statistical methods

Typical family study methodology would dictate the categorization of probands into discrete groups, allowing for the comparison of rates across groups of first-degree relatives (Faraone & Tsuang, 1995). However, as noted above, there are no accepted criteria with which to categorize children into overt CD cases and covert CD cases. Coupled with this hurdle are other drawbacks associated with categorizing a latent dimensional variable, namely, loss of information and efficiency and difficulties of interpretation stemming from the arbitrary distinction between 'cases' and 'non-cases' (Dunn, 2000). These considerations prompted us to adopt an alternate method utilized by Alsobrook & Pauls (2002), where the symptoms

of the disorder are consolidated into continuous measures. Then, associations are examined between the probands' symptom score and the relatives' symptom score.

Based on the extensive factor analyses in the literature (Loeber & Schmaling, 1985; Frick *et al.* 1993), we divided the DSM-III-R CD symptoms into two classes, one representing overt behavior and the other representing covert behavior. Overt symptoms include: (1) often starts physical fights; (2) used a weapon in more than one fight; (3) physically cruel to animals; (4) physically cruel to other people; and (5) stolen with confrontation of the victim. Covert symptoms include: (1) destroyed property of others; (2) deliberately set fires; (3) often lies; (4) has broken into someone's house, car, etc; and (5) stolen without confrontation of the victim. These symptoms are coded 0 for an absent symptom, 0·5 for a subthreshold symptom, or 1 for a full symptom. A subthreshold designation was assigned to a symptom if the behavior was present but lacked the frequency or duration to warrant full symptom status. Using the ADHD probands with complete data ($n=273$), we aggregated each proband's covert symptoms and overt symptoms, generating two symptom total scores. We excluded symptoms that document status offenses (i.e. is often truant, ran away from home overnight). This decision was motivated by the desire to study behaviors captured by CD symptoms that, perpetrated by individuals across a population, are harmful to society, such as violence (US Department of Health and Human Services, 2001) and property crimes (Moore *et al.* 1994). Also, a meta-analysis of factor analyses suggests that status offense CD symptoms, overt CD symptoms and covert CD symptoms aggregate in three distinct domains (Frick *et al.* 1993). Although we recognize that status offenses are a subtype of CD symptoms that are problematic and worthy of legal and clinical attention, we focus here on the two subtypes of CD symptoms, overt and covert, that generates victims and thus has a detrimental impact on the public health.

While factor analytic studies of disruptive behavior disorders included symptoms of both CD and oppositional defiant disorder (ODD; Frick *et al.* 1993), we chose to focus on only the symptoms of CD for this family study. This decision was motivated by the recognition that CD and ODD are separate disorders (APA, 1994) and, as stated above, the widely documented heterogeneity within CD. Given these conditions, we choose to limit our investigation to the familiality of symptomatic subtypes of CD. The inclusion of ODD symptoms would have introduced a great deal of complexity to the interpretation of the results and hindered the assessment of our hypotheses.

We adopted the methods of multivariate logistic regression for the familial aggregation of two disorders as developed by Hudson *et al.* (2001*a*, *b*). As described by Hudson *et al.*, this method has several advantages over more traditional familial aggregation techniques, such as increased power to detect coaggregation and enhanced interpretability of estimated parameters. In the Hudson analysis (Hudson *et al.* 2001*b*), regression models were performed using the logit link and Bernoulli distribution, because the outcomes in this study were binary disorder indicators. However, since our measures are not dichotomous, the use of the logit link and Bernoulli distribution was not appropriate. We modified the model described in the above-referenced papers to accommodate overt and covert CD symptom scores by using the Gaussian distribution and identity link. The identity link was chosen because the outcome and the linear predictor vector have a direct, or 'identical' relationship (Hardin & Hilbe, 2001). To enhance the interpretability of the regression coefficients that are produced by this model, they were transformed into a commonly used and readily understood statistic, the partial correlation coefficient (r), using the following formula (Kleinbaum *et al.* 1988):

$$r=(S_X/S_Y)\beta,$$

where S_X is the standard deviation of the independent variable, S_Y is the standard deviation of the dependent variable, and β is the estimated regression coefficient.

Multivariate regression, as stated above, describes the familial aggregation of two disorders, say disorder A and disorder B. In this model, the relatives of the probands are the units of analysis. Each relative is represented by two observations in the dataset, so, if there are 100 relatives, the data will contain 200 observations.

Table 1. *Competing hypotheses of the familial aggregation of overt and covert conduct disorder symptoms*

Description of parameter …	Predicted within person estimate Association of A and B within a given relative	Predicted overt aggregation estimate Association between proband A score and a given relative A score	Predicted covert aggregation estimate Association between proband B score and a given relative B score	Predicted coaggregation estimate Association between proband A(B) score and a given relative B(A) score
Competing hypotheses				
1 Neither subtype is familial	NP	N.S.	N.S.	N.S.
2 Only the overt subtype is familial	NP	SIG	N.S.	N.S.
3 Only the covert subtype is familial	NP	N.S.	SIG	N.S.
4 Conduct disorder symptoms exhibit a non-specific familial risk	SIG	SIG	SIG	SIG
5 Subtypes of antisocial behavior exhibit specific familial risk	NP	SIG	SIG	N.S.

A, overt; B, covert; N.S., not significant; SIG, positive significant association; NP, not predicted; both N.S. and SIG are consistent with hypothesis.

For the first observation of a given relative, his or her disorder A status is designated as the dependent variable. For the second observation of that same relative, his or her disorder B is designated as the dependent variable. So, the model has a single dependent variable, but is unique in that this dependent variable actually consists of two outcomes, relatives' disorder A status and relatives' disorder B status.

The model provides estimates for four parameters: (1) the association between disorder A and disorder B in relatives; (2) the aggregation of relative disorder A and proband disorder A; (3) the aggregation of relative disorder B and proband disorder B; (4) and the coaggregation of discordant proband/relative disorders. Specifically, coaggregation refers to the combined association between: (1) proband disorder A and relative disorder B, and (2) proband disorder B and relative disorder A. Conceptually, the second and third parameters estimate the degree to which the symptom subtypes independently breed true in families, while the fourth parameter estimates the degree to which there is non-specific familial transmission. See Table 1 for the formal interpretations of these parameters and their predicted estimates based on competing hypotheses about the familial aggregation of overt and covert CD subtypes.

