Co-occurrence of Aggressive Behavior and Rule-Breaking Behavior at Age 12: Multi-Rater Analyses

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Aggressive Behavior (AGG) and Rule-Breaking Behavior (RB) are two of the eight CBCL syndromes. The phenotypic correlation between AGG and RB ranges from .48 to .76, and varies depending on the rater and the sex of the child. Prevalence of AGG and RB (i.e., $T \geq 67$) is in the range of 6%–7% in both boys and girls. Fifty percent to 60% of the children who are deviant on AGG are also deviant on RB and vice versa. Why so many children show problem behavior in the clinical range for both syndromes is unclear. This co-occurrence could be due to genetic factors influencing both traits, to environmental factors influencing both traits, or to both. The purpose of this study is to use a genetically informative sample to estimate genetic and environmental influences on AGG and RB and to investigate the etiology of the co-occurrence of both behaviors. We do this using multiple informants to take into account underlying sources of parental agreement and disagreement in ratings of their offspring. To this end, mother and father ratings of AGG and RB were collected by using the Child Behavior Checklist in a large sample of 12-year-old twins. Parental agreement is represented by an interparent correlation in the range of .53–.76, depending on phenotype (AGG or RB) and sex of the child. Genetic influences account for 79% and 69% of the individual differences in RB and AGG behavior (defined as AGG and RB on which both parents do agree) in boys. In girls 56% and 72% of the variance in RB and AGG are accounted for by genetic factors. Shared environmental influences are significant for RB in girls only, explaining 23% of the total variance. Eighty percent of the covariance between AGG and RB, similarly assessed by both parents, can be explained by genetic influences. So, co-occurrence in AGG and RB is mainly caused by a common set of genes. Parental disagreement seems to be a combination of so-called rater bias and of parental specific views.

KEY WORDS: Twins; rater bias; CBCL; heritability; aggression; rule breaking; multivariate genetic analysis.

INTRODUCTION

In past years, differential diagnosis was the key concept of professionals who provide clinical services. In other words, in childhood psychopathology one

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carefully considered all possible diagnoses and picked the one that best fit the symptoms. However, nowadays the concept of co-occurrence, the co-occurrence of several disorders in the same person, is winning ground. The study of co-occurrence is of general interest to both researchers and clinicians. Research scientists will need to understand how best to refine phenotypes for future molecular genetic research. From a clinical perspective, population-based and genetic studies on co-occurrence can help by answering questions about whether or not a syndrome most often occurs alone or in concert with other conditions and can address the etiology of the co-occurrence. Most children with problem behavior in the clinical range seem to be co-morbid for several problem behavior syndromes (Caron and Rutter, 1991; Kessler, *et al.,* 1994; Verhulst and

Van der Ende, 1993). The high co-occurrence rates obtained from both parents' and teachers' ratings indicate that co-occurrence between behavioral syndromes is not a methodological artifact resulting from the use of a single informant but may be regarded as an aspect of the complexities of child psychopathology (Yang *et al.,* 2001). For Aggressive Behavior (AGG) and Rule-Breaking Behavior (RB) the presence of co-occurrence is well established. Both syndromes are derived from the Child Behavior Checklist (CBCL, Achenbach, 1991) and are represented by items that point to the same direction of problem behavior. Factor analyses of CBCL items clearly result in two distinct syndromes (Achenbach *et al.,* 1987b; Cole, 1987; De Groot *et al.,* 1994; Verhulst *et al.,* 1988). In Achenbach and Ruffle (2000) AGG and RB are independent but related syndromes on the CBCL, TRF (Teacher Report Form), and YSR (Youth Self Report). It is clear that the two syndromes are highly correlated, but are discrete, like many if not most of the psychopathologies. Similar correlations have been reported between attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD), anxiety disorders and depression, and personality disorders and depression. Evidence for independence has been collected through the use of factor analyses of the type used by Achenbach and Rescorla (2000). Many conduct disorder (CD) experts have argued for the importance of studying aggressive CD and delinquent CD as two different constructs (Frick *et al.,* 1993, Lahey *et al.,* 2003).

A phenotypic correlation of .7 between AGG and RB was observed in an adoption study of 78 pairs of unrelated adoptive siblings and 94 pairs of biologically related siblings who were rated by their parents and teachers (Deater-Deckard and Plomin, 1999). Further, high co-occurrence of RB and AGG is found based on parent (CBCL) ratings in a sample 854 randomly selected students (Yang *et al.,* 2001). These high rates of co-occurrence replicate the finding of previous studies (Faraone *et al.,* 1991; Spitzer *et al.,* 1990; Verhulst and Van der Ende, 1993; Walker *et al.,* 1991). The evidence for the co-occurrence of AGG and RB thus appears to be strong.

The literature on AGG and RB and the related DSM disorders ODD and CD indicate remarkable differences in prevalence and types of symptoms between boys and girls. Thus any study of behaviors such as these must take into account potential gender bias. One source of bias can be the informant, and we therefore paid special attention to how parents rate their boys and girls AGG and RB. It is well established that mothers rate their children as having more problem behavior than do fathers. Finally, from a scientific point of view, testing

for sex-differences seems appropriate to search for the most reliable results and, as pointed out by Zoccolillo *et al.* (1996), sex differences in the demonstration of aggressive and delinquent subtypes of CD need to be further explored.

The sources or etiology of the co-occurrence of AGG and RB and whether or not sex differences are significant is as yet unexplained. Rutter (1997) suggested a number of possible explanations for co-occurrence, one of which is the proposal that co-occurrence may arise from the same or correlated risk factors. For instance, is the source of the co-occurrence genetic or environmental factors or both? It is this hypothesis that we will test using twin data. Do AGG and RB co-occur because of environmental factors, genetic factors, or some combination of both? Answers to these questions would provide useful information in understanding childhood psychopathology. For instance, AGG has been shown to be predictive of ODD and later CD, and RB has been shown to be predictive of CD (Achenbach and Rescorla, 2001). There is a large body of literature discussing the many phenotypes of ODD/CD, and experts in this field struggle with the question of whether or not the aggressive and delinquent subtypes of CD exist as independent, yet correlated, phenotypes or whether they are best described as a single syndrome with variable expression (Burke *et al.,* 2002). Therefore a behavioral genetic study of the co-occurrence between AGG and RB has the potential not only to provide information on these questions but also to provide an estimate of the unique and shared genetic and environmental influences on the two main subtypes of CD. If research verifies that genes associated with one problem behavior syndrome are also typically associated with another as well, perspectives on the ways in which co-occurrence is characterized must change. These changes will then likely lead to more successful gene-finding expectations.

Genetics of AGG and RB

Evidence from twin studies suggests that individual differences in AGG as well as in RB are influenced by genetic and shared environmental factors. Twin studies of parent- and teacher-reported AGG and RB show low to high genetic variation (explaining 24%–70% of the variance) and low to moderate shared environmental variation (Deater-Deckard and Plomin, 1999; Edelbrock *et al.,* 1995; Eley *et al.,* 1999; Schmitz *et al.,* 1995). Studies using self-reported delinquency in junior and senior high school twins report monozygotic twin correlations in the range of .65, with dizygotic twin correlations in the range of .48, resulting in a heritability

estimate of 34%. In a meta-analysis on AGG an overall genetic effect was reported that accounted for 50% of the variance in AGG (Miles and Carey, 1997). A sibling-adoption study, with 111 biological siblings and 221 nonbiological international adopted sibling pairs (mean age 12.4) reported heritabilities of 70% for AGG and of 30% for RB. There was also evidence for the significance of shared environmental influences on RB (Van den Oord *et al.,* 1994; Van der Valk *et al.,* 1998). This range of genetic and environmental estimates could be due to the fact that the samples used consist of children of several ages. Further, varying sample sizes—and in that respect varying power—may cause differences in heritability estimates. Hudziak *et al.* (2003, this issue) report the genetic influences on AGG to be roughly 60% on children ages 3, 7, and 10, regardless of gender or informant and based on large samples. A study on the causes of stability of childhood AGG in a large longitudinal sample of Dutch twins shows that stability is mainly explained by genetic factors (65%), expressing a simplex pattern. Twenty-five percent of the stability is accounted for by a common set of shared environmental factors (Van Beijsterveldt *et al.,* 2003, this issue). Based on the knowledge that genes and shared environmental factors influence AGG as well as RB, it will be important to study the possibility that similar genes or similar environmental influences are significant to both. Based on previous studies on externalizing problem behavior, it is found that externalizing behavior in boys and girls is influenced by the same set of genes (absence of heterogeneity) but that the genetic influences on these kinds of behaviors are of different strength.

Multiple Informants

In studies on childhood psychopathology, such as AGG and RB, researchers commonly use parental ratings for behavioral assessment, such as the Child Behavior Checklist (Achenbach, 1991). This approach, which quantifies children's problem behavior by asking the parents to score behavioral and emotional problems on behavioral questionnaires, has both advantages and disadvantages. Parents have the advantage that they observe their children over long periods and can witness both frequent and rare behaviors. Additionally, using more than one rater will give more reliable results by decreasing measurement error. Disadvantages are that the disagreement between mother and father ratings are sometimes interpreted as yielding conflicting, rather than complementary data. A meta-analysis by Achenbach *et al.* (1987a) showed a mean correlation of .60 between maternal and paternal ratings of problem behavior of the same child. This underscores that parents are able to assess their child's behavior; for if parental ratings would reflect nothing but error, the correlation between their ratings would be low. On the other hand, this interparent correlation is less than perfect. This may be explained by different forms of parental disagreement. Parental disagreement could arise if the parents' own traits influenced ratings (a projection bias) or if parents exhibited response biases (e.g., stereotyping, employing different normative standards, or having certain response styles, i.e., judging problem behaviors more or less severely), resulting in so-called rater bias. However, disagreement could also reflect the fact that each parent assesses a rater-specific aspect of his or her child's behavior. This will occur when the parent observes the child in distinct situations or is exposed to distinct samples of the child's behavior. For instance, the parent who usually brings the child to school may be more familiar with the child's behavior outside the home. Moreover, each parent may interact differently with the child (Achenbach *et al.,* 1987a). These unique interactions between a parent and a child may allow each parent to provide additional information about the child's behavior, apart from the information on which they both agree.

Data on unrelated singletons do not have the statistical properties to disentangle the sources of disagreement, whereas using multiple raters in a genetically informative sample gives rise to the opportunity to distinguish between rater bias/unreliability or rater-specific view as the major source of disagreement. In prior studies on the issue of rater bias and parental-specific view it was found that rater differences do not merely reflect measurement error or rater bias, but indicate that parents assess different aspects of the child's behavior. Rater bias accounts for at most 13% of the variance in externalizing behavior (Bartels *et al.,* 2003a, b, c; Hewitt *et al.,* 1992; Van der Valk *et al.,* 2001, 2003). Gaining insight into the magnitude of the effect of rater bias and rater-specific views is essential in order to get correct estimates of genetic and environmental influences on the phenotype under investigation. If the issue of rater bias is ignored, it results in an overestimation of shared environmental influences. This overestimation could lead to intervention procedures that focus on the child's (family) environment, while in fact this influence of shared environment is a representation of issues at the rater's levels instead of a representation of real environmental influences on the behavior of the child. So from a clinical and scientific perspective, disentangling rater bias from real shared environmental effects is important for both phenotype definition and intervention. All the above mentioned issues on the use of

multiple informants are, of course, applicable for studies on co-occurrence. For these studies it is essential to know whether the significant co-occurrence is really present in the behavior of the child or whether the significant co-occurrence is a result of rater bias, such as stereotyping, employing different normative standards, or having certain response styles.

METHODS

Subjects

All participants are registered by the Netherlands Twin Registry (NTR), kept by the Department of Biological Psychology at the Vrije Universiteit in Amsterdam. Of all multiple births in the Netherlands, 40%–50% are registered by the NTR (Boomsma, 1998; Boomsma *et al.,* 1992, 2002). This study is part of an ongoing longitudinal study on the development of intelligence and problem behavior. For the present analyses, data collected at age 12 years from twins from the birth cohorts 1986–1990 were used. Questionnaires were mailed to families within 3 months of the twins' twelfth birthday. After 2–3 months, reminders were sent, and 4 months after the initial mailing, persistent nonresponders were contacted by phone. Families whose addresses were no longer available were included in the nonresponse group. From the original sample, 80 twin pairs were excluded because either one or both of the children had a disease or handicap that interfered severely with daily functioning at age 12 or at a younger age. Of the parents who responded to the first questionnaire, received directly after registration of their twin at birth, around 60% still attend the study after a 12-year interval. The final data set for analysis consists of 1481 mother ratings and 1156 father ratings.