In observations where relative disorder A is the dependent variable, the first, second and fourth of the independent variables are coded as follows: (1) the given relative's disorder B status (i.e. association between disorders A and B within relatives); (2) the proband's disorder A status (i.e. familial aggregation of disorder A); (4) the proband's disorder B status (i.e. coaggregation of relative disorder A and proband disorder B). The third independent variable is coded as a nuisance variable with a value fixed at zero. This nuisance variable is coded as zero when relative disorder A is the dependent variable and is coded as the proband's disorder B status when relative disorder B is the dependent variable. As will be described in the next paragraph, this variable provides the estimate of the familial aggregation of disorder B.

Likewise, in observations where relative disorder B is the dependent variable, the first, third and fourth of the independent variables are coded as follows: (1) the given relative's disorder A status (i.e. association between disorders B and A within relatives); (3) the proband's disorder B status (i.e. familial aggregation of disorder B); (4) the proband's disorder A status (i.e. coaggregation of relative disorder B and proband disorder A). The second independent variable is coded as a nuisance variable with a value fixed at zero. This nuisance variable is coded as zero when relative disorder B is the dependent variable and is coded as the proband's disorder A status when relative disorder A is the dependent variable. As was described in the previous paragraph, this variable provides the estimate of the familial aggregation of disorder A. See Hudson *et al.* (2001*a*, *b*) for a more detailed description of the model.

Based on the literature, we decided *a priori* to present the results in the full sample as well as stratified by the gender of the proband.

https://doi.org/10.1017/S0033291703001788 Published online by Cambridge University Press

Table 2. *Demographic characteristics of probands and relatives, stratified by proband gender*

	Families ascertained by male probands		Families ascertained by female probands	
	Probands ($n=138$)	Relatives ($n=423$)	Probands ($n=135$)	Relatives ($n=384$)
Age	$10{\cdot}6 \pm 3{\cdot}0^{b+}$	$29{\cdot}8 \pm 14{\cdot}7$	$11{\cdot}2 \pm 3{\cdot}4$	$31{\cdot}8 \pm 14{\cdot}7^{a-}$
Gender (male)†	138 (100)	$211\ (50)^{a+b+}$	0 (0)	$195\ (51)^{a+b+}$
SES‡	$1{\cdot}9 \pm 1{\cdot}0$	$1{\cdot}9 \pm 1{\cdot}0^{b+}$	$1{\cdot}9 \pm 0{\cdot}9$	$1{\cdot}9 \pm 0{\cdot}9^{a+b+}$

Values in table represent mean ± standard deviation or frequency (%).
† Positive associations with symptom scores indicate higher scores in males.
‡ Smaller values indicate high SES, larger values indicate low SES.
[a+] Significant positive association with overt score, $p<0{\cdot}05$; [a−] significant negative association with overt score, $p<0{\cdot}05$.
[b+] Significant positive association with covert score, $p<0{\cdot}05$; [b−] significant negative association with covert score, $p<0{\cdot}05$.

However, we assessed the interaction between proband gender and the overt and covert aggregation parameters. This analysis will explicitly test whether the familial risk for overt and covert behaviors are statistically different for males *versus* females.

As secondary analyses, we repeated the analytical plan outlined above using dichotomized measures of overt and covert CD symptoms. This analysis, while losing information and thus precision by collapsing data, allows for more readily interpretable estimates (i.e. odds ratios) of familial aggregation. These binary variables are coded positive if the symptom score is greater than or equal to 0·5, and zero otherwise. While this dichotomization provides a low threshold for defining a 'case', it is useful in that the risk estimates provided by the resulting odds ratios are in reference to the complete absence of symptoms. For example, we can say that the odds of having at least one overt CD symptom in relatives of probands with least one overt CD symptom is some quantity times the odds of relatives of probands with no overt symptoms. This analytical plan provided more meaningful estimates of effect compared to those that would result from using an arbitrary cut-off somewhere along the symptom distribution. While other psychiatric diagnoses employ this approach (i.e. ADHD), these cut-offs are validated with statistical and clinical consensus. In the absence of any validated criteria with which to define overt and covert CD cases, we considered the use of a liberal threshold to be a reasonable trade-off in exchange for interpretability.

Because we are analyzing relatives, the assumption that each observation is independent of all other observations is violated in these data. To account for correlation among family members, we used robust sandwich estimates of variance in all regression models so that p values would not be underestimated. Associations between binary and continuous demographic variables and the CD symptom scores were assessed using Wilcoxon rank-sum tests and Spearman correlations, respectively. All statistical tests were two-tailed and alpha was set at 0·05, with statistical trends recognized at alpha = 0·10.

RESULTS

The demographic characteristics of the probands and relatives are presented in Table 2, stratified by the gender of the proband. Age was positively associated with the covert CD symptom score in male probands and negatively associated with overt CD symptoms in relatives of female probands. Gender was significantly associated with both overt and covert CD symptom scores in the relatives of both male and female probands, with higher scores in males across all groups. Also, SES was significantly associated with both overt and covert CD symptom scores in the relatives of female probands, indicating increasing CD symptoms as SES decreases. A similar significant relationship with SES was found for covert CD symptom score in relatives of male probands. Thus, all familial analyses were adjusted for relative gender and SES.

Table 3 presents the frequencies of each symptom, stratified by proband and relative gender. As shown, males typically had higher symptom frequencies and mean symptom scores compared

https://doi.org/10.1017/S0033291703001788 Published online by Cambridge University Press

Table 3. *Prevalence of selected DSM-III-R conduct disorder symptoms used to generate overt and covert symptom counts*