Zygosity was determined for 472 same-sex twin pairs by DNA analyses or blood group polymorphisms. For all other same-sex twin pairs, zygosity was determined by discriminant analysis using questionnaire items. Parents were asked how much the twins resembled each other in facial structure, hair color, facial color, eye color, and whether they were ever mistaken for each other by the parents themselves, family, or strangers. They were also asked if the twins were as much alike as two peas in a pod, whether it was difficult for the parents to separate the twins on a recent picture, and how similar the twins' hair structure was (for details see Rietveld *et al.,* 2000).

This gave a sample of 283 monozygotic males (MZM), 231 dizygotic males (DZM), 315 monozygotic females (MZF), 228 dizygotic females (DZF), and 424 dizygotic opposite-sex (DOS) twin pairs. In general, mothers' response rate outnumbers fathers' response rate. Therefore the data could be further divided into twin pairs for which both mother and father had replied (225 MZM, 180 DZM, 240 MZF, 187 DZF, and 324 DOS) and twin pairs for which only mothers had replied (58 MZM, 51 DZM, 75 MZF, 41 DZF, and 100 DOS).

Measures

The Child Behavior Checklist (CBCL4-18) (Achenbach, 1991) was developed for parents to score the behavioral and emotional problems of their 4-to-18-year-old children. It consists of 120 problem items that are scored by parents on a 3-point scale based on the occurrence of the behavior during the preceding 6 months: 0 if the problem item was not true of the child, 1 if the item was somewhat or sometimes true, and 2 if it was very true or often true. The syndrome scales Aggressive Behavior (AGG) and Rule-Breaking Behavior (RB) were composed by adding the scores on syndrome-specific questions (see Table I), according to the 1991 profile (Achenbach, 1991). Dutch syndrome scales and comparability with the syndrome scales as developed by Achenbach are reported in the Dutch manual (Verhulst *et al.,* 1996).

The data were square-root transformed to approximate normal distributions that are required for maximum likelihood estimation. After transformation, all skewness and kurtosis indices were between −1.0 and 1.0, implying that not much distortion is to be expected (Muthén and Kaplan, 1985).

Data Analyses

Descriptive statistics and prevalence of the occurring co-occurrence between AGG and RB were calculated using SPSS/windows 10. Pearson correlations were used to test the phenotypic association between AGG and RB and to calculate the interparent correlation within and between the syndromes. Significance of difference in means for boys and girls were tested using ANOVA for the oldest and the youngest of the twin pair separately. Differences in means based on mother or father ratings were tested using a paired-samples *t*-test for the oldest and the youngest of the twin pair separately.

Genetic Model-Fitting

Data from monozygotic and dizygotic twins were used to decompose the variance in scores on AGG and

Table I. Items (item#) of the Child Behavior Checklist Used to Define Rule-Breaking Behavior and Aggressive Behavior

Rule-Breaking Behavior (RB)	Aggressive Behavior (AGG)
Doesn't seem to feel guilty after misbehaving (26)	Argues a lot (3)
Hangs around with others who get in trouble (39)	Bragging, boasting (7)
Lying or cheating (43)	Cruelty, bullying, or meanness to others (16)
Prefers being with older kids (63)	Demands a lot of attention (19)
Runs away from home (67)	Destroys his/her own things (20)
Sets fires (72)	Destroys things belonging to his/her family or others (21)
Steals at home (81)	Disobedient at home (22)
Steals outside the home (82)	Disobedient at school (23)
Swears or uses obscene language (90)	Easily jealous (27)
Thinks about sex too much (96)	Gets teased a lot (37)
Truancy, skips school (101)	Physically attacks people (57)
Uses drugs for nonmedical purposes (105)	Screams a lot (68)
Vandalism (106)	Shows off or clowns (74)
	Stubborn, sullen or irritable (86)
	Sudden changes in mood or feelings (87)
	Talks to much (93)
	Teases a lot (94)
	Temper tantrums or hot temper (95)
	Threatens people (97)
	Unusually loud (104)

RB into a contribution of the additive effects of many genes, environmental influences that are shared by twins (e.g., style of parenting, socioeconomic level, or religion), and environmental influences that are not shared by twins (e.g., illness, relationships with peers, or measurement errors). For a summary of the twin method, the various assumptions, and the plausibility of these assumptions, see, for example, Boomsma *et al.* (2002); Eaves (1982); Kendler and Eaves (1986); Martin and Eaves (1977); Neale and Cardon (1992); and Plomin *et al.* (2000).

Twin correlations and cross correlations for the five zygosity groups give a first impression of the genetic and environmental influences on AGG and RB. The cross correlations represent cross-trait-cross-twin-cross-rater correlations and give information on the genetic and environmental influences on the co-occurrence of AGG and RB and give information on the underlying causes of parental agreement and disagreement.

The 8×8 variance-covariance matrix of AGG and RB rated by mothers and fathers for twin 1 and twin 2 can be decomposed into a matrix of genetic, shared environmental, and nonshared environmental variances and covariances for behavior similarly assessed by both parents and for parts of the behavior on which parents disagree. The decomposition is obtained by fitting multivariate genetic models. First, a bivariate Cholesky decomposition was fit to the data for mother and father ratings separately. These models served as a first step to gain insight into the etiology of co-occurrence of AGG and RB. This saturated model, also known as a

triangular decomposition, is an unconstrained model for the (co)variances among phenotypes (in this case AGG and RB), wherein disagreement between parents is not taken into account. Standardized estimates of genetic and environmental influences on the variance of AGG and RB and on the covariance between the two problems behaviors were calculated for mother and father ratings separately. However to disentangle the sources of parental disagreement and to estimate the influence of rater bias on the variances and covariance a bivariate psychometric model was used. Although there are alternative ways for modeling twin data with multiple raters, in previous studies we found this model the most appropriate (Bartels *et al.,* 2003a, b, c; Van der Valk *et al.,* 2001, 2003).

The psychometric model (Hewitt *et al.,* 1992) (Figure 1) estimates the influence of a genetic (A), a shared environmental (C), and a nonshared environmental factor (E) on the behavior similarly assessed by both parents and on the covariance between the two phenotypes as rated by both parents (parental agreement). This behavior similarly assessed by both parents (parental agreement) is drawn as a latent variable in Figure 1 (AGG T_1, RB T_1, AGG T_2, RB T_2) and represents a more reliable measure of AGG or RB because it is based on the agreement of two raters. In addition, rater-specific genetic ($A_{m/f}$), rater-specific shared environmental ($C_{m/f}$), and rater-specific nonshared environmental factors ($E_{m/f}$) are estimated for the ratings of mother/father separately (parental disagreement; lower part of the path diagram in Figure 1). Disagreement between
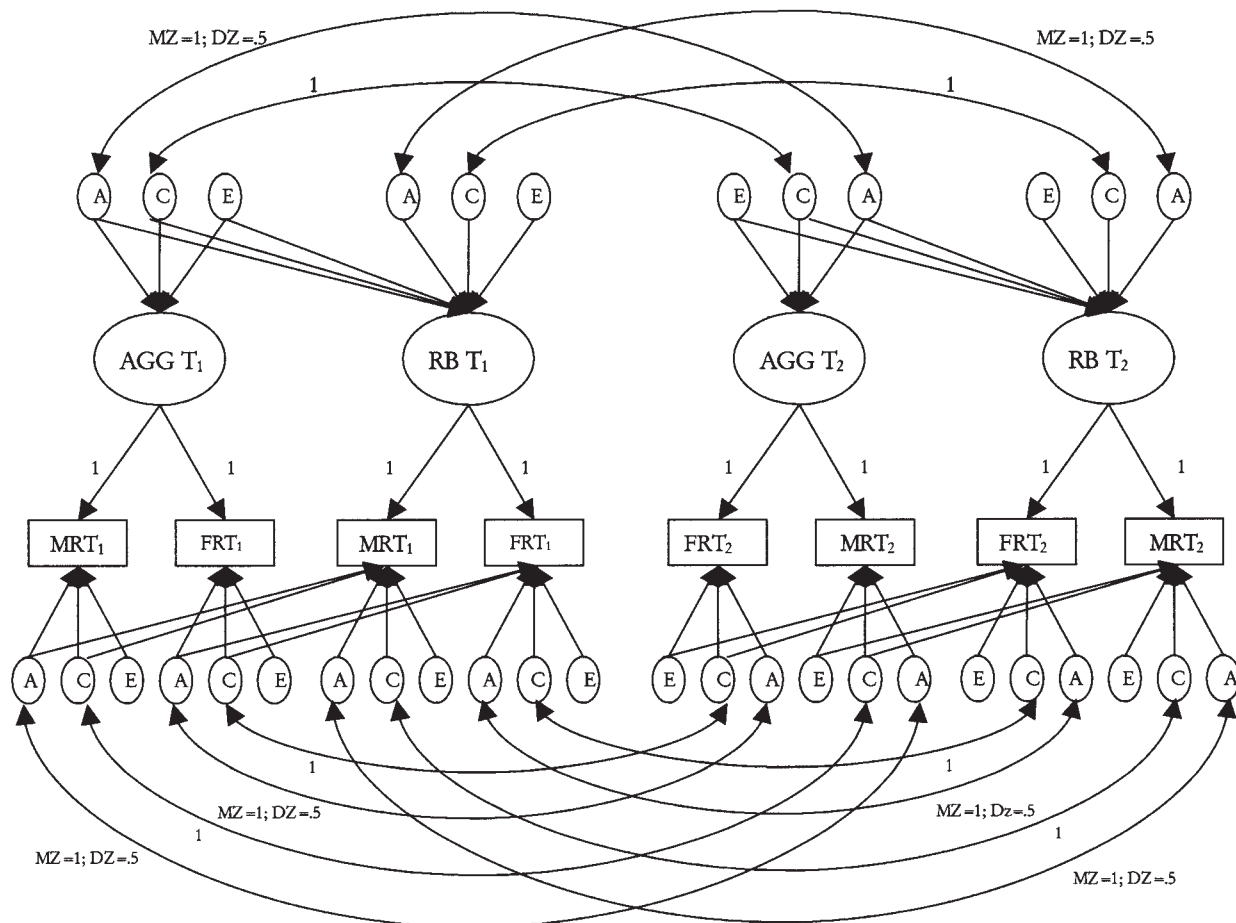
Fig. 1. Bivariate psychometric model.

parents in this model can be caused by rater-specific behavioral views, leading to different but valid information of each rater. The psychometric model tests this possibility by examining whether there are significant genetic effects on the rater-specific part of each parent's rating. If the behaviors uniquely rated by the parents are shown to be influenced by the genotype of the child, the parent must have been assessing a "real" but unique aspect of the child's behavior. Error and unreliability cannot cause the systematic effects necessary for the model to estimate these genetic influences. Disagreement can also be caused by rater bias, which will confound the rater-specific shared environmental effects. Rater bias, which represents, for instance, certain response styles, stereotyping, or the use of specific normative standards, will be estimated in the rater-specific shared environmental factors, because the rater will bias the ratings of both children of a twin pair in the same way. However, it is not expected that both mothers and fathers do show the same form of rater bias at the same

time. Finally, disagreement between mother and father ratings can be caused by unreliability, which will confound the rater-specific nonshared environmental effects.

The three factors loading on the twins' latent phenotypes and on the co-occurrence between these latent AGG and RB phenotypes contain only reliable estimates (without rater bias and measurement error) of A, C, and E on the variance and covariance of AGG and RB, which causes the additive genetic factors to contain only pure genetic influences, the nonshared environmental factor to contain only pure independent (idiosyncratic) environmental effects (McArdle and Goldsmith, 1990), and the shared environmental factor to contain only pure shared environmental effects.

Model Fitting

The program Mx (Neale *et al.,* 2002) was used to analyze the data making use of a Cholesky decomposition

for each parent separately and the bivariate psychometric model. To make optimal use of all available data, the analyses were performed on raw data. Means were estimated freely for MZ vs. DZ twins, youngest vs. oldest twin, and boys vs. girls. First we fitted a bivariate Cholesky decomposition with additive genetic, shared environmental, and nonshared environmental influences (ACE model), including sex differences in these parameter estimates, for mother and father ratings separately. Next, we fit a saturated (Cholesky decomposition) bivariate psychometric model (Figure 1), again with sex differences in these parameter estimates. In this model, influences of genetic, shared environmental, and nonshared environmental influences on AGG, RB, and the co-occurrence of both syndromes were estimated for behavior similarly assessed by both parent (upper part of the path diagram in Figure 1). Rater-specific additive genetic, rater-specific shared environmental, and rater-specific nonshared environmental influences were estimated for both syndromes and the co-occurrence, giving information on rater bias and specific parental view. Finally, it was tested whether significant differences in parameter estimates of A, C, and E between boys and girls are present or absent for AGG and RB.

RESULTS

Children who have a raw score on AGG or RB that yields a T-score of ≥ 67 (defined per gender and based on this sample) are defined as falling in the borderline clinical range. Co-occurrence of AGG and RB occurs in 3.7% of the boys and girls, based on mother ratings. Based on father ratings, 4.6% of the boys and 2.6% of the girls show deviant behavior for both AGG and RB. Further, over 50% of the boys and girls tend to show deviant behavior on RB when showing deviant behavior on AGG as well, and vice versa (see Table II).