	Families of male ADHD probands			Families of female ADHD probands		
	Probands ($n=138$)	Male relatives ($n=211$)	Female relatives ($n=212$)	Probands ($n=135$)	Male relatives ($n=195$)	Female relatives ($n=189$)
Overt symptoms						
Often starts physical fights	52 (38)	32 (15)	12 (6)	28 (21)	25 (13)	13 (7)
Used a weapon in more than one fight	23 (17)	15 (7)	3 (1)	6 (4)	12 (6)	3 (2)
Physically cruel to animals	13 (9)	7 (3)	0 (0)	3 (2)	13 (7)	1 (1)
Physically cruel to people	20 (14)	11 (5)	5 (2)	7 (5)	8 (4)	2 (1)
Stolen with confrontation	2 (1)	2 (1)	2 (1)	0 (0)	4 (2)	0 (0)
Mean overt symptom count	0·72±1·0	0·30±0·6	0·09±0·3	0·27±0·6	0·31±0·7	0·09±0·4
Covert symptoms						
Destroyed property of others	34 (25)	30 (14)	8 (4)	22 (16)	27 (14)	6 (3)
Deliberately set fires	28 (20)	21 (10)	6 (3)	7 (5)	22 (11)	3 (2)
Often lies	50 (36)	32 (15)	25 (12)	46 (34)	32 (16)	22 (12)
Broken into house, car or building	8 (6)	21 (10)	3 (1)	5 (4)	14 (7)	4 (2)
Stolen without confrontation	21 (15)	34 (16)	25 (12)	21 (16)	36 (18)	24 (13)
Mean covert symptom count	0·91±1·1	0·60±1·0	0·29±0·6	0·69±1·1	0·62±1·0	0·30±0·7

ADHD, attention-deficit hyperactivity disorder.
Values for individual symptoms represent frequency (%) of subjects with a full or subthreshold symptom.
Values for means of symptom counts represent mean±standard deviation.
Percentages may not be consistent with total *n* because of missing data.

to females. Also, covert symptoms were more common than overt symptoms. The most frequently occurring overt symptom across all strata was 'often starts physical fights', while the most common covert symptoms were 'often lies' and 'stolen without confrontation of the victim'.

To determine whether the familial risk for overt and covert CD symptom scores significantly differed by the gender of the proband, we tested the interaction between gender and the symptom scores. The overt CD symptom score-by-proband gender interaction term was not significantly different from zero ($z=1·03$, $p=0·30$). However, we found evidence that the covert CD symptom score-by-proband gender interaction term was significantly different from zero ($z=2·81$, $p=0·01$). Consequently, we estimated the main effects both in the full sample of all relatives as well as in the subsamples stratified by proband gender, as exhibited in Table 4.

In the full sample of all relatives, there was a significant within-person association of overt and covert CD scores. This parameter was transformed into a partial correlation coefficient of 0·42, indicating a moderate degree of association between overt and covert CD symptoms within relatives. Also, there was a significant, positive association between proband overt CD symptoms and relative overt CD symptoms, with a modest partial correlation coefficient of 0·14. We also found significant aggregation of the covert CD score, with a partial correlation coefficient of 0·10. However, the coaggregation term yielded a non-significant, negative coefficient. These results remained the same after additional statistical adjustment for relative age. Also, these results were identical when repeated in siblings only and parents only, with the exception of the overt aggregation estimate in the parent sample, which failed to reach statistical significance.

In the relatives of male probands, there was a significant within-person association of overt and covert CD scores. When transformed, we found a partial correlation coefficient of 0·41. In addition, there was a significant, positive association between male proband overt CD scores and relative overt CD scores, indicating aggregation. This estimate yielded a modest partial correlation coefficient of 0·16. The covert CD score in the relatives of male probands, although recognized as a trend ($p=0·08$) did not pass our threshold for statistical significance. Additionally, the coaggregation term yielded a non-significant, negative coefficient.

Table 4. *Bivariate familial aggregation models of covert and overt conduct disorder symptom scores*

Estimates of familial aggregation	All relatives ($n=807$)		Relatives of male probands ($n=423$)		Relatives of female probands ($n=384$)	
	β (95% CI)	Adjusted r	β (95% CI)	Adjusted r	β (95% CI)	Adjusted r
Within person	**0·26 (0·18–0·34)**	0·416	**0·27 (0·17–0·36)**	0·408	**0·26 (0·14–0·39)**	0·423
Overt aggregation	**0·09 (0·02–0·16)**	0·144	**0·08 (0·02–0·15)**	0·156	0·12 (−0·08–0·33)	0·132
Covert aggregation	**0·08 (0·03–0·13)**	0·101	0·06 (−0·01–0·12)	0·074	**0·11 (0·04–0·18)**	0·128
Coaggregation	−0·02 (−0·06–0·02)	−0·032	−0·02 (−0·07–0·03)	−0·039	−0·03 (−0·09–0·04)	−0·031

Values in table represent β [95% confidence interval (CI)]; significant effects are in bold font.
All analyses adjusted for SES and relative gender.
All parameter estimates conditional on the overt and covert scores of the proband.

Table 5. *Bivariate familial aggregation models of dichotomized covert and overt conduct disorder symptoms*

Estimates of familial aggregation	All relatives ($n=807$) OR (95% CI)	Relatives of male probands ($n=423$) OR (95% CI)	Relatives of female probands ($n=384$) OR (95% CI)
Within person	**4·56 (3·02–6·90)**	**5·41 (3·03–9·68)**	**3·87 (2·10–7·11)**
Overt aggregation	**1·69 (1·04–2·75)**	**2·18 (1·09–4·37)**	1·19 (0·57–2·47)
Covert aggregation	**1·69 (1·17–2·45)**	1·39 (0·82–2·36)	**2·05 (1·20–3·50)**
Coaggregation	0·79 (0·59–1·07)	0·76 (0·49–1·18)	0·83 (0·55–1·26)

All values are for odds ratios (OR) and 95% confidence intervals (CI); significant effects are in bold font.
All analyses adjusted for socio-economic status and relative gender.
All parameter estimates conditional on the overt and covert scores of the proband.

In relatives of female probands, there again was a significant within-person association of overt and covert CD scores, with a partial correlation coefficient of 0·42. The overt CD aggregation estimate was not significant, although of a similar magnitude to that of the overt parameter in the relatives of male probands ($r=0·16$ and 0·13, for relatives of male and female probands, respectively). However, there was a significant, positive association between the female proband covert CD score and the relative covert CD score, indicating familial aggregation of this measure, with a correlation coefficient of 0·13. There was no significant coaggregation in relatives of female probands.

To further explore the potential role of gender as a moderator in the familial aggregation of overt and covert CD symptoms, we examined the interaction between relative gender and each aggregation term. We did not find significant evidence that familial aggregation differed by relative gender for either the overt CD symptoms ($z=1·67$, $p=0·09$) or covert symptoms ($z=0·75$, $p=0·45$).

As secondary analyses we used dichotomized measures of overt and covert CD symptoms and repeated the analyses described above. First, we tested the interaction between proband gender and the binary symptom indicator variables. The overt CD symptom indicator-by-proband gender interaction term was not significantly different from zero ($z=0·27$, $p=0·79$). The covert CD symptom indicator-by-proband gender interaction term was identified as a statistical trend ($z=1·92$, $p=0·06$).