Comparing boys and girls for the oldest of the twin pair, both mothers and fathers gave significantly higher ratings to the boys for AGG and RB (AGG: mother: $F(1,1476) = 48.329$, $p = .000$; fathers: $F(1,1163) = 37.617$, $p = .000$; RB: mothers: $F(1,1469) = 42.905$, $p = .000$; fathers: $F(1,1158) = 29.080$, $p = .000$). Comparing mother and father ratings, a paired t-test showed that the ratings for both AGG and RB given by mothers were significantly higher than ratings given by fathers for both boys and girls (AGG: boys: T = 5.438, $df = 572$, $p = .000$; girls: T = 5.215, $df = 572$, $p = .000$; RB: boys: T = 2.564, $df = 570$, $p = .011$; girls: T = 2.184, $df = 566$, $p = .029$). These analyses gave a similar picture for the youngest of the twin pair (results available from the author on request).

Interparent correlations and phenotypic cross-trait correlations for the whole sample are presented in Table III. The interparent correlations are around .6, which is in line with parental agreement found in previous studies (Achenbach *et al.,* 1987a). The cross-trait correlations (.7) are high and similar to the correlations presented by Deater-Deckard and Plomin (1999) in an adoption study of teacher and parent reports.

Table IV presents the twin correlations (boldface type) and the cross-twin-cross-trait-cross-rater correlations. The MZ twin correlations are higher than the DZ twin correlations, indicating genetic influences on both AGG and RB. The MZ correlations, though, are less than twice as high as the DZ correlations, which is an indication of the influence of shared environmental factors or rater bias for both behaviors. No differences between same-sex DZ twin correlations and opposite-sex DZ twin correlations are observed, so no heterogeneity is expected. However, in the absence of heterogeneity a difference in the strength of genetic and environmental effects for boys and girls could still occur. In our model fitting procedure we conducted a final test by constraining the parameter estimates for

Table II. Means, Standard Deviations, and Prevalence of Co-occurrence ($T \geq 67$) for Aggressive Behavior and Rule-Breaking Behavior, Calculated per Gender

	Descriptives						Prevalence Co-occurrence		RB if AGG		AGG if RB	
	♂	Mean	SD	♀	Mean	SD	♂	♀	♂	♀	♂	♀
RB_m	1438	1.10	1.55	1496	.69	1.15	3.7%	3.7%	56.4%	52.9%	51.5%	50.9%
AGG_m	1441	5.79	5.56	1500	4.27	4.37						
RB_f	1137	.96	1.57	1180	.55	.99	4.6%	2.6%	63.1%	46.3%	63.9%	50.0%
AGG_f	1135	4.91	5.19	1187	3.50	3.87						

Note: RB_m = Rule-Breaking Behavior based on mother ratings; AGG_m = Aggressive Behavior based on mother ratings; RB_f = Rule-Breaking Behavior based on father ratings; AGG_f = Aggressive Behavior based on father ratings.

Table III. Co-occurrence and Interparent Correlations for Aggressive and Rule-Breaking Behavior for Boys (below diagonal) and Girls (above diagonal)

	BOYS			
	RB_m	AGG_m	RB_f	AGG_f
RB_m	1	.67 (.64–.70)	.53 (.48–.57)	.48 (.43–.52)
AGG_m	.68 (.65–.71)	1	.48 (.43–.52)	.69 (.66–.72)
RB_f	.63 (.63–.66)	.60 (.56–.63)	1	.61 (.58–.65)
AGG_f	.55 (.55–.59)	.76 (.73–.78)	.76 (.73–.78)	1

Note: RB_m = Rule-Breaking Behavior based on mother ratings; AGG_m = Aggressive Behavior based on mother ratings; RB_f = Rule-Breaking Behavior based on father ratings; AGG_f = Aggressive Behavior based on father ratings.

common and rater-specific genetic and environmental influences for boys and girls to be equal. This procedure reveals significant differences in the strength of genetic and environmental influences between boys and girls ($\chi^2 = 92.379$, $df = 27$, $p = .00$).

The cross-trait correlation for mother and father ratings separately are higher in MZ than in DZ twins, but, as for the twin correlations, less than twice as high, indicating genetic and shared environmental influences or rater bias on the covariance between AGG and RB. The cross-twin-cross-parent correlations in Table IV indicate, by higher cross-twin-cross-parent correlations for MZ twins compared to DZ twins, that rater-specific parental view and rater bias are possible underlying causes of parental disagreement in both AGG and RB. Possible influences of rater bias and rater-specific parental view on the co-occurrence of AGG and RB are also expected based on the higher cross-trait-cross-twin-cross-rater correlations for MZ twins than for DZ twins.

The proportion of the total variance and covariance accounted for by additive genetic, shared environmental, and nonshared environmental factors for mother and father ratings separately and for the variance in behavior on which both parents agree are presented in Table V. The upper part of Table V represents proportions of the total variance of AGG and RB and the co-occurrence accounted for by genetic and environmental influences *for mother and father ratings separately.* The lower part of the table represents the percentage of the variance of AGG and RB and the co-occurrence, *similarly assessed by both parents,* accounted for by genetic and environmental influences. The differences in the estimates of the parents separately and the behavior similarly assessed by both parents give insight into the presence and absence of rater bias. As mentioned in the introduction the presence of rater bias will result in an overestimation of shared environmental influences, so if the shared environ-

mental component is larger in analyses of mother and father ratings separately in comparison to the estimates based on the psychometric model, as is the case in this study, rater bias, besides some rater-specific shared environmental influences, is present for AGG and RB and for the co-occurrence between both behaviors.

The most informative estimates of additive genetic, shared environmental, and nonshared environmental influences on AGG and RB and the co-occurrence between both are presented in the lower part of the table, because these estimates are based on behavioral observations on which both parents do agree. Heritabilities of AGG and RB are moderate to high for boys and girls, explaining 56%–79% of the total variance (Table V, lower part). The covariance between AGG and RB, representing co-occurrence, is highly influenced by additive genetic factors (84%). After correction for possible influences of rater bias, shared environmental influences seem to be of significance only for RB in girls.

Table VI presents the result of the analyses with the psychometric model on mother *and* father ratings and gives insight into the sources of rater agreement and disagreement. Estimates of rater-specific parental view and rater bias/rater-specific shared environmental influences and the proportion of total variance and covariance accounted for by these manifestations are presented in Table VI. The percentages in parentheses sum to 100%, which represents the total observed variance per rater. Parental-specific view, represented by rater-specific additive genetic influences (A_u) plays no part in explaining individual differences in RB in girls. However the parental-specific view seems to be important for AGG in boys and girls, explaining about 50% of the total variance in boys and about 40% of the total variance in girls. This parental-specific view also seems of significance for the co-occurrence between AGG and RB, explaining 45% of the covariance in boys and 28% of the covariance in girls.

Table IV. Twin Correlation (bold faced) and Cross-Twin-Cross-Trait-Cross-Rater Correlations for Rule-Breaking Behavior and Aggressive Behavior for the Five Zygosity Groups Separately

		RB_ma[1]	AGG_ma	RB_fa	AGG_fa	RB_mb[2]	AGG_mb	RB_fb	AGG_fb
MZM	RB_ma	1							
	AGG_ma	.67	1						
	RB_fa	.58	.58	1					
	AGG_fa	.51	.75	.69	1				
	RB_mb	**.83**	.62	.55	.49	1			
	AGG_mb	.62	**.86**	.57	.68	.67	1		
	RB_fb	.55	.57	**.85**	.67	.58	.58	1	
	AGG_fb	.49	.68	.67	**.88**	.51	.75	.69	1
		RB_ma	AGG_ma	RB_fa	AGG_fa	RB_mb	AGG_mb	RB_fb	AGG_fb
DZM	RB_ma	1							
	AGG_ma	.60	1						
	RB_fa	.57	.51	1					
	AGG_fa	.48	.70	.69	1				
	RB_mb	**.53**	.38	.34	.30	1			
	AGG_mb	.38	**.49**	.31	.34	.60	1		
	RB_fb	.34	.31	**.58**	.49	.57	.51	1	
	AGG_fb	.30	.34	.49	**.56**	.48	.70	.69	1
		RB_ma	AGG_ma	RB_fa	AGG_fa	RB_mb	AGG_mb	RB_fb	AGG_fb
MZF	RB_ma	1							
	AGG_ma	.65	1						
	RB_fa	.45	.48	1					
	AGG_fa	.52	.68	.56	1				
	RB_mb	**.75**	.58	.42	.44	1			
	AGG_mb	.58	**.83**	.46	.58	.65	1		
	RB_fb	.42	.46	**.77**	.51	.45	.48	1	
	AGG_fb	.44	.58	.51	**.79**	.52	.68	.56	1
		RB_ma	AGG_ma	RB_fa	AGG_fa	RB_mb	AGG_mb	RB_fb	AGG_fb
DZF	RB_ma	1							
	AGG_ma	.58	1						
	RB_fa	.57	.45	1					
	AGG_fa	.42	.72	.55	1				
	RB_mb	**.58**	.39	.35	.29	1			
	AGG_mb	.39	**.52**	.25	.38	.58	1		
	RB_fb	.35	.25	**.52**	.39	.57	.45	1	
	AGG_fb	.29	.38	.39	**.55**	.42	.72	.55	1
		RB_ma	AGG_ma	RB_fa	AGG_fa	RB_mb	AGG_mb	RB_fb	AGG_fb
DOS	RB_ma	1							
	AGG_ma	.63	1						
	RB_fa	.53	.49	1					
	AGG_fa	.47	.71	.57	1				
	RB_mb	**.52**	.42	.36	.30	1			
	AGG_mb	.42	**.58**	.34	.40	.63	1		
	RB_fb	.36	.34	**.57**	.39	.53	.49	1	
	AGG_fb	.30	.40	.39	**.54**	.47	.71	.57	1

[1] "a" is the oldest of the twin and the boy in the twins of opposite sex; [2] "b" is the youngest of the twins and the girl in twins of opposite sex.

Note: MZM = Monozygotic male twins; DZM = dizygotic male twins; MZF = monozygotic female twins; DZF = dizygotic female twins; DOS = dizygotic twins of opposite sex.

Significant influences of rater bias and/or rater-specific shared environmental influences, represented by C_u, are found for both AGG and RB. Rater bias is also significant for the co-occurrence of AGG and RB. About 35% of the covariance in boys and 45% of the covariance in girls is explained by rater-specific shared environmental influences. So the use of multiple raters in studies on co-occurrence is highly recommended, although part of this rater-specific C can reflect real shared environmental influences observed by the

Table V. Proportion of Total Variances and Covariance Accounted for by Additive Genetic, Shared Environmental, and Nonshared Environmental Influences for Rule-Breaking Behavior and Aggressive Behavior in 12-Year-Olds Based on Mother Ratings (Bivariate Cholesky), Father Ratings (Bivariate Cholesky) and Behavior Similarly Assessed by Both Parents (Bivariate Psychometric Model)

Mother Ratings

Boys

	A		C		E	
	RB	AGG	RB	AGG	RB	AGG
RB	50%		32%		18%	
AGG	49%	61%	44%	25%	7.0%	14%

Girls

	A		C		E	
	RB	AGG	RB	AGG	RB	AGG
RB	49%		26%		25%	
AGG	44%	54%	45%	29%	11%	17%

Father Ratings

Boys

	A		C		E	
	RB	AGG	RB	AGG	RB	AGG
RB	49%		36%		15%	
AGG	51%	60%	46%	27%	3.0%	13%

Girls

	A		C		E	
	RB	AGG	RB	AGG	RB	AGG
RB	51%		27%		22%	
AGG	37%	48%	54%	33%	9.0%	19%

Reliable Trait Variance (Mother-Father Agreement)

Boys

	A		C		E	
	RB	AGG	RB	AGG	RB	AGG
RB	79%		1.0%		20%	
AGG	84%	69%	2.0%	1.0%	14%	30%

Girls

	A		C		E	
	RB	AGG	RB	AGG	RB	AGG
RB	56%		23%		21%	
AGG	82%	72%	6.0%	0.0%	12%	28%

mother or the father of the child instead of rater bias per se.