Next, using these binary measures, we estimated the main effects both in the full sample as well as in the subsamples stratified by proband gender, as exhibited in Table 5. In all three instances, the pattern of statistical significance was identical to that of analyses using symptom scores. For example, the odds of a relative having at least one overt CD symptom, given that the proband has at least one overt CD symptom, was 1·7 times the odds of a relative with a proband lacking any overt symptoms, a significant effect. Similarly, the odds of a relative having at least one covert CD symptom, given

https://doi.org/10.1017/S0033291703001788 Published online by Cambridge University Press

that the proband has at least one covert CD symptom, was 1·7 times the odds of a relative with a proband lacking any covert symptoms.

For relatives of male probands, the analysis of binary symptom indicators, as in the analysis of symptom scores, yielded a significant estimate of overt aggregation. The odds of a relative having at least one overt CD symptom, given that the male proband has at least one overt CD symptom, was 2·2 times the odds of a relative with a male proband lacking any overt symptoms.

Analyses using binary symptom indicators in the relatives of female probands, parallel to the analysis of symptom scores, found a statistically significant relationship between proband covert CD symptoms and relative covert CD symptoms. The odds of a relative having at least one covert CD symptom, given that the female proband has at least one covert CD symptom, are 2·1 times the odds of a relative with a female proband lacking any covert CD symptoms.

DISCUSSION

In a large sample of families ascertained by male and female ADHD probands with and without CD, we found evidence for the familial aggregation of both overt and covert CD symptoms. Also, there was evidence that the aggregation of covert symptoms was conditional on the gender of the proband, being stronger in the families of females. In addition, there was no statistical evidence of coaggregation between the two behavioral constructs, indicating that they are independently transmitted. While these results cannot speak to genetic effects, taken together they are most consistent with Hypothesis 5, which states that overt and covert CD symptoms, within the context of an ADHD sample, are distinct from a familial perspective.

Findings in families of male probands

The familial aggregation of overt CD symptoms in families of male probands is consistent with several studies that found familial influences on aggressive or violent behavior in samples of adults (Lappalainen *et al*. 1998; Manuck *et al*. 1999, 2000; Samochowiec *et al*. 1999) and children (Edelbrock *et al*. 1995; Lahey *et al*. 1998). However, our findings are inconsistent with a twin study of a community sample of 434 male twin pairs (Simonoff *et al*. 1998) that found a genetic effect for both aggression and property offenses. This discrepancy may be explained by sampling differences, as that study used a community sample and our study a referred ADHD sample with and without co-morbid CD. However, it should be noted that the familial effect for overt CD symptoms in our study was greater than the familial effect for covert CD symptoms, and that the aggregation of covert CD symptoms approached statistical significance ($p = 0{\cdot}08$). Also, the proportion of genetic variance was greater for overt behavior than for covert behavior in the Simonoff study. Thus, it may be that both patterns of antisocial behaviors are familial in boys with the overt effect being of greater magnitude, but our study did not have the statistical power to detect weaker familial loading of covert CD symptoms.

In another twin study, Edelbrock *et al*. (1995) did not find a genetic effect for delinquent (covert) behavior in a community sample of 181 same-sex twin pairs, approximately half of which were male. This null finding is difficult to interpret in light of our results, due to the mixture of male and female subjects. However, it should be noted that the p value of the genetic effect for delinquent behavior in that study was identified as a trend ($p < 0{\cdot}10$). Perhaps a re-analysis stratified by gender would have revealed a pattern of results more consistent with our findings. Also, it is difficult to reconcile our findings with the European adoption studies that found a significant effect for property crimes, but not for violent crimes (Bohman *et al*. 1982; Mednick *et al*. 1984). Several factors could account for this discrepancy, including different sampling schemes (community sample *v*. referred sample), age of subjects (adults *v*. children), and measures of antisocial behavior (criminal convictions *v*. DSM criteria for CD).

Findings in families of female probands

Our results partially support the hypothesis of a greater familial risk in families of female probands but the predicted interaction was found only for covert CD symptoms. These results are consistent with a large adoption study that found biological parents of female property criminals to have a higher proportion of property offenders compared to the biological parents of male property criminals (Sigvardsson

https://doi.org/10.1017/S0033291703001788 Published online by Cambridge University Press

et al. 1982; Brennan *et al*. 1991). Also, the rate of repeated convictions in that study was significantly greater in parents of female criminals relative to the parents of male criminals (Bohman, 1996). Based on these and similar data, it has been suggested that the threshold for genetic liability for developing criminality was higher in women than in men. That is, women require a greater genetic risk to manifest criminality as compared to men (Bohman, 1996). This idea is partially consistent with our findings, which showed stronger familial risks for covert behavior in families of female probands compared to families of male probands. These results are also consistent with findings that demonstrated increased rates of covert CD symptoms in female adolescents relative to males (McGee *et al*. 1990).

The failure to detect a greater magnitude of familial risk for overt CD symptoms in the families of female probands may be due to the low base rate of such behaviors in females. Evidence for this notion can be found in the wide confidence interval for the overt aggregation parameter in relatives of female probands in Table 4, indicating an imprecise estimate. Another reason for the failure to detect aggregation of overt CD symptoms in families of female probands could be that aggression was manifested differently in females. For example, in a review of gender differences in patterns of aggression, it was noted that women tend to use indirect or verbal assaults such as alienation and character deformation, as opposed to physical aggression (Loeber & Stouthamer-Loeber, 1998). Also, aggression in girls may take a similar, non-physical form, and may be more verbal and relational in nature, such as spreading derogatory rumors and excluding peers from play groups (Crick, 1995; Crick & Grotpeter, 1995). Thus, it may be that the measurement of overt CD symptoms in females may have been incomplete, hampering our ability to detect familial aggregation. This potential measurement error, coupled with the imprecision noted above, suggests that this null finding should be interpreted cautiously.