DISCUSSION

AGG and RB are highly heritable behaviors. They are also significantly associated. Individual differences in RB similarly assessed by both parents are for 79% (boys) and 56% (girls) accounted for by genetic influences. The remaining part of the variance in boys is accounted for by nonshared environmental influences, whereas for girls 23% of the total variance of the behavior on which both parents agree is accounted for by shared environmental influences and 21% by nonshared environmental influences. For AGG, 69% of the variance of the behavior on which both parents agree in boys and 72% of this variance in girls is accounted for by genetic factors. The remaining variance in both boys and girls is accounted for by nonshared environmental influences. The focus of this study was to determine what factors contributed to the co-occurrence of AGG and RB. This study made use of the unique characteristics of data of multiple traits rated by multiple raters in genetically related subjects in order to simultaneously investigate the etiology of co-occurrence patterns and plausibility of different models for (dis)agreement between multiple raters. Over 80% of the reliably assessed covariance between AGG and RB, defined as the covariance on which both parents agree, can be explained by additive genetic factors. Of the remaining 20%, 12%–14% can be explained by nonshared environmental factors and 2%–6% by shared environmental influences. Based on these results it can be concluded that genetic factors are primarily responsible for the co-occurrence between AGG and RB. The results of this study may be useful in diagnostic and research settings. It should be realized that children who suffer AGG or RB in the clinical range are at equal risk to have the comorbid problem behavior as well. In our sample 50%–64% of the children who are deviant on AGG are also deviant on RB and vice versa. Although the high rates of co-occurrence between AGG and RB are not a surprise, the finding that the majority of the influences on the comorbid condition are due to genetic factors will be useful in designing molecular genetic studies aimed at discovering gene-behavior relations.

Although the absence of shared environmental influences on the co-occurrence of both behaviors appears to argue that adverse family environments are not the only cause of these behavior problems, clinicians may benefit from considering that the robust genetic influences reported here on children may also play a role in

Table VI. Parameter Estimates and Percentages of Total Variances (diagonal) and Covariances (off diagonal) for Boys and Girls Based on the Bivariate Psychometric Model with Mother and Father Ratings for Rule-Breaking and Aggressive Behavior

		Mother rating		Father rating	
Boys					
		RB	AGG	RB	AGG
A_c[a]	RB	.19 (33%)		.19 (35%)	
	AGG	.10 (14%)	.17 (10%)	.10 (13%)	.17 (10%)
		RB	AGG	RB	AGG
C_c[b]	RB	.00 (0.0%)		.00 (0.0%)	
	AGG	.00 (0.0%)	.00 (0.0%)	.00 (0.0%)	.00 (0.0%)
E_c[c]	RB	.05 (9.0%)		.05 (9.0%)	
	AGG	.02 (2.0%)	.08 (4.0%)	.02 (2.0%)	.08 (.04%)
A_u[d]	RB	.12 (21%)		.11 (20%)	
	AGG	.32 (45%)	.96 (54%)	.31 (43%)	.87 (50%)
C_u[e]	RB	.16 (27%)		.19 (34%)	
	AGG	.23 (33%)	.35 (20%)	.28 (39%)	.43 (25%)
E_u[f]	RB	.06 (10%)		.01 (2.0%)	
	AGG	.04 (6.0%)	.21 (12%)	.02 (3.0%)	.20 (11%)
Girls					
		RB	AGG	RB	AGG
A_c[a]	RB	.10 (24%)		.10 (29%)	
	AGG	.07 (13%)	.15 (10%)	.07 (16%)	.15 (11%)
C_c[b]	RB	.04 (10%)		.04 (12%)	
	AGG	.01 (1.0%)	.00 (0.0%)	.01 (1.0%)	.00 (0.0%)
E_c[c]	RB	.04 (9.0%)		.04 (11%)	
	AGG	.01 (2.0%)	.06 (4.0%)	.01 (2.0%)	.06 (4.0%)
A_u[d]	RB	.03 (8.0%)		.03 (8.0%)	
	AGG	.14 (28%)	.67 (44%)	.13 (29%)	.62 (43%)
C_u[e]	RB	.14 (32%)		.12 (33%)	
	AGG	.24 (46%)	.41 (27%)	.20 (45%)	.36 (25%)
E_u[f]	RB	.07 (17%)		.03 (7.0%)	
	AGG	.05 (10%)	.23 (15%)	.03 (7.0%)	.24 (17%)

[a] Additive genetic influence on the behavior similar assessed by both parents; [b] shared environmental influence on the behavior similar assessed by both parents; [c] nonshared environmental influence on the behavior similarly assessed by both parents; [d] parental-specific genetic influences/parental-specific view; [e] parental-specific shared environmental variance and/or rater bias; [f] parental-specific nonshared environmental variance/measurement error.

parents behavior, and thus directly affect the adverse family environmental factors reported in families of children with these problems. It may well be, as Jenkins *et al.* (2003) point out, that these family factors (both within and between family factors), are not only important in the evolution of these behaviors, but these factors themselves may be heavily influenced by the same genetic factors that influence AGG and RB in the off-spring. Therefore these data may compel clinicians to focus treatment aimed not only at minimizing the effects

of adverse family environment, but also consider that parental core psychopathology may need treatment of similar or related behaviors that are expressed by their children. Although this twin study does not directly test or measure the contribution of genes to parental psychopathology, most clinicians recognize the contribution of parental psychopathology to adverse family environment. It may well be that future family studies testing for AGG and RB across pedigrees will yield family-based interventions to minimize both parental

and childhood AGG and RB in treatment settings. Our group (Hudziak *et al.,* 2003) has a family study underway testing this hypothesis. In this way, the adverse family environmental factors may be reduced by improved the health of both the children and the parents.

Further, it should be realized that adverse family environmental factors could influence one of the children of a twin pair and in that matter show up as nonshared environmental influences. These influences, even after correction for measurement error, are of significance for both RB and AGG and for the co-occurrence of both. Future studies are necessary to gain more insight into the shared and nonshared environmental factors and the way to define and disentangle both influences.

A strength of the study is that the analyses were performed on a population-based sample. If one was to assume that psychopathology is caused by environmental hazards or pathogenic genes that are qualitatively distinct from those that cause variation in the normal range (Rutter *et al.,* 1990), our result would have little clinical importance. There is, however, evidence that clearly suggests links between normal and abnormal behavior. First, several CBCL studies have shown correlations between behavior problem syndromes and DSM diagnoses (Costello *et al.,* 1985; Edelbrock and Costello, 1988; Ferdinand *et al.,* 1999; Kasius *et al.,* 1997). This convergence indicates that behavior problem syndromes as studied in this article are relevant for psychiatric conditions. Second, several studies supported the view that the sources of normal variation may also affect psychopathology in children and adolescents. So latent class analyses have been used to identify subgroups of individuals with normal or pathological behavior (Eaves *et al.,* 1993; Hudziak *et al.,* 1998; Neuman *et al.,* 1999). Results tend to suggest that these groups differ in degree rather than in kind. Furthermore, using methods from item response theory, Van den Oord *et al.* (2003) found that liability distributions for behavior and emotional problems show very little or no evidence of non-normality. This also seems to suggest that psychopathology may often be an extreme on the same continuum that describes variation in the normal range. Thus, although we used a nonclinical sample, it can be argued that our finding that co-occurrence between AGG and RB is mainly due to genetic factors is also important for understanding psychopathology.