Overt and covert CD as distinct familial disorders

Given the statistical trend for covert aggregation in families of males and the measurement issues hampering the precision of the overt aggregation estimate in families of females, the aggregation results taken as a whole coupled with the null coaggregation results are compatible with the hypothesis that overt and covert subtypes of CD may represent distinct familial conditions, each independently transmitted. This is consistent with research that has shown differential associations between these two constructs and other risk factors such as birth complications (Raine *et al*. 1994, 1997), cortisol (Virkkunen, 1985; McBurnett *et al*. 2000) and serotonin (Moffitt *et al*. 1998) levels. However, this observed statistical specificity does not rule out other, more complex causal models (Garber & Hollon, 1991). For example, the familial risk for covert CD symptoms in families of male probands may become statistically evident when interacting with another, unmeasured factor. These results, if replicated, need to be incorporated into a more comprehensive causal model that explains the association between important risk factors and subtypes of CD.

The strong within person association between overt and covert CD symptoms is not incompatible with the hypothesis that these symptom subtypes are distinct disorders. For instance, the two subtypes of CD may share a common causal factor, perhaps environmental in origin, yet have distinct genetic causes. Such a scenario could produce etiologically separate, yet correlated, disorders (Garber & Hollon, 1991). To develop this notion in the context of the present study, it is important to note that ADHD is associated with early-onset CD (Moffitt, 1990; Loeber *et al*. 1995), marked by both overt and covert symptoms (Lahey *et al*. 1998, 1999). We can therefore hypothesize that a common environmental etiologic factor of the two behavioral subtypes may be prevalent within ADHD families. Thus, although overt and covert CD symptoms may have distinct genetic risks, the causal chain of each may be completed by a common environmental factor that could be widespread in families of ADHD children, leading to etiologically distinct yet commonly co-occurring CD symptom patterns in ADHD children.

Finally, it should be noted that while the within person correlation was moderately sized and highly significant, there were many relatives who exhibited only one subtype of CD

https://doi.org/10.1017/S0033291703001788 Published online by Cambridge University Press

symptoms. Out of all the relatives with at least one CD symptom ($n=296$), only 27% had at least one symptom of each subtype. Thus, the great majority of relatives with CD symptoms had either overt symptoms (15%) or covert symptoms (58%), but not both. Thus, the degree of symptomatic overlap may not be as extensive as the within person correlations may suggest, and does not rule out the hypothesis of overt and covert CD symptoms as distinct disorders.

Dimensional measures of psychiatric disorders

This study, like that of Alsobrook & Pauls (2002), is distinct from other studies examining familial aggregation of disorders in the use of continuous measures, rather than the conventional binary disorder indicators. This approach avoids the loss of information, inefficiency, and difficulty in interpretation resulting from dichotomizing (Dunn, 2000). Also, it has been suggested that CD symptoms should be analyzed as a continuous measure because of the linear association found between symptom counts and measures of impairment (Robins & Price, 1991). However, the clinical relevance and generalizability of results derived from continuous measures could be questioned, compared to similar analyses using binary indicators, which provide odds ratios as a measure of association.

In comparing the two methods, it was found that a dimensional approach to the measurement of child psychopathology performed roughly as well as a categorical approach in terms of agreement with external validators (Jensen *et al.* 1996). However, as noted by Kasius *et al.* (1997), the divergence between the two approaches may be enough to warrant use of both to attain the most information about child psychopathology. As such, the strength of our results is enhanced by the identical pattern of results found using the two methods, although the cut-point used here (no symptoms *v.* any symptoms) was not empirically based. Future research should define clinically and nosologically meaningful cut-offs to define overt CD and covert CD 'cases'.

Limitations

These findings should be considered in the light of some methodological limitations. First, these analyses were conducted with data from an ADHD family study, not in families ascertained on the basis of proband CD. However, studies of CD youth document a very high co-morbidity with ADHD (Offord *et al.* 1986; Lahey *et al.* 1998). CD co-morbid with ADHD is marked by a poor long-term outcome (Moffitt, 1990; Hinshaw *et al.* 1993; Mannuzza *et al.* 1993; Loeber *et al.* 2000) and tends to onset in early childhood (Loeber *et al.* 1995; Lahey *et al.* 1998). Early-onset CD cases also tend to exhibit more overt symptoms (Lahey *et al.* 1998, 1999) that are more heritable (DiLalla & Gottesman, 1989). In contrast, late-onset CD is characterized by lower rates of ADHD (Lahey *et al.* 1998), an acute course (Moffitt, 1993), and a lesser degree of heritability (Lyons *et al.* 1995). In addition, Moffitt (1993) predicts that late-onset CD cases primarily commit covert acts and status offenses, a hypothesis supported by empirical work (Lahey *et al.* 1998, 1999). Thus, it is reasonable to speculate that a sample ascertained through CD probands would contain a greater degree of late-onset CD cases relative to a sample ascertained via ADHD probands. If so, then such a study may not detect the familial aggregation of overt and covert CD symptoms found in the present study. Considering this, the generalization of our results must be limited to ADHD families until further research extends the findings to other samples. Another limit to the generalizability of these results is the racial distribution of the sample since the probands were 97% Caucasian.

Also, it should be noted that the symptoms of CD used in this analysis represent a limited sampling of the total set of antisocial behaviors. While symptoms as taken from the DSM represent behaviors deemed clinically relevant, a more exhaustive sampling of antisocial behaviors could yield different results, especially for females. Additionally, while we did not find evidence that familial aggregation differed by relative gender, this analysis may have been underpowered. Considering the borderline significance of the overt interaction term, there may be meaningful differences between males and females in the familial aggregation of overt symptoms that could be detected with larger samples. Future studies should explore this issue while taking the methodological difficulties associated with the measurement of overt symptoms in females described above into account. It should also be noted that the estimates of

familial aggregation, while statistically significant, yielded rather modest correlations. Although the results could indicate that the familial transmission of CD symptom subtypes is weak, it is also possible that the relationship between proband and relative symptom scores deviates to some degree from linearity. If the assumption of linearity is not met, our models may underestimate the size of the effect. While our analysis of dichotomized measures of the symptom scores avoids this problem and provides effect sizes that are statistically and clinically significant, future studies with more power are needed to clarify the nature of the familial aggregation of CD symptom subtypes.

Another concern stems for the use of maternal interviews for children younger than 12 years old, which may have decreased the sensitivity of detecting CD symptoms. However, children younger than 12 years old are less likely than older children to spend a great deal of time beyond the watch of adult supervision. Thus, the loss of information suffered through the use of maternal reports should be minimal. Also, there is evidence that young children have limited expressive and receptive language abilities, questioning the reliability of their self-report (Loeber *et al*. 1991). A study of interview techniques for young children also casts doubt on the reliability of their reports (Achenbach *et al*. 1987). Another related limitation is that younger siblings may not have passed through the age of risk for some of the CD symptoms, leading to the misclassification of their symptom status and a reduction of statistical precision. Thus, the estimates of overt and covert aggregation may be stronger than found here.

Finally, it should be noted that the results document familiality and do not necessarily imply genetic causality. Conclusions about the genetic influence on overt and covert CD symptoms await twin, adoption, and molecular genetic studies.

Conclusions

Despite these limitations, familial risk analysis in a large sample of male and female ADHD probands found evidence for the independent familial aggregation of overt and covert CD symptoms. While not implying genetic influences, these findings support the hypothesis that, in an ADHD sample, overt and covert CD symptoms represent distinct disorders. If replicated in other samples with differing ascertainment strategies, these results could inform twin, adoption and molecular genetic studies searching for the genetic liability for subtypes of CD symptoms, calling attention to the idea the subtype of CD symptom should be considered when conducting research on CD and related constructs. Ultimately, intervention and prevention programs charged with decreasing CD and antisocial behavior in children may need to be tailored to the symptomatic subtype.

ACKNOWLEDGEMENTS

This work was supported, in part, by grants from USPHS (NIMH) grant RO1 MH-41314-01A2 (J.B.). The authors thank Dr Stephen V. Faraone and Dr David L. Pauls for their contributions to this manuscript.

REFERENCES

Achenbach, T. M., Howell, C. T., Quay, H. C. & Conners, C. K. (1991). National survey of problems and competencies among four- to sixteen-year-olds: parents' reports for normative and clinical samples. *Monographs of the Society for Research in Child Development* **56**, 1–131.

Achenbach, T. M., McConaughy, S. H. & Howell, C. T. (1987). Child/adolescent behavioral and emotional problems: implications of cross-informant correlations for situational specificity. *Psychological Bulletin* **101**, 213–232.

Alsobrook, J. P. & Pauls, D. L. (2002). A factor analysis of tic symptoms in Gilles de la Tourette's syndrome. *American Journal of Psychiatry* **159**, 291–296.

APA (1994). *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV*. American Psychiatric Association: Washington, DC.

Beitchman, J. H., Inglis, A. & Schachter, D. (1992). Child psychiatry and early intervention. IV. The externalizing disorders. *Canadian Journal of Psychiatry* **37**, 245–249.

Biederman, J., Faraone, S. V., Keenan, K., Benjamin, J., Krifcher, B., Moore, C., Sprich-Buckminster, S., Ugaglia, K., Jellinek, M. S., Steingard, R., Spencer, T., Norman, D., Kolodny, R., Kraus, I., Perrin, J., Keller, M. B. & Tsuang, M. T. (1992). Further evidence for family-genetic risk factors in attention deficit hyperactivity disorder. Patterns of comorbidity in probands and relatives in psychiatrically and pediatrically referred samples. *Archives of General Psychiatry* **49**, 728–738.

Biederman, J., Faraone, S. V., Mick, E., Williamson, S., Wilens, T. E., Spencer, T. J., Weber, W., Jetton, J., Kraus, I., Pert, J. & Zallen, B. (1999). Clinical correlates of ADHD in females: findings from a large group of girls ascertained from pediatric and psychiatric referral sources. *Journal of the American Academy of Child and Adolescent Psychiatry* **38**, 966–975.

Biederman, J., Mick, E., Faraone, S. V., Braaten, E., Doyle, A., Spencer, T., Wilens, T. E., Frazier, E. & Johnson, M. A. (2002). Influence of gender on attention deficit hyperactivity disorder in children referred to a psychiatric clinic. *American Journal of Psychiatry* **159**, 36–42.

Bohman, M. (1996). Predisposition to criminality: Swedish adoption studies in retrospect. *Ciba Foundation Symposium* **194**, 99–109.

Bohman, M., Cloninger, C. R., Sigvardsson, S. & von Knorring, A. L. (1982). Predisposition to petty criminality in Swedish adoptees. I. Genetic and environmental heterogeneity. *Archives of General Psychiatry* **39**, 1233–1241.

Brennan, P. A., Mednick, S. A. & Gabrielli Jr, W. F. (1991). Genetic influences and criminal behavior. In *Genetic Issues in Psychosocial Epidemiology* (ed. M. Tsuang, K. S. Kendler and M. J. Lyons), pp. 231–246. Rutgers University Press: New Brunswick.

Cadoret, R. J., Yates, W. R., Troughton, E., Woodworth, G. & Stewart, M. A. (1995). Genetic-environmental interaction in the genesis of aggressivity and conduct disorders. *Archives of General Psychiatry* **52**, 916–924.

Caron, C. & Rutter, M. (1991). Comorbidity in child psychopathology: concepts, issues and research strategies. *Journal of Child Psychology and Psychiatry* **32**, 1063–1080.

Crick, N. R. (1995). Relational aggression: the role of intent attributes, feelings of distress, and provocation type. *Development and Psychopathology* **7**, 313–322.

Crick, N. R. & Grotpeter, J. K. (1995). Relational aggression, gender, and social-psychological adjustment. *Child Development* **66**, 710–722.

DiLalla, L. F. & Gottesman, I. I. (1989). Heterogeneity of causes for delinquency and criminality: lifespan perspectives. *Development and Psychopathology* **1**, 339–349.

Dunn, G. (2000). *Statistics in Psychiatry*. Oxford University Press: New York, NY.

Earls, F. (1994). Oppositional-defiant and conduct disorders. In *Child and Adolescent Psychiatry. Modern Approaches* (ed. M. Rutter, E. Taylor and L. Hersov), pp. 308–329. Blackwell Scientific Publications: Oxford.

Edelbrock, C., Rende, R., Plomin, R. & Thompson, L. A. (1995). A twin study of competence and problem behavior in childhood and early adolescence. *Journal of Child Psychology and Psychiatry* **36**, 775–785.

Faraone, S. V., Biederman, J., Jetton, J. G. & Tsuang, M. T. (1997). Attention deficit disorder and conduct disorder: longitudinal evidence for a familial subtype. *Psychological Medicine* **27**, 291–300.

Faraone, S. V., Biederman, J. & Monuteaux, M. C. (2000). Attention-deficit disorder and conduct disorder in girls: evidence for a familial subtype. *Biological Psychiatry* **48**, 21–29.