Further, the finding of high genetic influences on the co-occurrence between AGG and RB has important implication for phenotype definition and future gene finding. If molecular genetic research verifies that genes associated with one phenotype are also typically associated with other phenotypes, more attention should be paid to the sample selection for gene finding.

Shared environmental influences are only significant for RB in girls. The influence of such family shared environmental factors has been demonstrated in numerous other studies (for a review see Loeber and Hay, 1997). It is important to note that the influence of shared environment on RB in girls remains significant after correcting for rater bias. These shared environmental influences are not necessarily confined to the home environment. For instance, there are indications that these environmental effects are not merely shared by siblings but also by cousins (Van den Oord and Rowe, 1998, 1999). This suggests that shared environment reflects the wider community in which families are embedded as well (Bronfenbrenner, 1979; Parke and Kellam, 1994, p3). The influence of peers on aggressive and nonaggressive antisocial behavior has been demonstrated in numerous studies in adolescents (see for example Fergusson and Horwood, 1996). This influence of peers could be considered a strong candidate for nonshared environmental influences. Most children have frequent contact with their peer group, and this is likely to contain many features that do not affect both members of a twin pair in the same way. However, it should be noted that the peer group could also be a reflection of the genetic material of the individual, who chooses his or her peers based on his or her genetic background (G-E correlation).

The finding of moderate to high heritabilities for AGG and RB similarly assessed by both parents for both boys and girls is in line with results of previous studies (see Introduction) and consolidates the possibilities of the use of these phenotypes to investigate the complex interplay between genotype and phenotype. For example, genetic deficiencies in MAOA have been linked with aggression in mice and humans (Manuck *et al.,* 2000; Rowe, 2001). The MAOA gene is located on the X chromosome (Xp 11.23-11.4) and it encodes the MAOA enzyme, which metabolizes neurotransmitters such as norepinephrine (NE), seretonin (5-HT), and dopamine (DA). Increased aggression and increased levels of brain NE, 5-HT, and DA were observed in a mice lacking MAOA (MAOA knockouts) (Cases *et al.,* 1995), and aggression was normalized by restoring MAOA expression (Shih and Thompson, 1999). In humans, a null allele at the MAOA locus was linked with male antisocial behavior in a single large family studied in the Netherlands (Brunner *et al.,* 1993). However, this mutation is very rare. Further preliminary evidence of an association between polymorphic variation in the gene for *MAOA* and interindividual variability on aggression, impulsivity, and central nervous system serotonergic responsivity was found by Manuck *et al.* (2000). Recently, a significant G × E

interaction was reported between *MAOA* and maltreatment. Caspi *et al.* (2002) found that maltreated children with a genotype conferring high levels of *MAOA* expression were less likely to develop antisocial behavior. However, if this X-linked gene is very important in explaining individual differences in AGG, a different correlation pattern would have been found for same-sex females twins in comparison to same-sex males twins and twins of opposite sex (Mather and Jinks, 1963).

This study also provides more insight into the value of the use of multiple raters in studying AGG and RB. On one hand, no impact of rater bias is expected for behavior that is relatively easily observable like AGG. On the other hand, though, AGG and RB are likely candidates to influence parental-specific reports. Mothers may react different to AGG and RB than fathers. Using both mother and father ratings enabled us to sort out sources of parental agreement and disagreement. Both the parental specific view of behavior and rater bias are contributors to the overall measure of parental disagreement. Forty-five percent of the total covariance in boys and 29% of the total covariance in girls, taking both behavior based on parental agreement and disagreement into account, is accounted for by parental-specific views. This finding emphasizes the necessity of the use of multiple raters. The use of mother and father ratings does give a more complete picture of the child's behavior. In addition, about 35% of the covariance in boys and 46% of the covariance in girls can be explained by rater bias. This finding emphasizes the necessity of the use of multiple raters. In this paper we showed that data of multiple raters of genetically related subjects give rise to the possibility to disentangle rater bias from rater-specific views. Although the finding of significant rater-specific views by using parental ratings supports the need for studies with multiple raters of child psychopathology, the fact remains that there is a debate on how to best combine these informants. Some argue for finding the "single best informant" whereas other argue for combining informants. Our data on this, although not new, adds to the evidence that combining informants, each as representing a unique and possibly important viewpoint is the best way to proceed. Nonetheless, we need to do more work on this subject, for instance, by implementing raters from different settings and age-groups. We believe that the use of teacher ratings and self-reports will be a valuable extension of the present study. Teachers observe the behaviors of the child in a different setting, resulting in a more complete picture of the childs' behavior when using both parental and teacher ratings.

The rater bias components of mother and fathers could be correlated because of the combination of two mechanisms. First, parents tend to have similar levels of psychopathology. Significant spousal correlations are found for internalizing behaviors such as depression and anxiety as well as externalizing behaviors such as antisocial behavior (Dufouil and Alperovitch, 2000; Krueger *et al.,* 1998; Mathews and Reus, 2001; Stallings *et al.,* 1997). These correlations could be a result of either assortative mating or contagion/interaction effects. Second, levels of parental psychopathology affect ratings of problem behavior in their children. Several studies suggest that depression in mothers may lead to them overestimating their children's symptomology (Fergusson and Horwood, 1996). In one study (Breslau *et al.,* 1988), mothers who were depressed rated their children as showing a greater number of symptoms of all psychiatric syndromes. Like mothers', fathers' reports of their children's behavioral problems are influenced by their own level of psychological symptoms (Jensen *et al.,* 1988; Phares *et al.,* 1989). Because this shared rater bias component will affect MZ and DZ twin correlations in the same way, it will show as shared environmental effects on the common part of the parental ratings. The inclusion of measures of parental psychopathology or the use of a different types of raters, such as teachers, will be helpful to account for these correlated rater bias effects. However as most assortative mating correlations are significant but low, we do not expect this phenomenon to significantly overshadow our results.

In conclusion, individual differences in AGG and RB are accounted for by genetic, shared, and nonshared environmental influences. Co-occurrence between AGG and RB could be a result of an overlapping set of genes, accounting for over 80% of the covariance. The use of multiple raters in studying these externalizing problem behaviors and co-occurrence is highly recommended, because both rater bias and parental specific views explain large parts of the variance of both behaviors and the covariance of both behaviors.

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