Faraone, S. V. & Tsuang, M. T. (1995). Methods in psychiatric genetics. In *Textbook in Psychiatric Epidemiology* (ed. M. Tohen, M. T. Tsuang and G. E. P. Zahner), pp. 81–134. John Wiley: New York, NY.

Fergusson, D. M., Horwood, L. J. & Lynskey, M. T. (1994). Structure of DSM-III-R criteria for disruptive childhood behaviors: confirmatory factor models. *Journal of the American Academy of Child & Adolescent Psychiatry* **33**, 1145–1155; discussion 155-157.

Frick, P., Lahey, B., Loeber, R., Tannenbaum, L., Horn, Y., Christ, M., Hart, E. & Hanson, K. (1993). Oppositional defiant disorder and conduct disorder: a meta-analytic review of factor analyses and cross-validation in a clinical sample. *Clinical Psychology Review* **13**, 319–340.

Garber, J. & Hollon, S. D. (1991). What can specificity designs say about causality in psychopathology research? *Psychological Bulletin* **110**, 129–136.

Ghodsian-Carpey, J. & Baker, L. A. (1987). Genetic and environmental influences on aggression in 4- to 7-year-old twins. *Aggressive Behavior* **13**, 173–186.

Hardin, J. & Hilbe, J. (2001). *Generalized Linear Models and Extensions*. Stata Press: College Station, TX.

Hinshaw, S., Lahey, B. & Hart, E. (1993). Issues of taxonomy and comorbidity in the development of Conduct Disorder. *Development and Psychopathology* **5**, 31–49.

Hollingshead, A. B. (1975). *Four Factor Index of Social Status*. Yale Press: New Haven.

Hudson, J. I., Laird, N. M. & Betensky, R. A. (2001*a*). Multivariate logistic regression for familial aggregation of two disorders. I. Development of models and methods. *American Journal of Epidemiology* **153**, 500–505.

Hudson, J. I., Laird, N. M., Betensky, R. A., Keck Jr, P. E. & Pope Jr, H. G. (2001*b*). Multivariate logistic regression for familial aggregation of two disorders. II. Analysis of studies of eating and mood disorders. *American Journal of Epidemiology* **153**, 506–514.

Institute of Medicine (1989). *Research on Chidren and Adolesents with Mental, Behavioral, and Developmental Disorders*. National Academy Press: Washington, DC.

Jensen, P. S., Watanabe, H. K., Richters, J. E., Roper, M., Hibbs, E. D., Salzberg, A. D. & Liu, S. (1996). Scales, diagnoses, and child psychopathology. II. Comparing the CBCL and the DISC against external validators. *Journal of Abnormal Child Psychology* **24**, 151–169.

Kasius, M., Ferdinand, R., van den Berg, H. & Verhulst, F. C. (1997). Associations between different diagnostic approaches for child and adolescent psychopathology. *Journal of Child Psychology and Psychiatry* **38**, 625–632.

Kleinbaum, D. G., Kupper, L. L. & Muller, K. E. (1988). *Applied Regression Analysis and Other Multivariate Methods*. Wadsworth Publishing Company: Belmont, CA.

Lahey, B., Loeber, R., Quay, H., Applegate, B., Shaffer, D., Waldman, I., Hart, E., McBurnett, K., Frick, P., Jensen, P., Dulcan, M., Canino, G. & Bird, H. (1998). Validity of DSM-IV subtypes of conduct disorder based on age of onset. *Journal of the American Academy of Child and Adolescent Psychiatry* **37**, 435–442.

Lahey, B. B., Goodman, S. H., Waldman, I. D., Bird, H., Canino, G., Jensen, P., Regier, D., Leaf, P. J., Gordon, R. & Applegate, B. (1999). Relation of age of onset to the type and severity of child and adolescent conduct problems. *Journal of Abnormal Child Psychology* **27**, 247–260.

Lappalainen, J., Long, J. C., Eggert, M., Ozaki, N., Robin, R. W., Brown, G. L., Naukkarinen, H., Virkkunen, M., Linnoila, M. & Goldman, D. (1998). Linkage of antisocial alcoholism to the serotonin 5-HT1B receptor gene in 2 populations. *Archives of General Psychiatry* **55**, 989–994.

Loeber, R., Burke, J. D., Lahey, B. B., Winters, A. & Zera, M. (2000). Oppositional defiant and conduct disorder: a review of the past 10 years, part I. *Journal of the American Academy of Child & Adolescent Psychiatry* **39**, 1468–1484.

Loeber, R., Green, S. M., Keenan, K. & Lahey, B. B. (1995). Which boys will fare worse? Early predictors of the onset of conduct disorder in a six-year longitudinal study. *Journal of the American Academy of Child & Adolescent Psychiatry* **34**, 499–509.

Loeber, R., Green, S. M., Lahey, B. B. & Stouthamer-Loeber, M. (1991). Differences and similarities between children, mothers, and teachers as informants on disruptive child behavior. *Journal of Abnormal Child Psychology* **19**, 75–95.

Loeber, R. & Hay, D. (1997). Key issues in the development of aggression and violence from childhood to early adulthood. *Annual Review of Psychology* **48**, 371–410.

Loeber, R. & Schmaling, K. B. (1985). Empirical evidence for overt and covert patterns of antisocial conduct problems: a meta-analysis. *Journal of Abnormal Child Psychology* **13**, 337–353.

Loeber, R. & Stouthamer-Loeber, M. (1998). Development of juvenile aggression and violence. Some common misconceptions and controversies. *American Psychologist* **53**, 242–259.

Lyons, M. J., True, W. R., Eisen, S. A., Goldberg, J., Meyer, J. M., Faraone, S. V., Eaves, L. J. & Tsuang, M. T. (1995). Differential heritability of adult and juvenile antisocial traits. *Archives of General Psychiatry* **52**, 906–915.

Mannuzza, S., Klein, R. G., Bessler, A., Malloy, P. & LaPadula, M. (1993). Adult outcome of hyperactive boys. Educational achievement, occupational rank, and psychiatric status. *Archives of General Psychiatry* **50**, 565–576.

Manuck, S. B., Flory, J. D., Ferrell, R. E., Dent, K. M., Mann, J. J. & Muldoon, M. F. (1999). Aggression and anger-related traits associated with a polymorphism of the tryptophan hydroxylase gene. *Biological Psychiatry* **45**, 603–614.

Manuck, S. B., Flory, J. D., Ferrell, R. E., Mann, J. J. & Muldoon, M. F. (2000). A regulatory polymorphism of the monoamine oxidase-A gene may be associated with variability in aggression,

impulsivity, and central nervous system serotonergic responsivity. *Psychiatry Research* **95**, 9–23.

McBurnett, K., Lahey, B. B., Rathouz, P. J. & Loeber, R. (2000). Low salivary cortisol and persistent aggression in boys referred for disruptive behavior. *Archives of General Psychiatry* **57**, 38–43.

McGee, R., Feehan, M., Williams, S., Partridge, F., Silva, P. A. & Kelly, J. (1990). DSM-III disorders in a large sample of adolescents. *Journal of the American Academy of Child & Adolescent Psychiatry* **29**, 611–619.

Mednick, S. A., Gabrielli Jr, W. F. & Hutchings, B. (1984). Genetic influences in criminal convictions: evidence from an adoption cohort. *Science* **224**, 891–894.

Moffitt, T. E. (1990). Juvenile delinquency and attention deficit disorder: boys' developmental trajectories from age 3 to age 15. *Child Development* **61**, 893–910.

Moffitt, T. E. (1993). Adolescence-limited and life-course-persistent antisocial behavior: a developmental taxonomy. *Psychological Review* **100**, 674–701.

Moffitt, T. E., Brammer, G. L., Caspi, A., Fawcett, J. P., Raleigh, M., Yuwiler, A. & Silva, P. (1998). Whole blood serotonin relates to violence in an epidemiological study. *Biological Psychiatry* **43**, 446–457.

Moore, M. H., Prothrow-Stith, D., Guyer, B. & Spivak, H. (1994). Violence and intentional injuries: criminal justice and public health perspectives on an urgent national problem. In *Understanding and Preventing Violence*, vol. 4 (ed. A. J. Reiss and J. A. Roth), pp. 167–216. National Academy Press: Washington, DC.

Offord, D. R., Alder, R. J. & Boyle, M. H. (1986). Prevalence and sociodemographic correlates of conduct disorder. *American Journal of Social Psychiatry* **6**, 272–278.

Offord, D. R. & Bennett, K. J. (1994). Conduct disorder: long-term outcomes and intervention effectiveness. *Journal of the American Academy of Child & Adolescent Psychiatry* **33**, 1069–1078.

Orvaschel, H. & Puig-Antich, J. (1987). *Schedule for Affective Disorders and Schizophrenia for School-Age Children: Epidemiologic Version*. Nova University: Fort Lauderdale, FL.

Raine, A. (1993). *The Psychopathology of Crime: Criminal Behavior as a Clinical Disorder*. Academic Press: San Diego.

Raine, A., Brennan, P. & Mednick, S. A. (1994). Birth complications combined with early maternal rejection at age 1 year predispose to violent crime at age 18 years. *Archives of General Psychiatry* **51**, 984–988.

Raine, A., Brennan, P. & Mednick, S. A. (1997). Interaction between birth complications and early maternal rejection in predisposing individuals to adult violence: specificity to serious, early-onset violence. *American Journal of Psychiatry* **154**, 1265–1271.

Robins, L. N. & Price, R. K. (1991). Adult disorders predicted by childhood conduct problems: results from the NIMH Epidemiologic Catchment Area project. *Psychiatry* **54**, 116–132.

Samochowiec, J., Lesch, K. P., Rottmann, M., Smolka, M., Syagailo, Y. V., Okladnova, O., Rommelspacher, H., Winterer, G., Schmidt, L. G. & Sander, T. (1999). Association of a regulatory polymorphism in the promoter region of the monoamine oxidase A gene with antisocial alcoholism. *Psychiatry Research* **86**, 67–72.

Sigvardsson, S., Cloninger, C. R., Bohman, M. & von Knorring, A. L. (1982). Predisposition to petty criminality in Swedish adoptees. III. Sex differences and validation of the male typology. *Archives of General Psychiatry* **39**, 1248–1253.

Silberg, J., Rutter, M., Meyer, J., Maes, H., Hewitt, J., Simonoff, E., Pickles, A., Loeber, R. & Eaves, L. (1996). Genetic and environmental influences on the covariation between hyperactivity and conduct disturbance in juvenile twins. *Journal of Child Psychology and Psychiatry* **37**, 803–816.

Simonoff, E. (2001). Genetic influences on conduct disorder. In *Conduct Disorders in Childhood and Adolescence* (ed. J. Hill and B. Maughan), pp. 202–234. Cambridge University Press: Cambridge, UK.

Simonoff, E., Pickles, A., Meyer, J., Silberg, J. & Maes, H. (1998). Genetic and environmental influences on subtypes of conduct disorder behavior in boys. *Journal of Abnormal Child Psychology* **26**, 495–509.

Smalley, S. L., McGough, J. J., Del'Homme, M., NewDelman, J., Gordon, E., Kim, T., Liu, A. & McCracken, J. T. (2000). Familial clustering of symptoms and disruptive behaviors in multiplex families with attention-deficit/hyperactivity disorder. *Journal of the American Academy of Child & Adolescent Psychiatry* **39**, 1135–1143.

Spitzer, R. L., Williams, J. B., Gibbon, M. & First, M. B. (1990). *Structured Clinical Interview for DSM-III-R: Non-Patient Edition* (*SCID-NP, Version 1.0*). American Psychiatric Press: Washington, DC.

US Department of Health and Human Services (2001). *Youth Violence: a Report of the Surgeon General*. US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Injury Prevention and Control; Substance Abuse and Mental Health Services Administration, Center for Mental Health Services; and National Institute of Mental Health, National Institute of Mental Health: Rockville, MD.

Virkkunen, M. (1985). Urinary free cortisol secretion in habitually violent offenders. *Acta Psychiatrica Scandinavica* **72**, 40–44.

Wamboldt, M. Z. & Wamboldt, F. S. (2000). Role of the family in the onset and outcome of childhood disorders: selected research findings. *Journal of the American Academy of Child & Adolescent Psychiatry* **39**, 1212–1219.

Wechsler, D. (1974). *Manual for the Wechsler Intelligence Scale for Children – Revised*. The Psychological Corporation: New York.

WHO (1986). ICD-10: Draft of Chapter V – Mental, Behavioural and Developmental Disorders. World Health Organization, Division of Mental Health.